Growing Teratoma Syndrome: A Rare Case Report

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Abstract:
Introduction - Growing teratoma syndrome (GTS) refers to metastatic masses from non-seminomatous germ cell tumors (NSGCT) containing mature teratoma, enlarging during or after chemotherapy. Surgery is the only chance of cure for these patients and is often difficult. Early exploration optimizes the chance of complete resection which is necessary for long term survival. Case report - We report a case of growing teratoma syndrome in a 24 year old male who had undergone orchiectomy for NSGCT in the right undescended intraabdominal testis in a private hospital in January 2010 after which he received 4 cycles of BEP (Bleomycin-Etoposide-Cisplatin) and 2 cycles of EP (Etoposide - Cisplatin) chemotherapy. The initial stage was stage IIIB (T1 N2 M1a S2). After completion of chemotherapy he had no residual disease on CT scans of chest and abdomen and his tumour markers were normal. But on followup CT scan done in September 2010, he had developed a retroperitoneal mass with normal serum markers. He was followed up in the same hospital with serial CT scans and tumour markers till June 2012. The tumour markers were constantly normal and the mass was growing slowly. With these findings he presented to our department in June 2012. He was evaluated for metastatic disease and underwent laparatomy and excision of the mass. The post-operative histopathology was consistent with mature teratoma. Conclusion - Growing teratoma syndrome occurs in 1.9-7.6 percent of patients with metastatic nonseminomatous germ cell tumours. Vigilant and frequent imaging helps in its early diagnosis. Prompt and complete surgical resection are essential in giving the best chance for cure, preventing local complications and development of second malignancies.

Keyword: Growing teratoma syndrome, NSGCT, Retroperitoneal mass

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Case report:
We report a case of growing teratoma syndrome in a 24 year old male who had underwent orchiectomy for NSGCT in the right undescended intra-abdominal testis in a private hospital in January 2010 after which he received 4 cycles of BEP (Bleomycin-Etoposide-Cisplatin) and 2 cycles of EP (Etoposide - Cisplatin) chemotherapy. The initial stage was stage IIIB (T1 N2 M1a S2). After completion of chemotherapy he had no residual disease on CT scans of chest and abdomen and his tumour markers were normal. But on follow up CT scan done in September 2010, he had developed a retroperitoneal mass with normal serum markers. He was followed up in the same hospital with serial CT scans and tumour markers till June 2012. The tumour markers were constantly normal and the mass was growing slowly. With these findings he presented to our department in June 2012. He was evaluated for metastatic disease and underwent laparotomy and excision of the mass. The postoperative histopathology was consistent with mature teratoma.

Conclusion:
Growing teratoma syndrome occurs in 1.9-7.6 percent of patients with metastatic non-seminomatous germ cell tumours. Vigilant and frequent imaging helps in its early diagnosis. Prompt and complete surgical resection is essential in giving the best chance for cure, preventing local complications, and development of second malignancies.

