Diagn Interv Radiol 2023; DOI: 10.5152/dir.2022.21317

ABDOMINAL IMAGING

PICTORIAL ESSAY

Ovarian dysgerminoma: clues to the radiological diagnosis

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ABSTRACT

Ovarian dysgerminoma (OD) is a rare germ cell tumor accounting for 1%–2% of all malignant ovarian tumors and is generally associated with a good prognosis. The condition is more frequent in young women and can arise in dysgenetic gonads that contain gonadoblastomas. While the definitive diagnosis of OD is only possible histologically, certain radiological features can provide facilitating clues. A large, unilateral, solid, lobulated ovarian tumor with markedly enhancing septa should raise the suspicion of OD in young women. Serum lactate dehydrogenase is characteristically elevated in this tumor type and can complement its diagnosis and postoperative follow-up; however, it is a nonspecific marker. Moreover, knowing the mimickers of OD is essential to optimizing the radiological image interpretation and allowing for adequate management and timely treatment. Therefore, in this article, the radiological and clinical-pathologic features of ODs were reviewed to allow radiologists to become familiarized with them and narrow the diagnostic possibilities when facing this type of tumor.

KEYWORDS

Computed tomography, magnetic resonance imaging, ovarian dysgerminoma, radiology, ultrasound

Ovarian tumors are divided into epithelial neoplasms, mesenchymal neoplasms, sex cord-stromal tumors, and germ cell tumors.[1] According to the 2020 World Health Organization Classification of Tumors, ovarian germ cell tumors include mature and immature teratoma, dysgerminoma, yolk sac tumors (YSTs), embryonal carcinoma, non-gestational choriocarcinoma, mixed germ cell tumors, monodermal teratomas and somatic type, and germ cell-sex cord-stromal tumors.[1] Ovarian dysgerminoma (OD) is a rare malignant tumor that derives from primordial germ cells and constitutes the female equivalent of testicular seminoma.[1-9] This type of tumor accounts for 1%–2% of malignant ovarian tumors and constitutes the most common ovarian malignant germ cell neoplasm, with an incidence rate of 32.8%–37.5%.[1-10]

While OD can occur at any age, females in their second to third decades of life are the most affected, and 15%–20% are diagnosed during pregnancy or post-childbirth.[4-9] However, the pathogenesis is still not well understood. The attendant theories suggest that OD can emerge from gonadoblastomas associated with gonadal dysgenesis or directly from primordial germ cells with spontaneous *KIT* gene mutations.[5,6,10] In rare cases, gonadoblastomas can arise in females without chromosomal abnormalities or gonadal dysgenesis.[10] In contrast to other germ cell tumors, OD can occur in both ovaries in 10%–15% of cases,[1-3] while the right ovary is generally the most affected, largely due to its slower differentiation.[2] While most patients are symptomatic, presenting a palpable pelvic or abdominal mass, OD may be present in asymptomatic women.[6,8] Menstrual disorders, abdominal enlargement and severe pain, explained by torsion, hemorrhage, or tumor rupture, are among the attendant complaints.[2-6]

High lactate dehydrogenase (LDH) levels are often associated with OD and can be used to complement the diagnosis and assist in postoperative follow-ups; however, this presents a non-specific laboratory finding.[2-6,8-12] In 3%–5% of cases, OD also contains syncytiotrophoblastic cells, which produce low quantities of human chorionic gonadotropin.[1,4-7] This feature can be responsible for endocrine abnormalities and for stimulating pregnancy.[5,6]

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Received 22 March 2021; revision requested 27 April 2021; last revision received 2 September 2021; accepted 4 October 2021

Epub: 21.12.2022

Publication date: 31.01.2023

DOI: 10.5152/dir.2022.21317

You may cite this article as: Amante S, Félix A, Cunha TM. Ovarian dysgerminoma: clues to the radiological diagnosis. *Diagn Interv Radiol.* 2023;29(1):18-23.

Generally speaking, OD spreads late, typically through the lymph system (28% of cases).[4] Peritoneal implantation occurs when tumor rupture is present.[4] This malignancy generally has an excellent prognosis, with almost 100% at the five-year survival rate, even when chemotherapy is needed.[1-6] Furthermore, around 75% of ODs are detected at an early stage, with surgery the main treatment option.[8,9]

Studies have reported that OD imaging reveals a large, multilobulated mass, predominantly solid, with lobules divided by fibrovascular septa.[6-10] While various radiological clues can help in diagnosing OD, accurate preoperative diagnosis using radiologic findings alone remains a challenge. Nonetheless, radiologists must be aware of this tumor's main characteristics, both in terms of the different imaging methods and the attendant pathology and markers, to reduce the differential diagnosis. This article thus reviews the imaging appearance of OD using a multimodal approach and explores its differential diagnoses.

