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Giant dysgerminoma with pelvic metastases at the time of puberty: A case report and review of the literature

Disgerminoma gigante con metástasis pélvica en la pubertad: Un reporte de caso y revisión de literatura

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Abstract

This study aims to provide a comprehensive insight into the clinical presentation, diagnostic challenges and management strategies associated with a rare occurrence of giant dysgerminoma with pelvic metastases in an adolescent patient. We intend to add valuable information to the medical literature that may help to better understand and manage similar cases in the future, making this case report potentially valuable to clinicians and researchers in the fields of gynaecological oncology and paediatric oncology. Germ cells, the precursors of the ova in women and sperm in men, can give rise to germ cell tumours if their migration goes wrong during embryogenesis. These tumours, which can be malignant or benign, are generally rare. In particular, germ cell lesions in women are usually benign, whereas in men they are often malignant. These tumours can present as intra- or extragonadal masses due to the migratory nature of the germ cells. Dysgerminoma, a rare malignant germ cell tumour, is more common in men than testicular seminoma. In women, dysgerminomas account for 1-2% of malignant ovarian tumours and present as exotic lesions. They are usually relatively small, but giant lesions have been reported. They also exhibit rapid growth and a characteristic lobulated surface, retaining the ovarian shape. Extra-ovarian presentations are rare but may extend into the abdominal region. In men, seminomas may occur extra-testicularly, particularly in the mediastinum. Dysgerminomas respond well to radiotherapy and chemotherapy, with survival rates of over 90% at five years with timely and appropriate treatment worldwide.

Resumen

El objetivo de este estudio es ofrecer una visión exhaustiva de la presentación clínica, las dificultades diagnósticas y las estrategias de tratamiento asociadas a un caso poco frecuente de disgerminoma gigante con metástasis pélvicas en una paciente adolescente. Pretendemos añadir información valiosa a la literatura médica que pueda ayudar a comprender y tratar mejor casos similares en el futuro, haciendo que este informe de caso sea potencialmente valioso para clínicos e investigadores en los campos de la oncología ginecológica y la oncología pediátrica. Las células germinales, precursoras de los óvulos en la mujer y de los espermatozoides en el hombre, pueden dar lugar a tumores de células germinales si su migración sale mal durante la embriogénesis. Estos tumores, que pueden ser malignos o benignos, suelen ser poco frecuentes. En particular, las lesiones de células germinales en la mujer suelen ser benignas, mientras que en el hombre suelen ser malignas. Estos tumores pueden presentarse como masas intragonadales o extragonadales debido al carácter migratorio de las células germinales. El disgerminoma, un tumor maligno raro de células germinales, es más frecuente en los hombres que el seminoma testicular. En las mujeres, los disgerminomas representan el 1-2% de los tumores malignos de ovario y se presentan como lesiones exóticas. Suelen ser relativamente pequeños, pero se han descrito lesiones gigantes. También presentan un crecimiento rápido y una superficie lobulada característica, conservando la forma ovárica. Las presentaciones extraováricas son raras, pero pueden extenderse a la región abdominal. En los hombres, los seminomas pueden aparecer extratesticularmente, sobre todo en el mediastino. Los disgerminomas responden bien a la radioterapia y la quimioterapia, con tasas de supervivencia superiores al 90% a los cinco años con un tratamiento oportuno y adecuado en todo el mundo.

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Introduction

Ovarian dysgerminoma (OD) is a subgroup of malignant tumours characterised by rapid growth, a marked propensity for lymphatic dissemination, and a remarkable responsiveness to chemotherapy coupled with an increased sensitivity to radiation [1]. This malignancy originates from the primordial germ cells within the ovary and represents a distinct category among ovarian neoplasms [2]. In particular, dysgerminomas differ from other ovarian tumours in the absence of precursor lesions, adding a unique facet to their pathogenesis [1,3]. The etiological basis of OD remains elusive, adding to the complexity of its origins. The World Health Organization (WHO) classification identifies OD as tumours composed of primitive germ cells that lack a specific differentiation pattern [1,4]. This classification provides a framework for understanding the histological nature of dysgerminomas [4].

Statistically, dysgerminomas account for a relatively small proportion of all ovarian malignancies, ranging from 0.9% to 2%, but they represent a significant proportion, accounting for approximately one third to almost half (33-37%) of malignant ovarian germ cell neoplasms [1-5]. This prevalence underscores the uniqueness and clinical importance of dysgerminomas within the spectrum of ovarian tumours, necessitating a comprehensive investigation of their characteristics and clinical behavior [5].