INTRODUCTION:
Testicular tumors account for 1 percent of all male neoplasms and are the most common cancers in the 20-30 year age group. The dissemination route primarily involves the retroperitoneal lymph nodes and hematogenous metastases occur at a later stage in the course of the disease. The prognosis of these tumors has improved with chemotherapy and today over 90 percent of patients have good prognosis. Even those with extensive metastatic disease can be cured [1]. Following chemotherapy, the retroperitoneal metastases may either regress completely or persist as a residual mass that remains stable or increases in size over a period of time. A retroperitoneal mass usually enlarges during the course of chemotherapy due to treatment failure but on rare occasions due to an enlarging mature teratoma, as has been termed the ‘growing teratoma syndrome’ by Logothetis et al [2]. The growing teratoma syndrome (GTS) occurs in about 1.9-7.6 percent of metastatic non-seminomatous germ cell tumors. It is characterized by clinical or radiological enlargement of metastases during or after chemotherapy, in the presence of normal serum tumor markers. Surgery is the only curative treatment and histological analysis after resection usually reveals mature teratoma, without active tumor evidence. We report a case of growing teratoma syndrome. The natural history of the GTS is difficult to predict and is characterized by local complications, a potential for metastasis, malignant transformation and the risk of late recurrence. Complete surgical resection is the treatment of choice for GTS which avoids most of these complications.
CASE REPORT:
We report a case of growing teratoma syndrome in a 24 year old male who had underw ENT ORCHIECTOMY FOR NSGCT IN THE RIGHT UNDescENDED INTRA ABDOMINAL TESTIS IN A PRIVATE HOSPITAL IN JANUARY 2010. The post-operative histopathology was reported as non-seminomatous tumor - mixed cell type (predominant of embryonal type with yolk sac tumor and occasional teratomatous element seen). He had bilateral lung metastasis, multiple paraaortic, para-caval nodes, peri-pancreatic and mediastinal nodes on CT scans of chest and abdomen. His tumor markers were HCG - 40,650 mIU/mL, Alfa-fetoprotein - 95ng/ml, LDH - 185 IU/. The initial stage was stage IIIB (T1 N2 M1a S2). He received 4 cycles of BEP (Bleomycin-Etoposide- Cisplatin) and 2 cycles of EP (Etoposide -Cisplatin) chemotherapy in the same hospital. After completion of chemo therapy, a CT scan of chest and abdomen taken in April 2010 revealed no residual lesions and his serum tumor markers were normal. He was on regular follow up in that hospital where a CT scan done in September 2010 revealed no residual lesions and his serum tumor markers were normal. He was on regular follow up in that hospital where a CT scan done in September 2010 revealed no-contrast enhancing cystic and solid retroperitoneal mass 5x7 x5 cm with features suggestive of a teratoma. His tumor markers were normal. He was kept on regular follow up in the same hospital with serial CT scan and tumor markers. The tumours markers were normal and the mass was slowly growing to 10x8x5 cm size in June 2012. With this history the patient presented to our department in June 2012. On examination, his performance status was ECOG-1. General Examination was normal. He had no peripheral lymphadenopathy. Per abdomen, there was a 15x10 cm retroperitoneal mass in the epigastrium extending to umbilical region, multi-lobulated and hard in consistency. There was no organomegaly or free fluid. Right testis was absent and scrotal sac was hypo-plastic. Left Testis was normal. Supraclavicular and inguinal region were normal. His Routine blood counts, liver functions and renal parameters were normal. CT Chest and Chest X Ray were normal. CT scan of the Abdomen showed a well demarcated, multicystic and hypo intense mass lesion abutting IVC and Left renal vein. Serum tumor markers were normal. There was no evidence of other metastases. We planned for a laparotomy and excision of the mass. He underwent laparotomy in July 2012. During laparotomy, there was a large retroperitoneal mass of 12 x 10 cm size situated behind the duodenum and pancreas and adherent to IVC. The mass was excised in toto after carefully separating the adhesions. A small iatrogenic tear in IVC was repaired. The post-operative period was uneventful. The post-operative Histopathology revealed a 12x 10 cm solid and cystic mass shows multiple cystic spaces lined by ciliated columnar epithelium, some foci showing stratified epithelial some foci lined by flattened cuboidal cells with intervening areas of fibrocollagenous tissue, hemorrhage, hemosiderin laden macrophages, areas of necrosis. Few foci show dense inflammatory cells composed of mature lymphocytes. The Impression was of features consistent with mature teratoma.

