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AMAAAC Introduction
The Arab Medical Association Against Cancer (AMAAAC) 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 (AMAAAC) 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.

The Executive Board of AMAAC

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Breast Cancer among Patients Admitted into Al-Thawra Teaching Hospital in Sana’a, Yemen

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Key words: Breast Cancer, Teaching Hospital, Sana’a, Yemen

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Abstract

Breast Cancer continues to be a major cause of morbidity and mortality worldwide. It is the most frequent malignancy among women in the developed countries. This study was carried out in oncology unit at Al-Thawra Teaching Hospital-Sana’a-Yemen, to recognize the clinical feature, histopathological types and outcome of breast cancer. During 5- year study period (March 2006 –February 2010), 245 patients admitted into hospital with confirmed histopathologically breast cancer. From hospital record we reviewed the demographic data, clinical manifestations and histological characters and outcome of patients. Of two hundred and forty (98%) were female and only 5 (2%) male patients. The mean age of patients with breast cancer was 49 ± 8.2 years. The peak incidence occurred in the age group of 30-50 years, affecting 205 (83.67%). The common presenting symptoms and signs were painful breast lump and axillary painful mass presented in all patients. 83.67% of the patients had left side breast cancer.

Lymph nodes, lungs, liver and bones were the common sites of breast cancer metastasis accounted for (100%, 81.63%, 80.81%, 77.55%) respectively. The most frequent histological type was infiltrated ductal carcinoma represented 68.16%. All patients presented in advanced stages, (stage III 44.89% and stage IV 68.16%). The mortality rate of breast cancer in this study reached into 68.16%. All patients underwent the following investigations; complete blood picture, the breast ranks first among malignant tumors affecting females (³⁴). However, a study conducted between (1982-1992) in Gizan province in Saudi Arabia, showed that breast cancer constituted the fourth most common malignant tumors among Yemeni and Saudi females treated in that province (³⁵).

A study in United Arab Emirates reported that, breast cancer was an important health problem and considered as the most common malignancy among female patients (³⁶). In Yemen, the lack of a definitive catchments area for each health institution and the lack of a proper and defined referral system for each district hinder epidemiological studies at single institution. These factors plus the lack of a National Cancer Registry make it difficult to determine the real incidence and prevalence of breast cancer in Yemen. However, limited studies were carried out and indicated that breast cancer was frequent cancer among Yemeni females. Aulaqi et al in their study in Yemen conducted between1982-1992 showed that breast cancer ranked the third common cancer in Yemeni women, after cancer of the genital tract and lymphomas, represented 7.64% of female cancers (³⁷).

Another study conducted by Al-Thobhani A.K et al during 1999-2000 reported that breast cancer ranked first cancer among Yemeni women represented of 15.36% of all female cancers (³⁸). This study was taken to describe the pattern of breast cancer among patient admitted into Al-Thawra Teaching Hospital. This hospital is a well equipped with modern medical care facilities and act as a main referral hospital receiving patients from all parts of Yemen.

Conclusion: Breast cancer is frequently seen in our unit. Yemeni patients seek medical advice in advanced stage of the disease where the benefit of therapy is minimal and targeted only the improvement of the quality of life.

Introduction

Breast Cancer continues to be a major cause of morbidity and mortality worldwide. It is the most frequent malignancy among women in the developed countries and also in other nations (³⁹). In the United States, the most common malignancy in females is breast cancer. According to the American Cancer Society, about 1.3 million American women annually are diagnosed with breast cancer and about 465 000 die from the disease (²). Several reports from Gulf countries and Yemen had reported that breast cancer was the most frequent cancer affected women. In Saudi Arabia carcinoma of breast cancer is the breast ranks first among malignant tumors affecting females (³⁴). However, a study conducted between (1982-1992) in Gizan province in Saudi Arabia, showed that breast cancer constituted the fourth most common malignant tumors among Yemeni and Saudi females treated in that province (³⁵).

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Patients and Methods

The data was collected from patients presented to Oncology Unit at Al-Thawra teaching hospital during March 2006 –February 2010. All Patients with breast cancer attended the Oncology Unit in our hospital were subjected to the following procedures:- 1- history taken included age, sex, marital status, parity, age of menarche, age at first pregnancy, duration of breast feeding, age at menopause, family history for cancer, and type of treatment.2- clinical examination ,site of tumor , it’s metastasis and histopathological type of tumor. All patients underwent the following investigations; complete blood picture,
liver and renal function tests, chest x-ray, mammography, Ultrasonography and brain CT scan. Informed consent was taken from each patients participated in this study at the time of admission.

The diagnosis of breast cancer in our study was made histopathologically, by examination of specimens taken through True-cut needle biopsy in 210 (85.71%) patients, fine needle aspiration in 25 (10.20%) patients and 10 (4.08%) patients by axillary lymph node/s biopsies.

Staging of the disease at presentation was categorized based on TNM staging system of the Union International Contre le Cancer (UICC) (10).

Surgical management either modified radical mastectomy, simple mastectomy or lumpectomy was done and recorded. Postoperatively, the patients received hormonal therapy and chemotherapy consisted of CMF regimen (Cyclophosphamide, Methotrexate and 5-Flourouracil) or CAF regimen consisted of (Cyclophosphamide, Doxorubicin and 5-Flourouracil) (11, 12).

Some patients were referred abroad for radiotherapy due to the non-availability of this type of therapy in our country.

All data were recorded and entered into Personal computer. Statistical analysis of results was done by SPSS program. Mean and standard deviation were calculated and P value of 0.05 was taken as significance.

Results

A total of 245 cases of breast cancer were diagnosed in the period of March 2006 –February 2010, with the mean of 64 cases/ year. The majority of patients were females 240 which represented 98% and a minority of the patients was males, 5 cases only represented 2% of the total cases.

The age of the patients at diagnosis ranged between 20-70 years with a mean of 49 years. The most involved age groups were between 30-50 years comprised of 83.67% of the patients. The other age groups involved are illustrated in (table 1).

Table 1: Distribution of breast cancer according to age of the patient at the time of diagnosis

<table>
<thead>
<tr>
<th>Age group in years</th>
<th>No. of Patient.</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>20-30</td>
<td>22</td>
<td>8.98</td>
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<tr>
<td>31-40</td>
<td>85</td>
<td>34.69</td>
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<tr>
<td>41-50</td>
<td>120</td>
<td>48.98</td>
</tr>
<tr>
<td>51-60</td>
<td>10</td>
<td>4.08</td>
</tr>
<tr>
<td>&gt;60</td>
<td>8</td>
<td>3.27</td>
</tr>
<tr>
<td>Total</td>
<td>245</td>
<td>100</td>
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</table>

The study of the laterality of the disease showed that the majority of patients 205 (83.67%) had left breast cancer, Involvement of the right breast was found in 38 (15.5%) patients. Only 2 (0.82%) had bilateral involvement.

All patients in the study presented to our unit complaining of painful breast lump and axillary painful mass. In addition to the above-mentioned clinical manifestations, some patients presented with watery and/or bloody nipple discharge and/or retraction, skin retraction, erythema and oedema. The majority of patients 240 (98%) also presented with arm swelling, table 2.