Once the presence of ovarian dysgerminoma (OD) has been confirmed, a thorough preoperative paraclinical evaluation is essential. This comprehensive evaluation should include routine quantification of specific tumour markers in serum, including lactate dehydrogenase (LDH), carcinoembryonic antigen (CEA), cancer antigen 125 (CA125) and beta-human chorionic gonadotropin (Bhcg) [6]. Elevated levels of these markers often help to rule out alternative diagnoses and guide the subsequent surgical approach and technique. For the definitive diagnosis of dysgerminoma, histopathological examination using immunohistochemical techniques remains the gold standard [3]. This meticulous analysis allows precise identification and characterisation of the tumour, contributing to a nuanced understanding of its histological features and facilitating accurate classification [7].

Given the propensity of dysgerminomas for lymphatic metastasis, imaging studies are an integral part of the diagnostic process. Ultrasound and computed tomography (CT) play a key role in delineating the extent of lymphatic involvement and guiding treatment decisions [3,8]. These modalities provide critical insight into the staging of the disease and help to formulate an informed therapeutic strategy. Surgery is becoming an essential intervention, not only for definitive diagnosis, but also for staging and initiating the initial phase of treatment. Surgery is a critical step in the management of ovarian dysgerminoma, allowing accurate assessment, determination of the extent of disease spread, and implementation of therapeutic interventions tailored to the individual patient's needs [9].

Case presentation

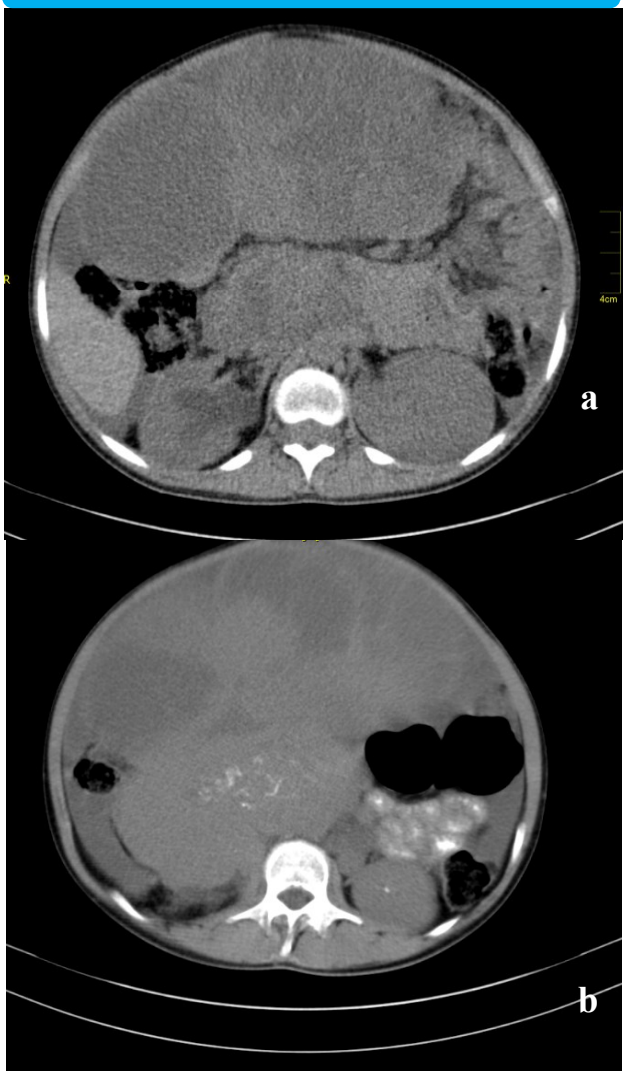
This is a 13-year-old female adolescent with suspected abdominopelvic neoplasia dependent on the right ovary, for which the gynaecology department ordered outpatient investigations, which reported the presence of a solid, nodular image without evidence of fluid content or necrosis, measuring 177 x 140 mm, at the abdominopelvic level and dependent on the right adnexa. According to the images, the lesion rejected the intestinal loops. No further investigation or follow-up was performed after the above study. 12 months later, the patient presented to the referral centre with progressive growth of the mass and abdominal distension associated with abdominal pain. Physical examination by the paediatric surgery department, revealed a hard abdomen on palpation with the presence of a giant mass involving all lower quadrants, with a stony consistency and non-tender to palpation, with no signs of peritoneal irritation.

