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Case Report

Laparoscopic Excisional Surgery for Growing Teratoma Syndrome Presenting 19 Years after Initial Treatment: A Case Report

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ABSTRACT: Growing teratoma syndrome (GTS) is rare. The optimum treatment strategy is complete surgical excision. We describe a 42-year-old woman with GTS who was treated with laparoscopic excisional surgery. Initially, we performed right salpingo-oophorectomy; she was diagnosed with grade 2 immature teratoma, which was treated with four courses of peplomycin, etoposide, and cisplatin chemotherapy. Postoperatively, her tumor marker (alpha-fetoprotein) was not elevated; however, 19 years later, she developed an enlarged mass in her pelvic cavity. Laparoscopic surgery revealed some of the enlarged tumors detected by preoperative magnetic resonance imaging in the pouch of Douglas. We resected the retroperitoneal tumors. The histological diagnosis was mature teratomas. We concluded that these tumors were GTS. No recurrent disease was observed 12 months thereafter. This case represents one of the longest reported interval periods before the development of GTS. Laparoscopic surgery is an effective alternative diagnostic and therapeutic approach in cases suggestive of GTS. Laparoscopic surgery might be feasible in cases of GTS, but further study will be needed, given that only a few reported cases have been managed laparoscopically.

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KEYWORDS: Growing teratoma syndrome, Laparoscopy, Immature teratoma, Laparoscopic surgery, Case report

Introduction

Growing teratoma syndrome (GTS) was originally defined by Logothetis et al. in 1982 as the phenomenon of subsequent growth of a benign tumor following the removal of a primary malignant tumor during or after chemotherapy.[1] The syndrome is defined as an increase in the size of a mature teratoma or the appearance of a new germ cell tumor mass with any initially elevated tumor markers remaining normal. As GTS is resistant to chemotherapy and radiotherapy, such a patient should be managed with complete surgical resection. We describe a patient who had a long interval period before the development of GTS and was effectively treated with laparoscopic excisional surgery.

Case Report

A 42-year-old woman had a history of an immature ovarian teratoma (grade 2) (Fig. 1) and was treated with right salpingo-oophorectomy in 1999 followed by four cycles of

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peplomycin (30 mg/body), etoposide (100 mg/m^2), and cisplatin (20 mg/m^2) chemotherapy. At initial laparotomy, we only found a right ovarian tumor measuring 5 cm, with no pelvic dissemination or ascites. Results of the preoperative serum tumor marker analysis showed an elevated alpha-fetoprotein (AFP) level at 517 ng/mL (normal range $<$8.78 ng/mL), and it returned to normal within 1 month postoperatively. In the following 18 years, her serum tumor marker had not been elevated. She felt slight abdominal discomfort at 19 years after the primary surgery. Magnetic resonance imaging revealed peritoneal lesions measuring 6 cm with fat and calcification in the pouch of Douglas, but the AFP level was not elevated (Fig. 2A, B). We could not differentiate between a diagnosis of GTS and a recurrent immature teratoma. After counseling, the patient consented to laparoscopic surgery and excision of the lesions.

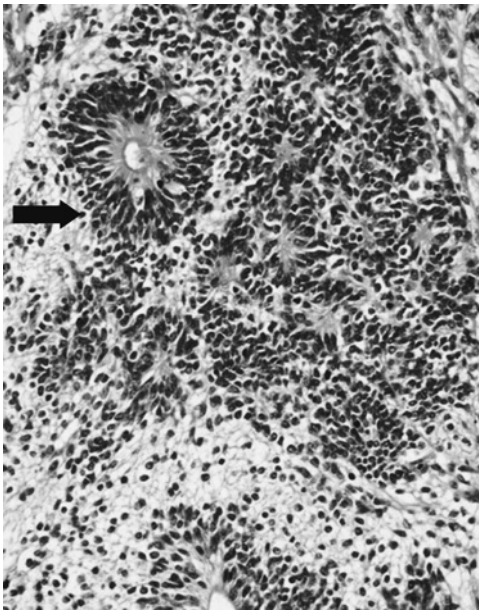

Fig. 1 Section showing rosette-forming immature neuroepithelial cells (arrow) in the ovarian tumor (hematoxylin and eosin, ×4)

Laparoscopic surgery revealed a 6-cm diameter tumor in the pouch of Douglas and additional 0.5-cm to 1-cm multiple nodules in the peritoneum of the deep pelvis (Fig. 3). The uterus, left ovary, and oviduct were normal. We could easily see the upper abdominal peritoneum, omentum, and liver and could not detect another disease. All these lesions were resected laparoscopically. The histological report revealed that the tumors were composed of mature cartilage, neural tissue, and skin; thus, the tumors were diagnosed as mature teratomas (Fig. 4A, B). Immature elements were not seen in any of the sections studied. Hence, a final diagnosis of GTS was made.