Table 2: Clinical features of the patients presented with Breast Carcinoma

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast lump</td>
<td>245</td>
<td>100</td>
</tr>
<tr>
<td>Breast Pain</td>
<td>245</td>
<td>100</td>
</tr>
</tbody>
</table>

Clinical examination of the lymphatic system revealed that the lymph nodes at presentation were palpable in the majority of patients 186 (75.91%). Most of them 230 (93.87%) had nodal size of 2-5cm in diameter. In a minority of patients with palpable lymph nodes 15 patients (6.12%) had the diameter of the lymph nodes of >5cm.

Those patients with impalpable lymph nodes represented 24.08% (59) patients see (table 3). the nodes, were also positive for malignancy.

Table 3: Status of the lymph Nodes

| Palpable         | 186             | 75.91%     |
| Not palpable     | 59              | 24.08%     |
| Axillary         | 189             | 77.14%     |
| Supraclavicular  | 125             | 51.02%     |
| Nodal size 2-5cm | 230             | 93.87%     |
| Nodal size>5cm   | 15              | 6.12%      |

Only (4) histopathological types of the tumors were found in this study. The most frequent type was infiltrating ductal carcinoma in 167 (68.16%) patients. The other histopathological types are shown in (Figure I).

Figure 1: Histopathological types of breast cancer

At presentation all patients had advanced disease locally and distant. The majority of patients 135 (55.10%) were in stage III and 110 (44.89%) were in stage IV. No patients were found in stage II & I as it is shown in (Figure II).

Figure 2: Stages of breast cancer at presentation
All patients underwent surgical intervention. The majority of them 200 (81.63%) had only lumpectomy while 45 (18.37%) patients had modified radical mastectomy. All patients received chemotherapy either CMF or CAF regimen. The majority of patients 215 (87.75%) received hormonal therapy in form of tablets Tamoxifen 20 mg/day. Those patients who did not receive hormonal therapy were negative for estrogen receptors and these were tested outside the country. Only 25 (10.20%) patients received palliative radiotherapy outside the country. With regards to metastasis, lymph node metastasis was detected in all patients, followed by the lungs affected in 200 (81.63%), the liver in 198 (80.81%) and the bones in 190 (77.55%) patients. The other organs such as pleura, brain, skin, kidneys and uterus in female were the sites of breast metastasis affected in different proportions.

The outcome of the patients with breast cancer is shown in figure (III). The mortality rate reached into (22.44%).

The frequently involved organs by breast cancer metastasis in this study were the lymph nodes, the lungs the liver and the bones in decreasing order. These are the same organs mostly involved by breast cancer metastasis mentioned in the literature review (2, 18, 19). The most frequent histopathological types of the breast tumors in this study were infiltrating ductal carcinoma followed by invasive ductal carcinoma. Other histopathological types such as: medullary carcinoma and Paget’s disease were not recorded. This data is corresponding to the histopathological types found in Saudi patients where infiltrating ductal carcinoma represented was the most frequent type (2, 19).

Analysis of the tumor size, histopathological typing, lymph nodes involvement, and presence of distant metastasis showed that all patients in our study presented too late for medical advice in stage III & IV which are terminal stages and no patients presented in an early stage I & II that potentially curable. This may explained the high mortality rate in our cases. This figure is completely different from Saudi study where they reported that 40% of Saudi patients presented in an early stage I & II for medical consultation (19, 20). Our data reflect the low awareness of Yemeni women about breast cancer and the lack of medical facilities in the rural areas where the majority of our population live. However, it is not known whether these patients with advanced disease is due to the delay in presentation and seeking medical advice, (due to cultural and social customs), or to a more aggressive disease in this part of the world. The current study cannot explain the differences in trends of breast disease. Factors like age, racial, social, cultural, genetics and dietary may play a role in explaining these differences. Therefore, further combined studies are needed to elucidate the real pattern of breast cancer among Yemeni females.

Conclusion

It is concluded that breast cancer is frequently seen in oncology unit at Al-Thawra teaching Hospital in Yemen ranks as a first cancer affected female. The frequency of male breast cancer is high in comparison with western countries. Yemeni patients usually seek medical advice in very advanced stages of the disease where the benefit of therapy is minimal and targeted only the improvement of the quality of life. Further studies are needed to look for the probable risk factors for breast cancer in Yemeni people where cultural, social, and dietary customs are different.
Recommendations

1. Further study is needed to clarify prevalence, incidence and risk factors for development of breast cancer.
2. Establishment of the National Cancer Registry as soon as possible to help the researchers to evaluate the exact incidence and prevalence of cancer in Yemen particularly, the breast cancer and to help the health policy makers to manage accordingly.
3. Intensify medical education to the general population and particularly to Yemeni women, through health workers and health institutes as well as through the media and schools of girls became mandatory to reduce the diseases.

Disclosure: The authors report no conflicts of interest in this work
Acknowledgment: We would like to thank Mrs. Nadia the head nurse of medical department, Dr. Zayed Atif deputy of director of Al-Thawra Teaching Hospital for their help and in obtaining the necessary permission to perform this study.

References

Acute coronary syndrome in a breast cancer patient treated with tamoxifen

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Key words: Breast cancer, Tamoxifen, Coronary syndrome.

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Abstract

Tamoxifen is a non-steroidal antioestrogen widely used in the treatment of breast cancer. Prolonged exposure to this therapy may result in cardio vascular undesirable events particularly thrombotic events. Arterial effects are rare. We report a case acute coronary syndrome in a locally advanced post menopausal breast cancer treated with neoadjuvant chemotherapy, surgery, adjuvant chemotherapy, radiotherapy and tamoxifen for 2 years. Then we discuss the controversial protective effect of tamoxifen against myocardial infarction.

Introduction

Tamoxifen is a non-steroidal antioestrogen and is considered to be the front line endocrine treatment for breast cancer. It was approved in 1978 by the US Food and Drug Administration for treatment of advanced postmenopausal breast cancer. Subsequently it was widely used in postmenopausal and premenopausal women both as adjuvant treatment for early disease and for advanced disease. Toxicity is known to be low. Nevertheless, the possibility that prolonged exposure may result in premature osteoporosis, endometrial adenocarcinoma and thrombotic events. Most cases reported are of venous thromboembolism; arterial events are rare. In this article, we report a case of an acute coronary syndrome in a post menopausal woman treated with tamoxifen for breast cancer.

Case report

A 46 years old woman with no history of vascular disease or source of cardiac emboli had a history of a locally advanced breast cancer diagnosed five years ago. Biopsies revealed an invasive ductal carcinoma grade 3. Immunocytochemical staining was positive for hormonal receptors and negative for c-erb B2. The staging of the neoplastic disease, revealed a IIIB stage according to AJCC breast staging 7th edition. The patient undergone 4 cycles of neoadjuvant chemotherapy (AC60 regimen) modified radical mastectomy and axillary lymph node curage. Macroscopic examination of the resection has revealed a single tumor nodule measuring 30x32 mm. Histologically, the tumor was classified as grade 4 according to Chevallier’s classification. Two lymph node metastases were detected. Post operatively, the investigations didn’t reveal any metastatic localization. The patient received adjuvant chemotherapy (4 Docetaxel), external beam radiation and hormonotherapy with tamoxifen. She has received 2 years of tamoxifen 20 mg/day when she developed an acute coronary syndrome. The patient presented to the department of emergencies with chest pain. There was no evidence of ST segment elevation on the electrocardiogram. Troponin was positive and urgent coronary angiography revealed a stenosis of 40% of the anterior interventricular (AIV) artery. A medical treatment based on aspirin, clopidogrel, β Blockers, and statin was carried out. Tamoxifen was stopped. As the patient was in amenorrhea for almost three years, we discussed with her benefice and cardio vascular risks of the treatment with aromatase inhibitors. The estimate survival gain calculated with Adjuvant online scoring system was almost 12% at 10 years. The patient preferred this therapeutic option with cardiovascular examination, electrocardiogram and biological lipid assessment every 3 months. After 3 years of follow up, she remains disease free without any cardio-vascular event.

