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CASE REPORT

Growing Teratoma Syndrome Following Treatment for Immature Teratoma of Ovary-A Case Report and Review of Literature

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Introduction

Growing teratoma syndrome (GTS) refers to enlarging metastatic masses detected during or following chemotherapy for non-seminomatous tumours of testes/malignant ovarian germ cell tumours (GCTs) with teratomatous element; in a background of normal tumour

markers, the surgical excision of which confirms the presence of mature teratomatous element only.

We report the case of a premenarcheal girl who was treated for immature teratoma by surgery and chemotherapy, who later developed multiple peritoneal lesions, surgical resection of which revealed mature teratoma.

Case Report

A 13-year-old premenarcheal girl was evaluated for abdominal distension at a peripheral hospital. Ultrasound scan showed a complex cyst in the right adnexa. She underwent a laparotomy with right salpingo-oophorectomy through a Pfannenstiel incision. Histopathology suggested immature teratoma grade II (Fig. 1). She did not receive any adjuvant therapy. Three months later, she presented with progressive abdominal distension and vomiting. MRI of abdomen and pelvis showed a large heterogenous abdominopelvic mass with peritoneal deposits and massive ascites. Serum alpha-fetoprotein (AFP) was 790 ng/ml and serum lactate dehydrogenase (LDH) was 584 IU/L. Other tumour markers were normal. Since the ovarian mass was inseparable from the uterus, she underwent hysterectomy and left salpingo-oophorectomy. Optimal cytoreduction was achieved by performing infracolic omentectomy and excision of peritoneal deposits. Histopathology was reported as grade II immature teratomatous element admixed with mature teratomatous element with omental metastases.

At this point, she was referred to a tertiary cancer centre. Here, a repeat CT scan showed perihepatic fluid collection. Serum AFP was 35 ng/ml. Other tumour markers were normal. She was treated with 4 cycles of bleomycin, etoposide and cisplatin (BEP) regimen. Two more cycles of etoposide and cisplatin (EP) were added as ultrasonography revealed residual peritoneal disease. After the completion of treatment, patient was asymptomatic and clinical examination was normal. Two weeks after completing chemotherapy, she underwent a CT scan (Fig. 2) which showed diffuse heterogenous lesions in the perihepatic and perisplenic regions, with areas of fat densities and calcifications. Serum tumour markers were normal. On laparotomy, there were multiple subdiaphragmatic, subhepatic and splenic surface deposits. She underwent splenectomy (Fig. 3) with complete excision of deposits. The

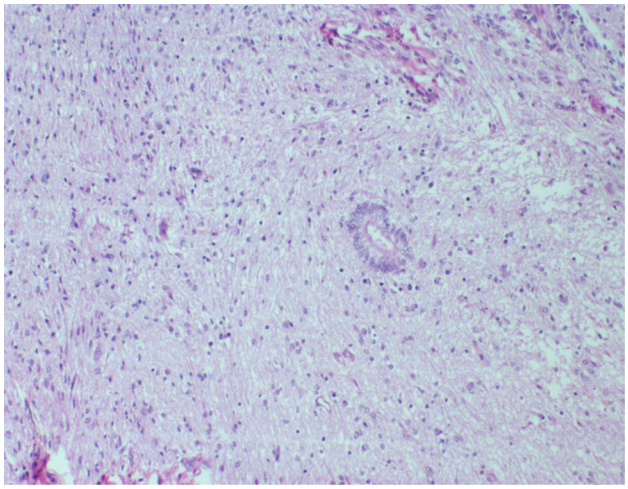

Fig. 1 Histopathological picture of specimen resected prior to chemotherapy showing immature teratomatous element—neuroepithelial tubule with glial tissue (×20)