The patient has been followed up every 6 months with ultrasonographic imaging and has exhibited no subsequent evidence of disease for 12 months.

Discussion

This is an unusual case with an increasing number of masses 19 years after chemotherapy for an ovarian immature teratoma, but all the subsequently resected masses were shown to contain only mature teratomas. Hence, the patient was diagnosed with GTS.

GTS is characterized by an increase in metastatic masses after complete eradication of a primary malignant ovarian germ cell tumor and by normalization of serum tumor markers, either during or after chemotherapy.[2] The pathogenesis of GTS has remained controversial. There are three predominant theories regarding the mechanism

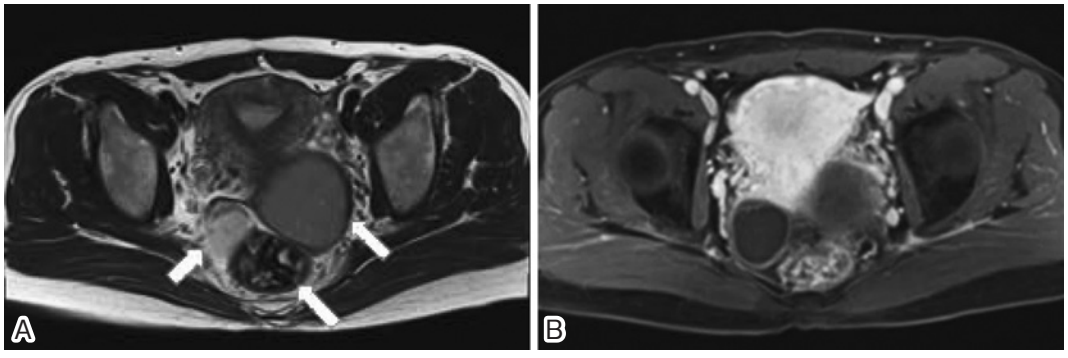

Fig. 2 (A) T2-weighted magnetic resonance image shows the mass with a heterogeneous internal signal intensity with punctate high signal intensity (arrows). (B) Suppression of the high signal intensity of the lesion is observed on fat-saturated T2-weighted images

of GTS: (1) chemotherapy stimulates differentiation of immature teratomatous tissue into mature tissue, and (2) the benign tumor is the result of chemotherapeutic-induced epigenetic retroconversion of the tumor cells.[3] Evidence for clonal selection of a less abnormal phenotype in post-chemotherapy mature teratoma suggests that the latter theory may be correct, and this view is strengthened by the observation that the presence of a mature teratoma in non-seminomatous germ cell tumors conveys an increased risk of GTS following treatment.[3] The third hypothesis is inherent and spontaneous differentiation of malignant cells into benign tissues, as suggested by the experimental murine teratocarcinoma mouse model.[4] There is still much uncertainty around GTS because of the limited number of cases. In addition, either or both of the inferences are possible because they can play important roles in the development of GTS.

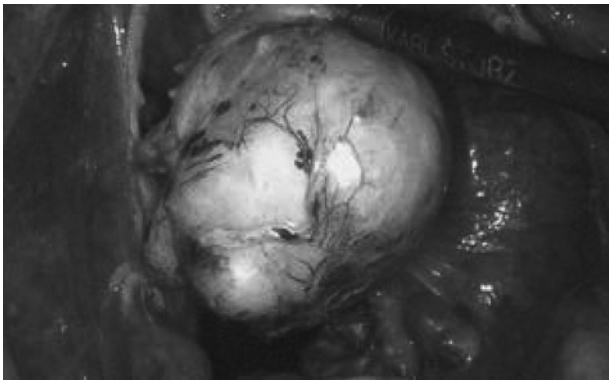

Fig. 3 Laparoscopic view of the tumor

GTS can occur in 2-7% of malignant ovarian germ cell tumors, but it develops most commonly in the retroperitoneum. Despite usually being seen during chemotherapy or shortly after, GTS has been reported up to 9 years following completion of treatment for ovarian immature teratoma; however, the median interval was 26.6 months.[5] The interval time from the first treatment to the onset of GTS in this case is the longest reported; this case highlights the fact that close attention should always be paid to rapidly enlarging tumor and/or normalization of serum tumor markers after initial treatment.

