Pan Arab Journal of Oncology

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Retinoblastoma
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Gastric Cancer
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**AMAAC Introduction**

The Arab Medical Association Against Cancer (AMAAC) is a medical body that was established in 2001 as part of the Arab Medical Association where its main office is located in Cairo - Egypt, and it is also a continuation of the Arab Council Against Cancer that was founded in 1995. The Executive Committee of (AMAAC) is represented by two members who are named officially by the Oncology Society of each Arab Country.

The Arab Medical Association Against Cancer aims at strengthening relationships between members in different Arab Countries to raise the level of cooperation in the field of oncology on both scientific and practical aspects. Exchanging information and researches between members through Regional and Arab Conferences and Publications. Holding Public Awareness Campaigns in the field of oncology that are organized by Arab Countries. Participating in scientific activities with International Oncology Societies. Finally, encouraging researchers and doctors to meet and exchange experiences together with finding training opportunities in the field of oncology inside and outside the Arab World.

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Clinicopathological Features of Gastric Cancer; Single Center Experience

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Key words: Gastric cancer, Clinicopathological features.

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Abstract

Gastric carcinoma remains a common disease worldwide with a dismal prognosis. This investigation was undertaken to define the demographic, clinicopathological and treatment modalities in patients with gastric adenocarcinoma.

Methods: We did a retrospective study of 56 patients with primary gastric cancer who had been at King Abdullah Medical city In Holy capital; a tertiary care hospital in KSA from January 2011 to December 2012, and follow up till December 2013.

Results: The mean patient age at diagnosis was 60.3 years (range= 26-94 years), and 62.2% were male. The male to-female ratio of patients was 1.6/1. 88.8%of the patients were Saudis and 11.2% were non Saudi (3 Yamani and 1 Pakistani). No family history of gastric cancer. 82.2% presented with stages III and IV disease. Histological types of adenocarcinoma lesions were present as intestinal, diffuse, and mixed with percent; 46.7%, 33.3% and 20% respectively. The H. pylori infection was documented in 20% of patients. Common chief complaint was abdominal pain (88.9%). 71.1% of our patients died within the first year and only 11% of them lived more than 2 years.

Conclusion: Gastric cancer is the second most common GI malignancies after colorectal cancer in King Abdullah Medical city. Most of our patients presented with advanced cancer stage which reflect its poor prognosis. This fact will need to be confirmed by a longer period of observation and enough sample size.

Key words: gastric cancer, clinicopathological features.

Introduction

Gastric cancer (GC) is a major contributor to the global burden of cancer morbidity and mortality. It is the fourth most commonly occurring worldwide (1). Moreover, because of its poor prognosis, it is the second most common cause of cancer death after the lung cancer. There are substantial variations in the incidence of GC by region and nation, with highest rates being observed in East Asia, Eastern Europe, and parts of Central and South America. Changes in the histology and location of upper GI tumors in some parts in Europe (2). In Western countries, the most common sites of GC are the proximal lesser curvature, cardia, and EGJ (3). It is possible that in the coming decades these changing trends to will also occur in South America and Asia. In 2013, an estimated 21,600 people were expected to be diagnosed and 10,990 would be eventually died of their disease in the United States (4).

GC, like other cancers, is the end result of the interplay of many risk factors as well as protective factors. Environmental and genetic factors are also likely to play a role in the etiology of the disease (5). Various epidemiological and pathological studies have suggested that gastric carcinogenesis develops with the following sequential steps, chronic gastritis, gastric atrophy, intestinal metaplasia and gastric dysplasia (6). Genetic factors play an important role in gastric carcinogenesis. The most common genetic abnormalities in gastric cancer tend to be the loss of the heterozygosity of tumor suppressor genes, particularly of p53 or “Adenomatous Polyposis Coli” gene (7).

GC is difficult to cure as it is often either asymptomatic or it may cause only nonspecific symptoms in its early stages. By the time symptoms occur, the cancer has often reached an advanced stage and may have also metastasized, which is one of the main reasons for its relatively poor prognosis. The modest efficacy and considerable toxicities associated with chemotherapy in advanced gastric cancer has prompted the pursuit of novel systemic treatment strategies (8). The difficulties encountered in the development of targeted therapy in advanced gastric carcinoma are caused by the lack of biomarkers to guide patient management. In the clinic to date, except for HER2, there are no established biomarkers predictive of tumor response to targeted agents. Few potential biomarkers are pending clinical validation, including amplification of MET (9), and fibroblast growth factor receptor 2 (FGFR2) (10) while others are more controversial. Moreover, the process of gastric carcinogenesis is complex. Several reports from the Kingdom of Saudi Arabia have studied general patterns of cancer (11), and patterns of gastrointestinal tract malignancies (12, 13). Only a few reports have been devoted to the study of the pattern of gastric cancer (14). The aim of this study was to describe the clinicopathological features and our experience in management of these patients in our local setting and suggesting ways to improve treatment outcome. Which might gives us a clue about whether or not screening programs are needed in our regions.
Methods

The current retrospective study included 45 patients with histological diagnosis of gastric carcinoma treated at oncology center in King Abdullah Medical City (KAMC) January 2011 and December 2012. The details of patients were retrieved from patients’ files kept in the medical record department and histopathology laboratory. Information retrieved included socio-demographic data, clinical presentation, anatomical site, TNM stage, histopathological type, grade, presence of metastasis and treatment modalities. The clinical stage of the disease was assigned to each patient by using TNM; this is a staging system which is an expression of the anatomical extent of the disease based on the extent of the primary tumor (T), absence or presence of and extent of regional lymph node metastasis (N) and absence or presence of distant metastasis (20). The histological classification was based on Lauren’s (1965) classification as follows: (1) Intestinal type, (2) Diffuse type and (3) Mixed type (15). Treatment modalities included surgery, chemotherapy, radiotherapy and palliative. Patients were followed up for one year or death.

Statistical analysis

Descriptive statistics included frequencies, means, medians, ranges, and percentages. Analytic statistics included chi-square tests and unpaired Student t test. P value of <.05 was considered statistically significant.

Ethical consideration

Ethical approval to conduct the study was sought from the IRB review committee before the commencement of the study.

Results

Demographic data

Out of 1471 patients who were registered with malignancies at our center during the study period, 56 patients were cases of gastric cancer representing 3.8% of cases. Of these, 4 patients were excluded from the study due to incomplete data. Seven patients were non carcinoma, (one NHL, one liomyosarcoma, one neuroendocrinal, and 4 GISTs; one low risk, two intermediate and one high risk). There were 28 (62.2%) males and 17 (37.8%) females giving a male to female ratio of 1.6:1. The ages ranged from 26 to 94 years with a mean age of 60.3 years. The peak incidence was in the age group of > 60 years (53.3%), followed by the age group of 40- 60 years (33.3%), and ages less than 40 years (13.3%). 88.7% of patients were Saudi and 11.3% were non Saudi (3 Yamani and 1 Pakistani) ; table 1.

Table 1: Demographic features.

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<th>Age in years</th>
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<tr>
<td>Median</td>
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<td>Range</td>
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Anatomical site, TNM staging and histopathologically type

The noncardiac region was the most frequent anatomical site involved in (64.4%) of cases. The gastric adenocarcinoma was the most common histopathologically type, occurring in 86.5% of cases, and most of the tumors had a poorly differentiated grade in 66.7% of cases. According to Lauren classification of gastric adenocarcinoma, 21 patients (46.7%) were intestinal, 15 patients (33.3%) were diffuse and 9 patients (20%) were mixed. According to TNM staging, 82.2% of the patients were diagnosed with advanced gastric cancer (Stages III and IV); table 3.

Diagnosis of gastric cancer

The diagnosis of gastric cancer was confirmed pathologically by upper GI endoscopic biopsies in 39 (86.7%) patients and the remaining 6 (13.3%) patients were diagnosed during laparotomy for gastric obstruction or definite surgery; table 3.

Treatment modalities

Out of 45 patients, 17 (37.8%) patients underwent surgical procedures for gastric cancer and the remaining 28 (62.2%) patients were not candidate for surgery with gastro-jejunostomy was the most frequent performed procedure; accounting for 58.8% of cases. 31.1% of patients were under palliative care from the start; table 3.
Discussion

GC is one of the most frequent cancers in the world; in terms of geographic distribution, almost two-thirds of gastric cancer cases and deaths occur in less developed regions. High rates apply to Japan, China, Korea, Central and South America, Eastern Europe, and parts of the Middle East, and low rates to North America, Australia and New Zealand, Northern Europe, and India (16). It is usually easier to treat if it is diagnosed early with a highly favorable prognosis and avoid extended surgery, which may produce complications, especially in the elderly people. However, many of the symptoms are similar to less serious conditions, which mean it can be difficult to recognize GC in the early stages and when symptomatic patients experience epigastric pain, discomfort and definitive symptoms such as weight loss or obstructive symptoms and metastases that often impede curative radical resection.

Although there are improved surgical techniques and adjuvant treatments, still the results of GC treatment do not differ markedly from the past results. Five-year relative survivals of around 20% or less are frequently reported (17).

In this review, gastric cancer accounted for 3.8% of all histopathologically-diagnosed malignancies seen during the studied period in our setting. These data are comparable with other studies which reported the incidence of gastric cancer up to 6.0% of all cancers (18, 19).

Our figure for GC in this study may actually be underestimated by the retrospective nature of the study. A better picture of its incidence in this region requires a prospective comprehensive data collection.

According to the Saudi Cancer Registry (SCR) between January and December 2004, 3158 gastric cancer male patients were diagnosed and analyzed with gastric cancer percentage 4.4% which represent the second common GIT cancers post colorectal (20). The cause of the high incidence of gastric cancer in our country is unclear and may be due to rapid change in Saudi life style including the increase in the prevalence of smoking among all age groups in comparison to other countries (21, 22) and dietary habits as Canned food, hot spices, salt and animal proteins which constitute a good media for foods fermentation and nitrosamine production. Both nitrosamine production and salt have been implicated as a risk factor for GC in many studies (23, 24). However, to further investigate this association we need more comprehensive and detailed data. In most developed countries, there has been a persistent and progressive decline in both the incidence and the mortality of gastric cancer in the past 50 years. This is principally related to changes in diet and food preparation and preservation (25).

In agreement with other studies (26), the peak age incidence of gastric cancer in this study was found to be in the sixth decade of life.

The male predominance demonstrated in this study was in keeping with previous observations reported in studies done elsewhere (27). The exact reason for this male preponderance is not known; although the higher prevalence of smoking among men with the possible protective effect of estrogen may explain this predominance (28).

Many studies confirm the importance of lifestyle and environmental factors including H. pylori-induced inflammation, atrophy of the gastric mucosa and a diet rich in salt and nitrates and poor in fruit and vegetables (29).

Retrospective studies of the risk of GC in relation to H. pylori infection underestimated the true risk, due to loss of infection with onset of cancer. H. pylori does not colonise areas of cancer, intestinal metaplasia, or atrophy, and there is evidence that with the development of advanced gastric disease the organism can be lost from the stomach (30), which partially explain the lower percentage of documented H. pylori in our results (only 20%) . One estimate attributed more than 70% of distal gastric cancers to H. pylori, and the presence of cytotoxin CagA-positive H. pylori increases the risk of gastric cancer 20-fold compared with CagA-negative (31). H. pylori eradication treatment can reduce risk of gastric cancer (32).

Determination of H. pylori seroprevalence was not performed in this retrospective study, because tests for H. pylori status were not routinely performed in patients with gastric cancer during the study period and, therefore, it was difficult to establish the association between H. pylori infection and gastric cancer.

A meta-analysis published in 1997 and in 2008 suggested a risk of stomach cancer among smokers of the order of 1.5-1.6 compared to non-smokers and the risk seen among current smokers was significant higher than that seen among ex-smokers (33). In this study, we could not determine the association among gastric cancer and smoking due to insufficient data in the files about the smoking history and type.

The most important method that is likely to improve the survival rates is early detection of GC. In the present study, the majority of patients presented late with an advanced stage of cancer (stage III and IV), which is in keeping with other studies in developing countries (34). Although there are sufficient endoscopic services. Which can be can be explained by many factors; firstly, the frequent visits to non-specialist physicians who prescribe medications to treat the symptoms without treating or investigating the underlying cause. Subsequently, these patients will be diagnosed either with late stage GC or one of its complications. Secondly, elderly people usually fail to make use of available medical services. Lastly, still there is no public screening system for gastric cancer detection in our area. So to improve chances of early detection we need a long term plan including patients and physicians as general practitioners should be more liberal in referring patients for endoscopy especially in high risk people ,open-access endoscopy ,greater efforts in education of patients and the improvement of diagnostic technical skills.

