CASE REPORT

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Growing ovarian teratoma syndrome: Case report and literature review

Síndrome de teratoma creciente: reporte de caso y revisión de la literatura

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ABSTRACT

The growing teratoma syndrome (GTS) is a rare condition in which patients with germ cell tumors present an increase in tumor size or the appearance of new lesions, during or after chemotherapy. The hallmark of this tumor is the unique presence of mature teratoma components, as well as tumor marker values that become negative with chemotherapy, and remain low thereafter. We report the case of a 28-year-old female who presented a mixed germ cell tumor of the ovary, for which she underwent surgery and subsequent chemotherapy. Later, she developed multiple pelvic tumors that corresponded to mature teratoma. It was crucial in this patient to identify the syndrome to avoid additional treatment with chemotherapy.

Key words: Neoplasm, Germ Cell, Embryonal cell, Teratoma, Peru

RESUMEN

El síndrome de teratoma creciente (STC) es una condición infrecuente en la que se evidencia aumento de tamaño de los tumores de células germinales o la aparición de nuevas lesiones, durante o después del tratamiento con quimioterapia. Lo más característico de este tumor es la presencia exclusiva de componentes de teratoma maduro, así como valores de marcadores tumorales que negativizan durante la quimioterapia, y se mantienen negativos durante el seguimiento. Se presenta el caso de una mujer de 28 años con un tumor de ovario de células germinales mixtas sometida a cirugía y luego quimioterapia. Durante el seguimiento, desarrolló múltiples tumores pélvicos que correspondieron a teratomas maduros. En esta paciente, fue crucial identificar el síndrome de teratoma creciente para evitar tratamiento adicional con quimioterapia.

Palabras clave. Neoplasia, Células germinales, Células embrionarias, Teratoma, Perú.

Introduction

The growing teratoma syndrome (GTS) was initially described in 1982, by Logothetis et al.[1], in male patients with non-seminomatous germ cell tumors. It is defined by the presence and enlargement of tumors, during or after chemotherapeutic treatment for non-seminomatous germ cell tumors, accompanied by the normalization of previously elevated tumor marker values and the exclusive presence of mature teratoma components in the histological evaluation of the tumor[2]. There are previous reports that describe a similar phenomenon in women, known as the "chemotherapeutic retroconversion syndrome", although in the latter there is no increase in the size of the tumors[3].

An incidence between 1.9% and 11.7% is reported in patients with non-seminomatous germ cell cancer[4–7], and different hypotheses are postulated regarding the cause of this pathology. The main places where growing tumors are located are the pelvis, abdomen or retroperitoneum, although they have been found less frequently in lymph nodes and lungs[5].

We present the case of a 28-year-old female with a diagnosis of mixed germ cell tumor, managed with surgery and chemotherapy, and in whom GTS was diagnosed a year later due to the presence of pelvic masses in images.

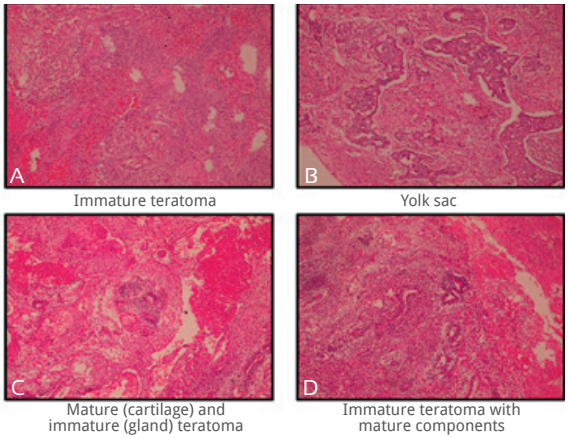
Case report

A 28-year-old nulliparous woman presented to the consultation with a disease time of 2 months, characterized by the presence of an abdominal tumor that increased in volume progressively, associated with pain and amenorrhea. Due to the clinical picture, an abdominopelvic multislice spiral tomography was obtained, in which a lobulated pelvic tumor was evidenced, with heterogeneous parenchyma, approximately 22 x 17 cm, dependent on the right adnexa and with signs of carcinomatosis. Likewise, elevated tumor marker values were found (Table 1).

In the initial surgery, the tumor was very extensive, had ruptured the capsule and compromised both ovaries, for which reason the contralateral ovary was not preserved.