Morphology and histopathology

Macroscopically, ODs are large, solid, multinodular tumors, which appear fleshy, yellow, or cream-colored (Figure 1).[4-6] Areas of necrosis, hemorrhage, and cystic degeneration may occur,[1,4-6] while calcifications can also be seen in dysgerminomas, typically with a speckled or spotted pattern.[1,2] Grossly visible calcifications only occur in dysgerminomas arising from a pre-existing gonadoblastoma with calcifications described as mottled or punctate. However, calcifications may also be detected in dysgerminomas without an underlying recognizable gonadoblastoma.[2]

Main points

- Ovarian dysgerminoma (OD) is a rare germ cell tumor with good prognosis that affects young females.
- Imaging can provide clues for the diagnosis of OD, revealing a large, predominantly solid, and multilobulated lesion with fibrovascular septa, which typically have low signal intensity on T2-weighted images without edema and marked enhancement on contrast-enhanced images.
- The condition typically presents with nonspecific elevated serum lactate dehydrogenase levels.
- The main treatment for OD is surgery that often allows for fertility preservation.

Microscopically, ODs are generally composed of round cell nests separated by thin fibrous septa infiltrated by lymphocytes (Figure 1).[1,4-6] Tumor cells are large and polygonal in shape with clear or eosinophilic cytoplasm containing a large central nucleus.[1,4-6] Mitoses are often abundant.[4-6] Immunohistochemically, OD can be positive for octamer-binding transcription factor 4, Sal-like protein 4, LIN28, NANOG, KIT (CD117) and D2-40, and negative for epithelial membrane antigen, CD30 and GPC3, while cytokeratins may be focally positive.[1]

Radiological findings

Ultrasound

On ultrasound imaging, OD frequently appears as a solid mass without specific features.[3] In most cases, it consists of a multilobulated tumor with smooth contours, well-defined borders, and heterogeneous echogenicity, characterized by prominent fibrovascular septa.[4-6] Necrosis, hemorrhagic areas, and speckled calcifications may also be depicted (Figure 1).[2-5] Under color or power Doppler ultrasound imaging, OD is highly vascularized, revealing a prominent flow in the septa (Figures 1-3).[4-6]

Computed tomography (CT)

While the classic septa of OD are generally thin, in the presence of stromal edema, they can become thickened or amorphous with low attenuation on CT examination (Figure 3).[2] Due to their fibrous content, septa frequently demonstrate avid enhancement on contrast-enhanced CT imaging (Figure 3).[2-5] Moreover, hyperdense and speckled calcifications have been observed in this type