This study showed a wide spectrum in the histopathological features. The common anatomical site for gastric cancer in this study was distal gastric non cardiac 64.4% (which is similar to studies done in developing countries (36, 35)
The most common histopathological type of gastric cancer in this study was adenocarcinoma, accounting for 86.5% of cases, which is consistent with what is reported in the literature. (37-39) Her 2 was not routinely done in our center during the study period. It is requested in 12 patients with 5 patients were positive. The treatment of gastric cancer requires a multidisciplinary approach. Treatment modalities of GC include surgery combined with chemotherapy and radiotherapy given either as neo- or adjuvant therapy. (40) Surgery is and, most probably, will remain the cornerstone of curative management of resectable disease; however, this benefit is limited to patients who present with early and, perhaps, localized disease. However, most of the patients we see in our environment present late with advanced disease at the time of diagnosis, for which only palliative surgery is possible. (41) In this study, only 4 patients had gastric resection with curative intent. 32 patients died during the first year and only 5 patients extended more than 2 years. The prognosis of GC has remained poor in most developing countries where most patients are already in an advanced stage of the disease at the time of diagnosis, which has been proven both in the present study and in most studies. (42-44) However, when it is diagnosed and treated early, gastric cancer is curable as a five-year survival rate of over 90% has been achieved in Japan. (45)

Limitations

The potential limitations of this study included the following: first, the fact that information about some patients was incomplete in view of the retrospective nature of the study might have introduced some bias in our findings. Second, we did not determine the association of H. pylori with gastric cancer because of lack of necessary facilities at the study center. Third, this study included small sample size patients who were evaluated and treated at a single institution, which may not reflect the whole population in this region.

Conclusion

Gastric cancer is the second most common gastrointestinal malignancy after colon cancer in our center. The majority of gastric cancer when become symptomatic, usually become beyond the cure. In absence of screening program, the only way to improve the prognosis is to change unhealthy dietary habits. Although this study has highlighted the general epidemiological and clinicopathological features of gastric malignancy in our center, further prospective studies with enough sample size are needed studies are needed to evaluate the environmental risk factors, treatment outcomes and survival rate.

Conflict of interest

The authors certify that is no potential or actual conflict of interest related to this research.

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Original Article

perspective, BANTA Book Group, 1997 Menasha, USA.


**Giant Cell Tumor: Rare Cases – Surgery vs. Medical Treatment**

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Key words: Giant sarcomas, Embolization, Sacrum.

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**Introduction**

Giant cell tumor (GCT) of bone is a rare neoplasm that accounts for approximately 5% of all primary bone tumors in adults. GCT most frequently occurs at the end of long bones, and the sacrum is the fourth most common site, accounting for between 1.7-8.2% of cases. Giant cell tumor also occurs in 2-4% of the cases in the spine. In all locations, the neoplasm occurs most commonly between the ages of 20-45 years of age, and it equally affects males and females.

Giant cell tumor has a 1 to 5% incidence of metastasizing to the lung. Pulmonary staging is an important component in the initial and follow-up evaluation of GCT of bone. Generally, lung metastases are late onset; their mean interval to progression is 4 years. The prognosis for survival when lung metastases develop is favorable in more than 70% of patients. Although surgical management of the metastatic lesions is the mainstay of treatment, nevertheless, in such cases approximately 15% of patients with metastatic disease may die.

Various treatment methods have been advocated including arterial embolization, curettage, surgical excision, radiation, and cryotherapy. Treatment is very successful in long bone lesions, but the optimal treatment and medical management of GCT in the spine and sacrum has not been well established.

We are presenting our experience with the diagnosis and management of one case of giant cell tumors of the spine and sacrum. We discuss the clinical presentation, treatments received, and outcomes of therapy.

**Prevalence and risk factors**

Giant cell tumor (GCT) of the sacrum is rare, representing about 3–4% of all giant cell tumors, but is particularly challenging to treat since the tumor is frequently diagnosed late and is often quite extensive within the bone and surrounds the sacral nerve roots, which often produce the initial symptoms, mistaken for sciatica. By the time of diagnosis, there is also often a large soft tissue mass involving bones and surrounding tissues.

Although regarded as a benign tumor, GCT represents a continuum of neoplasia, and clinical behavior is not predictable based upon clinical, radiographic, or histologic features. GCT can be locally aggressive, and it has the potential to recur locally after curettage alone. Furthermore, in about 2 to 3 percent of cases, distant metastases can occur, most often affecting the lungs.

**Case no 1 presentation**

A 24 years old female who initially attended the GP clinics with complain of lower back pain for the almost 9 months. Patient reported she had a fall before her back pain started and she was only treated with analgesics but was not responding to treatment; she had Urinary burning sensation and Constipation since that time as well. Has a family history of pancreas cancer. She was seen at our hospital and was evaluated by MRI and CT scan; MRI showed extensive destructive process involving sacrum with circumscribed lobulated soft tissue mass about 7x7 cm, multiple small cystic lesions were also seen and the largest lesion was about 4x4x6 cm (figure 1), CT scan of abdomen showed two small lesions in liver; laboratory blood values were all within normal limit except for slight anemia which was treated with supportive medications. Tumor markers were all negative. There were no signs of neurological or sensitive deficits. Patient underwent a tissue biopsy Under CT guidance, 2 core biopsies were obtained from the sacral mass which revealed Atypical spindle cell proliferation with giant cells suggestive of giant cell tumor of bone; tumor cells were negative for vimentin and SMA and no immunoreactivity was detected for Cytokeratin (AE1/AE3) and S100 protein; the surgery here was deemed inappropriate for the patient since this will cause instability of sacroiliac joint, inability to sit and urinary incontinence with overflow and chronic constipation which might...
require diverting stoma. As a supporting measures patient underwent pelvic angiogram and embolization which she tolerated well

Tumor board discussions recommended radiotherapy, patient had to go under ovaries transposition to protect them from radiation field and was treated with 54 Gy radiation doses followed by Denosumab monthly as patient was showing increase in the urinary N-telopeptide (NTX) with a value of 277 (NV Age 18 years or older – 21-66 nmol NTX/mmol creatinine)\(^1\)

Patient underwent angio/embolization of sacral mass which was repeated again after 6 months and was followed up monthly in the outpatient clinics; a repeat MRI revealed tumor to be of same size as described but showing some areas of necrosis (figure 2)

Patient up to date is followed up in the clinic and it was deemed through tumor board discussions that she would require major/extensive surgery but this type of surgeries cannot be performed at our institution.

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**Case no 2 presentation**

A 40 years old Male who started having intermittent swelling for 5 years in the left, patient was seen in multiple institutions and was treated conservatively until end of 2011 when a biopsy was done at a private hospital which revealed giant cell tumor in the tendon sheath of the left ankle. He underwent partial resection of the tumor followed by embolization of the left fibular artery mid-2012.

Patient was treated with monthly Denosumab and was followed up with MRI that revealed decrease in the mass size. He also underwent a PET scan as a follow up which was read as negative

Patient continued to have a stable disease but a Repeat MRI done in November 2013 showed mass increasing in size and encasing vessels/nerves (figure 2) and a re-embolization had to be performed on patient for the second time and he was continued on monthly Denosumab; a recommendation for surgery was decided by the tumor board committee but unfortunately the type of surgery required could not be performed at our institution. Currently patient still on monthly Denosumab but appears to progress as he complains of increasing pain and a repeated MRI showed increasing size of the mass.
Conclusion

In appropriately selected patients, surgery is a valuable approach to effect local tumor control and overall patient survival, despite potential complications. Before a decision for surgery is undertaken, an interdisciplinary surgical team including orthopedic oncology, general surgery, and spine surgery depending on the extent of the resection must be available.\(^\text{19-20}\)

Embolization may also prove palliative and/or curative in cases in which the lesion cannot be resected or in which the disease is refractory to other treatments; the risk of local recurrence is equal to 31% at 10 years and 43% at 15 and 20 years.\(^\text{21-22}\) Close follow-up evaluation for locally recurrent disease and pulmonary involvement is critical. Surveillance should include radiographic examination of the chest every 6 to 12 months for at least the first 2 to 3 years.

References

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Comparative study of two chemoreduction regimens with local therapy for the treatment of retinoblastoma

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Key words: Retinoblastoma, Chemoreduction regimens, Local therapy, Eye preservation.

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Abstract

Background: Retinoblastoma is the most common intraocular malignancy in childhood. Because of excellent survival in patients with intraocular disease; long term side effects and vision preservation are important factors. Chemoreduction with focal ophthalmic therapy have allowed cure of disease without the need for enucleation or external beam radiotherapy; which are associated with significant long term toxicities.

Aim of the Work: to compare 2 chemoreduction regimens with focal ophthalmic therapy for cases of retinoblastoma.

Patients and Methods: A total of 40 patients (63 eyes) with stage B, C or D retinoblastoma, seen in the department of clinical oncology, Alexandria University and department of pediatric oncology CHUV, Lausanne, Switzerland from November 2007 till November 2009. Patients were randomized into: group I (20 patients) received 4 cycles of carboplatin, vincristine and etoposide, and group II (20 patients) received 4 cycles of carboplatin, and vincristine. Both treatment groups received focal ophthalmic therapy. Salvage was done by enucleation or stereotactic radiotherapy. End points: event free survival, treatment toxicity, and prognostic factors.

Results: After a median follow up of 33 months, all patients were alive without residual disease. Eyes with stage B and C were preserved, while most of eyes with stage D needed salvage therapy. No difference in the event free survival between both groups. Acute side effects were less in group II. Stage at presentation was the only significant prognostic factor.

Conclusions: The 2 drug regimen is equally effective as the standard 3 drug regimen in terms of eye preservation and progression free survival.

Introduction

Retinoblastoma is the most frequent neoplasm of the eye in childhood, representing 2.5% to 4% of all pediatric cancers. Two thirds of all cases are diagnosed before the age of 2 years. Therefore, therapeutic approaches need to consider the need to preserve vision with minimal long-term effects. (1) Retinoblastoma presents in two clinical forms; bilateral which is hereditary in 25% to 35% of cases, characterized by germline mutations of the RB1 gene; and unilateral, which is usually nonhereditary. (2) For unilateral retinoblastoma, in the absence of extraocular disease, enucleation alone is curative for 85% to 90% of children.(3) In view of the success in treating bilateral intraocular disease with chemoreduction, a conservative approach is also adopted in single eyes with early-stage disease.(4) The treatment for patients with bilateral retinoblastoma, in the past, has been enucleation for the eye with advanced intraocular disease, and radiation of the other eye. However, irradiation of the orbit results in midfacial deformities and increased risk for sarcomas.(5,6) These concerns have resulted in the development of more conservative approaches with upfront chemoreduction, followed by focal therapies. The best results are achieved with a combination of vincristine, carboplatin, with or without etoposide.(7-11)

Aim of the Work

To compare two regimens of chemotherapy with focal therapy in patients with intraocular retinoblastoma regarding event-free survival, toxic effects, patterns of failure; and prognostic factors.

Patients and Methods

Forty patients (63 eyes), 9 patients seen at department of Clinical Oncology, Alexandria University Hospitals, Egypt and 31 patients seen at department of Paediatric Oncology, Lausanne University hospital, Vaud, Switzerland, between November 2007 and November 2009. Patients were randomized into 2 groups (20 patients each). They were subjected to: History and clinical examination, ophthalmic examination, RETCAM (retinal camera) fundus pictures under general anesthesia at diagnosis and 3 weeks after chemotherapy, laboratory investigations: before chemotherapy, and then every 2 months. Imaging: chest x-ray; MRI of the orbit and brain at diagnosis, then every 6 months.

Eligibility criteria

Unilateral or bilateral retinoblastoma by ophthalmologic examination. Age < 16 years. Stage B, C or D by International Classification System(12) for Intraocular
Retinoblastoma. Lansky performance status of 50-100% (13). No extraocular disease. No systemic metastases. Informed consent signed by the patient’s parents.

**Group I:** Received 4 cycles of Carboplatin 200 mg/m2/day, days 1-3, Etoposide 150 mg/m2/day, days 1-3 and Vincristine 1.4 mg/m2 (max 2 mg) day 1; repeated every 28 days. For children <10 Kg or <1 year old, mg/Kg dose was used. Focal ophthalmic therapy was delivered at any of the 3 days of chemotherapy; starting 2nd cycle. Transpupillary thermotherapy, using diode LASER, for posteriorly located lesions and Cryotherapy for anteriorly located tumors.