On admission, a routine serum tumour marker panel and a double-contrast abdominal CT scan were performed (Figure 1). Based on the results, conservative surgery was planned with a modified ovarian protocol: postoperative exploratory laparotomy, ovarian tumour resection and right adnexectomy, partial omentectomy, left ovarian biopsy, liver biopsy by trucut and appendectomy [10,11].

Intraoperative findings included: free ascitic fluid in the cavity, presence of a large giant tumour with an estimated weight (5 kg) (see Figure 2) of purplish colour, vascularised and fleshy appearance, crossing the contralateral midline, covering most of the abdominal cavity up to the pelvic cavity and including the ipsilateral uterine tube, numerous adhesions to the retroperitoneum were evident, multiple whitish and

friable seeding was also found on the peritoneal surface, predominantly on the right diaphragmatic dome.

Figure 1. Dual-contrast computed axial tomography

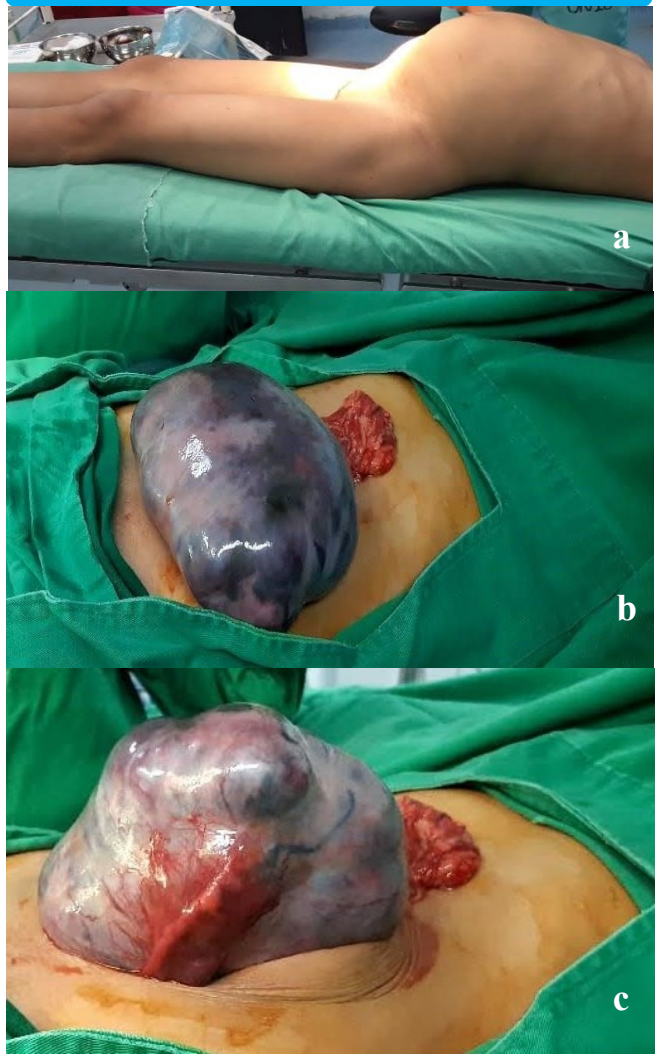


The uterus and left ovary were found to be macroscopically free of lesions. The patient was referred to anatomopathology for multiple sampling of the main lesion and associated findings for staging purposes. Following the diagnosis, the patient was referred to the oncology service for further management [12]. Postoperatively, an MRI of the abdomen and pelvis was performed (on day 6, Figure 3), which showed the absence of the right ovary, loops attached to the retroperitoneum, abundant lymphadenopathies, a small left ovary, and a small uterus and left ovary.

Pathological anatomy

The main lesion consisted of the right ovarian tumour weighing approximately 3000g, with cystic and solid areas interspersed on the surface. On sectioning, a solid, uniform, post-formalin-fixed, greyish-brown stroma was observed, interspersed with foci of haemorrhage and cystic structures of variable size. Samples of the omentum, cecal appendix, a liver biopsy obtained by tricut needle and the contralateral uterine tuba were also obtained.

