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Extra-uterine endometrial stromal sarcoma arising from deep infiltrating endometriosis

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ABSTRACT

We present a compelling case of a 45-year-old female with a history of endometriosis and leiomyomas, who presented to her gynecologist with chronic pelvic pain complaints.

Both a transvaginal ultrasound (US) and an MRI (magnetic resonance imaging) were ordered. The US demonstrated multiple uterine lesions, likely fibroids, and an endometrioma within the right ovary. The MRI of the pelvis with and without gadolinium identified a mass within the right ovary with homogenous intermediate T2-signal, restricted diffusion, and delayed enhancement relative to the myometrium. Several irregular-shaped lesions were also noted within the external myometrium, anterior pelvic wall, and the peritoneum, which were intermediate signal on T2-weighted images, restricted diffusion, and an enhancement pattern similar to the myometrium.

The patient underwent a right adnexectomy. The histopathology findings were consistent with a low-grade endometrial stromal sarcoma (low grade-ESS) arising from the endometrial stroma of the right ovary. A debulking surgery confirmed the involvement of external myometrium, anterior pelvic wall, and the peritoneum secondary to a low-grade ESS without the endometrial cavity's involvement.

The underlying hypothesis is that the endometriosis stroma from extra-uterine structures such as the right ovary, pelvic and anterior peritoneum, and external myometrium may have subsequently resulted in a low-grade ESS.

Low-grade extra-uterine ESS without endometrial involvement is a rare entity. Based on our literature search, this is one of the few reports covering the radiological features of low-grade extra-uterine ESS arising outside the uterus with a concomitant deep infiltrating endometriosis, but without the involvement of the endometrial cavity.

1. Introduction

Low-grade extra-uterine endometrial stromal sarcoma (ESS) without endometrial involvement is a rare disease and is closely associated with endometriosis. To the best of our knowledge, this is one of the few reports covering the radiological features of an ESS-low grade arising from extra-uterine structures such as the right ovary, pelvic and anterior peritoneum, and external myometrium with deep infiltrating endometriosis without the involvement of the endometrial cavity [1–5]. In this manuscript, we present a patient with the typical findings associated with low grade-extra-uterine ESS.

2. Case report

A 45-year-old G1C1 female with a history of endometriosis and leiomyomas presented to her gynecologist complaining of chronic pelvic pain. The referring physician ordered both transvaginal ultrasound (US) and an MRI (magnetic resonance imaging). The initial US

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demonstrated multiple uterine lesions, probably representing fibroids and an endometrioma in the right ovary (the images are not available for presentation). The pelvic MRI with and without IV gadolinium showed multiple ill-defined lesions infiltrating the external myometrium and the right ovary, with implants along the anterior pelvic wall, peritoneum, and recto-uterine and vesicouterine pouches (Fig. 1). All the lesions demonstrated homogenous low to intermediate signal on T2-weighted images with restricted diffusion. On post-contrast dynamic sequences, the right ovarian lesion (Fig. 2) had delayed enhancement compared to the myometrium, consistent with a type 1 perfusion curve. There were also peritoneal implants (Fig. 3), which had an enhancement pattern similar to the myometrium, consistent with a type 2 perfusion curve. The left ovary was normal. The primary differential diagnosis was an ovarian neoplasm of uncertain etiology and deep infiltrating endometriosis. Her Ca-125 level was 75 ng/ml.

After a multidisciplinary conference, the gynecologist decided to perform laparoscopy with biopsy. The laparoscopy showed an enlarged right adnexal mass with implants at the peritoneum, but the left ovary was normal. The uterus had multiple fibroids. A right adnexectomy was performed.

The gross pathology specimen showed irregular fragments of whitish-yellowish tissue with foci of hemorrhage. The right ovarian tissue was partially replaced by neoplastic proliferation of ovoid cells with scarce cytoplasm, monomorphic and homogeneous chromatin, and numerous arterioles with thick walls (Fig. 4) on histopathology. The immunohistochemistry staining (IHC) was positive for CD10, estrogen receptors, inhibin, and focal for calretinin. The pathology was consistent with low-grade ESS, which has arisen from the right ovary's endometrial stroma.

The patient underwent further surgical debulking and staging. Pathologic analysis confirmed the involvement of external myometrium, anterior pelvic wall, and the peritoneum secondary to a low-grade ESS without endometrial cavity's involvement, consistent with the diagnosis of a primary extra-uterine low-grade ESS. She subsequently received neoadjuvant therapy with tamoxifen. After seven months, the low grade-ESS recurred within the abdominal wall, which was resected. After five years, the patient is still on active surveillance but has no evidence of recurrence or metastatic disease.