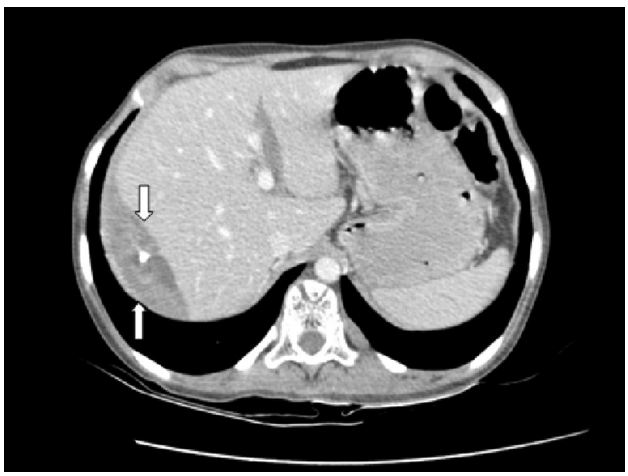

Fig. 2 CT scan taken after chemotherapy showing a heterogeneously enhancing soft tissue density lesion (marked by *arrows*) in the subcapsular region of liver with focal area of calcification

histopathology report was suggestive of mature teratoma (Fig. 4). Two and a half years after the last surgery, she remains asymptomatic, with no abnormalities on physical examination, imaging or tumour markers. She was given hormone replacement therapy (HRT).

Review of Literature

Logothetis coined the term growing teratoma syndrome (GTS) in 1982 to describe a clinical scenario reported in a case series of six patients with metastatic mixed GCTs of testes. Following treatment with appropriate chemotherapy, the patients were detected to have enlarging abdominal/

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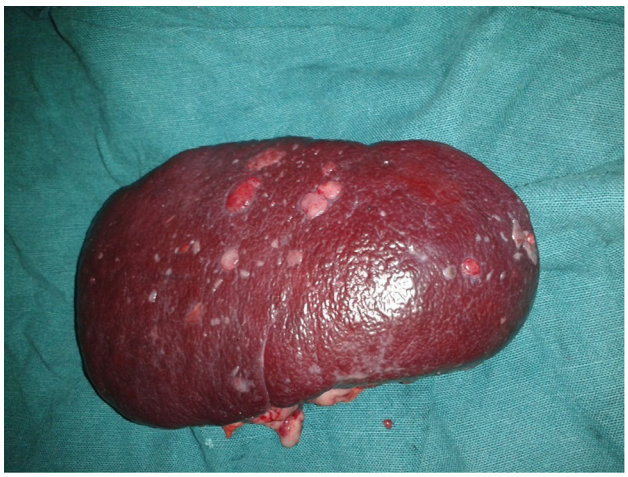

Fig. 3 Splenic subcapsular and hilar deposits on the splenectomy specimen

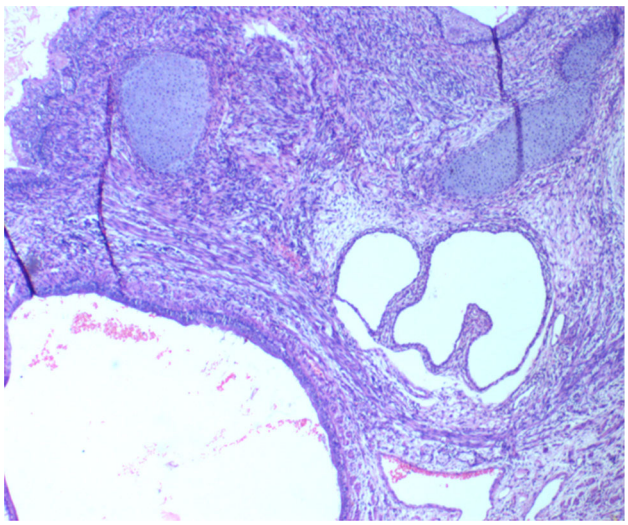

Fig. 4 Histopathological picture of specimen resected after chemotherapy showing only mature teratomatous element—cartilage and cystic spaces lined by mucinous epithelium (×20)

pulmonary masses in the presence of normal serum markers. The histopathology of these masses was consistent with mature teratoma.

The development of GTS may be from as early as during chemotherapy to even 12 years after completion of therapy [1]. The prevalence of GTS following ovarian GCTs is lower than the 1.9–7.9% reported for GTS following NSGCTs of testes [1]. The peak incidence of GTS occurs in the second and third decades of life.

