

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

Dr Kamal E.H.Mohamed, FFRRCSI,DMRT,DSN¹; Dr Muna M.A. Kaboush, MD²; Dr Mohamed O. Omer³

(1) Assoc Prof of Oncology, Faculty of Medicine, University of Khartoum

(2) Consultant Oncologist, RICK.

(3) Consultant Oncologist MD,RICK.

✉ Corresponding Author: Dr. Kamal E.H.Mohamed, FFRRCSI, DMRT, DSN

Assoc. Prof. of Oncology

Faculty of Medicine, University of Khartoum, Sudan

e-mail: kamaledein4@yahoo.com

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 its 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 and Curettage, 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.

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.

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

< 20 Years	32	40 %
21 – 30	14	17.5%
31 – 40	6	7.5%
41 – 50	28	35%

Mean Age = 30 years

Median = 30.1

Age Range = 19-50 years

Parity:		
First Abortion	39	48.7%
Para one	14	17.5%
Para	34	5%
Para	46	7.5%
Para 5	7	8.7%
Para 6	6	7.5%
Para 7	4	5%

Residence:		
Khartoum	38	47.5%
Central Sudan	16	20%
Northern Sudan	10	12.5%
Western Sudan	8	10%
Eastern Sudan	8	10%

Clinical Presentation of Cases:

Symptom	Number of cases	Percentage
Vginal Bleeding	74	92.5%
Passage of Moles	63	78.5%
Lower Abdominal pain	54	67.5%
Vomiting	43	53.7%

Some patients have multiple symptoms

BHCG Level at Presentation:

<500	22	27.5%
500 – 1000	24	30%
1000 – 10 000	14	17.5%
10 000 – 40 000	6	7.5%
40 000 – 100 000	8	10%
>100 000	6	7.5%

Number of Cycles of Chemotherapy ,before Normalization of BHCG Level:

3 Cycles	10	12.5%
4 Cycles	20	25%
5 Cycles	22	27.5%
6 Cycles	24	30%
Progressive Disease, EMACO Chemo.	2	2.5%

Discussion

Gestational Trophoblastic Disease encompasses a unique group of uncommon but interrelated conditions, derived from the placental trophoblasts, with a wide 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 6,7, the sperm then duplicates, making a 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, 7,8,9, in the spectrum of malignant potential they are intermediate between Hydatidiform Moles and Choriocarcinomas, ref 8,9,10. Invasive Mole – Chorionadenoma destruens, are locally invasive, rarely metastatic, characterized by trophoblastic invasion of the Myometrium, with

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 Actinomycin 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, Mucositis 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 or any other form 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.

Conclusion

Invasive Moles form less than 1% of all female Cancers in Sudan, but they mainly affect very young women at child bearing age, hence it is important to cure them, in this study they are curable in almost 100% of cases, we used low dose MTX in low risk Patients, with minimum morbidity and Complete response in all of them, and MTX, Actinomycin D, and or Etoposide.

In Medium Risk and HIGH Risk Patients, no patient had Hysterectomies, in Nizam study, from Pakistan, ref 3, 13.3% of Patients had Hysterectomies, 96.7%

of their sample recovered and 3.3% died of Metastatic disease, so our results are much better .

Its 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

1. Jefers MD, OdwerP, Curran B, Partial Moles ,Int.J.Gynae. pathology ,Oct 1993,12(4),315 – 323.
2. Lurian JR, Brewer J, MorrowCP, Natural History of Hydatidiform Moles, Am.J.ofObs and Gynae.Feb 1993,145,(5),519 –525.
3. Nizam K, HaiderG, Memon N, Haider A, Gestational Trophoblastic Disease, experience of Nawabashah hospital, J of Ayoub Med Coleg Abotabad,2009, Jn – Mrch,21,(1),94 – 97.
4. Goto S, Yamada A, Ishizaka T, Development of post Molar Pregnancy,J. Gynae Oncol, Feb1993,48,(2),165 – 70.
5. Cheung AN, Yamada A ,Ishizuka T, Metastatic Trophoblastic Disease after Partial Moles, Cancer ,April 2004,100,(7),141 – 7.
6. Menczer J, Girthero, Zajdel L, Glezerman Metal, Metastatic Trophoblastic Disease following Partial Moles review, J.GynaeOncol., August 1999,64,(2),304- 7.
7. FIGO Oncology Committee .FIGO staging for GTD,2000, Int J. OF gynae. Obstet.2002 June,77(3):285 – 7.
8. McCarthy A, etal, Master in Obst and Gynae..2nd edition, UK: Churchil and Livingstone;2003.
9. Seckl MJ, Smith EB, SzulmanAE, HinshawW, Choriocarcinoma and Partial Mole. Lancet, 2000 Jul,1;356(9223):36 – 9.
10. Barakat RR, etal, Hand Book of GynaeOncol ..UK, Martin Duntiz,2001.
11. Meneish IA, McNeish IA, StricklandS, Holdenl L, low risk GTD after treatment with low Methotrexate and Folinic Acid from 1992 – 2000 .J clinOncol 2002, Apr. 1,20 (70),1838 – 44.
12. Nizam K, Haider G, Memon N, Haider A, Ayoub Medical Coll.,2009, Jan –March,21,(1), 94 – 97.
13. Shakutala, Chabra, Ambreen Qureshi. J. Obst. Gyn. India., vol57, no2, March-April, 2007, 124-129

Acknowledgement: We would like to acknowledge all our patients for agreeing to be included in this study, and our colleages at the Radiation and Isotopes Centre of Khartoum for thire support.

This Study was a pproved by our Ethical committee.

All authors have no conflict of interest to declare.