Case Report

An Ultralate Female Growing Teratoma Syndrome: 19 Years after Aggressive Treatment for Advanced Ovarian Immature Teratoma

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Abstract

We report a rare case with the late occurrence of growing teratoma syndrome (GTS). A 24-year-old woman with Grade 3 immature teratoma of ovary underwent complete surgery and chemotherapy. Nineteen years later, she developed hematuria and pelvic mass that was completely resected and pathology revealed mature cystic teratoma. She has regularly followed up with tumor marker and computed tomography every three months. No evidence of disease has been detected throughout 14 years. In addition, we present a brief review of literature of ovarian GTS in the last decade. We have found that advanced stage, high grade, or early recurrence of germ cell tumor (GCT) could be the risk factors of GTS. It tends to appear within 1 year if the patients had the incomplete resection of primary disease. We stress the importance of long-term follow-up after treatment GCT to early recognition and treatment.

Keywords: Growing teratoma syndrome, immature teratoma, late occurrence, neoplasm, ovary

Introduction

Growing teratoma syndrome (GTS) of the ovary is uncommon which is characterized by enlargement of mature teratoma mass, combined with the normal tumor marker. It can appear at any time during or after the treatment of germ cell tumor (GCT). This condition should be differentiated from recurrence disease. Early recognition is a key to curative resection and good outcome. We report on a case of GTS, diagnosed 19 years after primary treatment of immature teratoma.

Case Report

A 24-year-old woman, G3P2, was diagnosed with ovarian tumor during pregnancy. She underwent ovarian cystectomy at the local hospital. Six months later, she came to our hospital due to pelvic discomfort and pelvic mass. On exploration, frozen section pathology reported immature teratoma. Due to advanced cancer status, total hysterectomy and bilateral salpingo-oophorectomy were performed with no residual disease. Final pathology confirmed the diagnosis of immature teratoma Grade 3. Postoperative adjuvant chemotherapy was arranged with 3 cycles of bleomycin, etoposide and cisplatin, 3 cycles of PE (etoposide and cisplatin), and 6 cycles of vincristine, adriamycin, and cyclophosphamide. After chemotherapy, the serum tumor markers (alpha-fetoprotein [AFP], CA 125) fell within normal range. Unfortunately, the patient was lost to follow-up and

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Table 1: Reported cases of ovarian growing teratoma syndrome; literature search during 2008-2017 period

	Age at diagnosis GCT	Histology	Stage	grade	Treatment	Surgical outcome of GCT	Interval between GCT and GTS (months)	Site of GTS	Surgical outcome of GTS	Last status	FU (months)
Hariprasad *et al*., 2008[1]	18	IT	III	3	Biopsy, 4 BEP	R2	After CMT	Uterus rectum and sigmoid	R0	NED	36
	26	IT	III	3	TH, right ovarian cystectomy, 4 BEP	R2	After CMT	Persistent pelvic mass, peritoneum, external iliac node	R0	NED	60
	27	IT	III	NA	Biopsy, 4 BEP	R2	1st: During CMT 2nd: NA	1st: Pelvis, pouch of Douglas 2nd: Increased mass size, liver	R2 (liver)	AWD	9
Tzortzatos *et al*., 2009[2]	20	I	Ic	2	FSS: RSO then BEP	R0	24	Peritoneum, pouch of Douglas	NA	NED	96
Sengar and Kulkarni *et al*., 2010[3]	26	1st: IT 2nd: Recurrent (RFS 4 months)	I	1	1st: RSO, omental biopsy peritoneal lavage 2nd: 3 BEP	R0	After CMT	Pelvic mass, omentum sigmoid, abdominal mass	R0	NED	6
Lorusso *et al*., 2011[4]	33	Mixed GCT (DGM, YST IT)	IIB	-	FSS, 4 BEP	R0	NA	Multiple liver masses	R0	NED	6
	19	1st: IT 2nd: Recurrent (RFS 12 months)	Ia	3	1st: FSS (No CMT) 2nd: Remove left adnexal mass, peritonectomy of bladder and Douglas cavity, 4 BEP	R0	After CMT	Multiple liver masses	R0	NED	6
Kato *et al*., 2013[5]	30	IT	IIIa	3	FSS and BEP	NA	1st: 96 2nd: 120	1st: Peritoneum 2nd: Pelvis ileocecal, pouch of Douglas, vesicovaginal recess	1st: R0 2nd: R0	NED	96
	22	Mixed (IT, YST)	NA	3	FSS and VAC	NA	264	Peritoneal cavity omentum	NA	NED	144
De Cuypere *et al*., 2014[6]	19	Mixed (YST, IT)	NA	NA	Ovarian cystectomy, (FU PET postoperative: Abnormal uptake at ROV pelvic and PAN) 4 BEP	R2	24	Pelvic cavity, uterus ROV, left iliac vessel region, left rectus muscle below the left trocar port site	R0	NED	36
Shigeta *et al*., 2015[7]	20	IT	IIIb	3	LSO, right ovarian cystectomy disseminated tumor reduction, 3 BEP	R2 Peritoneal lesion 5 mm	17	Peritoneum Right paracolic gutter pouch of Douglas	R0	NED	12

Contd...