**Group II:** Received 4 cycles of Carboplatin, and Vincristine, together with focal therapy. No Etoposide was used; same schedule and dose as in group I.

Patients with residual vitreous seeds were enucleated (8 in group I, and 11 in group II); those with residual perimacular disease received 3-D conformal stereotactic radiotherapy; 50.4 Gy (3 in each group). Otherwise, salvaged by focal therapy.

**Measurement of Response**

Three weeks after chemotherapy, patients had ophthalmic examination under general anesthesia, and the type of regression was described (14): **Type 0:** Complete disappearance of the lesion. **Type I:** Calcification “cottage cheese”. **Type II:** Translucent Tissue “fish Flesh”. **Type III:** Mixed type I and II. **Type IV:** White chorioretinal scar. **Complete response (CR):** type 0 or 1 regression for all tumors. **Very good partial response (vPR):** at least 50% decrease in tumor areas with residual type II or III regression in only one tumor. **Partial response (PR):** less than 50% decrease in tumor areas with residual type II or III regression in one tumor.

**Adverse Events:** Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 (15); [http://ctep.info.nih.gov](http://ctep.info.nih.gov).

**Statistical analysis:** SPSS version 18.0, Chicago, IL, USA.

**Results**

Patients’ characteristics in the whole series were comparable (Table 1).

The mean age for bilateral cases was 14.43 months and for unilateral cases 24.64 months; with statistically significant difference (p=0.005).

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**Table 1:** Patients’ characteristics in both groups.

<table>
<thead>
<tr>
<th>Age (in months)</th>
<th>Study group</th>
<th>Test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GP (I)</td>
<td>GP (II)</td>
</tr>
<tr>
<td>0-&lt;6</td>
<td>5</td>
<td>25</td>
</tr>
<tr>
<td>6-&lt;12</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>12-&lt;18</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>18-&lt;24</td>
<td>5</td>
<td>25</td>
</tr>
<tr>
<td>24-72</td>
<td>3</td>
<td>35</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>100</td>
</tr>
</tbody>
</table>

---

**Table 2:** Tumor stage in both treatment groups.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Study group</th>
<th>Test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GP (I)</td>
<td>GP (II)</td>
</tr>
<tr>
<td></td>
<td>(n) eyes</td>
<td>%</td>
</tr>
<tr>
<td>A</td>
<td>2</td>
<td>6.1</td>
</tr>
<tr>
<td>B</td>
<td>3</td>
<td>9.1</td>
</tr>
<tr>
<td>C</td>
<td>12</td>
<td>36.4</td>
</tr>
<tr>
<td>D</td>
<td>15</td>
<td>45.5</td>
</tr>
<tr>
<td>E</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>100</td>
</tr>
</tbody>
</table>

No significant differences in response to treatment between both arms was observed, with CR and vPR in 25 eyes (75.7%) in group I, and in 18 eyes (60%) in group II. (table 3)

---

**Table 3:** Best response in both treatment groups.

<table>
<thead>
<tr>
<th>Response</th>
<th>Study group</th>
<th>Test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GP (I)</td>
<td>GP (II)</td>
</tr>
<tr>
<td></td>
<td>(n) eyes</td>
<td>%</td>
</tr>
<tr>
<td>CR</td>
<td>17</td>
<td>51.5</td>
</tr>
<tr>
<td>vPR</td>
<td>8</td>
<td>24.2</td>
</tr>
<tr>
<td>PR</td>
<td>7</td>
<td>21.2</td>
</tr>
<tr>
<td>SD</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>52.4</td>
</tr>
</tbody>
</table>
Table 4 shows that more eyes in group II needed enucleation or radiotherapy as salvage.

Table 4: type of salvage therapy in both treatment groups.

<table>
<thead>
<tr>
<th>Type of Salvage therapy</th>
<th>Study Group</th>
<th>Test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GP (I)</td>
<td>GP (II)</td>
</tr>
<tr>
<td>Enucleation</td>
<td>(n)</td>
<td>%</td>
</tr>
<tr>
<td></td>
<td>8/33</td>
<td>24.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>X² = 1.152</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>3/33</td>
<td>9.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>p = 1.0</td>
</tr>
<tr>
<td>Total Failures</td>
<td>11/33</td>
<td>33.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>46.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>X² = 1.167</td>
</tr>
</tbody>
</table>

Useful vision was obtained in 69.6 % of group I patients versus 56.6 % of group II. (P= 0.283). Treatment toxicity was generally higher in group I. Eighty percent developed grade 3/4 neutropenia, compared to 30% in group II (P= 0.135). Two patients (10%) in group I developed febrile neutropenia that required hospitalization. (Table 5).

Table 5: Treatment toxicity in both groups.

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Study group</th>
<th>Test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GP (I)</td>
<td>GP (II)</td>
</tr>
<tr>
<td></td>
<td>(n)</td>
<td>%</td>
</tr>
<tr>
<td>Anemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>G2</td>
<td>4</td>
<td>20.0</td>
</tr>
<tr>
<td>G3</td>
<td>13</td>
<td>65.0</td>
</tr>
<tr>
<td>G4</td>
<td>3</td>
<td>15.0</td>
</tr>
<tr>
<td>Neutropenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>G2</td>
<td>4</td>
<td>20.0</td>
</tr>
<tr>
<td>G3</td>
<td>14</td>
<td>70.0</td>
</tr>
<tr>
<td>G4</td>
<td>2</td>
<td>10.0</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1</td>
<td>3</td>
<td>15.0</td>
</tr>
<tr>
<td>G2</td>
<td>2</td>
<td>10.0</td>
</tr>
<tr>
<td>G3</td>
<td>4</td>
<td>20.0</td>
</tr>
<tr>
<td>G4</td>
<td>4</td>
<td>20.0</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1</td>
<td>2</td>
<td>10.0</td>
</tr>
<tr>
<td>G2</td>
<td>12</td>
<td>60.0</td>
</tr>
<tr>
<td>Vomiting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1</td>
<td>6</td>
<td>30.0</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1</td>
<td>1</td>
<td>5.0</td>
</tr>
<tr>
<td>G2</td>
<td>6</td>
<td>30.0</td>
</tr>
</tbody>
</table>

After a median follow up of 30.5 months, all patients in both groups were alive. PFS for patients in group I (66.7%) was higher than in group II (53.3%). However this difference was not statistically significant. (figure1) Patients with stage B and C had statistically significant better PFS than stage D (P= 0.003).

Discussion

There is no consensus on the optimal chemotherapy for intraocular retinoblastoma(3). Most recent publications use carboplatin, vincristine and etoposide(7), however others omit vincristine(8) or etoposide(9). In our study, elimination of etoposide was due to its leukemiogenic effect. (16).

Bilateral disease was highly represented in our study, 65% for group I and 50% for group II. In many publications(10,11,17), the rate of bilateral disease is 60-75%. In Bonanomi et al, (18) 28 patients with intraocular retinoblastoma treated by 4-9 cycles of carboplatin and etoposide, the rate of bilateral disease was 46%. In our study, 45.5 % of patients in group I and 46.7% of patients in group II had stage D at presentation. Bonanomi et al(18) reported that 100% of unilateral and 57.7% of bilateral cases presented with stage D and E. Similarly; in the report by Chantada et al, (10) 67% presented with R-E stage IV and V. The higher rate of late disease in these publications may be explained by late diagnosis.

Our study showed that retinoblastoma is highly responsive to chemotherapy in combination with focal therapy, with 75.7%, and 60% of eyes in Group I, and II respectively, had CR and vPR. The CR rate in the study by Beck et al(8) was 71.4% after carboplatin and etoposide with focal treatment. On the contrary, Rodriguez et al(11) achieved a response rate of only 52% after 8 cycles of carboplatin and vincristine. This may be due to deferring the focal treatment till the end of last chemotherapy.

The higher rate of enucleation in group II of this study; 36.7% (P= 0.283) can be attributed to the use of 2 drugs. Stereotactic radiotherapy was used to salvage around 10% of patients in each group.

In the RET-3 report of Saint Jude(11), the rate of enucleation and/or radiotherapy was 53.5%; however, 37% of their patients were stage V.

In the study by Beck et al(8), 27.1% of the eyes needed salvage therapy. Similarly
in the report by Shields et al(17), 33% of the eyes needed salvage. Focal stereotactic radiotherapy was used in this study for perimacular lesions to avoid thermotherapy to the macula with subsequent loss of vision and to deliver minimal dose to the bony orbit and normal tissues. All 6 patients have controlled tumors with radiotherapy and none needed enucleation. They all had useful vision in the irradiated eye. Sahgal et al(19) treated 5 eyes with focal stereotactic radiotherapy after failure of chemothermotherapy. All eyes showed CR and only one eye developed recurrence after 5 months that needed enucleation.

In this study, both regimens were well tolerated with only 2 episodes (2.5%) of febrile neutropenia in group I, versus none in group II. The rate of grade 4 anemia was only 15% in group I and 5% in group II. Forty percent of patients in Group I and 20% in group II developed grade 3/4 thrombocytopenia that required platelets transfusion. We used the 50,000/mm3 platelet count as the cut off for transfusion to avoid vitreous hemorrhage. Shields et al(20) and Chantada et al(10) reported a 3% and 6% rate of febrile neutropenia respectively; similar to group I patients since they used a 3 drug regimen. On the other hand, Rodriguez et al(11) who used a 2 drug regimen as in Group II patients, reported no cases of febrile neutropenia. The OS in both groups of our study was 100%. This is similar to reports by Rodrigues et al(11), and Shields et al(17). In Chantada et al(10) , 2 out of 39 patients died; they had bilateral retinoblastoma and developed distant metastasis. Comparison of PFS for both groups (66.7% vs 53.3%) at a median of 30.5 months was not statistically significant (p=0.207). Confirmatory studies are required to support the use of the less toxic and less expensive two drug regimen. Interestingly, PFS for unilateral was less than for bilateral cases; 47.1% vs 65.2% (p=0.235). This may be the result of more efforts of ophthalmologist with aggressive focal therapy to avoid enucleation.

In the report by Chantada et al(10) the 5 year PFS was 90% for the group treated with 2 drugs and 45% for the group treated with 3 drugs. However the group who received 3 drugs was the higher risk group; which may explain the paradoxical results. The only positive prognostic factor in the current study was the stage at presentation. All patients with stage B and 77% of patients with stage C did not need salvage therapy. This is in contrast to only 37.9% of patients with stage D who did not need salvage therapy, this difference was statistically significant (p = 0.003).

Shields et al (21) analyzed 103 patients treated by 6 cycles of carboplatin, vincristine and etoposide with LASER and/or Cryotherapy. They similarly found that the most important predictive factor is the tumor stage.

Conclusion

Two drug regimen (carboplatin, vincristine), is equivalent to 3 drug regimen (carboplatin, vincristine and etoposide), as regards the rate of eye survival, with lower acute toxicity and costs. The most important prognostic factor is the stage of disease at presentation. Focal stereotactic radiotherapy is a valid and feasible option for salvage. More studies and longer follow up are required to confirm these findings.

AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST: The authors indicated no potential conflicts of interest.

References


Neoadjuvant chemotherapy in ovarian cancer, the effect of the interval period on the results

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Key words: Interval, Neoadjuvant, Chemotherapy, Results, Surgery.
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Abstract

Background: The use of Neo-adjuvant chemotherapy (NAC) had been recently increased in patients with locally advanced epithelial ovarian cancer (EOC), the effect of the interval between the last chemotherapy cycle and start of surgery had not been studied well.

Patients and methods: Thirty patients with advanced EOC were treated with NAC followed by cytoreductive surgery. These patients were divided into two groups, 15 patients each, Group A: Underwent IDS within 42 days from last cycle of chemotherapy, Group B: Underwent IDS after 42 days from last cycle of chemotherapy.

Results: all patients in this study received NAC and underwent IDS, 27 patients (90% of cases) of both groups received postoperative chemotherapy. TAH & BSO was performed for all patients, 27 patients (90%) in both groups had infra-colic omentectomy (14 Group I & 13 in Group II), 6 patients (20%) (3 Group I & 3 in Group II) had small bowel resection and anastomosis. Lymphadenectomy (pelvic) was performed for 3 patients (16%) (2 Group I & 1 in Group II) and they were involved pathologically. Optimum cytoreduction was achieved in 15 patients in Group I (100% of cases of Group I) compared to 3 patients in Group II (20% of cases of Group II).

