Growing Teratoma Syndrome Presenting as Skin Nodules: A Rare Entity

Abstract
Growing teratoma syndrome (GTS) an extremely rare phenomenon complicating malignant ovarian germ cell tumours. Till date very few have been reported. Growing teratoma syndrome (GTS) is characterised by increase in the size of a tumour occurring during or after chemotherapy for mixed germ cell tumour. Complete surgical resection not only confirms the diagnosis, revealing mature teratoma component, but also is most effective therapy offering cure. GTS commonly occurs in previously diseased sites such as retroperitoneum, chest, while uncommon sites include supravacular lymph nodes, lung, mediastinum, inguinal lymph nodes, mesentery and liver. To the best of our knowledge (GTS) involving the skin has not been reported in the past. We hereby report a rare case of paediatric mixed ovarian germ cell tumour with skin metastasis, along with its review of literature. A 12-year-old female presented who had abdominal distension and skin nodules, on the anterior abdominal wall and right lower posterior chest wall. She had previously undergone ovarian cystectomy elsewhere, followed by cisplatin and etoposide based chemotherapy for a left ovarian immature teratoma one year back. Recent Imaging showed solid and cystic mass in pelvic and abdominal cavity with calcification and widespread diffuse peritoneal deposits. As tumour markers (AFP, LDH, betaHCG) were within the normal range, a clinical diagnosis of GTS was made. She underwent complete cytoreductive surgery and wedge resection of skin nodules. Histopathology of all sample revealed mature cystic teratoma.

Keywords: Growing teratoma syndrome, Skin nodules

Introduction
Paediatrics germ cell tumours are uncommon tumours comprising 2 to 3% pediatric malignancy, of which 80% are benign while only 20% are malignant [1]. Immature teratoma occurs in 1% of ovarian tumours, median age of presentation is 10 years [2]. The most common complaint is abdominal pain with palpable abdominal mass [3]. Primary treatment is surgery for GCTs and chemotherapy depending on stage and grade of immature teratoma [4].

Growing teratoma syndrome (GTS) is a rare metastatic complication of treatment of non-seminomatus germ cell tumour, which contain mature teratoma components in context of normalized serum markers [5]. The development of GTS had been reported from few months to few years after chemotherapy. The metastatic masses can occur anywhere in the pelvis, retroperitoneum, liver, lungs and mediastinum. Mature teratoma is resistant to radiotherapy and chemotherapy, complete surgical excision is the cornerstone of treatment and should be done as early as possible for several reasons, to confirm the diagnosis, to relieve pressure symptoms on surrounding organs, and to prevent malignant transformation. A long term prognosis is generally favourable [6]. Here we report the first case of growing teratoma syndrome with skin involvement.

Case Report
A 12-year-old female, presented with abdominal distension and two skin nodules since 2 months. She had undergone left ovarian cystectomy elsewhere one year back for adnexal mass. Previous histopathological reports showed a grade three immature teratoma for which she received four cycles etoposide, and cisplatin based chemotherapy. She was asymptomatic until 2 months back. On examination there was generalised distension of abdomen which moved with respiration. She had 2 skin nodules, one on anterior abdominal wall just below the xiphi-sternum (Figure 1) and second on right sided posterior chest wall at lower ribs (Figure 2). Each measured about 4 × 3 cm. They were both fixed to the skin but free from the underlying structures and were not-tender. The rest of her physical examination was essentially normal.

Figure 1: Shows skin nodules on anterior abdominal wall just below the xiphi-sternum.
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Contrast enhanced CT abdomen and pelvis showed 70 x 61 mm size heterogeneously enhancing soft tissue density with calcification noted posterior to urinary bladder (Figure 3) and metastatic peritoneal deposits and moderate ascites. Both ovary and uterus are not seen separately from lesion. There was no evidence of abdominal lymphadenopathy or liver metastasis. CT thorax was normal. Complete blood count, renal function and liver function tests were within normal limits. Tumour markers (alpha fetoprotein, beta human chorionic gonadotropin) were in normal range.

At multidisciplinary tumour board meeting, it was decided that diagnosis of growing teratoma syndrome (GTS) would require histopathology confirmation. Biopsy would be of little benefit as complete surgical excision of tumour would not only confirm the diagnosis, but also be the most effective therapy offering cure.