The proposed hypotheses of GTS are as follows:

1. Regression of immature component in the tumour with persistence and growth of the mature component, the latter being resistant to chemotherapy.
2. Conversion of immature teratomatous element into mature teratomatous element by chemotherapy, i.e. chemotherapeutic retroconversion.
3. Spontaneous differentiation of malignant cells into benign tissue as suggested by the experimental murine teratocarcinoma mouse model offered by Hong et al. [1], the role of chemotherapy being to prolong the course of the disease to permit spontaneous evolution.

GTS is usually detected on serial imaging of patients treated for GCT. Patients may present with pressure symptoms if the lesions have remained undetected and grown large enough. The common sites of GTS include peritoneum, retroperitoneum, mesentery, lung and mediastinum. Peritoneum is the commonest site of GTS following an ovarian GCT [2]. Gliomatosis peritonei, i.e. peritoneal implants of benign glial tissue explained by chemotherapeutic retroconversion of neuroectodermal elements have been described [3].

Regular imaging of patients on follow up for malignant GCTs is the key to early diagnosis and treatment. However, it is not possible to distinguish between recurrent malignancy and GTS based on CT/PET scan findings alone. Tumour markers, if elevated, may suggest recurrence. In case of marker negative immature teratoma, which constitutes one-third of all immature teratoma cases, preoperative differentiation is difficult.

Thorough surgical resection at the earliest is the mainstay of treatment. Delay in detection and treatment can make the tumour unrespectable, with the accompanying risks of vascular thrombosis, ureteric/bowel obstruction, colonic fistula and rarely malignant transformation. Delayed surgical intervention may increase the risk of major vessel/organ injury. Most of the mortality due to GTS is attributed to post-operative complications [1].

The completeness of resection is a major factor predicting prognosis. Andre et al. [4] reported a recurrence rate of 4% in case of total resection, and 83% following partial resection of GTS. A 5-year survival of 89% is reported with complete surgical resection [1].

The medical management of unrespectable GTS with interferon alpha, bevacizumab and CDK (cyclin-dependent kinase) 4/6 inhibitors is experimental [2].

Discussion

In this case report, the patient had a non-comprehensive staging at initial presentation. She did not receive any adjuvant therapy based on the assumption that it was a Stage Ia grade II immature teratoma. She presented with metastatic disease soon thereafter (3 months). This highlights the importance of meticulous staging and

appropriate adjuvant chemotherapy in malignant ovarian GCT. At recurrence, although the patient had peritoneal dissemination, hysterectomy may have been avoided by the administration of chemotherapy prior to surgery.

Andre et al. described the following as predictors for GTS:

1. The existence of mature teratoma in the first tumour,
2. Incomplete resection of primary tumour and.
3. The absence of response of the metastasis after chemotherapy [4].

The above three factors were present in this case.

Following complete surgical resection of GTS, the patient is disease free for the last two and half years. Hormone replacement therapy (HRT) is not known to have a deleterious effect on either GCT or GTS. Therefore, she is on HRT to improve her quality of life and to reduce the risk of cardiovascular events and osteoporosis.

This case report intends to increase the awareness of GTS, as well as highlight the importance of comprehensive staging and tailored chemotherapy in malignant ovarian GCTs to maintain the possibility of cure while preserving fertility.

Conclusion

Growing teratoma syndrome is a rare outcome following treatment of malignant germ cell tumours. It is suspected in patients with non-seminomatous GCT/GCT with immature teratomatous element (during/post-chemotherapy), when metastatic masses increase in size despite normal tumour markers. Complete surgical resection is the gold standard of treatment. The diagnosis is confirmed by the exclusive presence of mature teratomatous element in the resected specimen.

Compliance with Ethical standards

Conflict of interest Leena Rose Johnson, Suchetha S, Rema P, Rari P Mony, Jiss Elizabeth Sebastian, Iqbal M. Ahamed declare that they have no conflict of interest.

Ethical Statement All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

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