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Case report: Growing teratoma syndrome

Shrestha R[1*], Maity N[2], Dasgupta R[3], Shrestha S[4]
[1] Fellow in Gynaecological Oncology, Tata Medical Center, Kolkata, India. Assistant professor, Department of Obs/ Gynae, BPKIHS, Dharan, Nepal
[2, 3] Past-fellow in Oncopathology and Gynaecological Oncology, Tata Medical Center, Kolkata, India
[4] College of Nursing (Master of Nursing), Institute of Medicine, Kathmandu, Nepal

Abstract
The growing teratoma syndrome (GTS) was originally defined by Logothetis *et al*. in 1982 as a phenomenon of subsequent growth of the benign tumor, following the removal of a primary malignant tumor during or after chemotherapy with normalization of previously elevated serum tumor markers and absence of any non seminomatous germ cell tumor components. To date, only a few case reports of ovarian GTS have been documented in the medical literature.
There are two reported cases of GTS in Tata Medical Center, Kolkata. The first patient was a 21 years old girl - diagnosed as immature teratoma after staging laparotomy in July, 2016 for complex right adnexal mass. She successfully completed four cycles of chemotherapy in November, 2016. A year later, she underwent debulking surgery for complex pelvic mass with calcifications and fat in imaging but with normal tumor markers. Cut section showed multiloculated cyst with hemorrhagic, mucinous and calcified areas with teeth formation.[1] Final histopathology showed mature teratoma elements only suggestive of Growing Teratoma Syndrome. The second patient was a 50 years woman diagnosed as ovarian immature teratoma post TAH-BSO followed by completion of chemotherapy in[1] 2001. Follow up imaging in June, 2017 showed right sub diaphragmatic mass but with normal tumor markers clinically looks like Growing Teratoma Syndrome. Subsequently, she had excision of right sub diaphragmatic solid mass and final histopathology showed mature teratoma elements only suggestive of Growing Teratoma Syndrome. Complete surgical excision is the treatment of choice. GTS has an overall good prognosis. However, close follow up is essential even after the treatment.

Keywords: debulking surgery, teratoma, staging laparotomy, tumor markers

Introduction
The growing teratoma syndrome (GTS) was originally defined by Logothetis *et al.* in 1982 as a phenomenon of subsequent growth of the benign tumor, following the removal of a primary malignant tumor during or after chemotherapy with normalization of previously elevated serum tumor markers and absence of any non seminomatous germ cell tumor (NSGCT) components [1]. The incidence of GTS in metastatic NSGCTs of the testis is estimated to be around 1.9–7.6% while GTS is less common in ovarian NSGCT [1, 2]. Tonkin *et al.* [3] reported the first ovarian case of GTS in 1991.
The Logothetis criteria for diagnosis of GTS includes: (1) normalization of serum tumor markers, alpha fetoprotein (AFP), lactate dehydrogenase (LDH) and human chorionic gonadotropin (HCG); (2) enlarging or new masses despite appropriate chemotherapy for NSGCT; (3) the exclusive presence of mature teratoma in the resected specimen [4, 5].
To date, only a few case reports of ovarian GTS have been documented in the medical literature.

Case 1
A 21 years old, unmarried girl from Kolkata presented in Tata Medical Center (TMC), Kolkata on first of August, 2017 with complain of dull aching lower abdominal pain.
She was diagnosed with FIGO stage IIIB-Immature teratoma grade III on final histopathology outside following laparotomy with right salphingo-ophorectomy, omentectomy, right pelvic and para-aortic lymphadenectomy for a complex right adnexal mass in June, 2016. She had completed adjuvant four cycles of BEP (Bleomycin, Etoposide, cisplatin on November, 2016. She was on regular follow up with no clinical and biochemical evidence of recurrence with normal germ cell tumor markers (Inhibin, LDH, AFP, HCG) till her presentation in TMC. Computed tomography (CT) imaging on 12th of September, 2017 revealed large complex lesion measuring 9.6 cm in pouch of Douglas (POD) containing calcifications and fat and adherent to anterior rectal wall and posterior uterine wall (Figure 1); multiple subphrenic, subhepatic, Morrison's pouch

deposits and cardiophrenic nodes involved but with normal germ cell tumor markers - clinically suspicious of Growing Teratoma Syndrome. On ninth of October, 2017 she underwent laparotomy (Figure 2a) frozen and proceed to debulking surgery (Figure 2b) after frozen report from suspected peritoneal deposit suggest mature glial tissues only. Cut section of the pelvic mass showed multiloculated cyst with hemorrhagic, mucinous and calcified areas with teeth formation. Final histopathology showed mature glial tissues (Figure 3) only suggestive of Growing Teratoma Syndrome. Her postoperative hospital stay was uneventful with 30 days postoperative Clavien Dindo complication grade II. She was doing well till her last follow up visit on July, 2018 with no clinical, biochemical and radiological evidence of disease recurrence.