She underwent laparotomy with complete cytoreductive surgery involving hysterectomy, bilateral salpingo-oophorectomy, and debulking of tumour tissue from peritoneum, pelvis, and iliac fossa. Wide local excision of skin nodules was also done. Histopathology report of all submitted specimen revealed mature cystic teratoma without any malignant components (Figure 4 & 5). No further chemotherapy was needed. Currently, she has no evidence of disease and is undergoing regular follow up in cancer survivor clinic since 1 year.

Discussion

Paediatrics germ cell tumours are rare. In general, 80% of GCTs are benign while only 20% are malignant. Teratoma is the most frequent germ tumour of the ovary while immature teratoma represents only 1% of ovarian tumours. It is usually seen in women of the first two decades and contains immature neural tissues, determining the grade of the tumour [1]. Primary treatment is surgery for GCTs and chemotherapy depending on stage and grade of immature teratoma. Most patients with immature teratoma of ovary are in their reproductive years and wish to preserve fertility. As germ cell tumours are extremely chemosensitive, fertility preserving surgery (unilateral salpingo-oophorectomy) followed by combination chemotherapy has become the standard treatment for early stage of immature teratoma [4].
Growing teratoma syndrome (GTS) is an uncommon metastatic complication seen in mixed germ cell tumour, with an incidence of 1.9 to 7.6% in testicular NSGCT and is even rarer in ovarian immature teratoma [5]. GTS is known to occur few months to several years after chemotherapy.

Growing teratoma syndrome was firstly narrated by Logothetis et al. in 1982, as conversion of immature gonadal germ cell tumour to a mature form and increase in tumour size during or after chemotherapy [7]. In 1977, DiSaia et al. [8] reported a similar phenomenon called “chemotherapeutic retroversion” [8]. Three simultaneous ways of dissemination of GTS are suggested: peritoneal, lymphatic and haematogenous [9]. Distant relapses (liver, chest, and mediastinum) or retroperitoneal GTS (paraaortic lymph nodes) is more common in testicular germ cell tumours [6]. Distant GTS suggests the existence of metastatic malignant cells in these regions at the time of the initial diagnosis.

The metastatic masses may occur anywhere in the pelvis, retro peritoneum, liver, lungs or mediastinum and onset of their appearance after completion of treatment is variable. GTS commonly occurs in previously diseased sites such as retro peritoneum, chest, while uncommon sites include supraclavicular lymph nodes, lung, mediastinum, inguinal lymph nodes, mesentery and liver [10].

This is one of the first reported growing teratoma with skin involvement. The possible explanation for the appearance of growing teratoma syndrome may be due to micro metastases of the immature teratoma cells within the peritoneal cavity and skin. This may be as a result of intra- abdominal dissemination despite intact capsule which may occur spontaneously preoperatively.

The physiopathology of growing Teratoma syndrome is elusive and various theories have been postulated, stating it results from the metamorphosis of malignant cells into mature cells under chemotherapy [11] or chemotherapy is successful into extinguishing the immature component and allowing the mature tissue to thrive. Clinically both these processes can mimic malignant metastases. Similar phenomenon has been described with non-seminomatous germ-cell tumours arising from the testis, the mediastinum and the pineal gland [12].

Three criteria must be fulfilled for a diagnosis of growing teratoma syndrome: (1) Clinical or radiological enlargement of tumour during or after chemotherapy, (2) Normalization of previously elevated tumour markers, (3) Subsequent surgery revealing mature teratoma without malignant cells on histological examination.

The lesions often expand quickly and symptoms are often non-specific, usually consisting of mass effect or compressive symptoms, which require surgery. Since mature teratoma is resistant to radiotherapy and chemotherapy, complete surgical excision is the only curative treatment and should be done whenever possible for several reasons, to confirm the diagnosis, to relieve pressure symptoms on surrounding organs, to prevent malignant transformation. A long term prognosis is generally favourable. Early decision for complete resection had lowered morbidity in this patient as with delay, GTS that can grow rapidly may encase the blood vessels and other vital structures leading to pressure effect and potential risk of vascular thrombosis, ureteral obstruction, bowel obstruction, or colonic fistula [13].

The majority of mortality of GTS is related to postoperative complications.

GTS neither should be mistaken for signs of disease progression nor should chemotherapy be given, as lesions are chemo refractory. Though the final diagnosis depends on the histologic confirmation of mature elements, it is important for a clinician to be aware of this entity, for the proper diagnosis and to avoid mismanagement.

References
