

Growing teratoma syndrome in ovarian germ cell tumours — a diagnostic challenge, two case reports

Ayesha Saba, Rozilla Sadia Khan, Humera Ismail

Abstract

Growing teratoma syndrome (GTS) is a rare complication of ovarian germ cell tumours and occurs in young age group. It is characterized by clinical or radiological increase in tumour size during or after chemotherapy, with normalization of tumour marker levels. Histopathological tissue growth post chemotherapy is a mature teratoma without any malignant component. Mainstay of treatment is surgical excision of the disease to prevent progression of tumour as mature teratomas are resistant to both chemotherapy and radiotherapy. Diagnosis is a challenge as disease recurrence or chemoresistance can be difficult to distinguish. Benign nature of this disease entity is essential to avoid overzealous chemotherapy or radical surgery.

Keywords: Chemotherapy retroconversion, Germ cell tumour, Growing teratoma syndrome.

Introduction

Growing teratoma syndrome (GTS) is a rare clinical entity first described by Logothetis et al in 1982. GTS is chemotherapeutic retro-conversion characterized by an increase in metastatic mass after complete eradication of a primary malignant ovarian germ cell tumour and by normalization of serum tumour markers, either during or after chemotherapy.^{1,2} Incidence of GTS is 12% after ovarian germ cell tumours.^{3,4} There are one hundred one cases of ovarian GTS from literature published between 1977 and 2015.⁵ Reason for occurrence of GTS is not exactly known but hypothetically there are two major inferences of GTS formation that is chemotherapy transforms malignant cells into "benign" teratomatous elements and chemotherapy can only destroy malignant cells leaving chemoresistant teratoma behind.^{4,6} There are three criteria according to the Logothetis definition which include; (i) Normalization of serum tumour markers, (ii) Enlarging or new masses despite appropriate chemotherapy, (iii) The exclusive presence of mature teratoma in the resected specimen.⁷

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Aga Khan University Hospital, Karachi.

Correspondence: Ayesha Saba. Email: ayeshasaba880@gmail.com

Diagnosis is a challenge as disease recurrence or chemoresistance can be difficult to distinguish. Benign nature of this disease entity is essential to avoid overzealous chemotherapy or radical surgery. Mainstay of treatment is surgical excision as mature teratoma, are resistant to both chemotherapy and radiotherapy.⁸ We describe two patients with GTS who developed GTS after primary surgery and chemotherapy for immature teratoma of the ovary.

Case-1

A 21 years old lady, unmarried presented in March 2014 with two months history of abdominal distension and abdominal mass. She was diagnosed to have left ovarian mass with raised serum CA-125 258units/ml and raised alpha fetoprotein 8232ng/ml. B-HCG was normal 4.75miu/ml. Pre-chemotherapy Computerized tomography (CT) scan suggested a 13x6.5cm mass in the left adnexa with mild ascites. She was diagnosed to have mixed germ cell tumour. After three cycles of chemotherapy in the form of bleomycin, etoposide and cisplatin her alpha fetoprotein normalized to 31ng/ml but the pelvic mass progressively increased in size. CT scan revealed presence of large left adnexal mass extended up to upper abdomen around 34.7x20cm. Her alpha fetoprotein was 2.2ng/ml. GTS was suspected. She underwent staging laparotomy, left salpingoophorectomy, left pelvic lymphadenectomy, peritoneal lavage, infracolic omentectomy and right ovarian cystectomy.

Histopathology revealed a left sided mature teratoma around 27x19x10cms with no immature tissues element. Alpha fetoprotein was 4.7ng/ml. Patient is on follow-up for twenty four months post-surgery with no recurrence.

Case Presentation 2

A 23 years old lady, unmarried presented in June 2013 post surgically having had a left salpino-oophorectomy with histopathology report showing immature teratoma 85%, yolk sac tumour 15% and neuroepithelial element of right ovary. After receiving three cycles of chemotherapy in the form of bleomycin, etoposide and cisplatin, she presented with recurrent pelvic mass on right side. CT

scan showed a large soft tissue mass 7.1x4cms in size on the right side. Her alpha fetoprotein was 7.4ng/ml. She underwent exploratory laparotomy, removal of right adnexal mass, total omentectomy and peritoneal lavage. Histopathology showed mature teratoma with no immature element. Patient is on follow-up for six months post-surgery with no recurrence.

Discussion

GTS is defined as an enlarging mature teratoma that arises during or following chemotherapy for a malignant germ cell tumour. GTS may occur several years after diagnosis of the primary tumour. The main challenge is the correct diagnosis of this condition in the young patient in order to avoid misdiagnosis of recurrence, chemoresistant nature of the disease, fertility conservation issue and excessive courses of chemotherapy or radical surgery. The reason for occurrence of GTS is not exactly known but hypothetically there are two major inferences of GTS formation that chemotherapy transforms malignant cells into "benign" teratomatous elements and chemotherapy can only destroy malignant cells leaving chemoresistant teratoma behind.^{4,6} Very few cases are reported on young Asian women.⁹ Development of GTS had been reported as early as three months and delayed till eight years. Patients who had complete excision had longer disease-free interval up to eight years with lowered recurrence episodes.¹⁰ Malignant transformation has been reported up to 3%. GTS has an overall good prognosis with only a few reported deaths. The five years survival rate is 89%. Regular follow-up is essential as recurrence may ensue up to the ten years after the initial diagnosis.¹⁰ As this is a rare condition, there is no consensus to the number of cycles of chemotherapy required prior to surgery. There are few case reports in which three cycles of chemotherapy are mentioned. In our patient three cycles of chemotherapy in the form of BEP were given. Number of cycles also depends on level of serum CA-125 and progression of the

disease. Rebiopsy can up stage the tumour because of breach in capsule of the tumour. It is therefore advisable to remove the mass and confirm its nature by histopathology. There is no published study available to see the impact of pregnancy on disease relapse. Further studies are warranted.

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