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	Age at diagnosis GCT	Histology	Stage	grade	Treatment	Surgical outcome of GCT	Interval between GCT and GTS (months)	Site of GTS	Surgical outcome of GTS	Last status	FU (months)
Soufi *et al*., 2015[8]	36	1st: IT 2nd: Recurrent (RFS 4 months)	NA	3	1st: LSO (no CMT) 2nd: Left salpingectomy abdominal wall and peritoneal lesion removal, 4 BEP	NA	5	Liver, pelvic nodes colon pelvic mass right ureter	R0	NED	10
Daher *et al*., 2015[9]	4	Mixed: DGM YST and teratomatous element	NA	3	Debulking of tumors IEP	R0	1st: 1 2nd: 7 3rd: 5	Omentum, appendix, subdiaphragm, broad ligament, abdominal wall	NA	NED	48

AWD: Alive with disease, BEP: Bleomycin + etoposide + cisplatin, CMT: Chemotherapy, DGM: Dysgerminoma, FSS: Fertility-sparing surgery, FU: Follow-up, GCT: Germ cell tumor, GTS: Growing teratoma syndrome, IEP: Ifosfamide + etoposide + cisplatin, IT: Immature teratoma, LSO: Left salpingo-oophorectomy, NA: Not available, NED: No evidence of disease, PAN: Para-aortic node, RFS: Recurrent-free survival, RSO: Right salpingo-oophorectomy, R0: No residual disease, R2: Macroresidual disease, TH: Total hysterectomy, VAC: Vincristine + actinomycin + cyclophosphamide, YST: Yolk sac tumor, ROV: Right ovarian vein, PET: Positron emission tomography

returned to our clinic due to abdominal discomfort and hematuria 19 years later. Computed tomography (CT) showed huge cystic mass occupying the entire pelvic cavity with bilateral hydronephrosis. The multiple small cystic lesions at mesenteric, perihepatic, and subphrenic region were also noted. The level of the AFP was found to be within normal limit (4.19 ng/ml) but the CA-125 was raised to 147.54 U/ml. She was arranged for debulking of the tumor including pelvic mass excision, bilateral ureterolysis, omentectomy, retroperitoneal lymph node resection, small bowel resection, and Hartmann's procedure. During operation, there was a huge multicystic mass filling the entire pelvis and abdomen. An isolated mass invaded ileum 40 cm in length and multiple cystic mass, ranging from 0.2 to 5 cm in size, over peritoneum, intestinal serosa, and intestinal mesentery were also found. The huge tumor compressed bladder, rectum, and bilateral ureter resulting in bilateral hydroureters and hydronephrosis. Histology revealed a mature teratoma, confirming the diagnosis of GTS of the ovary. No further chemotherapy was administered. The patient has regular follow-up with tumor marker and CT at the 3-month interval. At the time of this report, she remains free of disease 14 years after the primary GTS was diagnosed.

Discussion

GTS is an unusual condition characterized by (1) enlargement of tumors during or after chemotherapy for GCT, (2) normalization of tumor markers, and (3) the absence of any germ cell component other than mature teratoma. The median age at diagnosis of GCT ranges from 22 to 26 years.[1-3] We reviewed the literature of ovarian GTS reported in the last decade [Table1]. The etiology, pathogenesis, and risk factor remain unclear. The previous study reported that the presence of mature teratoma in the first tumor, the incomplete resection, and the absence of volume mass reduction during chemotherapy were predictors.[4] Recent studies revealed that the patient who developed GTS tended to have more advanced stage and were more likely to have received chemotherapy.[1,3] The median interval from diagnosis of GCT to development GTS was 7–26.6 months.[2,5]

Our case exhibits a late occurrence of GTS, 228 months after chemotherapy. Differential diagnosis includes recurrent IT and GTS. Because of the growing mass with normal tumor marker, in the context of regression GCT after chemotherapy, GTS should be considered. The advanced stage of GCT may be the risk factor of GTS in this case. From the literature reviews, most of the primary GCT cases were in Stage III. There were three cases reported of patients with Stage I GCT. Two in three cases had high-grade histology. Another patient with Grade 1 had tumor recurrence at 4 months. This could be explained by a tendency for understaging from fertility-sparing surgery.[6-8] It seems possible that the advanced stage, high-grade histology, and early recurrent of GCT might be the risks of GTS. The most frequent metastatic site was the site involved in primary tumor.[1] Other sites involved are large bowel, small bowel, omentum, abdominal wall, and trocar port site. Despite its benign nature, GTS leads to serious morbidity including mechanical complication and malignant transformation which occurred in 3%–5%. For this reason, it is essential for early diagnosis and treatment as

much as possible. The problem is some locations of disease are not easy to be completely resected. Several types of chemotherapy and immunotherapy have been investigated to treat unresectable masses.[3,9] However, the evidence is far from being confirmed. Even after complete resection, long-term recurrence GTS may occur in 0%–4%.[5] Therefore, lifelong follow–up is mandatory. Close follow-up with serial tumor marker and imaging by CT or magnetic resonance imaging are highly recommended. In properly treated, the overall prognosis of GTS is good.

Conclusion

Unusual presentations and complications of GCT should be kept in mind.[10] GTS nodule can occur anytime. There is no prevention strategy for this condition. It highlights that the clinicians should be aware of this condition even in patients without definite risk. Long-term and regular follow-up is crucial. Early diagnosis and early treatment can increase chances of complete resection which is associated with good outcomes and minimal morbidity.

Ethical approval

This study was approved by the institutional review board of Chang Gung Medical Foundation (approval no. 202000995B0 obtained on June 15, 2020) and the IRB approved the waiver of the participants' consent.

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Conflicts of interest

There are no conflicts of interest.

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