Spontaneous Growing Syndrome of an Immature Teratoma

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Abstract: *Background*: Immature teratomas of the ovary represent less than 1% of all ovarian teratomas. Growing teratoma syndrome is an increase of tumor size containing a mature teratoma component, during or after chemotherapy for germ cell tumors.

Case: We report a case of an immature teratoma of the ovary in a 21-year-old girl treated by cystectomy only. She presented a few months later with a pelvic mass with widespread diffuse peritoneal involvement exhibiting a spontaneous growing teratoma syndrome.

Conclusion: Present case shows that spontaneous growing syndrome can occur in ovarian teratoma. Ovarian tumors in young girl should be always considered as being potentially malignant to offer hope for curative treatment and fertility.

Keywords: Spontaneous growing teratoma syndrome, immature teratoma, ovarian cancer, chemotherapy.

INTRODUCTION

Teratoma is the most frequent germ tumor of the ovary but immature teratoma represents only 1% of ovarian tumors. Treatment is based on surgery and chemotherapy depending on stage and grade [1]. Growing syndrome is a rare histological entity defined by an increase in tumor size containing a mature teratoma component during or after chemotherapy [2-4]. Exceptional cases of spontaneous growing syndrome in non- gynecological disease have been published [5].

We report the first case of spontaneous growing syndrome in a patient with an immature teratoma.

CASE REPORT

A 21-year-old woman was referred to our gynecological oncology department with a pelvic mass a few months after an ovarian cystectomy. The initial histology of the cyst was an ovarian mature teratoma associated with a limited immature component. The patient had not received either chemotherapy or additional surgery after initial surgery. A few months later she complained of abdominal distension and pain. Physical examination, pelvic sonography and magnetic resonance imaging (MRI) showed an 8 cm complex pelvic mass without suspicious pelvic lymph nodes (Fig. **1**). A second analysis of the initial histology showed several sites of grade 2 immature teratoma. CA125 serum level was 52.7 UI /ml and AFP serum level 102.3 UI/ml.

In accordance with our standard protocol, a diagnostic laparoscopy was recommended to evaluate resectability of the lesions. The laparoscopy confirmed the presence of a sizeable pelvic mass and peritoneal carcinomatosis with diaphragmatic involvement. A median laparotomy was performed with complete cytoreductive surgery including peritoneal cytology, left salpingo-oophorectomy, appendectomy, omentectomy, peritonectomy, bilateral pelvic and paraaortic lymphadenectomy, right diaphragmatic peritoneal stripping, omphalectomy, and a left liver lobectomy. A wedge biopsy of the apparently normal contralateral ovary was performed. Histology showed a mass measuring 10 cm composed of a grade 1 immature teratoma and a growing teratoma syndrome as described after chemotherapy. Histopathology revealed mature glial tissues in all samples and in two of 38 lymph nodes corresponding to a FIGO stage III ovarian cancer. Our oncological committee recommended adjuvant chemotherapy with BEP (Bleomycine, Etoposide, Cisplatine). One year after chemotherapy, the patient had no evidence of disease with normal serum marker levels and regular menstrual cycles.

DISCUSSION

We report the first case of spontaneous growing ovarian teratoma syndrome. Growing teratoma syndrome was first reported by Logothetis *et al*. in 1982 and corresponds to histological modifications of malignant tumors treated by chemotherapy [2]. Six years before, DiSaia *et al*. described a similar phenomenon called "chemotherapeutic retroversion" [3]. The physiopathology of growing syndrome remains unknown but one theory postulates that it results from the differentiation of malignant cells into mature teratoma under chemotherapy with slow growth of benign cells [6]. Another theory suggests that mixed elements (mature and immature) may coexist in the metastatic tissue as found in the omentum. Chemotherapy is successful in destroying the immature component allowing the mature tissue to flourish. This has been described with non-seminomatous germ-cell

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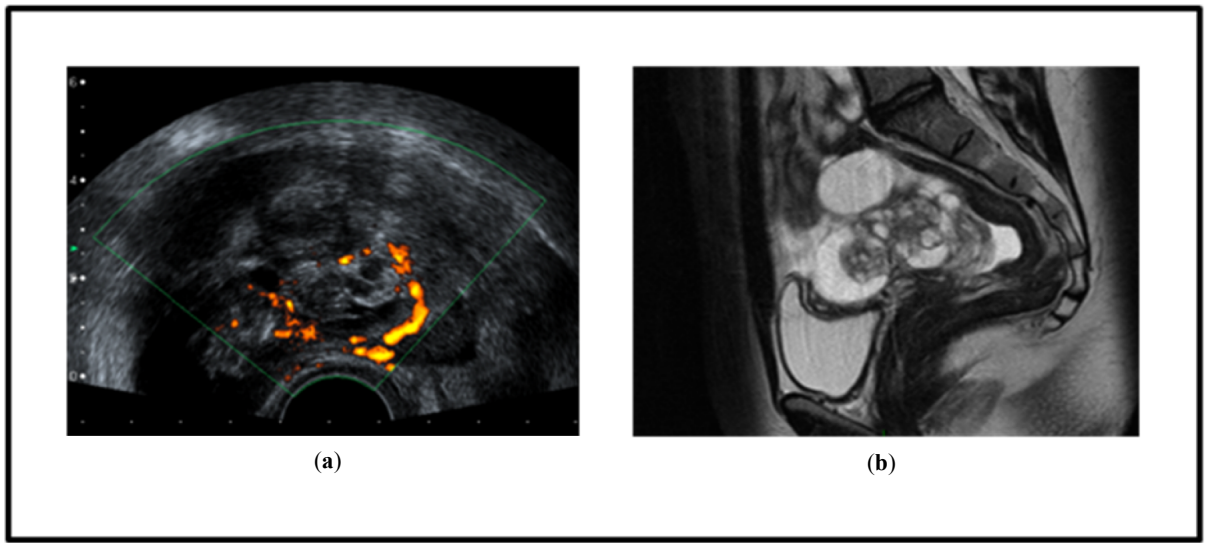