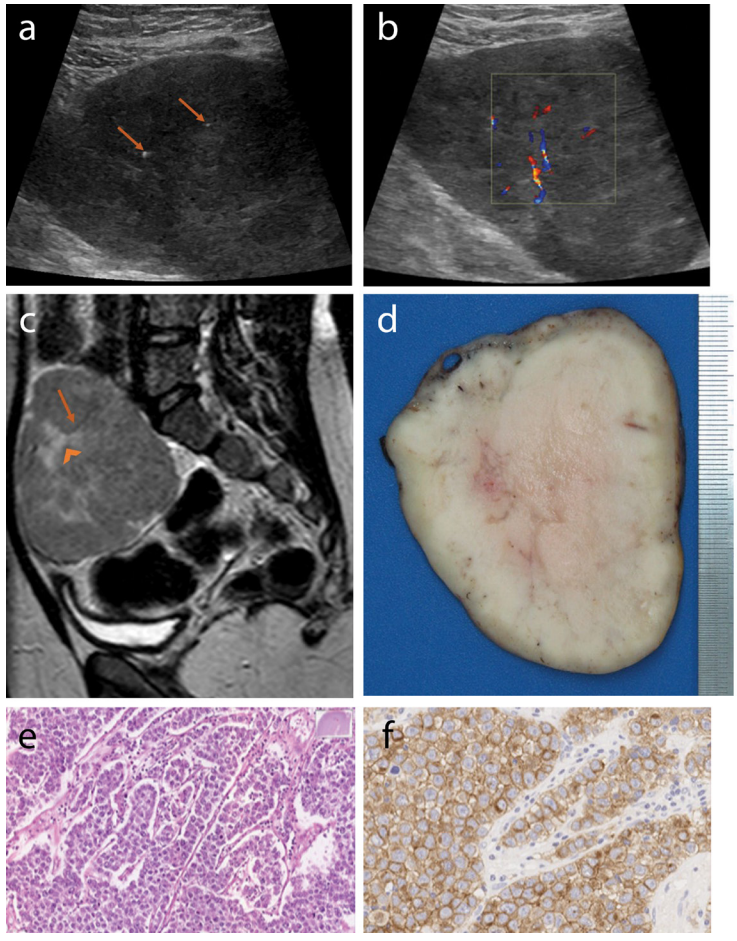

Figure 1. An eight-year-old female patient with Mayer–Rokitansky–Küster–Hauser syndrome was diagnosed with left ovarian dysgerminoma. Transabdominal pelvic ultrasound images **(a, b)** showing a heterogeneous, predominantly hypoechoic solid tumor with some scattered calcifications (*thin arrows*, **a**). Note the fibrovascular septa blood flow on the color Doppler study **(b)**. Sagittal T2WI **(c)** showing a large pelvic tumor with intermediate-SI and prominent septa with linear low-SI vessels (arrow) and high-SI edematous component (arrowhead). The section surface of the left adnexal specimen **(d)** shows a solid and capsulated cream-colored tumor. Hematoxylin and eosin staining of the dysgerminoma **(e)** reveals uniform large cells with empty nuclei and prominent nucleoli separated by fibrous septa with some lymphocytes. Anti-CD117 staining **(f)** reveals all cells stained in the cytoplasm and cell membrane; septa with disperse lymphocytes are negative. T2WI, T2-weighted imaging; SI, signal intensity.

of tumor, as well as in its retroperitoneal spread.[2,7,9] The nonspecific "ovarian vascular pedicle" sign was also identified in large ODs (Figure 3), which provides a clue for ovarian origin, allowing for narrowing the differential diagnosis.[2] Recently, Tsuboyama et al.[10] described the presence of central vessels that converge from the septa as a possible OD characteristic, while further studies are needed in this regard.[10]

Magnetic resonance imaging (MRI)

On MRI, OD manifests as a large, multilobulated, predominantly solid tumor with heterogeneous signal intensity (SI) and prominent fibrovascular septa.[6-10] Generally, it mainly has low- or intermediate-SI relative to muscle on T1-weighted imaging (T1WI) and intermediate-SI on T2-weighted imaging (T2WI) (Figures 2, 4).[2,4] On T2WI, tumoral septa typically appear as thin lines with low- or intermediate-SI, while on T1WI, they are difficult to grasp, commonly presenting low-SI (Figures 2, 4).[2-5] When edematous changes are present, the septa may become thickened with high-SI on T2WI ((Figure 1).[2,4] Depending on the degree of edema, they can be classified into thin non-edematous, thin edematous, thick edematous, and map-shaped edematous septa, which are predominant in large tumors.[2] Notably, 50% of ODs display more than one type of septa.[2] Large tumors generally exhibit heterogeneous SI, partly caused by necrosis or hemorrhage (Figures 2, 4).[2,7] Necrosis and hemorrhage do not enhance after contrast administration and exhibit high-SI on T2WI, while on T1WI, necrosis has low-SI and hemorrhage high-SI.

Following gadolinium administration, OD generally enhances less than normal myometrium and its septa demonstrate intense enhancement with mild or no enhancement of the edematous component (Figures 2, 4).[2-5] According to its malignancy and increased cellularity, OD is also associated with diffusion restriction, exhibiting high-SI on diffusion-weighted imaging (DWI) and low apparent diffusion coefficient (ADC) values (Figure 2).[2,9] Zhao et al.[2] reported a mean ADC value of $0.830 \pm 0.154 \times 10^{-3}$ mm^2/s for OD; however, further studies are needed.

