

Growing teratoma syndrome: A case report and review of the literature

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A rare case of growing teratoma syndrome (GTS) of the ovary is presented, with a review of the literature. A 36-year-old woman had 6 months' duration of back pain and abdominal fullness. She had undergone surgery elsewhere (right salpingo-oophorectomy) followed by chemotherapy for a histopathologically diagnosed immature teratoma of the right ovary 6 years previously. Imaging showed evidence of extensive peritoneal cystic metastases indenting the liver and in the pelvis and right suprarenal region. As tumour markers were within the normal range, a diagnosis of GTS was made. The patient underwent exploratory laparotomy with total hysterectomy and left salpingo-oophorectomy, and debulking of peritoneal deposits. Histopathological examination identified mature cystic teratoma. The available literature on this condition, with definitions, understanding of the pathophysiology and prognosis, is reviewed.

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Case report

A 36-year-old woman presented 6 years after oophorectomy for a right adnexal mass reported on histopathology as an immature teratoma. She underwent four cycles of chemotherapy (bleomycin, etoposide, cisplatin), and remained asymptomatic until 6 months before consulting us. In the intervening period (3 years previously), she had had a child, delivered by caesarean section with apparently normal intraoperative findings. She presented to us with backache and a sensation of abdominal fullness of 6 months' duration. She had mild hepatomegaly, but findings on abdominal, speculum and vaginal examination were otherwise normal. Magnetic resonance imaging of the abdomen showed well-defined multiloculated cystic lesions along the liver capsule indenting liver parenchyma. These were initially considered suggestive of peritoneal metastases. Peritoneal metastases were also noted in the pelvis and adjacent to the left kidney and right suprarenal region. As the tumour markers (CA-125, beta-human chorionic gonadotrophin and alpha-fetoprotein) were within the normal range, a working diagnosis of growing teratoma syndrome (GTS) of the ovary was made. She underwent exploratory laparotomy with total abdominal hysterectomy and left salpingo-oophorectomy, and debulking of tumour tissue from the pelvis, Morison's pouch, the diaphragm and the sub-hepatic region. Intraoperatively, deposits were noted on the left ovary and both uterosacral ligaments, and nodules on the undersurface of the diaphragm, in Morison's pouch, on the right side of the paracolic gutter, and between the liver and the kidney. There was no ascites, and the uterus and tubes were normal. She had blood loss of 3 L intraoperatively with subsequent disseminated intravascular coagulation that required correction and monitoring in the intensive care unit for 48 hours. She was discharged on the 8th postoperative day after an otherwise uneventful recovery. Histopathology was reported as mature cystic teratoma in specimens from the posterior surface of the uterus and nodules in the diaphragm, Morison's pouch and the infrahepatic region. There was an extensively hyalinised

nodule and no tumour in the mesothelium. Other findings were mild chronic cervicitis, secretory endometrium, myometrium with no specific lesion, and bilateral fallopian tubes with no specific lesion. The pathologists could find no immature teratomatous component in multiple sections examined. This was consistent with GTS.

Review of the literature

The diagnosis of GTS, first described in 1982, is based on three criteria:^[1] (i) an increase in tumour size or detection of metastases during or after chemotherapy for malignant germ cell tumour; (ii) normal tumour markers (which were high initially); and (iii) mature teratoma without evidence of malignancy on histopathology of the post-chemotherapy surgical specimen.

One of the initial suggested names for the diagnosis was 'chemotherapeutic retroconversion'; however, the pathogenesis remains uncertain.^[2] There is either selective elimination of the immature components of the teratoma or differentiation of malignant cells into mature teratoma cells. Clinically both these processes can mimic malignant metastases. In our patient radiographs suggested the possibility of malignant metastases, but clinically she was only minimally symptomatic for the extensive cystic peritoneal deposits. She had had initial surgery 6 years previously and had undergone a caesarean section 3 years previously.

At a multidisciplinary meeting, it was concluded that a diagnosis of GTS would need histopathological confirmation. A biopsy would serve no purpose, as both diagnosis and treatment depend on complete surgical removal and histopathological confirmation of the same. Although this involved fairly extensive surgery for this patient, with significant blood loss, it was hoped that the long-term outcome would be good.