Conclusion: The optimal timing for standard cytoreduction was within 42 days from last NAC cycle, longer interval between NAC and IDS has an adverse effect on the patient outcome.

Introduction

Ovarian cancer is the leading cause of death among all gynecological malignancies in developed countries. The incidence of ovarian cancer is up to 10 times higher in western countries than in rural Asian and African ones. Different reproductive characteristics, life styles and specific medical conditions are responsible for different pattern and incidence of ovarian cancer worldwide.

Eighty to ninety percent of ovarian cancers are epithelial, and more than two thirds are diagnosed at an advanced stage. Epithelial ovarian cancer is the most leading cause of death in females with pelvic malignancies, because the early symptoms of ovarian cancer are easily overlooked, a diagnosis of ovarian cancer is infrequently made before the cancer has progressed to stage III or IV.

The current standard of management for a patient with advanced (Stage III or IV) ovarian cancer is cytoreductive surgery followed by administration of systemic chemotherapy. The 1980s clinical trials demonstrated that platinum based chemotherapy improves survival in women with advanced disease, since mid-1990s a combination of platinum (cisplatin or carboplatin) and taxans (paclitaxel) have become the standard first-line chemotherapy regimen for treatment of ovarian cancer.

In certain cases, however, it is not prudent for the patient to undergo cytoreductive surgery at the time of diagnosis secondary to increased surgical risk. Often, these patients will have massive accumulating effusions or severe medical problems that prevent major surgery. In such patients, a presumptive diagnosis can be made by cytological examination of pleural fluid or ascites, or by fine needle aspiration of a soft tissue mass.

Diagnostic imaging criteria have also been developed to identify patients with advanced ovarian cancer in whom optimal cytoreduction is unlikely to be achieved at the initial surgery. Following diagnosis, these patients may benefit from (two or three cycles of) chemotherapy during which time the effusions or medical contraindications to surgery may resolve, after that cytoreductive surgery called “interval cytoreductive surgery” and additional (three cycles of) chemotherapy may be more feasible.

This technique, called “Neoadjuvant chemotherapy” has been evaluated in retrospective, matched-control trial, in Europe comparing 88 patient who underwent neoadjuvant chemotherapy with 244 patients who underwent standard therapy, all of whom had advanced ovarian cancer, the three and five years survival rates were not different between the groups, but the percentage of patients cytoreduced to less than 2 cm of residual tumor, quality of life, and disease-free interval were improved in patients who underwent neoadjuvant chemotherapy.

Recently, the efficiency of “Neoadjuvant chemotherapy” in ovarian cancer treatment has been widely discussed, and the equivalence and the possible advantage of NAC over initial debulking surgery were addressed in phase III EORTC/ NCIC trial including 670 patients.
**Patients and Methods**

Thirty patients (n=30) with locally advanced non metastatic epithelial ovarian cancer (stage III) were treated by (CP regimen; carboplatin and paclitaxel) as neoadjuvant chemotherapy followed by Interval debulking surgery. They were divided into two groups, 15 patients each, according to the time of surgery. (According to the time they were presented to the gynecology department).

**Group A:** Patients who underwent IDS within 42 days from last cycle of chemotherapy.  
**Group B:** Patients who underwent IDS after 42 days from last cycle of chemotherapy. All patients (n=30) received (CP regimen) as Neoadjuvant chemotherapy: Carboplatin (AUC = 6, Day 1) & Paclitaxel (175 mg/m², Day 1). The cycle was repeated every 3 weeks. Total numbers of cycles were 6 cycles for all responsive patients. Patients with stable disease (by CT), received different chemotherapy regimen (gemcitabine based) postoperatively. After the completion of neoadjuvant chemotherapy, all Patients were then referred for Interval debulking surgery and the surgico-pathologic response assessment.

Informed consent was taken from all patients before starting the treatment and the protocol was approved from the ethical committee.

**Results**

30 patients (100%) in our study received 3 cycles of NAC carboplatin paclitaxel (CP regimen) (15 Group I & 15 in Group II); {27 patients (90%) of both groups in our study received 3 cycles of preoperative chemotherapy, two patients (8%) had received preoperative 6 cycles and one patient (5%) had received 5 cycles). All patients (100%) underwent interval debulking surgery (15 Group I & 15 in Group II). 27 patients (90% of cases) of both groups received 3 cycles (CP regimen) of postoperative chemotherapy; as two patients (8%) who had 6 preoperative cycles and complete pathological response didn’t have post-operative chemotherapy.

The cycle was repeated every 3 weeks. Total numbers of cycles were 6 cycles for all responsive patients. Patients with stable disease (by CT), received different chemotherapy regimen (gemcitabine based) postoperatively. After the completion of neoadjuvant chemotherapy, all Patients were then referred for Interval debulking surgery and the surgico-pathologic response assessment.

**Discussion**

As the optimal number of chemotherapy cycles to be given before planned surgery is still a major unsolved issue. The number of cycles was determining according to the evidence of regression or progression of disease, response to CA125 level and patient’s ability to tolerate neoadjuvant chemotherapy. In this study, 90% of patients received 3 cycles, (3.3%) received 5 cycles and (3.3%) received 6 cycles of NAC.

It seems that the chance of achieving an optimal debulking increases in responding patients with the numbers of cycles before surgery. This potential advantage has to be balanced against the risk of drug resistance and cumulative drug toxicity associated with the increased number of chemotherapy cycles.
Since the amount of residual disease is the most important prognostic factor, every effort should be made to increase the optimal cytoreduction rate; NACT followed by surgical cytoreduction is one such approach. Hou JY et al.\(^\text{10}\) concluded that optimal cytoreduction rate was (95%) for neoadjuvant chemotherapy arm and (71%) for primary surgery arm. Hegazy et al.\(^\text{11}\) concluded that optimal cytoreduction rate was (72%) for neoadjuvant chemotherapy arm and (62%) for primary surgery arm.

In the present study, it was concluded that the optimal timing for standard cytoreduction surgery was within 42 days of last NAC cycle, we found that longer interval between neoadjuvant chemotherapy and interval debulking surgery (IDS) have an adverse effect on the residual tumor tissue left after surgery and thus may affect survival. (In our study, suboptimal cytoreduction >1cm was achieved in 75% of cases of Group II compared to 0% in group).

In accordance with this finding, Haupreased R et al.\(^\text{12}\) indicated better outcome for patients who undergo interval debulking surgery within 6 weeks after last cycle of neoadjuvant chemotherapy.

Several non-randomized trials, have reported an optimal cytoreduction rate of (60-95%) following neoadjuvant chemotherapy. In the current study, optimal cytoreduction rate was (60%) which is compatible with that reported in the literature using neoadjuvant chemotherapy.\(^\text{12,13,14}\)

In present study, in both groups, Optimum cytoreduction was achieved in 18 patients (60% of cases); these patients included: 8 patients had complete macroscopic resection; one of them had also complete pathological response, and suboptimal cytoreduction was achieved in 12 patients (40% of cases) with residual disease; mainly in pelvis, abdominal surface of diaphragm and liver surface in.

This data compared with Hegazy et al.\(^\text{10}\) who reported that non-standard surgery was performed in (22.2%) after neoadjuvant chemotherapy compared to (34.4%) for primary surgery group. However, A Bacili et al.\(^\text{15}\) Reported that only (14%) of patients who received neoadjuvant chemotherapy had non-standard surgery.

**Conclusion**

Neoadjuvant chemotherapy caused significant subjective and objective improvements before the surgical procedures which positively reflect on surgeon’s ability to achieve optimum cytoreduction surgery in advanced ovarian cancer. These occur in the view of adequate selection criteria for NACT, consideration of surgical morbidity and the possibility of successful debulking.

With the disease under control, relief of distressing symptoms as abdominal distension & discomfort and nutritional improvement result in improving patient’s performance status and perioperative outcome.

The optimal timing for standard cytoreduction surgery was within 42 days of last NAC cycle, we found that longer interval between neoadjuvant chemotherapy and interval debulking surgery (IDS) have an adverse effect on the patient outcome.

**References**

Ovarian dysgerminoma: Clinical features and therapeutics outcomes. Retrospective Tunisian study of 13 cases

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Abstract

Purpose: To report the epidemiologic, clinical features, treatment strategy, follow up and outcomes from a serie of dysgerminoma treated in Tunisia. Comparing them to literature and identifying prognosis factors.

Patients and methods: This retrospective study concerned 13 patients treated for an ovarian dysgerminoma (OD) at the medical oncology department of Farhat Hached hospital of Sousse in Tunisia. From 1994 to 2011.

Results: Median age was 16 years (85% under 18 years). 69% were nulliparous (31% on pre-menarche). Most common symptom was abdominal and/or pelvic pain (69%). According to FIGO classification, we found predominance of stage IIIc (31%). Preoperatively, the tumor markers were elevated in 60%, Alpha Foeto protein was normal in all cases. Postoperatively, tumor markers were elevated in 42%. After chemotherapy, they were high in 15, 4%. All patients underwent initial surgery, 92% of patients received a postoperative chemotherapy. BEP regimen was the most widely used (77%). Radiotherapy was performed for 31% of patients. The mean survival was 89 months (53 to 192 months). Overall survival at 5 years was 100% all stages combined. Among the 70% of patients who had conservative treatment: 22% had their menarche, 78% report the return of their cycle after the end of chemotherapy and only one of them is currently pregnant in the first quarter.

Conclusion: The OD has excellent prognosis. The new therapeutic approach combining conservative surgery and chemotherapy will further improve prognosis and reduce the number of recurrences while preserving the fertility of these young patients.

Introduction

Ovarian dysgerminomas (OD), the equivalent of seminoma in male are rare, representing 1-5% of ovarian cancers [1, 2] affecting younger women (often for of patients less than 30 years of age at diagnosis). Unlike epithelial ovarian cancer, approximately 75% of OD cases present with stage IA disease [2]. Early stage OD was often treated with conservative surgery to preserve fertility with or without adjuvant treatment. However, extraovarian disease is treated with chemotherapy. The exact protocol differs between oncologic centers. OD have a good survival after diagnosis even in disseminated form with an overall 5-year survival of over 90% [2, 3]. Relapses can occur within 2 years of diagnosis and the recurrence rate for stage IA is approximately 20% [2]. Because of absence of randomized trial evidence, data are limited and confined to case series that often include all types of ovarian germ cell tumors making specific information on dysgerminomas difficult to obtain. The aim of our study is to analyse epidemiologic, clinical features, therapeutic protocol and results of OD.

Patients and methods

This retrospective study concerned 13 patients treated between January 1994 and October 2011, for an histologically/immunohistologically confirmed OD. Initial work-up included: Anamnesis, clinical exam chest x-ray, abdominal ultrasound and thoracoabdominopelvic CT-scan. Tumors were staged according to FIGO classification (2000). Surgery was followed by adjuvant chemotherapy (CT) with BEP (Bleomycin-Etoposide-Cisplatin), EP (Etoposide-Cisplatin), VIP (Eoposide-Ifosfamide-Cisplatin) or VBP (Vinblastin-Bleomycin-Cisplatin). Pelvic radiotherapy has been used in cases with positive pelvic nodes. The last update for follow-up was performed in October 2011. Bibliography was made using Endnote program.

Results

Median age was 16 years (6 to 20 years) and 85% of patients were aged <18 years. Sixty-nine percent of patients were nulliparous, while 31% were on pre-menarche. We noted 2 cases a family history of head and neck cancer and metastatic cancer of unknown origin. Mean and median delays to consultation were 84 and 30 days (1 day to 1 year). OD was incidentally discovered in 2 cases. The most common symptom was abdominal and/or pelvic pain (69%) followed...
by an abdominal and/or pelvic mass and digestive disorders (31% each), weight loss or abdominal emergency were in 23% of cases. Imagery showed lesion linked to ovary in only 23% of cases with ascites in 61% of cases. Tumor mean volume was 16 cm³ of cystic aspect in 8% of cases, solid in 32% and mixed 60%, while calcifications were noted in 24% of cases.

Staging showed a right pleural effusion in 8% of cases, a peritoneal carcinomatosis in 24%, mesenteric, latero-aortic and iliac lymph nodes metastases in 24%, an invasion of the left kidney in 8% and a sheathing of the right iliac vessels in 8% of cases. According to FIGO classification, we found a predominance of stage IIIC (31%). Stage Ia was found in 23%.

Preoperatively, the tumor markers (BHCG, LDH) were elevated in 60% of patients, Alpha Foeto protein was normal in all cases. Postoperatively, tumor markers were elevated in 42% of patients. After chemotherapy, they were high in 15, 4%.