Discussion

Tamoxifen is the endocrine treatment of choice for selected patients with all stages of breast cancer. In post menopausal women, five years of adjuvant tamoxifen reduces the 15-year risk of breast cancer recurrence by approximately 40 percent and breast cancer mortality by 35 percent [1]. Tamoxifen is a selective estrogen receptor modulator (SERM) with both agonist and antagonist properties, depending on the individual target organ. The adverse effects associated with tamoxifen, including hot flashes, vaginal discharge, thromboembolic events, and endometrial cancer. Therefore, A number of studies, including the Early Breast Cancer Trialists Collaborative Group (EBCTCG) overview analysis and the large Breast Cancer Prevention Trials, have demonstrated that tamoxifen use is associated with an increased rate of venous thromboembolic events (2.8 percent), especially within the first two years of tamoxifen use, in elderly women, and that there is a significant additional procoagulant effect when tamoxifen is added to chemotherapy [2]. Additionally, this risk was increased in patients who had
surgery, immobilization, or fracture in the month prior to the event.

In contrast, arterial events particularly myocardial infarction, as shown in our case report is rare in women treated with tamoxifen. In fact, several studies have reported a significant reduction in myocardial infarction events among the tamoxifen-treated group. MacDonald and Stewart showed a 50% reduction in events among women treated with 20 mg/d tamoxifen for 5 years [3]. This beneficial effect may be due to the favorable effect of tamoxifen on lipid profiles. In a randomized trial in 57 normal postmenopausal women, tamoxifen in a dose of 20 mg/day led to significant reductions in total and LDL-cholesterol (12 and 19 percent, respectively) and an 18 percent fall in fibrinogen levels without any change in HDL-cholesterol. Moreover, Tamoxifen also has weak antioxidant properties, protecting LDL cholesterol from potentially harmful oxidation at least in vitro [5].

Tamoxifen is a coronary vasodilator in a porcine in vitro model and substantially increases endothelial function. Other mechanisms, such as anti-inflammatory effect and effects on insulin metabolism, should not be overlooked [6].

While these data suggest a potential protective effect against myocardial infarction, the available data from clinical suggest that in postmenopausal women both with and without cardiac heart disease, the use of tamoxifen is not associated with either a beneficial or adverse cardiovascular effect. Otherwise, other data suggest that the use of tamoxifen is not associated with a beneficial cardiovascular effect.

Finally, in all these trials, there were relatively few events reported, and myocardial infarction was not a prospective endpoint in any. Further studies are required to better define the effect of tamoxifen on cardiac risk.

References


Conflict of interest: None
The manuscript has never been presented before in another journal
Clinicopathological Features of Gastric Cancer; Single Center Experience

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Key words: Gastric cancer, Clinicopathological features.

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I and all co-authors confirm and certify that our paper has not been presented before to any conference or journal.

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 Holly 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.

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 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 between (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 (M). The histological classification was based on Laurens (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, tow 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 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-jejunosostomy 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.

Clinical presentation

Most patients presented with features of advanced disease such as, abdominal pain in 40 patients (88.9%), nausea and vomiting in 32 patients (71.1%), epigastric mass in 19 patients (42.2%), jaundice in 17 patients (37.8%), hematemesis in 12 patients (26.7%) and ascites in 7 patients (15.6%); table 2.
Original Article

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 may make it 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 study 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).

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 treatment the symptoms without treating or investigating the underlying cause.

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 predominance 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).

Discussion

<table>
<thead>
<tr>
<th>Lauren classification</th>
<th>Intestinal</th>
<th>Diffuse</th>
<th>Mixed</th>
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<tr>
<td></td>
<td>21</td>
<td>15</td>
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<td></td>
<td>46.7</td>
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<th>TNM staging</th>
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<tr>
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<td>82.2</td>
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<td></td>
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<td>6</td>
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<tr>
<td></td>
<td>29</td>
<td>16</td>
</tr>
<tr>
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<td>64.4</td>
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<th>Palliative chemotherapy</th>
<th>Palliative radiotherapy</th>
<th>Best supportive care from the start</th>
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<td>14</td>
<td>0</td>
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<td></td>
<td>8.9</td>
<td>28.9</td>
<td>31.1</td>
<td>0</td>
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</table>

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 with 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 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 (71.1%) 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 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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Trastuzumab associated cardiac toxicity: who is at risk in Saudi Arabia? A single institution study

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Key words: Breast Cancer, Cardiac Toxicity, Trastuzumab, Her-2 overexpression, Saudi patients.

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Abstract

Purpose: There is a growing concern about the long-term effect of trastuzumab-induced cardiotoxicity (TIC). Therefore, we retrospectively assessed the incidence of TIC and heart failure (HF) and tried to identify possible risk factors among a group of Saudi breast cancer (BC) patients.

Methods: This retrospective cohort study was conducted to review all Her2+ BC patients treated at KAMC, Riyadh KSA, with trastuzumab in the adjuvant and metastatic settings between 2003 and 2012. Of 150 patients, 104 were eligible with good quality baseline 2D-echocardiogram, and LVEF ≥ 55%. Cardiac function assessment was repeated every 3 months by echocardiogram thereafter.

Results: 104 Her2 positive breast cancer patients were eligible for analysis, with median age of 49 years and range (29–78 y). A significant decline in LVEF was observed in 16 patients (15.38%) at a mean exposure period of 15 months. On multivariate analysis a significant difference in LVEF decline was reported between patients diagnosed with hypercholesterolemia (64.71%) compared to (6.8%) in patients with normal cholesterol level (p-value 0.0001) as well as between patient who has been exposed to Anthracycline chemotherapy (p-value 1.0435). Diabetes was a significant risk factor for TIC on univariate analysis but this was not confirmed on multivariate analysis.

Conclusion: Given the limitations of this retrospective review, the results showed significant higher prevalence of TIC among Her2+ BC Saudi patients. The study highlighted significant correlation between hyperlipidemia and previous exposure to Anthracycline with development of TIC constituting a high risk group patients who may need to be closely monitored for cardio toxicity.