Thus, when facing a large, predominantly solid, multilobulated ovarian mass, with diffusion restriction and prominent septa, which characteristically demonstrates low-SI on T2WI and avid enhancement following contrast administration, the diagnosis of dysgerminoma in young women with elevated serum LDH values should be considered. The

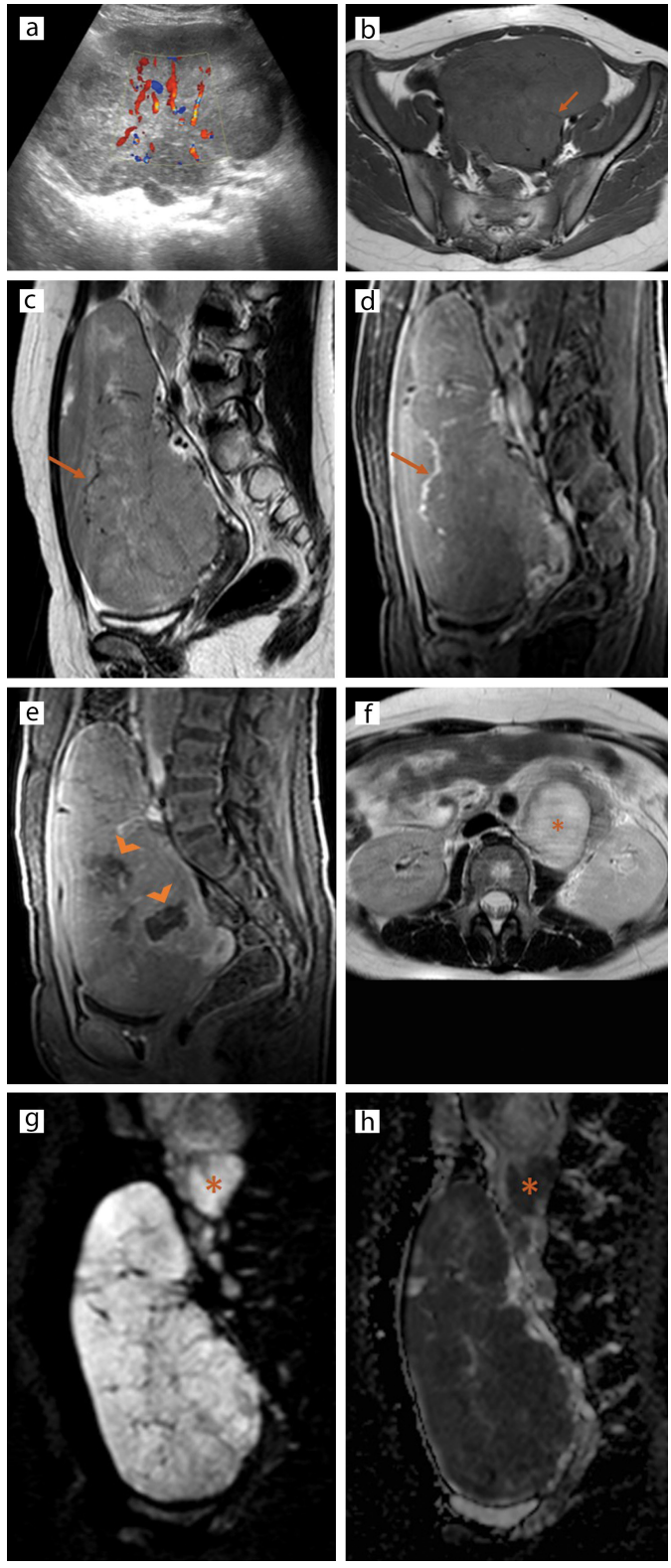

Figure 2. A 12-year-old female patient was diagnosed with left ovarian dysgerminoma and lymphatic dissemination. Transabdominal pelvic color Doppler ultrasound imaging **(a)** revealing a solid multilobulated tumor with heterogeneous echogenicity and marked vascularization. Axial T1WI **(b)** sagittal T2WI **(c)** and sagittal contrast-enhanced T1WI **(d)** revealing a large lobulated solid mass, divided into lobules by septa, which have low-SI on T1 and T2WI and avidly enhance following gadolinium administration (thin arrows, **b-d**). Sagittal gadolinium-enhanced image **(e)**: note the lower enhancement of the tumor compared to myometrium and the presence of concomitant areas of necrosis (arrowheads). Axial T2WI **(f)** revealing left para-aortic adenopathy (asterisk). Pelvic tumor and adenopathy (asterisks, **g, h**) clearly show diffusion restriction, with high-SI on DWI (b= 1000 s/mm^2) **(g)** and low ADC values **(h)** (tumor ADC value: 0.76 mm^2/s; adenopathy ADC value: 0.68 mm^2/s). T1WI, T1-weighted imaging; T2WI, T2-weighted imaging; SI, signal intensity; ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging.

best imaging method for assessing these radiologic features is the MRI method, which allows for an accurate characterization of OD fibrovascular septa and for evaluating the behavior of the lesion in DWI examinations. While these findings are not specific to OD, when integrated with appropriate clinic and laboratory markers, they can help narrow the differential diagnosis.