All patients underwent initial surgery. Ascites was noted in 54% of cases. The tumor was twisted in 23% of cases. Peritoneal carcinomatosis was present in 23% of cases but no case of liver metastases was identified. The mean tumor weight was 1730 g, varying from 6 to 24 cm with an mean size of 16 cm (Table 1).

The appearance of tumor was: cystic in 8% of cases, solid in 32% and solido-cystic in 60%. The capsule was intact and in 46% of cases and macroscopically reached in 54%. Necrotic and hemorrhagic areas were noted in 54% of cases. Histochemical study with PAS and PLAP was performed in 46% of cases and was positive in all of them.

Seventy percent of patients had a conservative surgery (defined as preservation of the contralateral ovary), and 30% had total hysterectomy and bilateral annexectomy (because of high tumour seize and/or tumour fixed to the intestine and omentum in 3 cases, and for bilateral tumour in 1 cases).

Ninetynine percent of patients received a postoperative chemotherapy. One patient received chemotherapy a year and a half after for a recurrence of dysgerminoma of the ovary (stage IIIC) treated by surgery alone. The BEP regimen was the most widely used (77%). The number of cycle was between 3 and 6. Radiotherapy (RT) was performed for 31% of patients, it consists in radiation under the diaphragm in 23% of cases or under and below diaphragm in 8% of cases (association to prophylactic treatment of the mediastinum).

The unilateral annexectomy with contralateral ovary conservation is considered the standard treatment of dysgerminomas mainly for tumor without locoregional extension, completely removed without distant metastasis. Conservative surgery includes not only unilateral salpingo-oophorectomy, It must include peritoneal washings for cytology, multiple biopsies (lymph node, peritoneal, omentum) and the realization of a wedge biopsy of the contralateral ovary (contralateral tumor estimated between 5 and 10% and are in 30 to 50% of cases invisible macroscopically). The unilateral annexectomy with contralateral ovary conservation is considered the standard treatment of dysgerminomas mainly for tumor without locoregional extension, completely removed without distant metastasis. Conservative surgery includes not only unilateral salpingo-oophorectomy, It must include peritoneal washings for cytology, multiple biopsies (lymph node, peritoneal, omentum) and the realization of a wedge biopsy of the contralateral ovary (contralateral tumor estimated between 5 and 10% and are in 30 to 50% of cases invisible macroscopically). The unilateral annexectomy with contralateral ovary conservation is considered the standard treatment of dysgerminomas mainly for tumor without locoregional extension, completely removed without distant metastasis. Conservative surgery includes not only unilateral salpingo-oophorectomy, It must include peritoneal washings for cytology, multiple biopsies (lymph node, peritoneal, omentum) and the realization of a wedge biopsy of the contralateral ovary (contralateral tumor estimated between 5 and 10% and are in 30 to 50% of cases invisible macroscopically).

Ninety-two percent of patients received a postoperative chemotherapy. One patient received chemotherapy a year and a half after for a recurrence of dysgerminoma in women who not desiring pregnancy or menopaused woman and in case of dysgerminoma occurring on gonadal dysgenesis because the probability of developing a tumor on the ovary remaining after conservative surgery is very important and on the other hand, the chances of pregnancy are excessively reduced.

Because of radio and chemosensitivity of dysgerminomas, lymphadenectomy was not done in a systematic way, it still controversial in terms of improving patient survival and some authors recommend to perform a sample biopsy (picking node) rather than lymphadenectomy. In a large series of 372 ovarian dysgerminoma, of the 244 that underwent lymph node dissection, lymph node metastasis was reported in 28.3%, while calcifications were noted in 24% of cases. Nowdays, non conservative surgery is reserved to ovarian dysgerminoma with large pelvic or peritoneal extension covering the ovary and uterus, in case of dysgerminoma in women who not desiring pregnancy or menopaused woman and in case of dysgerminoma occurring on gonadal dysgenesis because the probability of developing a tumor on the ovary remaining after conservative surgery is very important and on the other hand, the chances of pregnancy are excessively reduced.

Due to the major success of chemotherapy in advanced stages metastatic or recurrent dysgerminomas, it has been proposed by many authors to extend the indications of chemotherapy as adjuvant treatment in early stages in order to preserve ovarian function.

The BEP Protocol (Bleomycin, Etoposide, Cisplatin) has the advantage over the PVB protocol (vincristine, actinomycin D, cyclophosphamide) to reduce the frequency of toxicity especially myelosuppression, peripheral neuropathy, abdominal cramps and constipation. Due to the effectiveness, tolerability and preservation of hormonal function of the BEP regimen, he became the standard protocol used in the treatment of ovarian TGM. Others protocols can be proposed as second line treatment like VAC, VeIP and VIP protocol. In our series, twelve patients underwent postoperative chemotherapy. Different protocols were used. BEP protocol was must used (9 cases, 70%).

Like the testicular seminoma, OD can respond to low radiation doses of the order of 20 to 30 Gy. Radiation can be used to treat periaortic and pelvic lymph node metastases. Protection of remaining ovary by oophoropexy may be used to mechanically hold the remaining ovary away from the radiation field in attempt to preserve fertility. Radiation therapy may be used for any dysgerminomas stage Ib, II and III. Some authors have advocated radiation therapy for stage IA tumors larger
than 10 cm. The field of exposure extends from T11 to L5, with shielding of the contralateral ovary and the femur head. De Palo, Freed and Lawson developed radiation therapy protocols of the abdomen for node-positive disease and in prophylactic treatment of the mediastinum [16]. According Bewer, survival of dysgerminomas with surgery followed by radiotherapy ranged from 75 to 90% [5, 17]. In our series, radiotherapy was performed in 4 patients (31%). After irradiation for dysgerminoma, some side effects are described as acute toxicity (nausea and vomiting) and the risk of late radiation enteritis. In our study, tolerance was generally good. In fact, there was a minimal hematologic toxicity in one case, and a grade I dermatitis in other case. Pelvic or abdominopelvic recurrence after initial treatment was reported in 17% of cases within 19 months of diagnosis in the series of Danielle Vicus [2], similar to 12 months previously reported by Patterson and al. [8]. Late relapses are rare [5, 18]. In our series, only one patient (8%) had tumor recurrence 18 months after surgery alone without adjuvant therapy (lost of sight). On the other hand, age group 20 to 39 years seems to have better prognosis. Pregnancy does not seem to influence prognosis like rising HCG in condition that the rate is moderately high (< 100 IU/l) [19]. The thirteen OD of our work were pure without histological signs of poor prognosis (Table 2).

Overall survival in dysgerminoma in the literature varies from 82 to 100% For stage I OD there was any difference in survival at 10 years in the 2 groups of patients treated by conservative surgery or radical surgery. However, when these stages II, III or IV were treated by surgery alone, survival rates were statistically significantly lower than those obtained with surgery plus additional treatment, whether radiotherapy or chemotherapy [14, 17]. In our series, the 5-year survival was 100% for all stages combined, so we did not notice a change in survival according to tumor stage. Clinical surveillance must be strict: quarterly consultation during the first 2 years, then every 6 months until the fifth year and then annually. Marker assays is interesting, especially if positive preoperatively. Normalization reflects a good response; a subsequent rise is a warning sign and encourages research radio-clinical recurrence. The most useful markers for monitoring are HCG and LDH. Biological monitoring is done every 3 months for 2 years and then every 6 months for 5 years and then every year [14]. Lung radiography and abdominopelvic ultrasound are done every 3 months for 2 years and then every 6 months for 5 years and then annually. Thoraco-abdominopelvic computed tomography can search lung and liver metastases, it should be applied every 6 months for 2 years and then annually up to 5 years [14]. Gershenson [20] has reported that natural conception is possible after ovarian dysgerminoma, a finding similar to our cases. But natural course of pregnancy in cases of dysgerminoma is extremely difficult, due to large sizes of the tumors, irregular menstruation, and collection of fluid as well as tubal adhesions [19]. For AYHAN [5] in a series of 21 dysgerminomas treated conservatively, all patients irradiated has an amenorrhea and no patient treated with chemotherapy had menstrual disorders. Thus, many authors emphasize the need to chemotherapy rather than radiation to preserve future fertility. Whatever the type of chemotherapy used, no congenital abnormalities were observed in children of mothers treated for ovarian dysgerminoma [21]. Ovarian cortex cryopreservation (OCC) for future autotransplant can be proposed to prevent risk of ovarian failure and fertility disorders [22]. After laparotomy may appear peritoneal adhesions which may be responsible for infertility [9]. Authors found that after unilateral ovariectomy, functional cysts frequently occurs on the remaining ovary with an estimated frequency of 72% with a follow-up after surgery ranging from 12 to 215 months [23].

In our series, among the 9 patients who had conservative treatment: two are lost sight, two patients who had not yet reached puberty at the time of diagnosis had their menarche and five patients whose menstrual cycles were regular before treatment, had the return of menstruation in 100% of cases and only one patient is currently pregnant in the first quarter. Conclusion

The OD has excellent prognosis and have benefited in recent years from the experience of chemotherapy in the treatment of testicular cancer, especially seminomas. The new therapeutic approach combining conservative surgery and chemotherapy (current standard: BEP) even in early stages (Ia) will further improve prognosis and reduce the number of recurrences, while preserving the fertility of these young patients.

Tables

<table>
<thead>
<tr>
<th>Patients characteristics</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Patients</td>
<td>13 (100 %)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>Mean age (range)</td>
<td></td>
</tr>
<tr>
<td>&lt; 18 years</td>
<td>16 (6-20)</td>
</tr>
<tr>
<td>≥ 18 years</td>
<td>11 (85 %)</td>
</tr>
<tr>
<td>Gestational status</td>
<td></td>
</tr>
<tr>
<td>Nulliparus</td>
<td>9 (69 %)</td>
</tr>
<tr>
<td>Pre-menarche</td>
<td>4 (31 %)</td>
</tr>
<tr>
<td>Mean macroscopic seize (cm²)</td>
<td>16</td>
</tr>
<tr>
<td>Macropscopic aspect</td>
<td></td>
</tr>
<tr>
<td>Cystic</td>
<td>1 (8 %)</td>
</tr>
<tr>
<td>Solid</td>
<td>4 (32 %)</td>
</tr>
<tr>
<td>Mixte</td>
<td>8 (60 %)</td>
</tr>
<tr>
<td>Mean weigh (g)</td>
<td>1730</td>
</tr>
<tr>
<td>Mean delay to diagnosis (range) (days)</td>
<td>84 (1-365)</td>
</tr>
<tr>
<td>Tumor markers</td>
<td></td>
</tr>
<tr>
<td>BHCG, LDH elevated</td>
<td>8 (65 %)</td>
</tr>
<tr>
<td>Alpha Foeto protein elevated</td>
<td>0 (0 %)</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
</tr>
<tr>
<td>Ia</td>
<td>3 (23 %)</td>
</tr>
<tr>
<td>Ib</td>
<td>1 (8 %)</td>
</tr>
<tr>
<td>Ic</td>
<td>2 (15 %)</td>
</tr>
<tr>
<td>IIb</td>
<td>1 (8 %)</td>
</tr>
<tr>
<td>IIc</td>
<td>4 (30 %)</td>
</tr>
<tr>
<td>IIIc</td>
<td>1 (8 %)</td>
</tr>
<tr>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
</tr>
<tr>
<td>Conservative surgery</td>
<td>13 (100 %)</td>
</tr>
<tr>
<td>Total hysterectomy with bilateral annexectomy</td>
<td>9 (70 %)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td></td>
</tr>
<tr>
<td>BEP</td>
<td>12 (93 %)</td>
</tr>
<tr>
<td>VBP</td>
<td>9 (70 %)</td>
</tr>
<tr>
<td>VIP</td>
<td>2 (15 %)</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td></td>
</tr>
<tr>
<td>Under and below the diaphragm</td>
<td>4 (32 %)</td>
</tr>
<tr>
<td>Under diaphragm</td>
<td>1 (8 %)</td>
</tr>
<tr>
<td></td>
<td>3 (23 %)</td>
</tr>
</tbody>
</table>
Table 2: Poor prognosis factors

<table>
<thead>
<tr>
<th>Poor prognosis factors [1, 13]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surgical factors</strong></td>
</tr>
<tr>
<td>- High diseases stage</td>
</tr>
<tr>
<td>- Existence of capsular rupture in stage I</td>
</tr>
<tr>
<td>- Bleeding</td>
</tr>
<tr>
<td>- Ascitis</td>
</tr>
<tr>
<td>- Lymph node metastasis</td>
</tr>
<tr>
<td>- Presence of peritoneal granulations or intraperitoneal adhesion</td>
</tr>
<tr>
<td><strong>Histological factors</strong></td>
</tr>
<tr>
<td>- Combination of a dysgerminoma another TGMO whether choriocarcinoma, embryonal carcinoma, endodermal sinus tumor or immature teratoma</td>
</tr>
<tr>
<td>- Tumor size</td>
</tr>
<tr>
<td>- High number of mitosis</td>
</tr>
<tr>
<td>- Atypia</td>
</tr>
<tr>
<td>- Vascular emboli</td>
</tr>
<tr>
<td>- Absence of lymphocytic infiltration or granulomatous reaction or lack of septa partitioning or surrounding dysgerminomatosis cells</td>
</tr>
<tr>
<td>- Anaplastic dysgerminoma</td>
</tr>
<tr>
<td><strong>Therapeutic factors</strong></td>
</tr>
<tr>
<td>- Lack of response to chemotherapy containing platinum (platinum refractory or resistant)</td>
</tr>
<tr>
<td>- Interval of time between initial treatment and recurrence</td>
</tr>
</tbody>
</table>

**Conflict of Interest**

There is any financial and personal relationships with other people or organizations that could inappropriately influence this work.