Introduction

Breast cancer is the most common cancer among Saudi females, comprising 27.7% of all malignancies (13). Approximately 20 to 30% of all breast cancers overexpress human epidermal growth factor receptor 2 (Her2) (1). A variant of the disease associated with aggressive course and poor prognosis with a high risk of recurrence and metastasis (2). Trastuzumab, a monoclonal antibody targeting Her2 has led to a significant breakthrough in the treatment of breast cancer that over-expresses Erb-2 receptors, therefore, partnering trastuzumab with chemotherapy have improved the response rate, time to disease progression, and overall survival. At present, trastuzumab is considered part of the standard therapy for both advanced and early her2 positive breast cancer (3). Its use, however was associated with an unexpectedly high incidence of cardio toxicity usually occurring as asymptomatic LVEF reduction of >10% or overt heart failure (HF).

The risk factors for trastuzumab-induced cardio toxicity (TIC) have not been clearly defined. Moreover, the long-term impact of trastuzumab-related transient LVEF reduction is unknown, which raises concerns about breast cancer patients who are potentially cured. When trastuzumab is used as a single agent, cardio toxicity has been reported in up to 7% of patients. While, when combined with an anthracycline, TIC is notably increased up to 27% of cases, with NYGH Gr III or IV CHF being reported in 16% of patients in pivotal trials (4).

The NSABP B-31 (National Surgical Adjuvant Breast and Bowel Project) reported old age, baseline LVEF of 50%-54% and post-anthracycline LVEF of 50%-54% as significant risk factors of cardio toxicity (5). Cardiac arrhythmias and other cardiac risk factors were not found to be risk factors for cardiac toxicity in NSABP B-31 and (NCCTG N9831) of North Central Cancer Treatment Group (6,7). Nevertheless, other trials have not yet reported analysis of the predictive factors of trastuzumab induced cardiac dysfunction.

We aim to report the prevalence of cardio toxicity in her2 breast cancer Saudi population and to identify the subgroup of patients who are at higher risk to develop TIC by studying the various risk factors such as age, obesity, diabetes, hyperlipidemia and hypertension.

Patient and Methods

Using an institutional medical records database, we identified all early and advanced BC patients treated with trastuzumab at Adult Medical Oncology, KAMC-NGHA, Riyadh, from 1 March 2003 to 30 June 2012. 150 patients were identified and 104 were eligible for the study, they were Her2 positive breast cancer with good quality baseline 2D-echocardiogram, and LVEF ≥ 55%,
treated with trastuzumab and had received at least one dose of a trastuzumab-based regimen.

The following data were extracted retrospectively from electronic medical records for each patient: age, tumor characteristics, body mass index, chemotherapy use, smoking history, breast cancer side, use of radiation therapy, trastuzumab schedule and cardiac risk factors. These risk factors included hypertension (defined as blood pressure >140/90 mm Hg maintained over time or use of antihypertensive drugs), hypercholesterolemia (defined as total plasmatic cholesterol >200 mg/dl or use of lipid-lowering medications), diabetes mellitus (diagnosed by WHO criteria as fasting serum glucose ≥ 126 mg/dl, 2-h post challenge serum glucose ≥200 mg/dl or use of hypoglycemic medications).

All patients underwent a comprehensive baseline cardiac examination and echocardiography as part of their routine pre chemotherapy evaluation. Both evaluations were repeated before starting trastuzumab (baseline) and almost every 3 months thereafter for the duration of therapy. This study was approved by the Medical Scientific Committee of the Institute and by the Local Ethics Review Board.

Statistical Analysis

Descriptive statistics were used to describe the number of patients experiencing a LVEF reduction. Student t-test was used to compare the different groups in regard to continuous variables eg. EF results before and after trastuzumab. The association between patients who experienced a cardiac event and the risk factors under investigation was analyzed with the χ² test. Logistic regression was used to estimate OR and their 95% CI in order to evaluate the relation between cardiac risk factors and the development of cardio toxicity. All analyses were performed using SAS statistical (V9.1, SAS Institute, Cary, North Carolina, USA). Statistical significance for all tests was taken as p<0.05.

Results

Patient Characteristics

A total of 104 Her2-positive BC patients met inclusion criteria. All patients had undergone surgical removal of breast cancer before adjuvant chemotherapy. Full baseline characteristics are listed in table 1. Median age at the start of trastuzumab therapy was 49 years (range 29-78 years), 15% were <40 years, and 40% were between 41 and 50 years of age.

The median BMI was 30.5 (range 25-34) with 60% of study population having values >30. The median LVEF value at baseline (before trastuzumab treatment) was 54.86 (range 50-55). The majority of patients (62.5%) were not treated with an anthracycline-based, whereas 37.5% were anthracycline-based chemotherapy (FEC, AC or FAC). There was no concurrent use of trastuzumab and anthracycline in any study patient.

66 patients (63.46%) did not have any cardiac risk factors at baseline, while the remaining 38 patients (36.54%) showed at least one risk factor: hypertension 23 (22.12%), diabetes mellitus 22 (21.15%) or hypercholesterolemia 17 (16.35%), hypothyroidism was seen in only 2% of study population, and none of them was a smoker.

Cardiotoxicity and Potential Risk Factors

A cardiotoxic event was defined as an absolute LVEF reduction of at least 5 percentage points from baseline with signs and symptoms of heart failure (HF) or >10% without such symptoms. Recovery from the cardio toxic event was defined as LVEF recovery to values >50% or the complete resolution of symptoms. We used the term HF to denote New York Heart Association (NYHA) class III or IV cardiac dysfunction in the presence of decreased LVEF.

Of the 104 BC patients, only 16 (15.38%) experienced TIC event after a mean exposure duration of 15-month to trastuzumab (range 4-33 m), 8 patients stopped trastuzumab due to TIC after the first event and 3 patients after the second one. In our series trastuzumab induced significant decline in LVEF ended up with symptomatic CHF in 4 patients with subsequent irreversible none symptomatic EF < 55%.

Table 1: Baseline patients and disease characteristics (n=104)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N (%)</th>
<th>Median</th>
<th>Range</th>
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<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&lt;40</td>
<td>16 (15.38%)</td>
<td>49</td>
<td>29-78</td>
</tr>
<tr>
<td>41-49</td>
<td>37 (35.58%)</td>
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<tr>
<td>50-59</td>
<td>28 (26.92%)</td>
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</tr>
<tr>
<td>≥ 60</td>
<td>23 (22.12%)</td>
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<td></td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&lt;20</td>
<td>7 (6.73%)</td>
<td>30.51</td>
<td>25.47-34.01</td>
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<tr>
<td>20-24</td>
<td>11 (10.58%)</td>
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<tr>
<td>25-29</td>
<td>23 (22.12%)</td>
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<tr>
<td>≥ 30</td>
<td>63 (60.58%)</td>
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<tr>
<td>Baseline LVEF%</td>
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<tr>
<td>Hypercholesterolemia</td>
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<tr>
<td>Yes</td>
<td>17 (16.35%)</td>
<td>54.86</td>
<td>50-55</td>
</tr>
<tr>
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<td>87 (83.65%)</td>
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<tr>
<td>DM</td>
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<tr>
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<tr>
<td>No</td>
<td>82 (78.85%)</td>
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<tr>
<td>Anthracycline</td>
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<tr>
<td>Yes</td>
<td>39 (37.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>65 (62.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HTN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>23 (22.12%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>81 (77.88%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2 (1.92%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>102 (98.08%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Rate factors analysis