In April 2016, an exploratory laparotomy was performed, with resection of the pelvic tumor dependent on the right adnexa, hysterectomy with extension to the vagina, left salpingo-oophorectomy, infracolic omentectomy, resection of a nodule on the surface of the bladder with raffia of the same and aspiration of peritoneal fluid for cytology, considering this an optimal debulking. During surgery, approximately 250 mL of free peritoneal fluid was found, a 45 cm tumor with solid and cystic components, with necrotic and friable areas, with a broken capsule, adhered to adjacent structures and with involvement of both ovaries, as well as tumor implants in peritoneum and sigmoid mesocolon, reason for which the decision was made for left salpingo-oophorectomy, without being able to preserve fertility. The pathology report describes a mixed germ cell tumor, with components of the yolk sac (70%), mature teratoma (20%), and immature teratoma (10%) (Figure 1).

Figure 1. Initial pathological anatomy: (A) Immature teratoma with undifferentiated primitive tissue components, (B) Germinal tumor with presence of pseudoglandular components belonging to a yolk sac tumor, (C) Mature teratoma with presence of cartilage and sebaceous glands, (D) Immature teratoma with presence of primitive neuroectodermal tissue.



Subsequently, the patient received chemotherapy with a scheme of four cycles of bleomycin, etoposide and cisplatin, followed by two cycles of etoposide and cisplatin, which she completed in October 2016 with a complete response. In the following months, she underwent regular check-ups without evidence of disease and negative tumor markers. In November 2017, in a tomographic control, a 25 mm nodular image was found in the left iliac chain which captured contrast (Figure 2). Tumor marker values remained negative.

For this reason, an exploratory laparoscopy was performed, which was converted to open surgery due to the presence of multiple adhesions. Six nodules, measuring between 8 mm and 3 cm, were found in the parietal, visceral peritoneum, ileum, and mesocolon (Figure 3). In histology, mature teratomas were reported, with components of cartilage, hair follicles, sebaceous glands and glands of the digestive tract (Figure 4).

Table 1. Tumor marker values.

	29/03/16	18/05/16	05/08/16	08/09/16	26/09/16	18/10/16	10/12/16	10/1216	16/03/17	02/08/17	21/12/17
AFP	513.7	>50 000	37.3	12.1	10.4	8	5.1	4.2	2.5	2.4	2.35
βhCG		1	1	1							
DHL		575	606	611	493	503	530	418		485	488
Ca 125											4.02

First surgery
Start of the chemotherapy
End of the chemotherapy
Second surgery

AFP=alpha fetoprotein, βhCG=β human chorionic gonadotrophin, DHL=lactic dehydrogenase

Figure 2. Tomography (11/13/2017). 25 mm nodular image with marked contrast uptake.

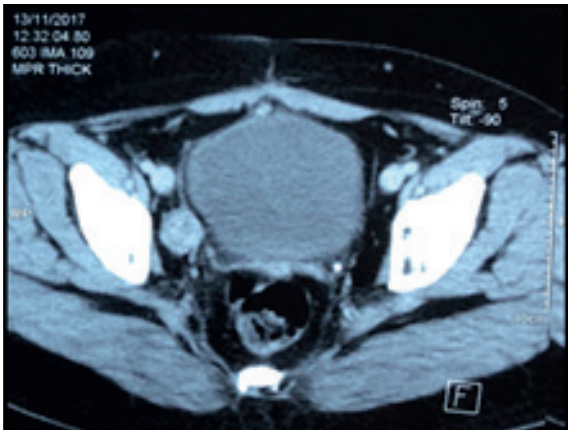


Figure 3. Surgical findings: vascularized solid tumor firmly adhered to the mesocolon and anterior peritoneal wall.