**References**

Objective

To determine the prevalence of nausea and vomiting and discuss the scope of management of nausea and vomiting in palliative care.

Methods

A retrospective review of patients admitted to the palliative care unit at King Abdullah Medical City for the period from January 2013 to December 2013 was conducted. The data were collected using a standardised chart review form. The prevalence of nausea and vomiting was calculated, and the management strategies were evaluated.

Results

A total of 100 patients were included in the study. The prevalence of nausea was 78%, and the prevalence of vomiting was 32%. The most common causes of nausea and vomiting were cancer and chemotherapy. The management strategies included antiemetic medications, psychological support, and alternative therapies.

Conclusion

Nausea and vomiting are common symptoms in patients with advanced cancer. Effective management strategies are crucial in improving the quality of life for these patients. Future research should focus on developing more effective management strategies and improving the understanding of the underlying mechanisms.
Epidemiology

Generally about 40% of patients with advanced cancer have nausea and 30% will vomit (7). These symptoms may be intermittent in palliative care patients, and are typically only mild to moderate in severity when present. They do appear to become more common as death approaches, so it is not surprising that nausea has been found to be a predictor of a shortened survival in one study (8). In patients admitted to specialist palliative care programs, nausea has been reported by 36% patients at the first contact with the service, (9, 10) 62% at 1–2 months before death, (11, 12) and 71% in the final week of life (13, 15).

Effect on quality of life

While nausea is an unpleasant experience and nobody likes to vomit, these symptoms may be intermittent in palliative care patients, and are typically only mild to moderate in severity when present. Nausea was rated only 3–4 out of 10 in intensity, and was moderate-to-severe (greater than 5 out of 10) in one study. In this sample, the impact of nausea and vomiting on general activity and emotional well being was rated as greater than 5 out of 10 by approximately 40% of patients (16).

Causes

An understanding of the likely causes of these symptoms is required for accurate assessment and treatment, resulting in better symptom control. The causes of nausea and vomiting in palliative care patients are usually multifactorial and rarely occur in isolation (table 1).

<table>
<thead>
<tr>
<th>Causes</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>Oropharyngeal diseases, Esophageal disease, Gastraparesis/gastric distention, Gastric irritation/peptic ulcer disease, Constipation/fecal impaction, Bowel obstruction, Liver capsule distention by tumor, Biliary tree distention</td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>Increased intracranial pressure, Meningitis, Hemorrhage, Vestibular</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Uremia, Liver failure, Hypercalcemia, Hypokalemia, Dehydration</td>
</tr>
<tr>
<td>Medication</td>
<td>Opioids, Digoxin, Chemotherapy agents, Antibiotics, Nonsteroidal anti-inflammatory drugs, Iron supplements, Theophylline, Antidepressants (tricyclics, selective serotonin reuptake inhibitors)</td>
</tr>
</tbody>
</table>

Table 1: Common causes of nausea and vomiting

Psychiatric

Fear, anxiety
Thoughts, visual and olfactory stimuli

Miscellaneous

Pain
Autonomic dysfunction
Tumor related toxins

Adapted from Rousseau P. (17)

Assessment

An accurate assessment of patients with nausea and vomiting will allow for appropriate management. Assessment of the patient may include: review history, medications and recent investigations. Examination - looking for underlying causes and likely physiological mechanisms. Investigations - only if will affect management.

Pharmacological treatment

Adequate symptom management frequently involves pharmacologic and no pharmacologic interventions. Patients, families, and members of the interdisciplinary team should participate in evaluating symptoms and choosing proper therapeutic options. Education of patients and families about the nature and progression of symptoms and potential treatment side effects is also crucial. Management of nausea and vomiting should be directed to the underlying cause, if identifiable (e.g., metabolic abnormalities, constipation) Table 2 showed the possible management of reversible causes.

Table 2: Possible management of reversible causes

<table>
<thead>
<tr>
<th>Cause</th>
<th>Specific Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Therapy</td>
<td>Stop or find alternative unless essential</td>
</tr>
<tr>
<td>Uncontrolled pain</td>
<td>Analgesia - non-oral route until vomiting settles</td>
</tr>
<tr>
<td>Cough</td>
<td>Cough suppressant</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>Catheterize</td>
</tr>
<tr>
<td>Constipation</td>
<td>Laxatives; bowel intervention</td>
</tr>
<tr>
<td>Anxiety Determine fears;</td>
<td>explanation; anxiolytics</td>
</tr>
<tr>
<td>Raised intracranial pressure</td>
<td>Corticosteroids (e.g. dexamethasone)</td>
</tr>
<tr>
<td>Electrolyte disturbances</td>
<td>Correct if possible and appropriate</td>
</tr>
<tr>
<td>Hypercalcemia</td>
<td>Rehydration and intravenous biphosphonate</td>
</tr>
<tr>
<td>Oral/esophageal candidosis</td>
<td>Antifungal (fluconazole, nystatin; imidazole)</td>
</tr>
<tr>
<td>Infection (URT1, UTI)</td>
<td>Antibiotic</td>
</tr>
<tr>
<td>Gastritis</td>
<td>Stop irritant drug; add PPI*</td>
</tr>
</tbody>
</table>

*Proton pump inhibitor

Pharmacological agents are the corner stone for palliating nausea and vomiting in patients with advanced cancer. The choice of drugs is either empirical or mechanistic. The empirical approach depends on physician preference, while, the mechanistic approach applies understanding of the emetic pathway in antiemetic selection (18), (see Figure 1).
Figure 1: Causes and proposed mechanisms of nausea and vomiting

These sites contain receptors for one or more neurotransmitter, including dopamine type 2 (D2), serotonin types 2–4 (5HT2–4), histamine type 1(H1), and acetylcholine (muscarinic receptors type 1 to 5, M1–5). Other receptors such as substance P, cannabinoid type 1 (CB1) and the endogenous opioids may also be implicated, although their precise sites are uncertain. Antiemetic selection is based on knowing which drugs block the receptors found in the structure where the cause of the nausea and vomiting is acting on.

While the mechanistic approach is based on clinical science, it has limitations in that the etiology of chronic nausea in advanced disease is often unidentifiable or multifactorial, many of the drugs act on multiple receptors (19). Therefore, a more empiric approach is justifiable. Because most cases are mediated via the chemoreceptor trigger zone, treatment should be initiated with dopamine antagonist. In patients who do not respond, agents from different classes are combined. In patients with refractory nausea and vomiting, a broad spectrum agent should be added, such as olanzapine (Table 3).

Table 3: Recommended drug management of nausea and vomiting

<table>
<thead>
<tr>
<th>Causes</th>
<th>First line drug</th>
<th>Stat dose (PO or SC)</th>
<th>24 HR Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric stasis and irritation</td>
<td>Metoclopramide +/- proton pump inhibitor/ H2-receptor Antagonist</td>
<td>10 - 20mg</td>
<td>30 - 60mg PO or SC</td>
</tr>
<tr>
<td>Bowel obstruction without colic</td>
<td>Metoclopramide</td>
<td>10 - 20mg SC only</td>
<td>30 - 60mg SC only</td>
</tr>
<tr>
<td>Bowel obstruction with colic</td>
<td>Cyclizine +/- Haloperidol +/- Hyoscine Butyramid</td>
<td>50mg SC only 1.5 – 5mg SC only</td>
<td>100-150mg SC 1.5 – 5mg SC 60 – 120mg SC</td>
</tr>
<tr>
<td>Chemical e.g • drugs • hypercalcaemia • uraemia</td>
<td>Haloperidol</td>
<td>1.5 - 5mg</td>
<td>1.5 - 5mg PO or SC</td>
</tr>
</tbody>
</table>

Raised intracranial Pressure

Dexamethasone plus Cyclizine +/- Ondansetron or Granisetron

8 - 16mg
50mg
150mg

Motion

Hyoscine hydrobromide OR Cyclizine

300micrograms SL
400micrograms SC
50mg

Indeterminate/Multifactorial

Levomepromazine

6 - 12.5mg tablet.
6.25 - 25mg PO or SC

PO— oral, SL—sublingually, SQ—subcutaneously.

Adapted from Yorkshire Cancer Network and North East Yorkshire and Humber Clinical Alliance: A guide to symptoms management in palliative care: version 5.1

Nonpharmacologic strategies for nausea and vomiting include; dietary alterations (providing small and frequent meals composed of foods chosen by the patient, encouraging frequent intake of carbonated beverages, and avoiding fatty or fried foods or foods that have strong odors ) relaxation techniques, behavioral therapy, acupuncture and acupressure (20-22)

Figure 2: The Cleveland clinic approach to managing nausea and vomiting in a palliative inpatient unit.

Conclusion

Pathophysiology of nausea and vomiting are helpful. Based on our experience, and in absence of complete obstruction; empiric single-drug therapy with
metoclopramide has the greatest evidence for benefit especially in first-line treatment in those who have not been on metoclopramide before. Haloperidol is also used particularly in the face of a complete bowel obstruction. Second-line agents used by our institution are the atypical antipsychotic, olanzapine, phenothiazine, or chlorpromazine. Nonpharmacologic approaches should be used depending on the evaluation of their overall status, including the stage of their disease trajectory and their goals of care.

**Conflict of Interest**

The authors certify that there is no actual or potential conflict of interest in relation to this article.

**References**

Myoepithelial carcinoma arising in a benign myoepithelioma of the palate.
Case report and literature review

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The study hasn’t been presented anywhere.

Abstract

Myoepithelial carcinomas are tumors arising from myoepithelial cells mainly or exclusively, they showed varied cell types and patterns leading to a wide range of differential diagnoses. Immunohistochemical analysis helped to determine the diagnosis. Recognition of myoepithelial carcinoma is clinically significant because, compared to its benign counterpart (myoepithelioma), It has increased frequency of local recurrences and metastases, which warrants close clinical follow-up. The aim of this case report was to present a rare neoplasm, myoepithelial carcinoma arising from a benign myoepithelioma of the palate, and to review its diagnostic criteria, pathologic and clinical characteristics, treatment options and prognosis.

Background

Myoepithelial tumors of the salivary gland including myoepitheliomas (benign) and myoepithelial carcinomas (malignant) are a rare group of tumors. Although myoepitheliomas were first described as early as 1943 by Sheldon [1], the best description of myoepithelial tumors was given in the landmark articles by Dardick et al in 1989 [2] and Dardick in 1995 [3]. Myoepithelial tumors have also been included as a separate entity in the second edition of the World Health Organization’s histological classification of salivary gland tumors (1991) [4-5]. Herein we present a case of malignant myoepithelial tumor arising in a benign myoepithelioma of the palate.

Observation

A 76 years old man consulted the clinic with chief complaint of a painful swelling in the hard palate which does not response to neither symptomatic nor antibiotic treatment. He underwent a biopsy of palate lesion which shows a benign myoepithelioma. A complete resection of the tumor was performed without any adjuvant treatment.

Nineteen years after, he presented to our institution with a history of recurrence of palate tissue mass that progresses since 3 years. The oral examination and the panendoscopy showed a great mass arising from the soft palate and packed the hole of oral cavity with invasion of: hard palate, tonsillar fossa, lateral wall of the oropharynx, and nasopharynx which was obstructed (Fig.1). A facial computed tomography (CT) confirmed the local tumor invasion, without any lymph nodes involvement (Fig.2).