Differential diagnosis

Differentiating dysgerminoma from other lesions and reaching a timely diagnosis is essential since it influences the treatment that can allow fertility to be preserved.[2-4, 8-10] Nevertheless, a differential diagnosis of OD can be challenging since some mimicking tumors may have nonspecific radiological features. In a young patient with an ovarian mass, radiological studies associated with clinical and laboratory parameters can be helpful in differentiating OD from granulosa cell tumors (GCT) (juvenile type), YST, Sertoli–Leydig tumors (SLT), and immature teratoma.[9] Furthermore, OD should also be differentiated from lymphoma, which can occur at a young age, as well as from benign tumors, such as sclerosing stromal tumors, ovarian fibroma, and subserosal uterine leiomyoma.

Juvenile GCT is an estrogen-producing tumor that typically presents with isosexual pseudoprecocity and menstrual alterations. On MRI, a sponge-like appearance (multiple cystic lesions within a solid mass) can be observed, which is not typical of OD (Figure 5).[3,13] Meanwhile, YST and SLT are generally unilateral lesions with non-specific radiological features.[9,13] Unlike OD, YST is usually associated with high alpha-fetoprotein values and SLT occurs with androgenic symptoms of virilization in 33% of cases.[9,13] Small areas of fat are important to distinguishing an immature teratoma from OD (Figure 6).[9]

Primary ovarian lymphoma without lymph nodes or bone marrow involvement is extremely rare and may be difficult to distinguish from OD.[9] The condition tends to appear as a bilateral, solid and large homogeneous mass, which enhances mildly and uniformly following contrast administration, without calcifications or ascites (Figure 7).[14] Studies have reported that ovarian lymphoma can course with septal structures with high-SI on T2WI and preserved ovarian follicles at its periphery.[15] These features can be useful diagnostic clues and help in differentiating OD, which generally presents low-SI septa on T2WI and with no peripheral follicles; however, the differential diagnosis can be difficult when OD reveals edematous septa.

While sclerosing stromal tumors occur predominantly in young women, much like OD, these tumors can be differentiated through their enhancement pattern. Sclerosing stromal tumors characteristically present avid and early peripheral contrast enhancement with centripetal progression, a pattern unassociated with OD (Figure 8).[5,7,12] Fibroma is the most frequent benign solid ovarian tumor, is uncommon at a young age and, unlike OD, is characterized by markedly low-SI on T2WI (Figure 9).[13] Cellular fibroma may have high-SI areas on T2WI, but septa are unusual.[13] Lastly, subserosal uterine leiomyomas should also be distinguished from OD. This type of tumor characteristically projects outward from uterine subserosa and reveals low to intermediate-SI on T1WI compared with myometrium and low-SI on T2WI. The presence of the bridging vessel sign on MRI (flow voids in the uterine feeding branches) reveals their uterine origin and can be a useful marker.[7]