The preferred treatment is complete surgical resection because GTS has a high recurrence rate of 72% to 83% in patients with partial resection compared to 0% to 4% in those who undergo complete resections, as GTS is resistant to chemotherapy and radiation therapy.[6] Kikawa et al. reviewed 48 cases of ovarian GTS and found that incomplete resection of GTS was an important risk factor for the recurrence of GTS.[7] They reported that 4 of 48 patients (8%) who did not undergo complete tumor resection experienced recurrence and that recurrence was rare in patients with GTS who underwent complete resection.[6] GTS has a small but real potential to undergo malignant transformation. In an assessment of only ovarian GTS,

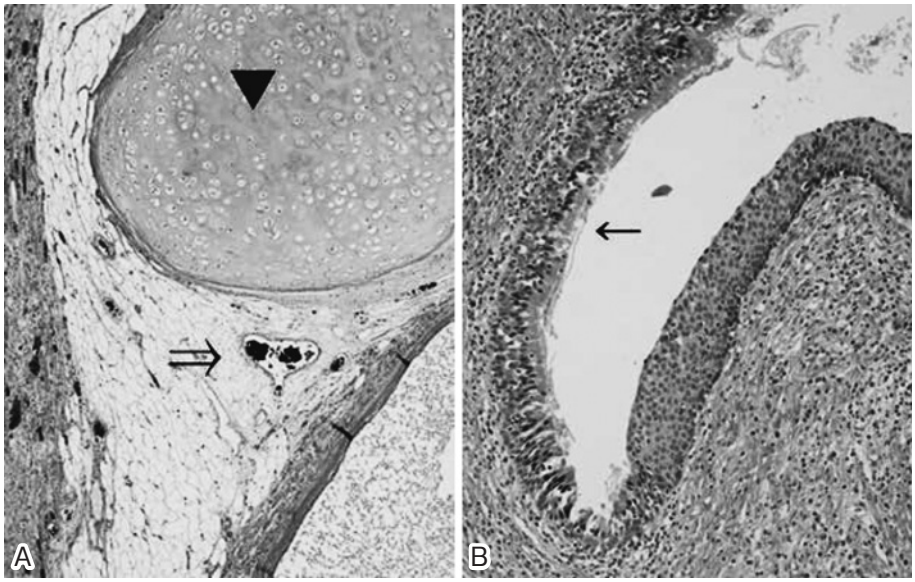

Fig. 4 Histological features of the tumor. (A) Mature cartilage (arrowhead) and an adipocyte cell (arrow). (B) Mature ciliated cell (arrowhead). Immature elements or viable carcinoma is not seen in any of the sections (hematoxylin and eosin, ×4)

Shigeta et al. showed that GTS recurred in 12.7% of cases and malignant transformation occurred in 5.4% of cases.[7] Therefore, complete surgical resection is a highly desirable treatment.[8]

Recent advances in laparoscopic technology have enabled surgeons to perform advanced laparoscopic surgical techniques. Laparoscopic surgery has many well-known advantages over laparotomy, including less blood loss, less pain, shorter recovery periods, and less adhesion formation.[9] In English literature, we found only four patients who were managed laparoscopically,[3, 8, 10, 11] and tumor recurrence did not occur after resection in these cases. We explained to the patient that laparoscopy is minimally invasive and suitable for visualizing details of the tumor even when the lesion is located deep within the pelvis but that it might be difficult to perform complete resection. After counseling, she chose to undergo laparoscopic surgery. We performed laparoscopic surgery and completely resected the tumors from GTS in the pouch of Douglas.

It is difficult to distinguish recurrence or metastasis of malignant germ cell tumors from GTS; therefore, surgery should be considered. Recurrent GTS occurs in some cases following laparoscopic surgery; thus, a minimally invasive method is a good option for possible frequent surgeries. Moreover, laparoscopy is suitable for visualizing details of the tumor even when the lesion is located deep within the pelvis. If there are multiple recurrent lesions, laparoscopy can be used as a curative method to treat GTS.

In conclusion, the case presented here represents the longest reported interval period before the development of GTS, as the patient presented at 19 years after the completion of therapy for immature teratoma. Furthermore, we demonstrated the feasibility of laparoscopic surgery in cases of GTS. Laparoscopic surgery should be considered as an effective alternative diagnostic and therapeutic method in cases suggestive of GTS, but further study is needed, given that only a few reported cases have been managed laparoscopically.

Ethical approval: The study protocol was approved by The Ethics Committee of Toho University Sakura Medical Center (No S 19037), and we provided a means of opting out for the patient.

Conflicts of interest: None declared.

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