An urgent tracheotomy was performed after the installation of an acute dyspnea. A biopsy was performed, the tumor showed proliferation of a double component: plasmocytoid-cells showing eccentric nucleus and pale eosinophilic cytoplasm, they also were weakly cohesive and were arranged in sheets or trabeculae (Fig.3); and spindle cells with centrally placed elongated nuclei, the mitosis was rare, there was no necrosis.

A fascicular arrangement of tumor cells was noted. These tumor-cells were disseminated in a variable amount of hyaline stroma. A tumor infiltration in the normal salivary glands and the adjacent adipose was found. Immunohistochemical stains were performed: the epithelial component was positive to keratine marker, the smooth muscle component positive for Protein S 100 (PS100), vimentine and calponin (Fig.4 and 5).

Despite the absence of frank histological criteria of malignancy (atypia, mitosis and necrosis), the invasive character referred to radioclinical and histological data (massive infiltration of salivary glands), lead to the diagnosis of low grade myoepithelial carcinoma arising in a benign myoepithelioma of the soft palate. The resection of tumor has been impossible due to the massive infiltration of the hole oral cavity and pharyngeal space, and in front of the advanced patient age, impaired karnofsky scale and nutritional condition, chemotherapy was not indicated in the first intension. We decided then to process by radiotherapy to reduce the tumor seize. He is actually under treatment.
Discussion

Myoepithelial tumors arise from myoepithelial cells that surround acini and ducts of salivary glands, these cells exhibit both epithelial and smooth muscle cell characteristics [6, 7]. These tumors commonly occur in major salivary glands but can arise in the submandibular, sublingual and rarely in minor salivary glands of the oral cavity [8-11]. In a large Indian series of 51 cases of myoepithelial carcinoma, tumors were located essentially in the parotid gland (29.4%), palate (29.4%), oral mucosa (13.7%), nasal cavity (9.8%), and maxilla, lower alveolus and tongue (16%) [5]. Myoepithelial carcinoma can appear de novo (77%) or develop in a pre-existing benign tumor (23%). The time between the onset of benign tumor and the occurrence of myoepithelial carcinoma is variable; it is 10 years in our case. Our patient is 76 years old, however, cases reported in the literature are of an age between 14 and 70, most patients were in their third to fifth decade of life; for the majority of them, the primary complain was a painless mass. Usually, myoepithelial carcinoma had a localized presentation at initial diagnosis with mean tumor seize of 4 cm [5]. Our case is different from other cases of the literature by the importance of local and regional extension of primitive tumor. At histological study, the tumor cells showed a wide morphologic variation: epitheliod (29%), plasmacytoid (14%), spindle (12%), stellate (16%) or mixed (24%). High-grade tumors showed nuclear pleomorphism and/or large areas of necrosis and mitosis [5]. The tumour cell may form solid and sheet-like formations, trabecular and reticular patterns, but they can also be dissociated, often within plentiful myxoid or hyaline stroma [12].

The diagnosis myoepithelial tumor can be helped by immunohistochemical (IHC) analysis that shows high expression of epithelial markers such as cytokeratin, epithelial membrane antigen (EMA), S-100 protein, and markers of smooth muscle origin such as smooth muscle actin and calponin on the tumor cells of myoepithelioamas. Current IHC criteria for the confirmation of myoepithelial differentiation are double positivity for both cytokeratins (pan CK or preferentially basal type CK) and one or more myoepithelial immunomarkers (S-100, calponin, p63, GFAP, maspin, actins, and a variety of myogenic markers) [13,14,15]. However, it must be noted that these markers are not always positively expressed in the tumor cells and that negative staining does not necessarily exclude myoepithelial differentiation [3]. IHC findings in our study are consistent with those of previous reports. In our cases, tumors positivity for both cytokeratins and myoepithelial markers (S-100 and Calponin) confirms the diagnosis of myoepithelial carcinoma. Indications of malignancy are based on features such as nuclear atypia, high mitotic rate and infiltrative growth into adjacent tissues. Currently, benign and malignant myoepithelialomas are differentiated by mitotic count, presence of invasive growth, cellular polymorphism, tumour necrosis, or their combination. Destructive growth and infiltrative character distinguishes myoepithelial carcinoma from benign myoepithelial tumors [12]. In our case, despite the absence of frank histological criteria of malignancy (atypia, mitosis and necrosis), the invasive character referred to radioclinical and histological data (massive infiltration of salivary glands), lead to the diagnosis of low grade myoepithelial carcinoma. The differential diagnosis of myoepithelial carcinoma includes a wide range of neoplasms, depending on the predominant cell type. It is sometimes difficult to differentiate myoepithelial carcinoma showing epitheliod morphologic characteristics from other salivary gland neoplasms showing myoepithelial differentiation, especially adenoid cystic carcinoma, polymorphous low-grade carcinoma [16]. In tumors with clear-cell morphologic characteristics, the differential diagnosis includes hyalinizing clear-cell carcinoma, epimyoepithelial carcinoma, and metastatic renal cell carcinoma [17]. Melanoma, high-grade lymphoma, or plasmacytoma must be ruled out when the tumor shows plasmacytoid differentiation. With spindle cell morphologic characteristics, the most common differentials diagnosis are sarcomatoid squamous carcinoma, spindle cell melanoma, and sarcoma [5, 16]. Given their rarity and only recent recognition, there is no consensus on the optimal treatment. Complete excision is the preferred treatment method for myoepithelioma. For myoepithelial carcinoma, complete excision with tumor-free margin with or without nodal dissection remains the first choice of treatment, in spite of the possibilities of local recurrence and distant metastasis [7, 16, 18].

Local radiation therapy and chemotherapy can be needed for myoepithelial carcinoma particularly in palliative situations. There is a case reported by Ibrahim and al [19] consisted in myoepithelioma of the hypopharynx and larynx with lymphatic invasion and liver metastasis treated by chemotherapy and palliative laryngeal radiotherapy with 3 month of follow-up, the patient was died of disease. There is a single published case report of a patient with metastatic myoepithelial carcinoma of the vulva who showed a complete response to chemotherapy with carboplatin/paclitaxel [20].

Compared with myoepithelioamas, myoepithelial carcinoma shows highly aggressiveness and high rate of recurrence even after adequate therapy [7, 21]. The most common site of metastasis is lung, followed by lymph nodes, bone and soft tissue with an average rate of 47%. Interestingly, this pattern of spread has features of both carcinomas (lymph nodes) and sarcomas (lung) [22]. Recurrence and metastasis are more common in children than in adult even with a negative excision margin [1]. Therefore, Yu suggested myoepithelialomas of the salivary gland should be classified as high-grade malignancies [2]. In the Indian study [5] of 51 cases of myoepithelial carcinoma main prognostic factors for local recurrence were stellate, clear, and spindle cell types; large tumor size; and perineural or bone invasion. Similarily, a high incidence of metastasis was noted with the presence of positive margins, large areas of necrosis, high mitotic count (> 4 per 10 hpf), Ki-67 labeling index of 4% to 10%, nuclear atypia, and spindle cell morphologic characteristics. There is no difference in clinical behaviour of “de novo” myoepithelial carcinomas and of those arising in pleomorphic adenomas and benign myoepithelioamas [12].

Conclusion

We report a rare case of myoepithelial carcinoma arising in a benign myoepithelioma of the soft palate. Myoepithelialomas showed varied cell types and patterns leading to a wide range of differential diagnoses. Immunohistochemical analysis helped to determine the diagnosis. Recognition of myoepithelial carcinoma is clinically significant because, compared to its benign counterpart (myoepithelioama), myoepithelial carcinoma has increased frequency of local recurrences and metastases, which warrants specific treatment and close clinical follow-up. Overall, the prognosis of a myoepithelial carcinoma is poor. However, a better clinical outcome can be expected if proper management and suitable operations are performed for patients.

References


Case Report

Gastric Adenocarcinoma Metastasizing to Urinary Bladder

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Key words: Gastric adenocarcinoma, Urinary bladder, Metastasis.
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Abstract

Transitional cell carcinoma comprises more than 95% of the primary bladder tumors and primary adenocarcinoma is found in 1% of cases. Secondary adenocarcinoma of urinary bladder is a rare entity, accounting for less than 2% of all bladder tumors and is mostly found in advanced stages with peritoneal dissemination. Metastasis to urinary bladder from gastric adenocarcinoma is extremely rare and is associated with grave prognosis. Here-in we report a case of a 62-year-old Saudi woman who was treated for gastric adenocarcinoma of lesser curvature four years ago; presented with the complaints of gross painless hematuria and on work-up was found to have a thickening of dome and left lateral wall of the urinary bladder. A transurethral biopsy of the bladder wall revealed well differentiated tubular adenocarcinoma metastatic from gastric carcinoma. After palliative radiotherapy to bladder, she was started on systemic chemotherapy.

This manuscript has not been presented before to any conference or journal
Consent: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.
Conflict of interest: The authors certify that there is no potential or actual conflict of interest related to this article.

Introduction

Metastasis to urinary bladder is a rare manifestation and most are discovered during autopsy reports [1]. Metastatic bladder adenocarcinoma accounts for less than 2% of all bladder malignancies and is mostly found in advanced stages with peritoneal seeding [2]. Most common primary sites which have tendency to metastasize to urinary bladder in descending order are gastric adenocarcinoma, malignant melanoma, breast and lung [3,4,5,6]. Urinary bladder metastases typically remain asymptomatic, but could present as gross painless hematuria and are considered as indicator of underlying high tumor burden and carry poor prognosis [7]. Urinary bladder metastasis of gastric origin were first reported by Hermann HB in 1929 and since that only thirteen more cases have been reported so far [8].

In this report, we describe a patient with gastric adenocarcinoma of lesser curvature who developed bladder metastasis, four years after Billroth II resection of the stomach, omentectomy and D2 lymph node dissection and adjuvant chemoradiation.

Case Report

A 62-year-old Saudi woman presented in our clinic for her routine visit with the complaints of off and on abdominal pain and gross painless hematuria. She had noticed these complaints for 2 months and these have been occurring frequently over 2 weeks, for which she was taking, antispasmodics and Tranexamic Acid 500mg, but minimal improvement. Her previous medical history revealed hypertension since last 20 years which were controlled on medications. She had no history of smoking and her weight was stable. Her past surgical history showed that four years back, she underwent Billroth II resection of the stomach, omentectomy and D2 lymph node dissection for gastric cancer of lesser curvature, Stage IIIB (pT3N3a). Histopathological findings of initial surgery were; well-differentiated adenocarcinoma, tubular type with highly desmoplastic stroma, positive margins (R1 resection), and lymphovascular space invasion (LVSI) and 15 lymph nodes were positive. After surgery, she received adjuvant chemoradiation (MacDonald JS protocol). Since that she was on regular follow-ups without any signs of locoregional recurrence or distant metastasis.

On physical examination, she was anemic but in good general condition and her vitals was stable. Per abdomen examination revealed deep tenderness in hypogastrium, however there was no palpable mass or visceromegaly. There was no palpable lymphadenopathy and examination of chest, heart and nervous system was normal. Baseline Hemoglobin levels were 8 g/dl (low) and her renal and liver function tests, tuberculin and serum electrolytes were found within normal limits. Clinical differential diagnosis was cystitis, bladder stones, primary urinary bladder cancer or metastasis.

Chest computed tomography (CT) scans did not show any distant metastasis. Abdominopelvic CT showed a semi –circumferential tumor like thickening of the urinary bladder more pronounced at the dome and left lateral wall with maximum thickness of 1.9cm and there was a partial loss of the fat planes
between the uterus and urinary bladder. Also there were three nodules; (a) epigastric subcutaneous nodule measuring 1.4x1.2 cm and (b) left retroperitoneal nodule just lateral to the left psoas muscle of size 1.2x1 cm and (c) left adnexal solid mass (Krukenberg’s tumor) measuring 4x3.5 cm. 

Cystoscopy revealed mucosal hyperemia and a tumor adjacent to the left ureteric orifice. A transurethral resection (TUR) of the left-sided bladder tumor was performed. Histopathology revealed mucosal inflammation, intact epithelium, muscle invasion of outer muscular layers and atypical glandular proliferation. 