DISCUSSION:
Growing teratoma syndrome (GTS) refers to enlarging retroperitoneal or other metastatic masses containing mature teratoma during or after chemotherapy for nonseminomatous germ cell tumors (NSGCT). Growing teratoma syndrome (GTS) was described as an independent entity in 1982 by Logothetis et al and occurs in 1.9-7.6 percent of patients with
metastatic nonseminomatous germ cell tumors who receive chemotherapy. The clinical definition of growing teratoma syndrome (7,9,13) includes:

(a) History of a nonseminomatous testicular neoplasm with a teratomatous component in the primary specimen
(b) Elevated serum levels of AFP, hCG and/or LDH with radiologic evidence of metastatic disease
(c) Normalization of biomarkers after chemotherapy
(d) Enlargement of the metastatic masses despite normal tumor markers during or after chemotherapy
(e) Mature teratoma in the resected metastatic specimen. There is no specific size or growth rate of a metastatic lesion that is diagnostic for growing teratoma syndrome. The presence of teratomatous elements in the orchiectomy specimen should raise the clinical suspicion of growing teratoma syndrome provided the previously mentioned criteria are met. The etiology of these masses is uncertain, but it is known that the embryonal cells are multipotential. Their origin is supposed to be the result of differentiation of tumour cells which may derive from yolk sac compounds. Yolk sac histology is frequently reported to associate with growing teratoma syndrome. Chemotherapeutic Retro conversion (CR), a similar terminology was first defined in 1977 by DiSaia (4) as a chemotherapy mediated transformation of a metastatic immature teratoma into mature teratoma where the masses do not increase in size. He hypothesized two possible mechanisms for this process (a) chemotherapy either promotes the conversion of immature teratomatous tissue into mature tissue (b) chemotherapy destroy only the immature component leaving the mature tissue behind. In growing teratoma syndrome, not only must the nodules undergo chemotherapeutic retro conversion, but they must also have the ability to grow in size. Growing teratoma syndrome has been reported in the retro-peritoneum (the most common site), lung, cervical & inguinal nodes, mediastinum, mesentery, forearm and liver (13). Although histologically benign, local expansile growth can cause compression and lead on to complications like arterial and venous thrombosis, ureter encasement, small bowel gangrene. An enlarging retroperitoneal mass in the presence of normal biomarkers needs an exploratory laparotomy not only because growing teratoma syndrome carries the risk of progressive compression on adjacent organs but also unresected mature teratoma in the retroperitoneum has the potential to metastasize or to differentiate into more aggressive tumours. In growing teratoma syndrome, CT scan may show a well circumscribed, increase or new onset of cystic changes in the mass, increase in low density with fat and calcifications may suggestive growing teratoma syndrome. FDG PET assists in identifying growing teratoma syndrome by separating viable tumour from necrosis and mature teratoma (14). Surgery is often difficult and early exploration optimizes the chances of complete resection which is necessary for long term survival. Such aggressive surgeries not without surgical challenges (12) include large vessel and ureteric injury. Post op complications like ileus, chylous ascites, pancreatitis and sepsis quite common. Multiple operations are necessary in some cases. Logothetis et al, Tongaonkar et al and Lorigan et al have all reported excellent survival rates of nearing

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100 percent with surgery alone and they emphasized the importance of early surgery. Several surgical approaches have been described (15) which include
(a) Resection of the mass only
(b) Template retroperitoneal lymph node dissection
(c) Complete bilateral retroperitoneal lymph node dissection. Drainage of cystic masses (13) has been used to palliate some patients with inoperable lesions. Early surgery is the only curative treatment and histological analysis after resection usually detects only mature teratoma, without active tumor evidence. Survival rates can approach 100 percent only through early exploration. Close follow-up is necessary as relapses are frequent. The administration of interferon and bevacizumab to induce shrinkage of some metastases composed only of differentiated teratoma has been reported. Both have shown to induce significant clinical improvement and stabilization of partially resected mass (16).

CONCLUSION:
Growing teratoma syndrome occurs in 1.9-7.6 percent of patients with metastatic nonseminomatous germ cell tumours. Vigilant and frequent imaging helps in its early diagnosis. Prompt and complete surgical resection is essential in giving the best chance for cure, preventing local complications and development of second malignancies.
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