(a) **(b)**

Fig. (1). Transvaginal sonography shows a large cystic mass with irregular heterogeneous solid portion displaying power Doppler flow suggestive of malignancy (**a**), Sagittal T2-weighted MR shows a mixed ovarian tumor. Note that the cystic portion of the mass has a similar intensity to urine, and the solid portion contains multiple hyperintense spots (**b**).

tumors arising from the testis, the mediastinum and the pineal gland [5].

Kattan *et al*. were the first to use the term "growing teratoma syndrome" to describe the presence of enlarging masses of mature teratoma growing after or during chemotherapy for malignant non-seminomatous germ-cell tumor [7]. Tumor masses grow at the initial tumor site and extend to several distant sites: the peritoneal cavity, liver, retroperitoneum and lymph nodes. Three criteria must be fulfilled for a diagnosis of growing teratoma syndrome: clinical or radiological enlargement of metastases during or after chemotherapy; normalization of previously elevated tumor markers; subsequent surgery revealing mature teratoma without malignant cells on histological examination. Our case report fulfills these criteria and thus confirms a diagnosis of spontaneous growing syndrome.

Several factors may explain the progression of our case of immature teratoma. First, although the initial surgical report did not mention the occurrence of intra-operative rupture of teratoma, this was probably a determinant factor of intra-abdominal dissemination. Intra-operative rupture of teratoma has already been reported after laparotomic or laparoscopic management of teratomas with a spillage incidence of 9 versus 88% respectively. This raises the issue of the indication of laparoscopy for large teratomas exposing women to the risk of chemical peritonitis, especially when a cystectomy is performed [8]. Second, the surgeon may have misinterpreted the histological report which led to an additional factor in allowing the disease to spread. Finally, the present case report raises the issue of indications of MRI for teratomas before surgery to rule out possible immature components. As in the present case, previous studies have shown the high accuracy of MRI in detecting malignant components in teratomas allowing to opt for an initial unilateral salpingo-oophorectomy and thus decreasing the risk of intra-operative rupture linked to cystectomy [9].

The therapeutic strategy for immature teratoma depends on the patient's age and the stage and grade of the lesion (Table **1**). Norris *et al*. reported that while size and stage were correlated to survival, grade was the best predictive factor for metastases: they found the risk of progression to be

Table 1. Review of the Literature: Immature Teratoma

Authors	Number of Patients	Grade of Tumors		
		Grade 1	Grade 2	Grade 3
Norris *et al*. [9]	58	40	9	9
Curry *et al*. [15]	25	NA	NA	NA
Carlson *et al*. [16]	4	1	3	0
Schartz *et al*. [17]	9	1	3	5
Iihara *et al*. [18]	7	6	1	0
Ohama *et al*. [19]	6	NA	NA	NA
Slayton *et al*. [20]	28	NA	NA	NA
Gershenson *et al*. [21]	41	NA	NA	NA
Koulos *et al*. [22]	35	2	12	11
Kawai *et al*. [23]	20	8	11	1
Nogales *et al*. [24]	2	0	2	NA
Heslan *et al*. [25]	3	NA	NA	NA
Bonazzi *et al*. [26]	32	NA	NA	NA
Culine *et al*. [27]	15	NA	NA	NA
Kojs *et al*. [28]	22	9	NA	2
Cushing *et al*. [29]	31	17	12	NA
Li *et al*. [30]	67	NA	NA	1
Biener *et al*. [31]	8	3	4	NA
Total	413	87/173 50.3%	57/173 32.9%	29/173 16.8%

NA: Not available.

18% for grade 1, 37% for grade 2 and 70% for grade 3 [10]. The AFP serum level could also be a useful marker of disease status but its level is only slightly correlated with grade [11,12]. In our case, we opted for conservative management to preserve the childbearing potential of our patient. This option appears logical as hysterectomy and removal of the contralateral ovary have not been proved to impact survival and the occurrence of bilateral immature teratomas is extremely rare [11,13]. An alternative might have been to perform ovarian cryopreservation as the chemotherapy recommended for advanced stages or grade 2-3 tumor includes the use of a BEP protocol which, though highly effective, carries the risk of infertility. However, a recent report has reported encouraging fertility outcomes after conservative surgery and chemotherapy for malignant germ cell tumors [14].

This case report reminds us that all ovarian tumors should be considered as being potentially malignant underlining the need to respect the rules of surgical oncology. Furthermore, we see here that spontaneous growing syndrome can occur in ovarian teratoma raising the issue of its physiopathology.

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