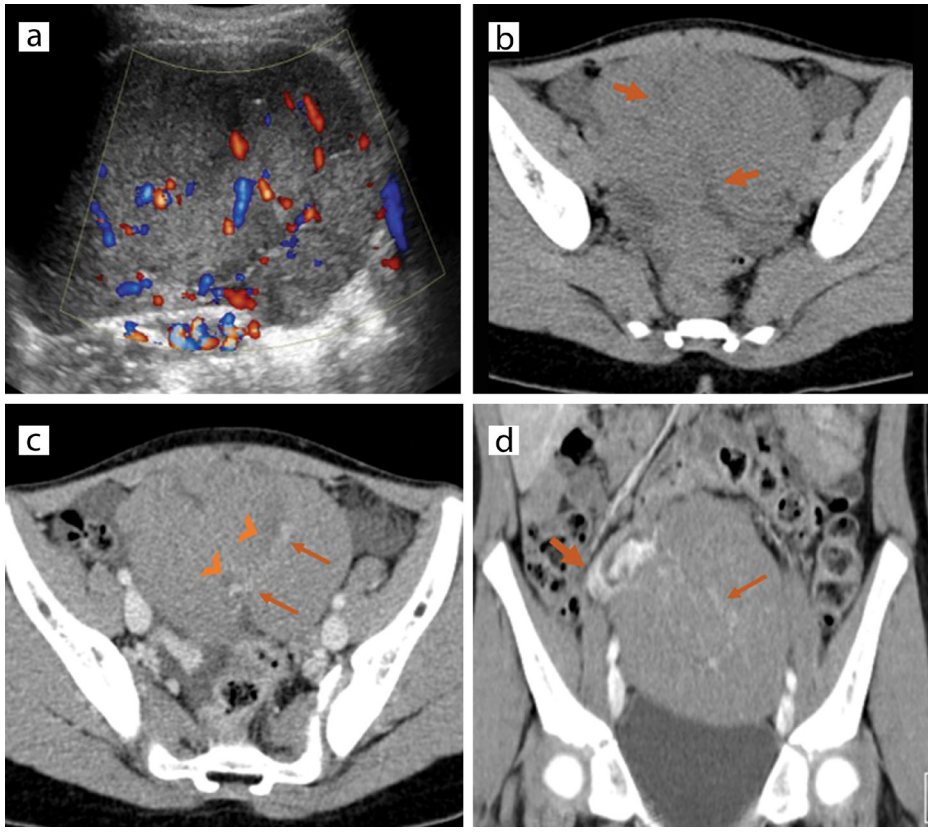

Figure 3. A 10-year-old female patient was diagnosed with right ovarian dysgerminoma. Transabdominal color Doppler US image **(a)** showing a solid mass with heterogeneous echogenicity and richly vascularized septa. Axial pre-contrast **(b)** and axial and coronal contrast-enhanced CT images **(c, d)** revealing a solid pelvic tumor with thick hypoattenuating septa (thick arrows, b) with enhancing vessels (thin arrows, **c, d**) and edematous non-enhancing components (arrowheads, **c**). Note the "ovarian vascular pedicle" sign, with enlarged right ovarian vein (thick arrow, **d**). CT, computed tomography.

Conclusion

OD is a rare germ cell tumor that can be challenging to diagnose. While diagnosis is only possible histologically, various radiological features should lead to its hypothesis, namely, the presence of a large, solid, and lobulated tumor with markedly enhancing septa in a young woman. The knowledge of the pathology, symptoms, and markers of OD is also essential to optimizing the radiological interpretation and enabling timely treatment and appropriate follow-ups. As such, radiologists must be familiarized with the characteristics of OD since they can be the first to suspect its presence.