Figure 2. Intraoperative findings

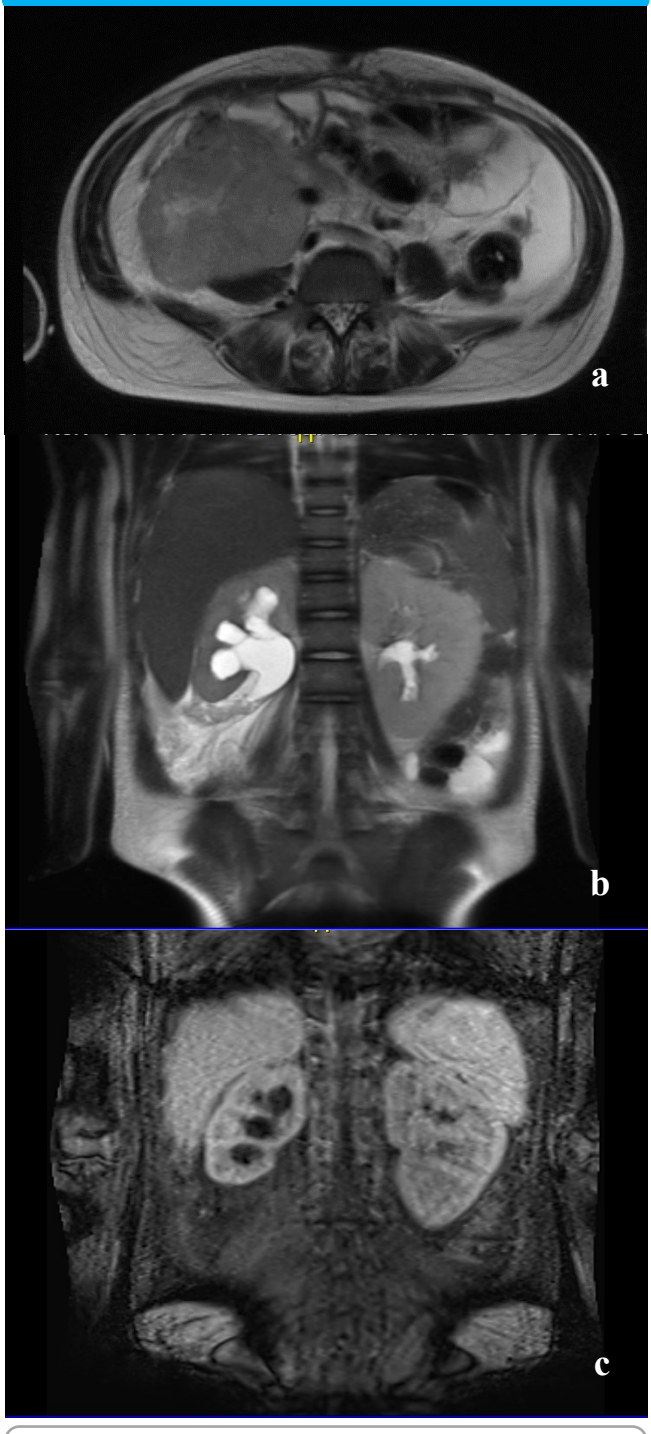


a: Increased abdominal volume in a paediatric patient; **b:** Giant tumour involving the right ovary as seen through the incision made during surgery; **c:** Volume of the tumour including the right uterine tube.

Histological sections of the right ovarian lesion showed the presence of a malignant neoplasm composed of polygonal, uniform, large cells arranged

in cords and nests, with microcystic formations in an interspersed reticular pattern. The mitotic rate of the lesion was high. Areas of haemorrhage and necrosis [13] were also observed.

Figure 3. Abdominal and pelvic MRI with contrast: Taken on postoperative day 6



a: Lesion in the right hypochondrium; **b:** Both right and left Skin Dilatation of the skin on the right and left; **c:** Enlarged kidneys.

The mitotic rate of the lesion was high. Areas of haemorrhage and necrosis were also observed. The sheets of tumour cells described were sometimes interrupted by tracts of fibrous connective tissue within which lymphocytes were identified in a histopathological pattern similar to that of a seminoma (Figure 4), confirming the known homology between this tumour in men and dysgerminoma in women. In the remaining specimens, there was evidence of tumour foci extending from the main lesion only in the omentum [12, 13].