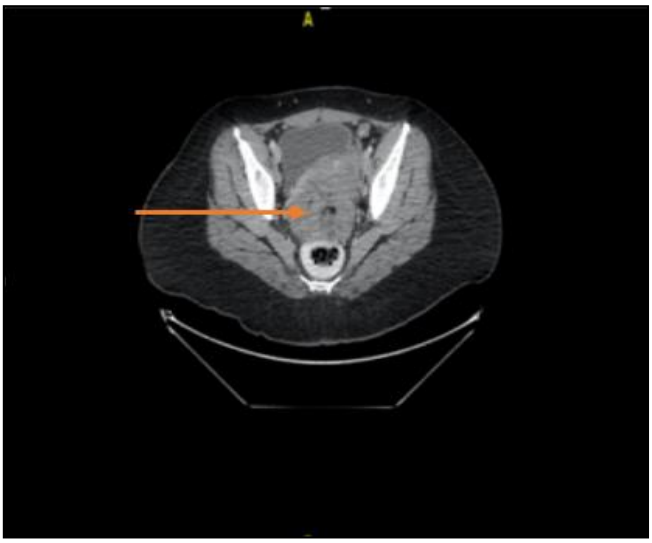

Fig 1: CT image of POD mass

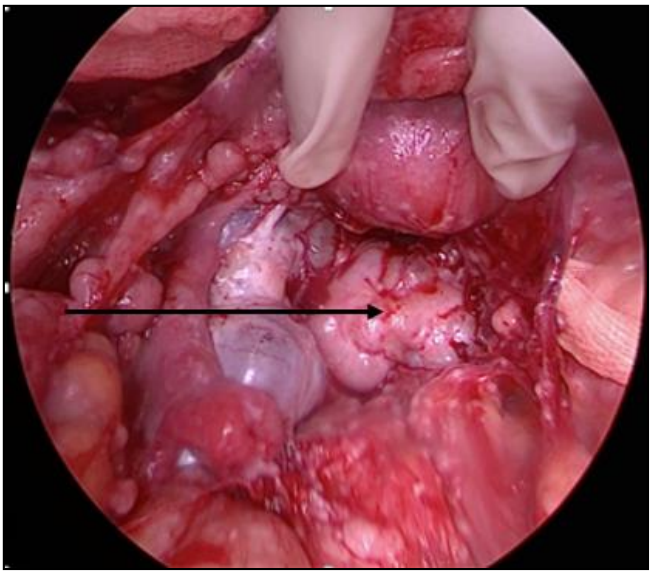

Fig 2a: Intraoperative picture of POD mass

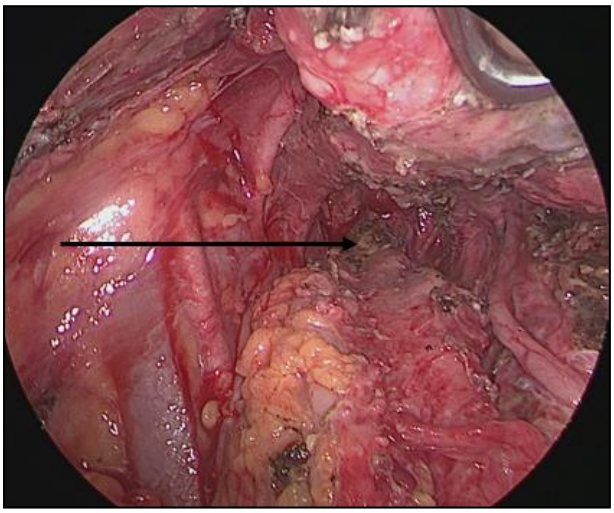

Fig 2b: Intraoperative picture after pelvic clearance

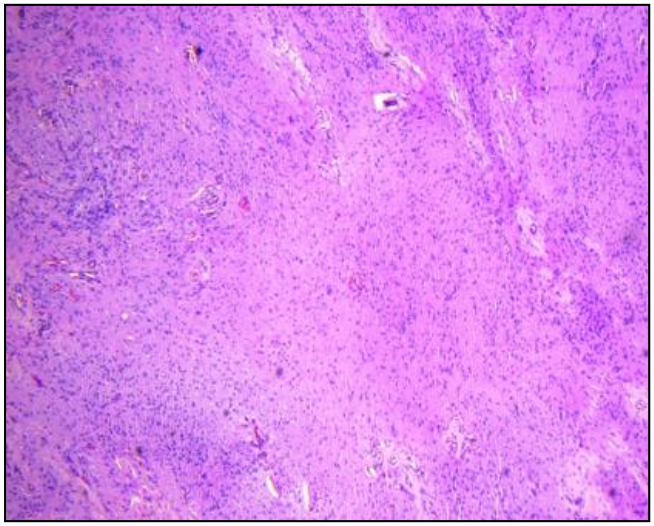

Fig 3: Histopathology section of the specimen showing mature glial elements.

Case 2

A 50 years woman from Mizoram presented in TMC, Kolkata in July, 2017 with one month long history of left flank pain and left upper quadrant pain. She was diagnosed with left ovarian immature teratoma following total abdominal hysterectomy and bilateral salpingo -oophorectomy in 2001 and completed adjuvant chemotherapy.

