CAS CLINIQUE / CASE REPORT

GROWING TERATOMA SYNDROME OF THE OVARY
Case Report and Review of the Literature

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Paul Henri TORBEY[1], Carla EL HABER[1*]

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ABSTRACT • Growing teratoma syndrome (GTS) is defined by Logothetis *et al.* in 1982 as a growth of a benign tumor after removal of a primary malignant germ cell tumor during or after treatment with chemotherapy. We report the case of a twelve year-old girl with immature ovarian teratoma who underwent surgery and chemotherapy. Her tumor markers normalized by the end of chemotherapy. However, she developed months later retroperitoneal masses that were subsequently and repeatedly resected. Histopathology revealed each time mature teratoma consistent with the diagnosis of GTS.

Keywords : ovary; immature teratoma; growing teratoma syndrome; chemotherapy; tumor markers; recurrence

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RÉSUMÉ • Le *growing teratoma syndrome* (GTS) est défini par Logothetis *et al.* en 1982 comme une croissance d'une tumeur bénigne suivant l'ablation d'une tumeur maligne primaire pendant ou après le traitement par chimiothérapie. Nous rapportons le cas d'une fille de douze ans ayant un tératome ovarien immature traité par chimiothérapie et chirurgie. Les marqueurs tumoraux se sont normalisés à la fin du traitement par chimiothérapie. Cependant, elle a développé des mois plus tard des masses rétropéritonéales réséquées à plusieurs reprises et l'histopathologie révélait invariablement un tératome mature constituant un GTS.

Mots-clés : ovaire; tératome immature; *growing teratoma syndrome*; chimiothérapie; marqueurs tumoraux; récidive

INTRODUCTION

The growing teratoma syndrome (GTS) is defined as a mature teratoma combined with normal tumor marker levels that may occur after treatment of malignant nonseminomatous germ cell tumors (NSGCT) [1]. It has been reported in 12% of ovarian germ cell tumors [2]. It typically affects young adults and adolescents [3]. Diagnostic criteria include: enlarging or new masses despite appropriate chemotherapy for nonseminomatous germ cell tumors, the exclusive presence of mature teratoma and normalization of previously increased tumor markers (AFP, β-HCG or both) [4]. These tumors can metastasize particularly to the retroperitoneum, mediastinum and cervical region. Although prognosis is excellent after complete excision, it is essential that the patient be regularly followed-up with serum tumor markers and imaging. We report a case of GTS with multiple recurrences to stress the need for early recognition of this syndrome in order to prevent unnecessary chemotherapy and optimize management.

CASE

A twelve-year-old prepubertal girl presented with a one-week history of nausea, progressive abdominal pain and vomiting. Physical examination revealed abdominal distension with a large palpable pelvic mass. Laboratory tests were normal, except for AFP, CA 125 and LDH which were 500 UI/ml, 313 UI/ml and 865 U/l respectively. Abdominal and pelvic MRI identified a mass in the lower abdomen and pelvis (Figure 1). At laparotomy, a left ovarian mass of cystic and solid nature measuring 19 x 12 x 6.5 cm was completely resected without preservation of the ovary, along with several suspicious nodules

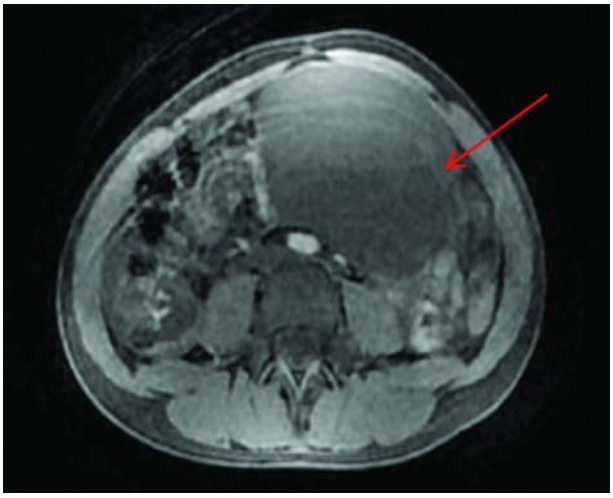

Figure 1. Abdominal and pelvic MRI showing the mass in the lower abdomen and pelvis

[1]Department of Pediatrics, Hôtel-Dieu de France University Hospital, Saint Joseph University, Beirut, Lebanon.
[*]Corresponding author: *Carla El Haber, MD*. e-mail: Carla_haber@hotmail.com

within the omentum. Liver, contralateral ovary, retroperitoneal, and pelvic lymph nodes were inspected and no suspicious lesions were found nor biopsied. Histopathologic diagnosis was grade II immature ovarian teratoma. She was started on a chemotherapy regimen based on vinblastine 3 mg/m^2/day x 2 days, bleomycine 15 mg/m^2/day x 2 days and cisplatin 100 mg/m^2/day x 1 day for three cycles according to the French protocol SFOP TGM 95.