The initial histopathological diagnosis was a germ cell tumour with a phenotype to be defined by immunohistochemistry. However, the initial pathological-paraclinical correlation indicated the elevated levels of alpha-fetoprotein, CA-125 and especially LDH, which was 4,238 U/l. In line with the histological findings [14], this could support the possibility of a mixed lesion with a dysgerminoma component and yolk sac tumour as the phenotype of the lesion observed, i.e. it was a biphasic or mixed tumour [15]. Immunotyping was performed with the markers glypican 3, SALL4, D2-40, OCT3/4, inhibin-A and AFP. Expression of tumour cells with the markers SALL4, D2-40, OCT3/4 was observed (Figure 5). Other markers were negative in the specimens. The observed immunohistochemical pattern supported the diagnosis of germ cell tumour, mixed dysgerminoma variety [14,15].

Post-diagnostic evolution

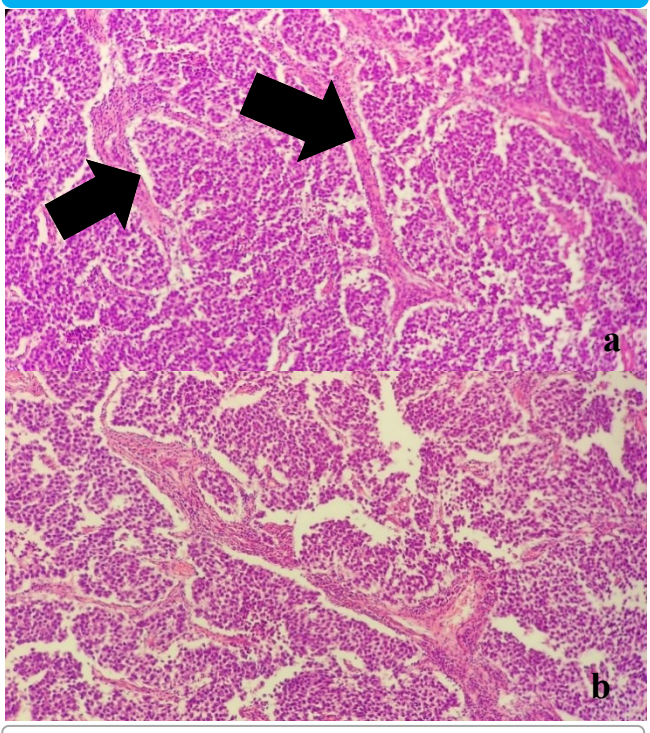
The patient was referred to the paediatric haemato-oncology service with a diagnosis of right ovarian tumour, mixed dysgerminoma without vascular invasion and confined to the ovary with omental pelvic metastases, classified by TNM and FIGO as T3CN1M1 and FIGO stage IIIC/IV. She was treated with curative intent according to the BEP chemotherapy protocol with no paraclinical changes in serum markers in the months following the start of chemotherapy, no evidence of collateral hepato-renal dysfunction, PET-CT and echocardiogram without findings of clinical relevance. At months 5 and 6, imaging controls were performed: chest x-ray and abdominal ultrasound, as well as negative tumour markers.

Discussion

Ovarian tumours of a malignant nature are rare in the

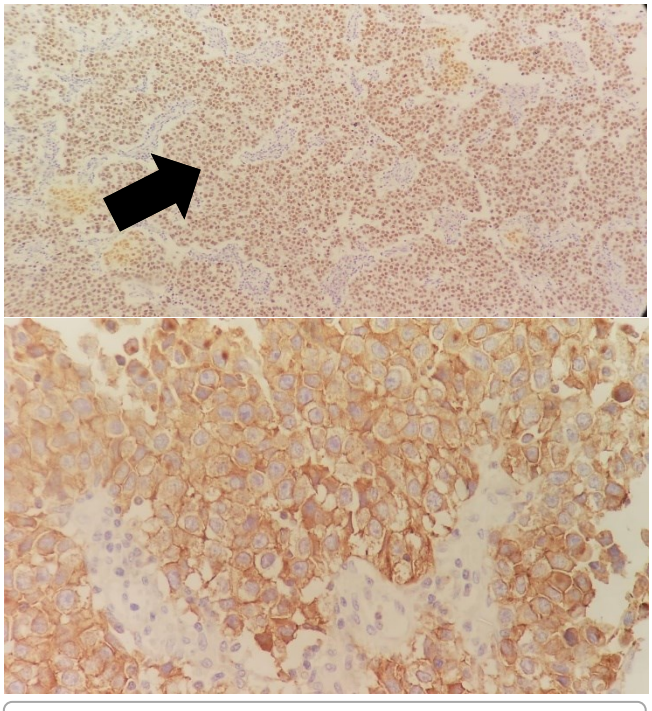
paediatric age group. Dysgerminoma is a rare malignant neoplasm affecting this cohort, requiring surgery and a diagnostic approach based on pathological anatomy and immunotyping of the case [16,17].