At initial presentation in TMC, she had good performance status but with tenderness in the right upper quadrant on deep palpation. CT imaging on July, 2017 revealed 11.2cm x 10cm x 9.5cm lesion in the right sub diaphragmatic space indenting the hepatic parenchyma with mural nodules and calcifications (Figure 4) and normal germ cell tumor markers - clinically looks like Growing teratoma syndrome. In August, 2017, she underwent laparotomy with excision of right sub-diaphragmatic solid mass with en bloc excision of a part of right hemi diaphragm. Tumor grossing

showed 14.5 cm solid-cystic mass with large amount of necrosis and caseous material with large areas of calcification. Final pathology report showed mature teratoma elements only with diverse histomorphology, consisting of foci of squamous epithelium with sebaceous glands, salivary glands, mucin secreting columnar cells, respiratory epithelium, transitional epithelium, uveal tissue along with bone and cartilaginous tissue (Figure 5) suggestive of growing teratoma syndrome.

Her postoperative hospital stay was uneventful with 30 days postoperative Clavein Dindo complication grade II. She was doing well till her last follow up visit in July, 2018 with no clinical, biochemical and radiological evidence of disease recurrence.

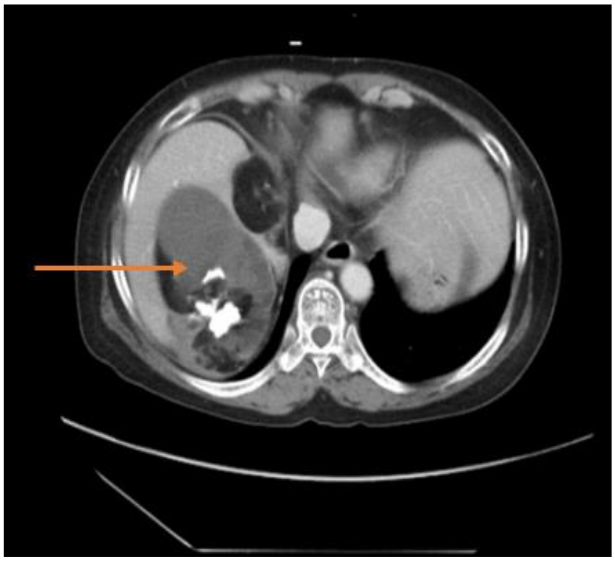

Fig 4: CT image of right subdiaphragmatic mass

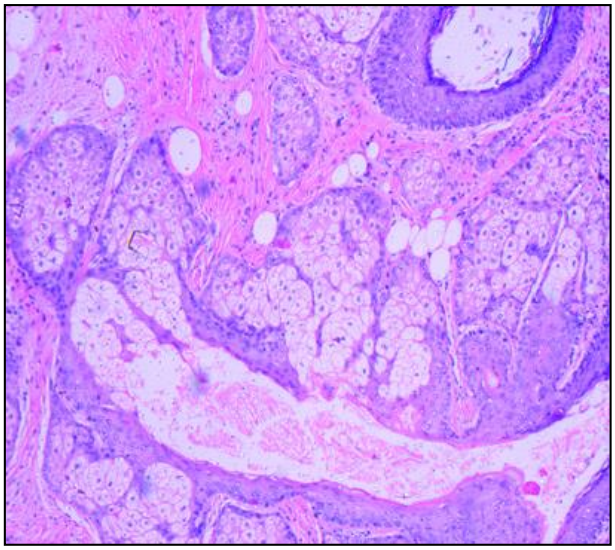

Fig 5: Histopathology section of specimen showing diverse histomorphology without immature teratoma elements.

Discussion

Although GTS was first described by Logothetis *et al.* [1] in 1982, DiSaia *et al.* [6] Had described a similar phenomenon 5 years earlier, which they called "chemotherapeutic retroconversion". It is now thought that GTS and chemotherapeutic retroconversion are different terms used for the same disease entity [7, 8]. Differentiation of malignant cells into mature teratoma components following exposure to chemotherapeutic agents or selective elimination of the malignant cells by chemotherapeutic agents leaving chemo resistant mature teratoma components behind or may be the two possible mechanisms for origin of GTS [9, 10]. Complete resection is the standard treatment for mature teratoma because there is risk of malignant transformation reported in about 3% of cases [8] and organ damage, owing to their uncertain growth rate.

The youngest age of GTS reported in the literature is 5 years old [11]. The development of GTS had been reported as early as three months and as delayed as eight years after primary treatment of ovarian germ cell tumor. In our second case report, the development of GTS was reported as late as 16 years.

Complete surgical excision with retroperitoneal lymph node dissection is the treatment of choice[11-13]. Early decision for complete resection has lower postoperative morbidities and complications as with delay, GTS can grow rapidly encasing the blood vessels and other vital structures leading to pressure effect and potential risk of vascular thrombosis and insufficiency, ureteral obstruction, bowel obstruction, or colonic fistula [11, 13].

Conclusions

GTS has an overall good prognosis with few reported deaths and five years overall survival of 89% following successful surgery. However, regular follow up is essential as recurrence may ensue up to the 10 years after surgical treatment [12].

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Disclosure

The authors report no conflicts of interest in this work.
No violation of human rights and safety.

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