There have been reports of carcinoids and sarcomatous conversion mimicking GTS;^[3-5] however, the pathologists were unable to find immature components in any of the specimens from our patient. Peritoneal gliomatosis has also been associated with GTS,

with some suggestion that initial association of immature teratoma with peritoneal gliomatosis may predict future development of GTS.^[1,2]

The outcome of GTS has uniformly been described as good; however, the key is early recognition so that resection can be as complete as possible, as chemotherapy is ineffective.^[6]

1. Umekawa T, Tabata T, Tanida K, Yoshimura K, Sagawa N. Growing teratoma syndrome as an unusual cause of gliomatosis peritonei: A case report. *Gynecol Oncol* 2005;99(3):761-763. [http://dx.doi.org/10.1016/j.ygyno.2005.07.029]

2. Mrabti H, El Ghissassi I, Sbitti Y, Amrani M, Hachi H, Errihani H. Growing teratoma syndrome and peritoneal gliomatosis. *Case Report Med* 2011;2011:1-4. [http://dx.doi.org/10.1155/2011/123527]
3. Djordjevic B, Euscher ED, Malpica A. Growing teratoma syndrome of the ovary: Review of literature and first report of a carcinoid tumor arising in a growing teratoma of the ovary. *Am J Surg Pathol* 2007;31(12):1913-1918. [http://dx.doi.org/10.1097/pas.0b013e318073cf44]
4. Al-Jumaily U, Al-Hussaini M, Ajlouni F, Abulruz A, Sultan I. Ovarian germ cell tumors with rhabdomyosarcomatous components and later development of growing teratoma syndrome: A case report. *J Med Case Rep* 2012;6(1):13. [http://dx.doi.org/10.1186/1752-1947-6-13]
5. Morency EG, Lerner D, Garcia R, Kalir T. High-grade sarcoma masquerading as growing teratoma syndrome after resection of ovarian immature teratoma: Report of a case. *Int J Gynecol Pathol* 2012;31(3):276-279. [http://dx.doi.org/10.1097/pgp.0b013e31823ef912]
6. Hariprasad R, Kumar L, Janga D, Kumar S, Vijayaraghavan M. Growing teratoma syndrome of ovary. *Int J Clin Oncol* 2008;13(1):83-87. [http://dx.doi.org/10.1007/s10147-007-0693-7]



Fig. 1. Contrast-enhanced computed tomography scan showing multiple space-occupying lesions in the liver.



Fig. 2. Magnetic resonance image showing solitary metastasis at D12 vertebra.

spine was done. This revealed collapse of the D12 vertebra (Fig. 2). Biopsy of the lesion confirmed bone metastasis. The patient was hospitalised for further management, and palliative radiotherapy (800 cGy, single fraction) was given to the involved vertebra along with monthly intravenous injections of zoledronate 4 mg. Gemcitabine-based chemotherapy was given with appropriate premedications. The CA-125 level came down to 29 U/mL at the end of six cycles of chemotherapy, and the patient was symptom-free at 6 months of follow-up.

Discussion

The course of ovarian cancer is highly variable, and the standard clinical predictors for metastasis and poor prognosis have met with limited success.^[8] Development of distant metastases in the liver, brain, and other sites is uncommon in carcinoma of the ovary.^[9,11] A number of authors have evaluated traditional clinical parameters such as histological features, grade, stage and ascites as predictors for prognosis in patients with ovarian cancer.^[10,12] Exposure to multiple chemotherapeutic agents and disruption of the blood-brain barrier by these agents may be the cause of distant spread. Carcinoma of the ovary has significant potential for distant metastasis, but bony metastases are rare. The mode of bony spread appears to be haematogenous, although no definite route of spread has been documented in the literature. Dauplat *et al.*^[4] analysed 336 patients with distant metastases from ovarian cancer in his autopsy series. Of these, four had bone metastases, two thoracic vertebra involvement, and one each clavicular and bone marrow involvement. According to the authors, bony metastasis is rare and the median time to development ranged from 13 to 49 months. In the present case report, bone involvement also appeared to be a part of haematogenous spread, since both liver and bone were involved. In an autopsy series, Rose *et al.*^[6] studied the metastatic pattern in 428 ovarian cancers and correlated different histologies with sites of metastasis. The incidence of bony metastasis was 0.06 - 0.19% with epithelial histology. This reflects the rarity of bony metastasis in this malignancy. There was no difference in the pattern of spread with different histological subtypes.^[5] Abdul Karim *et al.*^[8] did a clinicopathological audit of bone metastasis from different gynaecological malignancies. They analysed a total of 305 patients, of whom 113 had ovarian cancers. Bony metastasis was seen in seven patients only. Skeletal metastasis was seen in high-grade tumours. Rose *et al.*^[6] had observed that presence of lymph nodes in the abdominal cavity was associated with