The patient remained asymptomatic with normal serum tumor markers for four months (β-hCG 2.1 mUI/ml, AFP UI/ml and CA 125 16 U/ml) and when she reported lower abdominal discomfort, tumor markers at that time were negative. A pelvic ultrasound showed a right ovarian multilobulated mixed solid and cystic mass measuring 71 x 54 x 57 mm (Figure 2).

A second laparotomy showed right ovarian mass and many peritoneal implants that were all removed and sampled for pathologic examination with preservation of the right ovary. Histopathology showed mature teratoma with no malignant component.

Eight months later, a third exploratory laparotomy for recurrent abdominal masses showed multiple implants studding the right subdiaphragmatic space and hepatic capsular region. The lesions were all resected and histopathology revealed again mature teratoma with no malignant cells.

The patient was followed with serial ultrasonography and serum tumor markers which remained normal. At the time of this report, the patient is a healthy fourteen-year-old girl with no evidence of disease.

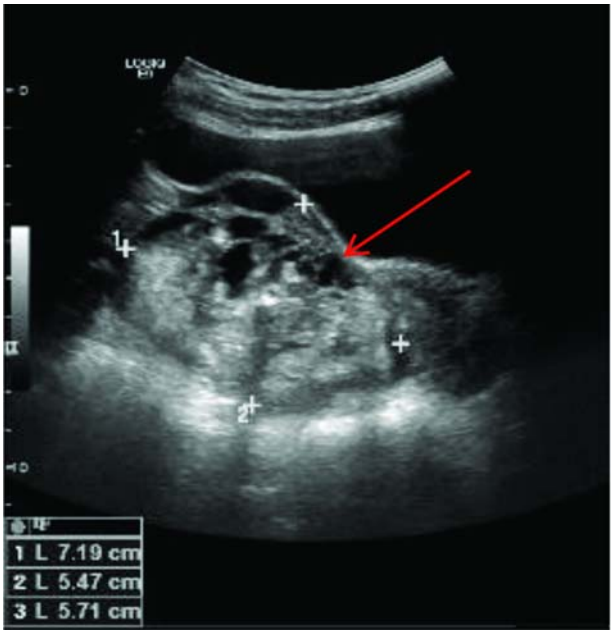

Figure 2. Abdominal and pelvic ultrasound identified a right ovarian multilobulated mixed solid and a cystic mass measuring 71 x 54 x 57 mm.

DISCUSSION

Germ cell tumors are rare in children under fifteen years, accounting for approximately 3% of cancers in this age group [1].. GTS is an unusual syndrome that may occur after treatment of malignant nonseminomatous germ cell tumors (NSGCT), with an incidence of 1.9 to 7.6% [4]. Three criteria are needed to define GTS: 1) An evolving tumor mass or occurrence of a new tumor mass during or after chemotherapy for NSGCT; 2) the normalization of previously increased tumor markers (AFP, β-HCG or both) and 3) the presence of mature teratoma only on histology [4].

The average age at presentation of germ cell tumors is 13.8 years (4-27 years) [5]. The incidence of extracranial GCTs in 0-4 and 10-14 years old girls is 5.8 and 7.8 per 1 million respectively [6]. The precise cause of GTS is unknown and its development has been reported as early as three months after an initial malignant tumor up to eight years after diagnosis. In patients with primary ovarian NSGCT and initial peritoneal extension, GTS occurs mainly in the peritoneum [7,8].

The initial presenting symptoms are usually abdominal distension or discomfort. Diagnosis is based on the combination of imaging with evidence of one or multiple masses increasing in size and containing fat, calcifications or cysts in a patient with a history of a germ cell tumor during or after completion of chemotherapy along with normal tumor markers [9]. Metastatic lesions may appear anywhere in the pelvis, retroperitoneum, liver, lungs or mediastinum. Peritoneal, lymphatic and hematogenous dissemination routes are suggested [10]. The appearance of distant GTS suggests that metastatic malignant cells are initially present in these sites at the time of initial diagnosis even before surgery and nonruptured tumor capsule. Despite normalization of serum tumor markers during chemotherapy, the metastatic tumor continues to grow.