Figure 4. Haematoxylin and eosin. 4x and 10x, respectively



Tumour cell sheets interrupted by vascularised fibrous tissue tracts (arrows) with presence of lymphocytes

Figure 5. OCT3/4 and D2-40 Immunohistochemistry



Note the nuclear and cytoplasmic-membranous expression patterns.

Serological tumour markers are useful in the initial pre-surgical evaluation to raise the differential suspicion of the phenotype and show their real utility in the post-treatment oncological follow-up for early detection of possible recurrences [18]; LDH is the most sensitive tumour marker. The gold standard for the diagnosis of the tumour is 100% the histopathological study, complemented by immunohistochemical analysis; the expression of the markers OCT3/4, D2-40 and SALL4 are elements of judgement that support the diagnosis of dysgerminoma in any case [18]. Dysgerminomas are generally malignancies with a good prognosis, with a high cure rate, and they are also chemo- and radiosensitive, which allows neoadjuvant protocols to be carried out in the case of giant lesions [19]. Recurrence rates are low. The new combined treatments of surgery and chemotherapy achieve survival rates of over 90% in some series if the tumour is treated in early stages and 87% in advanced stages, according to the literature [16-19]. During chemotherapy, up to 50% of patients experience amenorrhoea, but most of them recover normal ovarian function by the end of treatment [20].

Dysgerminomas may be associated with paraneoplastic syndromes, mainly hypercalcaemia. The reported mean age of patients at diagnosis is 12.5 years [3,5,20]. Semiologically, the clinical picture usually presents with progressive abdominal pain and a rapidly growing palpable abdomino-pelvic mass. In adolescents and even in women of childbearing age, pregnancy may be implicated as a triggering factor for the tumour, suggesting a hormonal component associated with tumourogenesis [21].

Timely medical attention, early surgical intervention and rapid histological diagnosis have a favourable effect on the response to treatment. It is therefore important to bear in mind that, until proven otherwise, any abdominal growth in prepubertal girls or adolescent women corresponds to a germline tumour, including a dysgerminoma; in the rare cases of tumours in adult women, the diagnosis is one of exclusion, often late, and the prognosis is usually less favourable [22,23].).

Because it is a fast-growing tumour with an early propensity for distant invasion, lymph node

involvement may be found concomitantly with the presentation of the primary tumour, mainly in the retroperitoneal and para-aortic lymphatic chains, making it essential to perform imaging studies prior to surgery: ultrasound, CT or nuclear magnetic resonance. However, ultrasound is not only the most cost-effective technique, but also the most useful and quickest to detect and characterise the different adnexal masses. Of the ultrasound findings, the description of solid tumour parenchyma is in itself the most prognostically significant piece of information suggesting the possibility of malignancy.

Conclusion

Dysgerminomas develop as aggressive tumours characterised by increased lethality in the absence of prompt intervention. The critical determinant of favourable outcomes is early diagnosis, coupled with surgical and oncological interventions tailored to the therapeutic needs of the lesion. Remarkably, when these criteria are met, success and survival rates exceed 90%, underscoring the efficacy of a well-coordinated treatment approach.

However, the prognosis of dysgerminomas depends on several key factors. Parameters such as tumour size, the presence of extraovarian extension at the time of diagnosis, histological subtype, degree of differentiation, the presence of a mixed component and the presence of peritoneal seeding collectively shape the prognostic landscape. The complex interplay of these variables underscores the nuanced nature of dysgerminoma prognosis.

In the case presented here, despite the delay in management due to the patient's non-attendance after the initial imaging, the diagnosis was made quickly after the semiological elements of the tumour worsened, thanks to the fact that a preoperative total tumour excision was performed, which, in addition to the lumpectomy, allowed other areas of macroscopic involvement to be removed and biopsies to be taken from areas of suspected involvement. Histologically, the lesion corresponded to a mixed ovarian dysgerminoma, which was completely resected without complications, with omental tumour seeding observed. At the time of writing, serial follow-up at 36 months post-treatment shows that the patient is asymptomatic and free of tumour recurrence after cancer treatment and without collateral organ involvement after chemotherapy.

Consent for publication

The authors read and approved the final manuscript.

Competing interest

The authors declare no conflict of interest. This document only reflects their point of views and not that of the institution to which they belong.

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