an increased incidence of bone metastasis. Advancing age is the most significant risk factor for the development of ovarian cancer. Marchetti *et al.*^[13] showed that out of 545 patients with epithelial ovarian cancer, 49 were under 35 years of age, with most of them having histopathological features of borderline tumour. Advancing age could therefore be an important prognostic factor. However, mucinous cyst adenocarcinoma in an 11-year-old girl has been reported by authors from the same institution, suggesting that no age is immune to the disease.^[14]

In the present case, a young woman without lymphadenopathy developed bony metastasis 4 months after treatment. The authors conclude that bony metastasis should be considered in the differential diagnosis of backache in patients with ovarian cancer, even in an early stage and in middle-aged women.

1. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Estimated Cancer Incidence, Mortality and Prevalence Worldwide: IARC CancerBase No. 11. Lyon: International Agency for Research on Cancer, 2013. www.iarc.fr (accessed 6 October 2014).
2. Kohn EC, Liotta LA. Molecular insights into cancer invasion: Strategies for prevention and intervention. *Cancer Res* 1995;55(9):1856-1862.
3. MacDonald NJ, Steeg PS. Molecular basis of tumour metastasis. *Cancer Surv* 1993;16:175-199.
4. Dauplat J, Hacker NF, Nieberg RK, Berek SJ, Rose PT, Sagae S. Distant metastasis in epithelial ovarian carcinoma. *Cancer* 1987;60(7):1561-1566.
5. Dvoretzky PM, Richards KA, Bonfiglio TA. The pathology and biologic behavior of ovarian cancer: An autopsy review. *Pathol Ann* 1989;24:1-24.
6. Rose PG, Piver SM, Tsukada Y, Lau TS. Metastatic patterns in histologic variants of ovarian cancer: An autopsy study. *Cancer* 1989;64(7):1508-1513.
7. Julian CG, Goss J, Blanchard K, Woodruff JD. Biologic behavior of primary ovarian malignancy. *Obstet Gynecol* 1974;44(6):873-884.
8. Abdul-Karim FW, Kida M, Wentz WB, et al. Bone metastasis from gynecologic carcinomas: A clinicopathologic study. *Gynecol Oncol* 1990;39(2):108-114. [http://dx.doi.org/10.1016/0090-8258(90)90414-g]
9. Geisler JP, Geisler HE. Brain metastases in epithelial ovarian carcinoma. *Gynecol Oncol* 1995;57(2):246-249. [http://dx.doi.org/10.1006/gyno.1995.1134]
10. Ansell SM, Rapoport BL, Falkson G, Raats JI, Moeken CM. Survival determinants in patients with advanced ovarian cancer. *Gynecol Oncol* 1993;50(2):215-220. [http://dx.doi.org/10.1006/gyno.1993.1195]
11. Seewaldt VL, Figge DC, Greer BE, Tamimi HK, Brown WS, Cain JM. Primary central nervous system recurrence after paclitaxel therapy for epithelial ovarian malignancy. *Gynecol Oncol* 1994;55(3):456-458. [http://dx.doi.org/10.1006/gyno.1994.1322]
12. Kastan MB, Onyekwere O, Sidransky D, Vogelstein B, Craig RW. Participation of p53 protein in the cellular response to DNA damage. *Cancer Res* 1991;51(23):6304-6311.
13. Marchetti M, Chiarelli S, Silvestri P, Peron ML. Epithelial ovarian tumors in young women under 35 years. *Eur J Gynaecol Oncol* 1995;16(6):488-493. [http://dx.doi.org/10.1097/00006254-199604000-00013]
14. Nangal JK, Narayan S, Kapoor A, Purohit R, Kumar HS. Mucinous cystadenocarcinoma of ovary in preadolescence: An ordinary tumor but at an unexpected age. *Clin Cancer Inv J* 2014;4(1)(in press).