Surgery is the cornerstone of the management of GTS. Early diagnosis is crucial as delay might result in significant symptoms due to mechanical compression and makes surgery more difficult with higher morbidity [8]. Surgery alleviates compressive symptoms and prevents the very rare probability of sarcomatous transformation within these lesions.

Although laparoscopic surgery is an option in small tumors, in many cases open surgery was preferred based on tumor size and spread [11].

Complete excision of GTS is mandatory, because ovarian GTS recurrence rates are 50 to 83% when incompletely resected versus 0 to 4% when completely resected [5,8]. Long-term follow-up with serum tumor markers is crucial as recurrence may develop up to ten

years after initial diagnosis and should be combined with imaging [9,12]. Long-term prognosis is generally favorable [13] and the 5-year overall survival rate of patients who underwent surgery following GTS is 89% [14].

CONCLUSION

The case we report here shows that ovarian GTS may occur in prepubertal girls despite good response to chemotherapy and complete initial germ cell tumor removal. Absence of malignant components in recurrent tumor, even when tumor implants are multiple, precludes the role of chemotherapy. Laparoscopy is a tool to differentiate GTS from recurrent immature teratoma. Recurrent lesions, even when multiple, can be removed and GTS cured. In some cases tumor may recur repeatedly and multiple successive surgical interventions may be required to relieve compression of adjacent structures [15].

REFERENCES

1. Logothetis CJ, Samuels ML, Trindade A et al. The growing teratoma syndrome. Cancer 1982; 50: 1629-35.
2. Zagame L, Pautier P, Duvillard P et al. Growing teratoma syndrome after ovarian germ cell tumors. Obstet Gynecol 2006; 108: 509-14.
3. Lai CH, Chang TC, Hsueh S et al. Outcome and prognostic factors in ovarian germ cell malignancies. Gynecol Oncol 2005; 96: 784-91.
4. Bentivegna E, Azais H, Uzan C et al. Surgical outcomes after debulking surgery for intraabdominal ovarian growing teratoma syndrome: analysis of 38 cases. Ann Surg Oncol 2015; 22 (Suppl 3): 964-70.
5. Spiess PE, Kassouf W, Brown GA et al. Surgical management of growing teratoma syndrome. The M.D. Anderson Cancer Center Experience. J Urol 2007; 177: 1330-34.
6. Tongaonkar HB, Deshmane VH, Dalal AV et al. Growing teratoma syndrome. J Surg Oncol 1994; 55 (1): 56-60.
7. André F, Fizazi K, Culine S et al. The growing teratoma syndrome: results of therapy and long-term follow-up of 33 patients. Eur J Cancer 2000; 36 (11): 1389-94.
8. Tangjitgamol S, Manusirivithaya S, Leelahakorn S et al. The growing teratoma syndrome: a case report and review of the literature. Int J Gynecol Cancer 2006; 16 (Suppl.1): 384-90.
9. Hain SF, Maisey MN. Positron emission tomography for urological tumours. BJU Int 2003; 92: 159-64.
10. Shibata K, Kajiyama H, Kikkawa F. Growing teratoma syndrome of the ovary showing three patterns of metastasis: A case report. Case Rep Oncol 2013; 6 (3): 544-49.
11. Matsushita H, Arai K, Fukase M, Takayanagi T, Ikarashi H. Growing teratoma syndrome of the ovary after fertility-sparing surgery and successful pregnancy. Gynecol Obstet Invest 2010; 69: 221-23.
12. Nimkin K, Gupta P, McCauley R et al. The growing teratoma syndrome. Pediatr Radiol 2004; 34: 259-62.
13. Hariprasad R, Kumar L, Janga D et al. Growing teratoma syndrome of ovary. Int J Clin Oncol 2008; 13: 83-7.
14. Gorbatiy V, Spiess P, Pisters L. The growing teratoma syndrome: current of the literature. Indian Journal of Urology 2009; 25: 186-89.
15. Shigeta N, Kobayashi E, Sawada K et al. Laparoscopic excisional surgery for growing teratoma syndrome of the ovary: Case report and literature review. J Minim Invasive Gynecol 2015; 22 (4): 668-74.