19 patients out of 104 (15.38%) developed trastuzumab induced cardiac toxicity (TIC). The distribution of possible risk factors in patients with and without trastuzumab-induced cardiotoxicity (TIC) is listed in table II. There was no statistically significant difference between the 2 groups for age, BMI, nor hypertension suggesting by this univariate analysis that those might not be an important risk factor for TIC, of the 16 patients with TIC, 4 patients (25%) were <40 years of age and only 1 patient (6%) was >60 years of age, compared to 12 patients (13.6%) and 22 patient (25%) of respectable age group from the 88 patients with no reported TIC, also the BMI of value >30 was seen in 10 patients (62%) in the TIC group vs 53 patient (60%) in patients without TIC, hypertension was reported in 6 patients (37%) from the TIC group vs 17 patients (19%) of patients without TIC, the difference was not statistically significant (P-value 0.1070).
On the other hand using the same univariate analysis, the presence of hypercholesterolemia, diabetes mellitus and the use of anthracycline were significant risk factor for the development of cardiac toxicity, as 11 patients of TIC group (64%) had hypercholesterolemia compared to 6 patients only from patients without TIC (7%), with highly statistical significant P-value of (0.001), as for the effect of diabetes, 7 patients from the TIC group (43%) had diabetes compared to 15 patients from patients without TIC (17%) with statistical significant P-value of (0.001), also 10 patients of TIC group (62%) had received anthracycline chemotherapy compared to 29 patients only from patients without TIC (33%) with statistical significant P-value of (0.025).

Table 2: Distribution of possible risk factors in patients with and without cardiotoxicity (n=104)

<table>
<thead>
<tr>
<th>Factors</th>
<th>Pt with cardiotoxicity</th>
<th>Without cardiotoxicity</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>4 (25.00%)</td>
<td>12 (13.64%)</td>
<td>0.2994</td>
</tr>
<tr>
<td>41-49</td>
<td>7 (43.75%)</td>
<td>30 (34.09%)</td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>4 (25.00%)</td>
<td>24 (27.27%)</td>
<td></td>
</tr>
<tr>
<td>≥ 60</td>
<td>1 (6.25%)</td>
<td>22 (25.00%)</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>0 (00%)</td>
<td>7 (7.95%)</td>
<td>0.5063</td>
</tr>
<tr>
<td>20-24</td>
<td>1 (6.25%)</td>
<td>10 (11.36%)</td>
<td></td>
</tr>
<tr>
<td>25-29</td>
<td>5 (31.25%)</td>
<td>18 (20.45%)</td>
<td></td>
</tr>
<tr>
<td>≥ 30</td>
<td>10 (62.50%)</td>
<td>53 (60.24%)</td>
<td></td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>11 (64.71%)</td>
<td>6 (6.81%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>No</td>
<td>5 (5.75%)</td>
<td>82 (93.29%)</td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic</td>
<td>7 (43.75%)</td>
<td>15 (17.05%)</td>
<td>0.0161</td>
</tr>
<tr>
<td>Non diabetic</td>
<td>9 (56.25%)</td>
<td>73 (82.95%)</td>
<td></td>
</tr>
<tr>
<td>Anthracycline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes anthracycline</td>
<td>10 (62.50%)</td>
<td>29 (32.95%)</td>
<td>0.0247</td>
</tr>
<tr>
<td>No anthracycline</td>
<td>6 (37.50%)</td>
<td>59 (67.05%)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertensive</td>
<td>6 (37.50%)</td>
<td>17 (19.32%)</td>
<td>0.1070</td>
</tr>
<tr>
<td>Non</td>
<td>10 (62.50%)</td>
<td>71 (80.68%)</td>
<td></td>
</tr>
</tbody>
</table>

On multivariate analysis (table III) statistically significant trastuzumab induced cardiac toxicity (TIC) was documented in association with hypercholesterolemia and the use of anthracycline on the other hand, it had failed to confirm the relationship of hypertension or diabetes to the development of TIC.

The OR for the presences of hypercholesterolemia was very high at 71.2 with very statistically significant P-value of .0001 while the OR for the use of anthracycline was 5.9 with P-value of 0.043. The differences observed for all other potential risk factors were not statistically significant.

Table 3: Multivariate analysis of risk factors in patients with and without cardiotoxicity (n=104)

<table>
<thead>
<tr>
<th>Factors</th>
<th>OR</th>
<th>(95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40 vs. ≥60</td>
<td>2.638</td>
<td>(0.122 – 56.842)</td>
<td>0.6785</td>
</tr>
<tr>
<td>41-49 vs. ≥60</td>
<td>8.013</td>
<td>(0.391 – 164.349)</td>
<td>0.2502</td>
</tr>
<tr>
<td>50-59 vs. ≥60</td>
<td>8.503</td>
<td>(0.407 – 177.624)</td>
<td>0.2318</td>
</tr>
<tr>
<td>BM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-24 vs. ≥30</td>
<td>1.073</td>
<td>(0.036 – 31.717)</td>
<td>0.6307</td>
</tr>
<tr>
<td>25-29 vs. ≥30</td>
<td>5.772</td>
<td>(0.746 – 44.648)</td>
<td>0.1450</td>
</tr>
</tbody>
</table>

Table 4: Multivariate analysis of risk factors in patients with and without cardiotoxicity (n=104)

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypercholesterolemia</td>
<td></td>
</tr>
<tr>
<td>High vs. normal</td>
<td>71.24</td>
</tr>
<tr>
<td>(4.217 – 555.657)</td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td></td>
</tr>
<tr>
<td>Diabetic vs. non</td>
<td>3.217</td>
</tr>
<tr>
<td>(0.656 – 15.774)</td>
<td></td>
</tr>
<tr>
<td>Anthracycline</td>
<td></td>
</tr>
<tr>
<td>Anthracycline vs.</td>
<td>5.928</td>
</tr>
<tr>
<td>anthracycline</td>
<td>(1.0153 – 33.358)</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>Hypertensive vs. non</td>
<td>2.372</td>
</tr>
<tr>
<td>(0.386 – 14.578)</td>
<td></td>
</tr>
</tbody>
</table>

Discussion

Approximately 20-25% of breast cancer overexpresses the human epidermal growth factor II (Her2) which confers aggressive behavioral traits (12). In Saudi Arabia, breast cancer ranked the highest among Saudi females, comprising 27.7% of all malignancies (13) in the range between 17% as reported in the eastern region of the kingdom to 30% in the central region (14,15).

Although trastuzumab is not known to cause the classical toxicities related with chemotherapy or other targeted therapy medications, one of the major concern is the occurrence of cardiac dysfunction. The risk for serious and life-threatening cardiotoxicity with combination anthracyclines and trastuzumab has been an ongoing concern (16). Therefore, we designed this study with the aim of identifying the potential risk factors for cardiac toxicity associated with trastuzumab treatment among Saudi women with Her-2 positive breast cancer.

In our study, TIC defined as significant decline in the LVEF to below 55% was reported in 15% of the patients. Compare to around 4-5% in international series, an observation which may indicate different natural history among Arab women. Our series constituted of relatively younger patient population (median 45 years) where anthracycline is more frequently used compared with older patients as the median age in published pivotal randomized trials is >50 years (17, 18). Such a rational, which was the impetus of a recent study assessing cardiac events in elderly breast cancer women between 72-90 years (19).