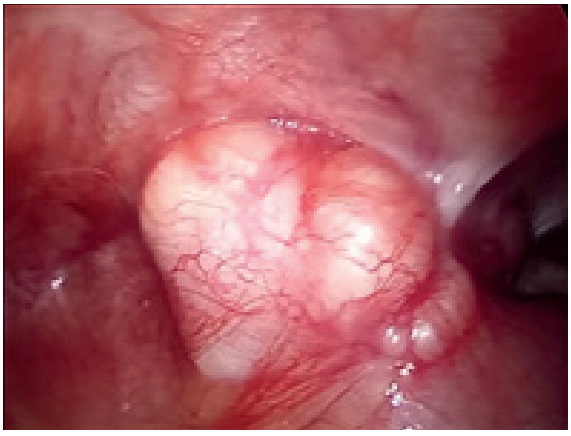
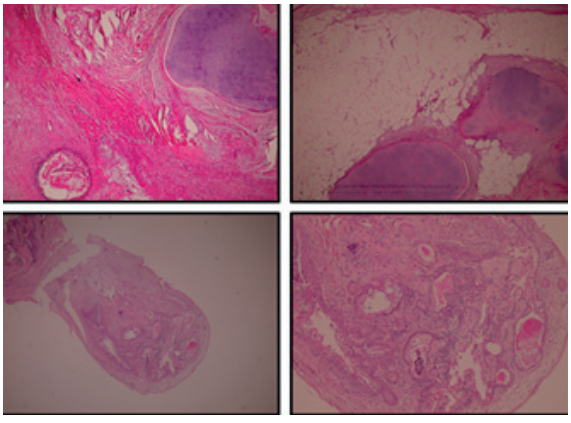


Figure 4. Mature teratoma, presence of well-differentiated structures of cartilage, sebaceous glands, follicles, adipose tissue and of the digestive tract, surrounded by connective tissue.



Discussion

Immature ovarian teratomas account for less than 1% of ovarian cancer cases, and are a rare type of germ cell tumor, mainly affecting young women, with diagnosis at age 19 average[6]. In Peru, the literature is limited, but this phenomenon has been reported in a case of testicular cancer[8]. These cases tend to respond favorably to surgical treatment with total or partial resection of the tumor, followed by chemotherapy with bleomycin, etoposide and cisplatin, given their high sensitivity to them[2]. Surgical treatment can preserve fertility even in cases of advanced disease if macroscopic evidence of disease is not found in the contralateral ovary. This achievement has been found in 52.6% of patients in a study, with subsequent pregnancy in 25% of them[9]. The finding of a tumor during subsequent follow-up may suggest recurrence. However, given the initial presentation of GTS, it should be ruled out for the establishment of the therapeutic plan[10].

GTS in an uncommon condition in which patients with germ cell tumors, as in this case, have an increase in size or the appearance of new tumor lesions during or after chemotherapy treatment. It is more common in cases of immature teratomas, but it also found in patients with mixed germ cell tumors[2]. Regarding these, the most frequent is dysgerminoma with endodermal sinus tumor. However, the composition of these tumors varies and determines the absence or elevation of different tumor markers, as reported in regional cases[9,11]. To meet the criteria established for diagnosis, the decrease and persistence of negative tumor marker values (alpha-fetoprotein and human chorionic gonadotropin) must be evidenced, as well as the exclusive presence of mature teratoma components in the tumors found, as with our patient.

Two probable mechanisms have been proposed for the development of this condition: the first is the selective eradication of the immature components of the initial tumor and the resistance of the mature components to chemotherapy, and the second, is the differentiation of immature to mature components induced by chemotherapy[12]. Likewise, the location of these tumors has been described in the abdominal, pelvic and retroperitoneal cavity in the vast majority of cases, although they have also been found in other organs such as the lungs or the brain, and in lymph nodes[5,13,14]. Distant disease is rare, but different routes of spread, such as direct invasion and hematogenous or lymphatic seeding, have been demonstrated, even in a single patient[12].

The presentation interval between the initial tumor and the GTS varies from 4 to 55 months approximately, with a median of 9 months, with reports from the second cycle of chemotherapy up to 12 years after the initial diagnosis. However, most cases present in the first two years, so the possibility of a recurrence must be present, as mentioned above[6]. In our patient, the appearance of new lesions occurred one year after the end of chemotherapy, and the location was the peritoneum. The diagnosis of GTS was made after the evaluation of the medical history, the pathology results and the tumor marker values, which defined appropriate management. Surgical management was decided, the patient did not receive more chemotherapy, and continued with periodic controls.

Surgical management of this entity is recommended due to the possible complications that may occur. First, the enlargement of the tumors could lead to compression of other organs, resulting in pain, intestinal obstruction, renal failure due to ureteral compression, or necrosis of the surrounding tissue. Second, the tumors can present a malignant transformation in 3-5% of cases, such as sarcomas, adenocarcinomas, carcinoids, or primitive neuroectodermal tumors[2,13–15]. Finally, resection of these lesions is recommended for histological analysis, in order to differentiate between GTS and recurrence of the disease, thus avoiding further cycles of chemotherapy.

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