Fig. 1A & B. Immunohistochemical (IHC) staining detected positivity for epithelial membrane antigen (EMA), caudal-type homeobox transcription factor (CDX2), cytokeratin -7 (CK7), CA19.9 and carcinoembryonic antigen (CEA) and negativity for CK20, which confirmed the diagnosis of metastatic gastric adenocarcinoma. An exploratory laparotomy was also performed which showed peritoneal deposits and biopsy were taken. Histopathology showed sheets of dyscohesive neoplastic cells with foamy to eosinophilic cytoplasm and few signet ring cells and IHC examination confirmed the metastases of the primary gastric adenocarcinoma origin (CDX2+, CK7+, CEA+, CK20–). For grade 3 bleeding (requiring transfusion) gross hematuria, she was given radiotherapy haemostatic dose of 8 Gy to bladder. Then she was started on systemic chemotherapy based on cisplatin and etoposide. At time of publication, she was alive without any hematuria and was receiving third cycle of chemotherapy.

Discussion

Urinary bladder metastases from gastric adenocarcinoma are extremely rare and are seen at advanced stages with peritoneal seeding. Among cases of bladder metastasis secondary to gastric adenocarcinoma published so far, the incidence is similar between genders, and mean age ranges from 44 to 63 years [8]. The potential routes contributing to the appearance of urinary metastasis in gastric adenocarcinoma are hematogenous or peritoneal dissemination [9]. It has also been hypothesized that the ovarian involvement is somehow related to the bladder and other pelvic visceral metastasis, since bladder metastases are very rare in the absence of Krukenberg’s tumor (ovarian cancers arising from gastrointestinal origin). Also in our patient bladder metastasis were seen in the presence of left Krukenberg’s tumor [10].

Clinical features of bladder metastasis are similar to primary bladder tumors. Cystoscopic examination and radiological imaging are also not much helpful in differentiating the primary (mostly at trigone) or secondary bladder adenocarcinomas (any site involvement). A panel for immunohistochemical (IHC) staining is confirmatory for the diagnosis of urinary bladder metastasis and to differentiate it from primary tongue carcinoma. Bladder metastases secondary to gastric adenocarcinoma show immunopositivity for CK7, CDX2 and CEA and CA19.9, and immunonegativity for thyroid transcription factor (TTF)-1 and CK20.

The treatment for bladder metastasis with curative intention is not possible due to the metastatic characteristics of the disease and presence of high tumor burden and systemic chemotherapy also has not shown satisfactory results (median survival time: 3–9 months) in previously published case reports. Palliative radiation therapy can be offered to such patient for symptomatic relief of gross hematuria or associated pain as in our case.

In conclusion, urinary bladder metastasis is rare entity and after diagnosing a bladder adenocarcinoma, the possibility of primary stomach shall be excluded since in a few cases this can be the first clinical manifestation in these patients. Immunohistochemistry is confirmatory in differentiating metastatic and primary bladder adenocarcinomas.
Figure 1: Sheets of dyscohesive neoplastic cells with foamy to eosinophilic cytoplasm and few signet ring cells (H & E stain, X 100 magnification) and (B) Neoplastic cells are positive for CDX2 (CDX2 immunostain, X 40 magnification).

References

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<td>Cervical Cancer Awareness Month</td>
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<td>FEBRUARY</td>
<td>Screening and Early Detection Awareness Month</td>
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<tr>
<td>MARCH</td>
<td>Colorectal Cancer Awareness Month</td>
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<tr>
<td>APRIL</td>
<td>Cancer Fatigue Awareness Month</td>
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<tr>
<td>MAY</td>
<td>Melanoma and Skin Cancer Awareness Month</td>
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<tr>
<td>JUNE</td>
<td>National Cancer Survivors Day</td>
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<td>JULY</td>
<td>Sarcoma Awareness Month</td>
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<tr>
<td>AUGUST</td>
<td>Pain Medicine and Palliative Care</td>
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<tr>
<td>SEPTEMBER</td>
<td>Gynecologic Cancer Awareness Month, Prostate Cancer Awareness Month, Leukemia and Lymphoma Awareness Month</td>
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<tr>
<td>OCTOBER</td>
<td>Breast Cancer Awareness Month</td>
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<tr>
<td>NOVEMBER</td>
<td>Lung Cancer Awareness Month, Smoking Cessation</td>
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<tr>
<td>DECEMBER</td>
<td>5 A Day Awareness Month</td>
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The Pan Arab Journal of Oncology (PAJO) is the official Journal of the Arab Medical Association Against Cancer (AMAAC). It is a quarterly publication targeting health professionals interested in the oncology field. It is a multidisciplinary peer-reviewed journal that publishes articles addressing medical oncology, malignant hematology, surgery, radiotherapy, pediatric oncology, geriatric oncology, basic research and the comprehensive management of patients with malignant diseases in addition to international oncology activities, congresses & news.

The journal will be addressed, as a first step, mainly to the professionals in the hematology & oncology field in the Middle East region and North Africa. The goal is to share local & regional research activities news and to be updated with international activities. We hope, with your support, to achieve our following objectives:

1. Promote and encourage research activities in the Arab World.
2. Disseminate & analyze epidemiological local, regional and international data.
3. Update health professionals with the most recent advances, news & developments in the field of oncology.
4. Improve the level of scientific publications arising form the Arab World.
5. Keep health professionals connected and exposed to the activities of different Arab cancer societies.
6. Share with our immigrant compatriots their activities & feedback in this field.
7. Involve all health professionals interested in the field of Oncology within the multidisciplinary scope of the Journal.
8. Encourage post graduates students to submit their research work.

### Instructions For The Authors

**1. Manuscript Categories**

**1.1. Clinical trials**
The Editor-in-Chief and an Associate Editor generally review Reports from clinical trials. Selected manuscripts are also reviewed by at least two external peer reviewers. Comments offered by reviewers are returned to the author(s) for consideration. Manuscript acceptance is based on many factors, including the importance of the research to the field of oncology & the quality of the study. Authors should focus on accuracy, clarity, and brevity in their presentation, and should avoid lengthy introductions, repetition of data from tables and figures in the text, and unfocused discussions. Extended patient demographic data should be included in a table, not listed within the text.

Reports from Clinical trials are limited to 3,000 words of body text, excluding the abstract, references, figures, and tables. They are limited to six total figures and tables. All abstracts are strictly limited to 250 words. Titles are to be descriptive, but succinct. Results of clinical studies should be supported by a clear description of the study design, conduct, and analysis methods used to obtain the results.

Reports of phase II & III studies should include from the protocol a clear definition of the primary end point, the hypothesized value of the primary end point that justified the planned sample size, and a discussion of possible weaknesses, such as comparison to historical controls.

Phase I studies will be well received if they have interesting clinical responses, unusual toxicity that pointed to mechanism of action of the agents, and important or novel correlative laboratory studies associated with the trials.

**1.2. Review Articles**
All reviews must be clinically oriented, i.e., at least half the review must describe studies that detail human impact, marker effect on prognosis, or clinical trials.

Review Articles should be prepared in accordance with the Journal’s Manuscript Preparation Guidelines, and will be reviewed in the same manner as Reports from Clinical Trials. Reviews are limited to 4,500 words of body text, excluding the abstract, references, figures, and tables. The editors also suggest a limit of 150 references.

**1.3. Editorials / Comments / Controversies**
The Editor-in-Chief may solicit an Editorial to accompany an accepted manuscript. Authors who wish to submit unsolicited Comments and Controversies should contact the Editor-in-Chief, before submission to determine the appropriateness of the topic for publication in the Journal.

Editorials should be no more than four to five pages in length.

**1.4. Articles on Health Economics**
Articles about health economics (cost of disease, cost-effectiveness of drugs, etc) are highly encouraged.

**1.5. Case Reports / Correspondence / Special Articles**
Correspondence (letters to the Editor) may be in response to a published article, or a short, free-standing piece expressing an opinion, describing a unique case, or reporting an observation that would not qualify as an Original Report. If the Correspondence is in response to a published article, the Editor-in-Chief may choose to invite the article’s authors to write a Correspondence reply. Correspondence should be no longer than three pages in length. Special Articles present reports, news from international, regional societies as well as news from our compatriots.
Instructions For The Authors

2. Manuscript submission procedure

All manuscripts should be submitted in word and PDF format directly to the Editor-in-Chief by e-mail at the following e-mail: editorinchief.pajo@yahoo.com. The manuscript should adhere to the journal requirements. Upon manuscript submission, corresponding authors must provide unique e-mail addresses for all contributing authors. Receipt of manuscripts will be acknowledged via e-mail. Upon completion of editorial review, the corresponding author will receive notification of the Editor’s decision, along with the reviewers’ comments, as appropriate, via e-mail.

3. Disclosures of Potential Conflicts of interest

In compliance with standards established and implemented by ASCO’s Conflict of Interest Policy (J Clin Oncol 24:519–521, 2006), it is the PAJO’s intent, as previously referred, to ensure balance, independence, objectivity, and scientific rigor in all of its editorial policies related to the Journal through the disclosure of financial interests, among other measures. All contributors to the Journal are required to disclose financial and other relationships with entities that have investment, licensing, or other commercial interests in the subject matter under consideration in their article. These disclosures should include, but are not limited to, relationships with pharmaceutical and biotechnology companies, device manufacturers, or other corporations whose products or services are related to the subject matter of the submission. Disclosures of financial interests or relationships involving the authors must be addressed on the Author Disclosure Declaration form. The corresponding author may complete the form on behalf of other authors, or authors may complete their own forms and forward them to the corresponding author. This information will be sent to the Editorial Board. Statements regarding financial support of the research must be made on the manuscript title page, and disclosed on the form. This form is available upon request from the Editorial Office. All disclosures will appear in print at the end of all published articles. The Journal requires all Editors and reviewers to make similar disclosures. Reviewers are asked to make disclosures when accepting a review.

4. Manuscript Preparation Guidelines

Title Page
The first page of the manuscript must contain the following information: (1) title of the report, as succinct as possible; (2) author list of no more than 20 names (first name, last name); (3) names of the authors’ institutions and an indication of each author’s affiliation; (4) acknowledgments of research support; (5) name, address, telephone and fax numbers, and e-mail address of the corresponding author; (6) running head of no more than 80 characters (including spaces); (7) list of where and when the study has been presented in part elsewhere, if applicable; and (8) disclaimers, if any.

Abstract
Abstracts are limited to 250 words and must appear after the title page. Abstracts must be formatted according to the following headings: (1) Purpose, (2) Patients and methods (or materials and methods, similar heading), (3) Results, and (4) Conclusion. Authors may use design instead of Patients and methods in abstracts of Review Articles. Comments and Controversies, Editorials and Correspondence do not require abstracts.

Text
The body of the manuscript should be written as concisely as possible and must not exceed the manuscript category word limits described herein. All pages of a submission should be numbered and double-spaced. Helvetica and Arial at 12pt size are the recommended fonts for all text (see Figures section for acceptable fonts for figures). The Journal adheres to the style guidelines set forth by the International Committee of Medical Journal Editors.

References
References must be listed and numbered after the body text in the order in which they are cited in the text. They should be double-spaced and should appear under the heading “REFERENCES.” Abbreviations of medical periodicals should conform to those used in the latest edition of Index Medicus and on MEDLINE. The «List of Journals Indexed in Index Medicus» includes the latest abbreviations. Inclusive page numbers must be cited in the reference. When a reference is for an abstract or supplement, it must be identified as such in parentheses at the end of the reference. Abstract and supplement numbers should be provided, if applicable. When a reference is a personal communication, unpublished data, a manuscript in preparation, or a manuscript submitted but not in press, it should be included in parentheses in the body of the text, and not cited in the reference list. Published manuscripts and manuscripts that have been accepted and are pending publication should be cited in the reference list.

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- Journal article with more than three authors

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- Supplement
results and prognostic factors among 138 patients with advanced Hodgkin’s disease treated with the alternating MOPP/ABVD chemotherapy. Ann Oncol 5:S53-S57, 1994 (suppl 2)

° Book with a single author

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° Chapter in a multi-authored book with editors

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Figures must be cited in the order they appear in the text using Arabic numerals. Figures should be submitted in a separate document. Figure legends are required for all article types. Figure legends must not exceed 55 words per figure and should be written below the figure. Images may be embedded in word or Power Point files.

Tables
Tables must be cited in the order in which they appear in the text using Arabic numerals. The table’s legend may include any pertinent notes and must include definitions of all abbreviations and acronyms that have been used in the table. Tables submitted with multiple parts will be renumbered. Tables should be submitted in a separate document. Legends must not exceed 55 words per table and should be written above the figure.

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Emirates Oncology Conference
& 14th Pan Arab Cancer Congress

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Working towards applying for CME accreditation