It is worth noting that our study have limitations in interpreting results given its retrospective nature and the small sample size, which limited its power to detect statistical have limitations in interpreting results given its retrospective nature and the small sample size, which limited its power to detect statistical significant parameters. However, such limitations are encountered and shared in recently published reviews in the west (20), as well as a single Saudi institution series (21) which retrospectively published data of 98 patients who received adjuvant trastuzumab from 2006 to 2009. More or less the results matched our report in terms of TIC detected among 12% of cases (11,98). Furthermore, 5 patients suffered CHF subsequent withdrawal of trastuzumab.

Moreover, our study demonstrated a significantly increased incidence of cardiac events with multivariate analysis among patients with history of DM and hyperlipidemia similar to published reports, but the only statistically significant risk factors identified on multivariate analysis was hypercholesterolemia and previous anthracycline exposure while other well-known established risk factors such as hypertension, left side breast and were not shown to have a significant impact on development of trastuzumab-induced cardiac toxicity among our population, (22), the reason might be the relatively small sample size of our study.
A median BMI of 31.22 was reported among the 16 patients who suffered trastuzumab induced cardiotoxicity compared to BMI of 30.51 of the whole study group with no statistical significant difference (P-value 0.56). Other studies had suggested that a BMI of more than 25 have been shown to increase the risk of cardiac toxicity but the results are inconsistent or uniform (3, 9). The main preventive strategy would be through early detection of high risk patients and prompt initiation of prophylactic treatment, so it seems of crucial importance to identify patients with DM and hyperlipidemia before treatment with trastuzumab, such patients require cautious follow-up and close monitoring and early intervention to avoid any deterioration of the cardiac function.

Detection of subclinical myocardial changes might be proven very important for better patient selection, the role of troponin I (TNI) in relation TIC was recently reported, 72% of patients who had elevated levels of TNI had TIC compared to 7% of those with normal levels (23, 24).

Several other methods are currently been explored for early detection of subclinical LV dysfunction as the new echocardiographic methods such as myocardial strain and strain rate (SR) are newer echocardiographic parameters using promising tools as tissue Doppler imaging (TDI) or speckle tracking (ST), cardio specific biomarkers NT-proBNP (25) or innovative Her-2 imaging techniques which may prove of use in the near future (26).

Whether we encourage the concept of substituting anthracyclines by evidence-based alternatives as TCH from BCIRG006 (27) which reported cardiac event rate of 0.4% is still controversial since we lack long term cardiac safety profile of the treated patients.

Conclusion and Recommendations

Although TIC is not a common adverse event, it is very important to know the patients who are at risk, as prevention and early treatment might be very effective to optimize outcome of trastuzumab therapy. In our study, we have found that hyperlipidemia and the use of anthracycline are considered significant independent risk factors for exacerbating trastuzumab induced cardiac toxicity. While, in our study, hypertension, diabetes nor high BMI values did not correlate with the development of trastuzumab induced cardiac toxicity, an observation which needed to be interpreted with a lot of caution due to small sample size, and the fact the majority of such patients are already taking AC inhibitors.

Risk factors for trastuzumab-related cardiotoxicity are still poorly defined and are generally considered to be similar to those for anthracycline-induced cardiac dysfunction. Further research is needed to determine predictive factors for the early occurrence of cardiotoxicity in order to prevent cardiac injury.

References


Is this manuscript presented before to any conference or journal No

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Everolimus with endocrine therapy as a treatment option in ER + MBC failing at least one line of endocrine therapy: a single institute experience

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Key words: Breast Cancer, Everolimus, MTOR Inhibitor, Endocrine Therapy, Secondary Resistance.

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Abstract

75% of MBC are hormone receptor positive; on ET the responders eventually will acquire resistance. One of the suggestive mechanisms for this resistance is the activation of the mTOR pathway. In the BOLERO-2 study, the addition of everolimus to exemestane was associated with a significant improvement in PFS. 

Purpose and Methods: To evaluate the response rate in heavily pretreated population and the safety of the drug in different genetic/ethnic backgrounds. We performed a retrospective analysis of all ER+, MBC who received everolimus during a period of 6 months. A few cases were reported based on their interesting findings.

Results:

19 patients, Median age was 58, 26% were pre-menopause. The combination was used after failure of at least one line of ET (1-4), 17 patients had it with exemestane and 2 with tamoxifen. The median duration of the treatment was 20 weeks. 8 had it for ≤4weeks. The reasons were poor patient selection (PS ≥3), poor tolerance or progressive disease. Response assessment, 10 had PR, 2 SD, 1 PD, in 6 patients no evaluation was possible for premature stoppage of the therapy. Toxicities: mucositis 78%. Less frequently hyperglycemia, weight loss, infection and non-infectious pneumonitis. Dose interruptions and adjustments were frequently reported >70%.

Conclusions: Everolimus combination was associated with a high RR, it may be less toxic than chemotherapy, but patients who are poor candidates for chemotherapy may not be a good candidates for this combination as well. Educating patients and physicians experience reduce the treatment toxicity and improve the tolerability.

Background

75% of metastatic breast cancers are hormone receptor positive but not all patients will respond to endocrine therapy. In fact, a small proportion is primary refractory while the others eventually will acquire resistance to endocrine treatment (secondary resistance). One of the suggestive mechanisms for this acquired resistance is associated with activation of the mammalian target of rapamycin (mTOR) intracellular signaling pathway. In early pre-clinical and clinical studies, the addition of the mTOR inhibitor everolimus to endocrine therapy showed antitumor activity.

In the BOLERO-2 study, the addition of everolimus to exemestane was associated with a significant improvement in progression-free survival, with observed medians of 6.9 and 2.8 months. This corresponded to a 57% reduction in the hazard ratio.

Objectives

• To evaluate the response rate in a heavily pretreated population, which differs from patients usually included in a clinical trial.
• To elaborate on the safety profile of the drug in patients who have worse PS and different genetic/ethnic backgrounds.

Methods

• We performed a retrospective analysis of all hormone receptor positive MBC who received everolimus as a combination with endocrine therapy during a period 6 months. 19 patients were included in this analysis.
• We reported the response rate which was defined by either radiological response according to (RECIST) criteria or a drop in tumor marker, as well as the median duration of treatment, Everolimus dosing, treatment interruptions, side effects, as well as other demographic data.
• A few cases were reported based on their interesting findings.

Results

Nineteen patients were eligible for evaluation. The median age was 58, (38 - 75 years). 5 patients (26%) were pre-menopause. All patients received the combination after failure of at least one line of hormonal therapy. Three patients received the combination as 1st line palliative hormonal treatment after failing adjuvant hormonal therapy, while 8 patients received it as...
2nd line therapy. Five patients received treatment as 3rd line, 2 patients as 4th line and 1 patient received it as 5th line hormonal treatment. (Fig. 2, table 1)
The everolimus combination was with exemestane in 17 patients and with tamoxifen in 2 patients.
In 41% of the 1st group, the exemestane was considered a re-challenge and in 1 of the 2 tamoxifen cases, the patient was progressing and everolimus was added to the tamoxifen. (fig. 3, table 2)
Patient exposure to endocrine therapy before the combination ranged from (1 to 4) drugs with an average of 2.3.