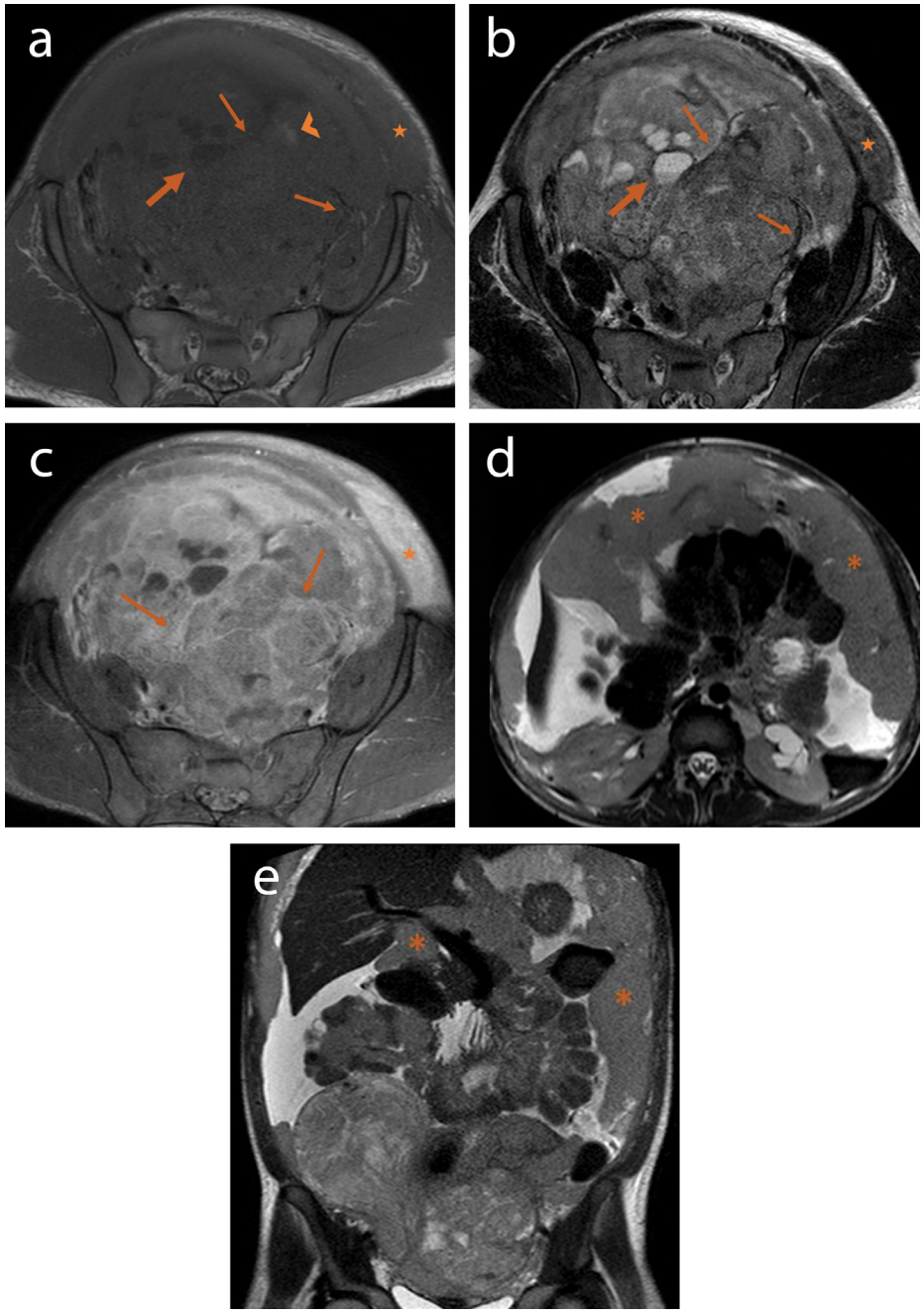

Figure 4. A 22-year-old female was diagnosed with bilateral ovarian dysgerminoma and peritoneal and lymphatic dissemination. Axial T1WI **(a)** and axial T2WI **(b)** show large, multilobulated, heterogeneous bilateral tumor, with septa of low-SI on T1WI and T2WI (thin arrows, **a**, **b**), some of them associated with edematous component. Hemorrhagic areas with high-SI on T1WI are observed (arrowhead, **a**), as well as multiple cystic areas, low-SI on T1WI and high-SI on T2WI (thick arrows, **a, b**). Axial gadolinium-enhanced image **(c)** revealing heterogeneous contrast enhancement of the tumor, with several enhancing and thickened septa (thin arrows). Axial and coronal T2WI **(d, e)** also reveal exuberant peritoneal metastases (asterisks). Note the presence of metastases in the left abdominal wall, anterior to the abdominal wall muscles, which were externalized through the entrance port of diagnostic laparoscopic surgery (stars, **a**, **b**, **e**). T1WI, T1-weighted imaging; T2WI, T2-weighted imaging; SI, signal intensity.

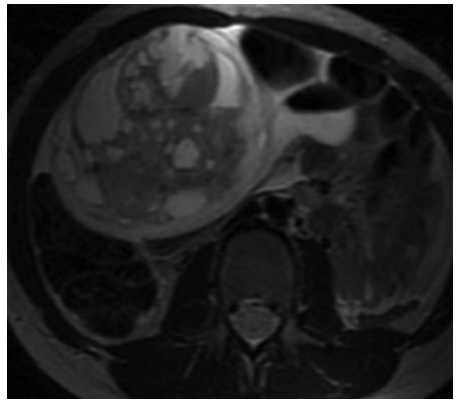

Figure 5. Axial T2WI showing a large right ovarian tumor, with a sponge-like appearance compatible with an ovarian juvenile granulosa cell tumor. T2WI, T2-weighted imaging.