The median duration of the combination treatment was 20 weeks, ranging from 2-64 weeks. Eight patients had treatment duration of ≤4 weeks. The main reason for this short duration was poor patient selection (poor PS ≥3) in 3 patients, 4 patients had poor tolerance and one patient had progressive disease. Eventually in all patients, the treatment was stopped for either progressive disease or poor tolerance (fig. 4, 5).

Response assessment (1st assessment) was available for 13 patients. Ten had PR, 2 SD, 1 PD, in 6 patients no evaluation was possible for premature stoppage of the therapy, (Table 3).

The toxicities reported were: mucositis (all grades) in 78% (fig 6). Less frequent Side effects included hyperglycemia, weight loss, infection (skin, UTI and URTI); two cases had non-infectious pneumonitis, which resolved with medical treatment. One of them the treatment was resumed at a lower dose.
Dose interruptions and dose adjustments were frequently reported >70%.
Cases

**Case 1**

42 y/o patient diagnosed in 2000 with right breast cancer, underwent Rt MRM, staged as pT1b, N1 +1/12 LN, M0, ER (+), PR (+). She received adjuvant chemotherapy with 6 cycles of CEF followed by adjuvant endocrine therapy consisting of tamoxifen for 3 years only cause patient became pregnant.

In March of 2008, she developed hip pain. Evaluation revealed diffuse bone metastases. She received palliative radiotherapy to pelvis and to D1-L2 spine. Cerb2 receptors were done on the initial breast tissue and this was negative. She was restarted on endocrine therapy with tamoxifen and goserelin, as well as zoledronic acid.

Re-evaluation in January of 2010 revealed stable disease. In October of 2010, she developed progressive bone disease without visceral involvement. She was switched to letrozole and continued on goserelin and zoledronic acid. A year later in October of 2011, CT scan revealed multiple liver metastases.

1st line palliative chemotherapy with nab-paclitaxel was given between October 2011 and June 2012. This was followed by 3rd line hormonal treatment fulvestrant 500mg. She was maintained on goserelin, and zoledronic acid was changed to denosumab. She continued to progress with increasing liver lesions.

Liver biopsy revealed metastatic breast cancer, ER (+80%) PR (+50%) Cerb 2 (0). 4th line hormonal treatment was exemestane and everolimus was started in October of 2012. This was maintained for one year until October of 2013.

**Case 2**

49 y/o premenopausal female diagnosed in May of 2010 with right breast cancer. PET-CT revealed multiple bone lesions with no visceral metastases.

1st line chemotherapy was paclitaxel + UFT + 5-fluorouracil and bevacizumab. She had 4 cycles between May 2010 and Sept. 2010. Follow up PET-CT showed partial response. She underwent Rt MRM in October 2010. Histopathology revealed invasive ductal carcinoma, ER (+), PR (+), Cerb2 (0). 1st line hormonal treatment consisted of tamoxifen. She was also maintained on monthly injections of zoledronic acid.

In January of 2012, she presented with back pain radiating to the left leg. MRI of the spine revealed progressive disease without cord or nerve root compression. Ovarian function assessment was consistent with postmenopausal state. She was switched to letrozole. Follow up PET-CT in June of 2012 revealed progressive bone metastases. Exemestane was started as 3rd line endocrine therapy. With no improvement in symptoms, Everolimus was added to exemestane in September of 2012. This led to a clinical and radiological improvement of 14 months.
Conclusions

- The combination treatment of exemestane and everolimus is associated with a high response rate in fit patients.
- This treatment may be less toxic than chemotherapy, but patients who are poor candidates for chemotherapy may not be good candidates for this combination as well.
- Education and experience of both parties (patients and physicians), will help in reducing the everolimus toxicity and improve the tolerability to this treatment.

References

Retrospective Review of Cases of Invasive Moles Treated At The Radiation And Isotope Centre of Khartoum (RICK), Sudan

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Key words: Invasive Mole, Trophoblastic Disease, Sudan, Chemotherapy, BHCG.

ISSN: 2070-254X

Abstract

Background: Invasive Moles are rare and highly Chemo sensitive and curable tumors, although the outcome of treatment for more than 98% of Women with Gestational Trophoblastic Disease is excellent, few women die mainly due to delayed presentation and late diagnosis and Drug resistance, so it’s important that they should be diagnosed and referred earlier. In this study our aim is to determine the frequency of Invasive Moles, clinical presentation, management and outcome.

Material and Methods: This is a retrospective Study of 80 Patients with Invasive Moles, treated at the Radiation and Isotopes Centre of Khartoum RICK, between 2000 and 2008.

Results: The Age distribution of the sample showed Age Range of 19 – 50 years, Mean Age = 30 years, Median age = 30.1 years, with 2 peaks of age, <20 years 40%, 41 – 50 years 35%, BHCG level were low risk level, < 1000 IU/ml, 47 patients = 57.5%, medium risk level, 1000 – 10000, =14 patients = 17.5%, high risk level, >10 000, 20 patients = 25%.

Conclusion: All patients had evacuation or Dilatation nad Curetage, D and C, and Histopathology first, followed by Chemotherapy, all patients achieved complete Response, CR, except 2 patients, who were given more aggressive Chemotherapy, EMACO Regimen, one of them was lost due to Septicemia, none of our Patients had Hysterectomy.

Method

This is a retrospective Study of A random sample of 80 Cases of Invasive Moles. Treated at the Radiation and Isotopes Centre of Khartoum, RICK, between 2000 and 2008, the case records of all this patients were analyzed.

Results

Most of the patients belong to the extremes of ages, 52 patients ,65% were below the age of 40, 28 patients ,35% between 40 and 50, most patients were from Khartoum and central Sudan, 54 patients ,67.5%, most patients presented with vaginal bleeding, 74 patients, 92.5%, passing Moles, 63 patients, 78.5%, lower abdominal pain, 54 patients, 67.5%, and vomiting, 43 patients, 53.7%.

Table 1: Age Distribution

<table>
<thead>
<tr>
<th>Age</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20 Years</td>
<td>32</td>
</tr>
<tr>
<td>21 – 30</td>
<td>14</td>
</tr>
<tr>
<td>31 – 40</td>
<td>6</td>
</tr>
<tr>
<td>41 – 50</td>
<td>28</td>
</tr>
</tbody>
</table>