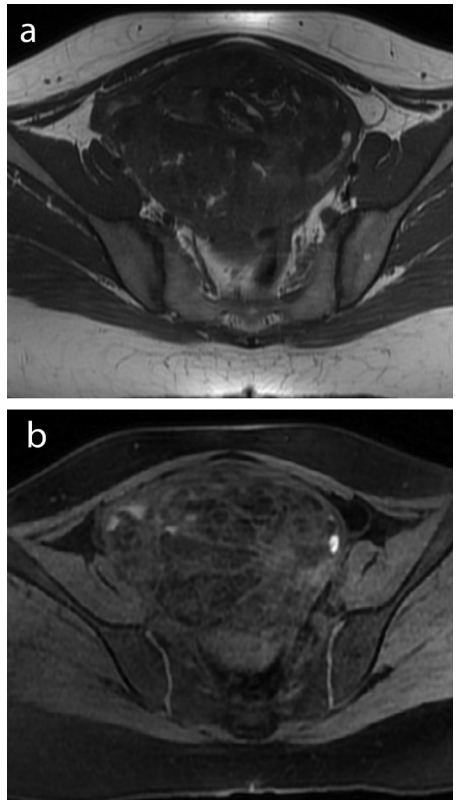

Figure 6. Axial T1WI **(a)** and fat-suppressed T1WI **(b)** revealing a large immature teratoma of the right ovary with small areas of fat. T1WI, T1-weighted imaging.

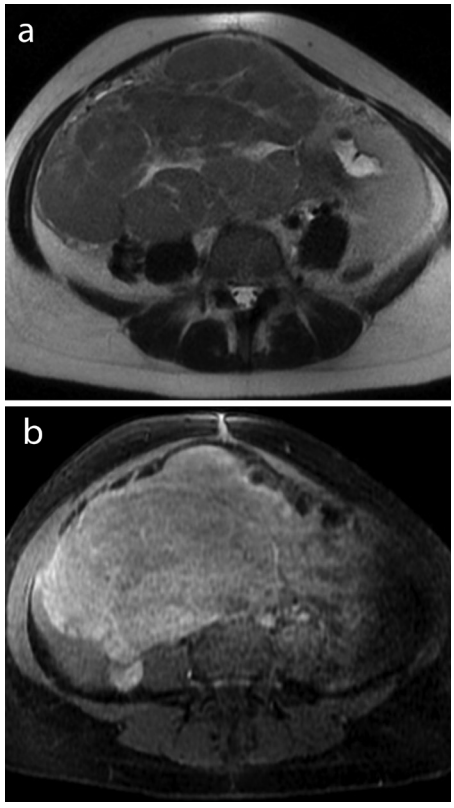

Figure 7. Axial T2WI **(a)** and gadolinium-enhanced image **(b)** revealing a bilateral primary ovarian B-cell lymphoma with high-SI septa on T2WI and progressive and homogeneous enhancement. T2WI, T2-weighted imaging; SI, signal intensity.

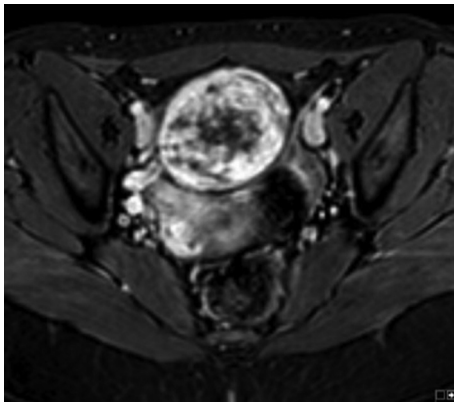

Figure 8. Axial gadolinium-enhanced image revealing a right ovarian sclerosing stromal tumor with avid and early peripheral contrast enhancement.

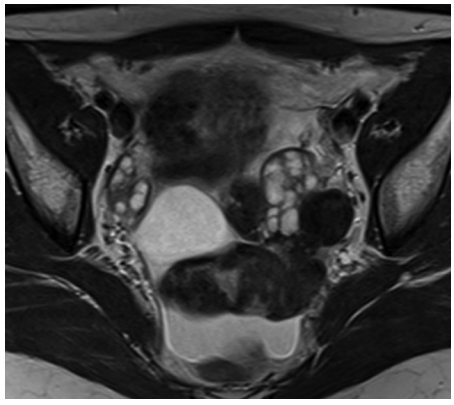

Figure 9. Axial T2WI revealing a left ovarian fibroma with markedly low-SI. T2WI, T2-weighted imaging; SI, signal intensity.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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