Mean Age = 30 years
Median = 30.1
Age Range = 19-50 years

Introduction

This is a retrospective Review of a random sample of 80 Cases of Invasive Moles treated at the Radiation and Isotopes Centre of Khartoum, RICK, between 2000 and 2008, to study the frequency of this disease, presentation, management and outcome. Invasive Moles form less than 1% of all females Cancers Treated at RICK, Gestational Trophoblastic Disease GPD encompasses several disease processes which originates from the Placenta, these include complete and Partial Moles, Placental Site Trophoblastic tumors, Invasive Moles and Choriocarcinomas, most Women with Malignant Gestational Trophoblastic Disease can be cured, ref 1. The incidence of Hydatidiform Moles Pregnancies, varies greatly in the World, ranging between 1/695 in Ireland to 1/100 Pregnancies in Indonesia and 1/695, ref 2, the highest incidence was reported from Turkey, 12.1, /1000, ref 3, the highest malignant potential was reported from South East Asia, where its 10 –15% compared to 2-4% in Western Countries, ref 4, 5. Malignancy is diagnosed in 15 – 20% of Complete Moles Cases and in 2-3% of cases of Partial Moles ref 3, 4, and Lung metastases are found in 4- 5% of Complete Moles cases and rarely in cases of Partial Moles, ref 5, 6, 7.
Gestational Trophoblastic Disease encompasses a unique group of uncommon but interrelated conditions, derived from the placental trophoblasts, with widespread range of histologic appearances and clinical behaviors, ref 7,8. The most common kind of Gestational Trophoblastic Disease, GTD, is Complete Hydatidiform Mole, ref 6, it arises from the fertilization of an empty ovum lacking maternal genes, ref 6, the sperm then duplicate, making diploid number of chromosomes which are therefore entirely male in origin, thus no embryonic tissue is present, ref 8, 9. The overgrowth of the Placenta is benign but can metastasize if left untreated. Invasive Moles occur as a result of local invasion of the Myometrium by a complete or partial mole, ref 7, 8, 9, in the spectrum of malignant potential they are intermediate between Hydatidiform Moles and Choriocarcinomas, ref 8, 9, 10. Invasive Mole – Chorioadenoma Destructans - are locally invasive, rarely metastatic, characterized by trophoblastic invasion of the Myometrium, which identifiable villous structure, they are more aggressive than Partial and Complete Moles, however unlike Choriocarcinomas they can regress spontaneously.

The age distribution of the Patients in this study showed 2 peaks, <20 Years, 40% of Patients and 41-50 Years 35% of Patients, Mean Age 30.3 years, Median 30.1, Age Range 19 - 50. As Hydatidiform Moles are more common at the extremes of reproductive age, in Women in the early teens age or perimenopausal women, this is similar to what is reported in the literature, ref 1. Invasive Moles occur in the First pregnancy in 39 Patients, 48.7% this is higher than what is reported in the literature, followed by Para 1, 14 Patients, 17.5%, 38 Patients, 47.5%, were from Khartoum State. 50 Patients, 46 patients, 57.5% presented with BHCG level less than 1000, low risk group, 14 patients, 17.5% with 1000 - 10 000, medium risk; 20 patients, 12.5% 10 000 - 40 000, high risk.

Medium Risk group, and 20% more than 40 000 High risk group. All patients had CXR, US Abdomen, BHCG Level, BHCG was the most sensitive detector, CBC, LFT and UE, at presentation and for follow up, and BHCG level after each cycle of Chemotherapy, in the Patients who had progressive rise of BHCG, CT Abdomen, Chest and Brain were done and were normal. All Patients had evacuation first by suction or by D and C, most patients 56.78% had positive pathology. The Chemotherapy used in the treatment, depended on the risk level, and consisted of low dose Methotrexate MTX Single agent in low risk group, MTX and Actinomycine D or Etoposide, are used in medium and high risk patients. EMACO was used in 2 patients with progressive rise in the BHCG level during Chemotherapy without evidence of distant metastases. 2 cycles of chemo were given after normalization of BHCG, main side effects were, Mucoisit and Nausea, asymptomatic elevation of Liver Function Tests, Alopecia and Myelosuppression were rare, as reported in other studies, ref 9, 10. Patients were advised to use Contraceptive Pills as progestational rhad of contraception during chemo and for one year after chemotherapy. All our patients achieved Complete response and Normal BHCG levels following Chemotherapy except the mentioned 2 patients who were switched to EMACO because of progressive rise in BHCG during Chemotherapy, we lost one of them due to Septicemia, one of them is still under follow up with plateauing of her BHCG. All Patients were followed by BHCG Levels every 3 months, and were discharged from follow up if the 3 BHCG levels were normal, 72 patients, 90%, the other 6 patients had arising BHCG after finishing the initial chemotherapy, and had more Chemotherapy and all of them were followed after chemotherapy monthly BHCG and were discharged from follow up after 6 consecutive normal BHCG levels.

There is no method to predict accurately the clinical behavior of Hydatidiform Moles by histopathology, the clinical course is defined by the serum level of BHCG curve after evacuation of the Mole, in 80% of benign Hydatidiform Moles, serum BHCG levels steadily drop to normal within 8 – 12 weeks after evacuation of the Molar Pregnancy, in the other 20% patients with malignant Moles, serum BHCG either rise or plateau, ref 11, 12.
of their sample recovered and 3.3% died of Metastatic disease, so our results are much better.

It's important that the disease be diagnosed earlier, and Chemotherapy should be given urgently, for this highly curable disease, which is often cured with a single Cytotoxic drug.

**References**


**Acknowledgement:** We would like to acknowledge all our patients for agreeing to be included in this study, and our colleagues at the Radiation and Isotopes Centre of Khartoum for their support. This Study was approved by our Ethical committee. All authors have no conflict of interest to declare.
Myoepithelial carcinoma arising in a benign myoepithelioma of the palate. Case report and literature review

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Key words: Head and neck cancer, Myoepithelial carcinoma, Palate tumor, Myoepithelioma, Salivary glands carcinoma.

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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: plasmocytoïd-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 submucosal, 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: epithelioid (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 myoepitheliomas. 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 myoepithelial tumours 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 epithelioid 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, epi-myoepithelial carcinoma, and metastatic renal cell carcinoma [17]. Melanoma, high-grade lymphoma, or plasmacytoid 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 tumour-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 myoepitheliomas, myoepithelial carcinoma shows higher 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 myoepithelial carcinomas 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. Similarly, 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 myoepitheliomas [12].

Conclusion

We report a rare case of myoepithelial carcinoma arising in a benign myoepithelioma of the soft palate. Myoepithelial carcinomas 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), 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


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The Eighth Regional Meeting of The Lebanese Society of HEMATOLOGY & BLOOD TRANSFUSION

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PRELIMINARY INVITED FACULTY

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<tbody>
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News From The Arab World

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- Discuss the latest advances in anti-angiogenic treatment approaches of different solid malignancies
- Recommend the most appropriate ways for them to implement clinical changes in their clinical environment
- Identify the priorities for implementation in their practice that will make the largest improvement in patient care

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<td>JANUARY</td>
<td>Cervical Cancer Awareness Month</td>
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<tr>
<td>FEBRUARY</td>
<td>Screening and Early Detection Awareness Month</td>
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<td>MARCH</td>
<td>Colorectal Cancer Awareness Month</td>
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<td>APRIL</td>
<td>Cancer Fatigue Awareness Month</td>
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<td>MAY</td>
<td>Melanoma and Skin Cancer Awareness Month</td>
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<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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<td>AUGUST</td>
<td>Pain Medicine and Palliative Care</td>
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<td>SEPTEMBER</td>
<td>Gynecologic Cancer Awareness Month Prostate Cancer Awareness Month Leukemia and Lymphoma Awareness Month</td>
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<td>OCTOBER</td>
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<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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Objectives & Scope Of The PAJO

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.
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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.

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All reviews must be clinically oriented, ie, 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.
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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.

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