3. Discussion

Endometrial stromal sarcoma (ESS) represents only 0.2% of all

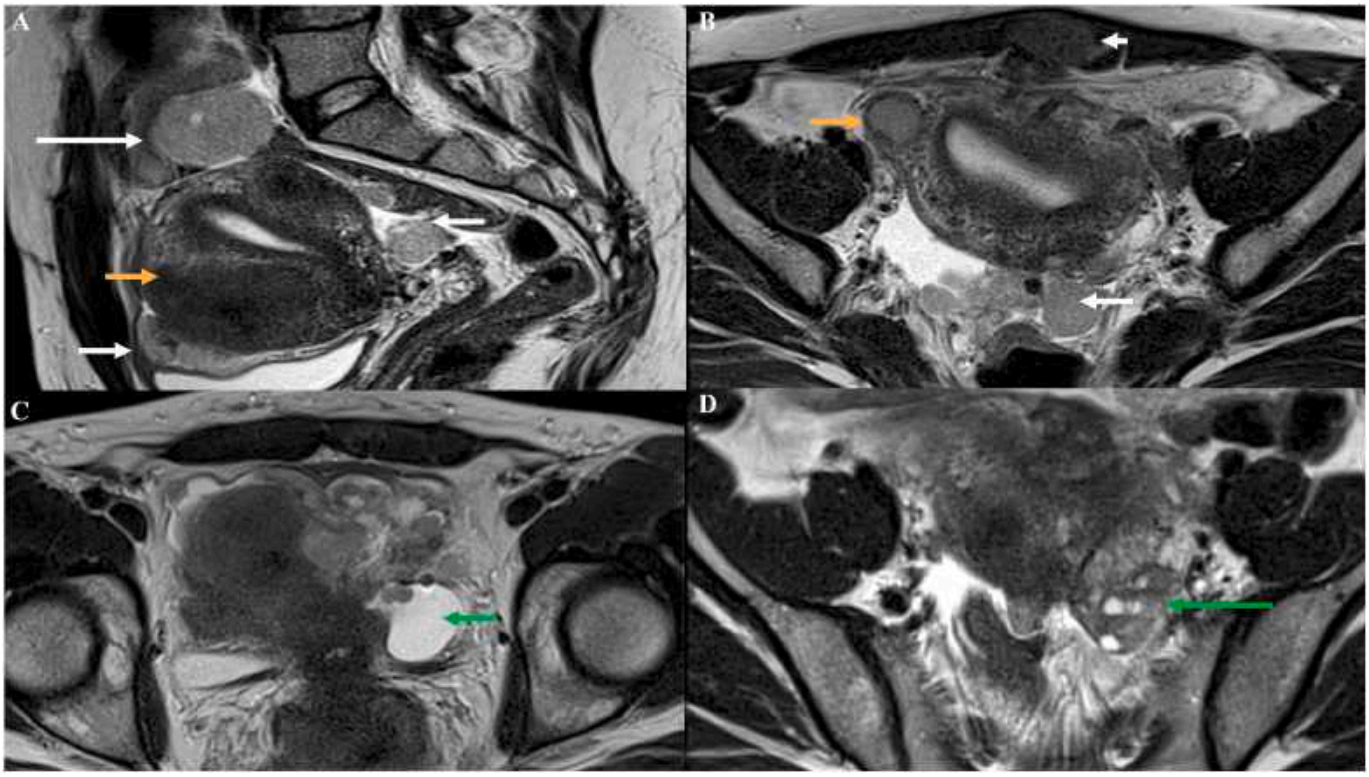

Fig. 1. T2-weighted images. Sagittal T2-weighted (A) demonstrates a homogenously intermediate signal mass within the right ovary (long white arrow), located above the uterus. There is also an infiltrative soft tissue within the anterior external myometrium (short orange arrows), with some areas showing low signal and other with intermediate-signal on T2-weighted images. Also, within the vesical-uterine pouch and pouch of Douglas (short white arrows), intermediate T2-weighted lesions are representing pelvic and peritoneal implants. Axial T2-weighted (B) shows an intermediate T2-weighed lesion within the right cornuate (short orange arrows), peritoneal implants in the pouch of Douglas (short white arrows), and a hypointense on T2-weighted lesion within the anterior abdominal wall, which likely represents an implant (white arrowhead). Finally, the axial T2-weighted (C and D) images show a left hydrosalpinx (C, short green arrow), and a normal left ovary (D, long green arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

uterine malignancies, 7%–25% of uterine sarcomas, and greater than 50% of cases are associated with endometriosis. Histologically, there are four subtypes of ESS, endometrial stromal nodule, low-grade, high-grade, and undifferentiated [5]. The most common is the high grade, which has the most aggressive features, with only a 33% 5-year survival rate [6]. Furthermore, each subtype can occur in the endometrial cavity (ESS-uterine) or the pelvis (ESS-extra-uterine) such as the ovaries, fallopian tubes, or peritoneum [6].

The low grade is a relative indolent variant, with 65% of the patients being FIGO stage I–II. There is a 90% 5-year survival rate and a 50% recurrence rate within the pelvis and thorax [4,5,7]. The low grade can arise either from the endometrial cavity (i.e., uterine-ESS) or from the ovaries, vulva, vagina, or abdominal or pelvic cavity (i.e., extra-uterine-ESS) [4,7]. Extrauterine-ESS may originate from ectopic endometrial stroma, which explains the strong correlation with endometriosis [4,5,7]. The mean age at diagnosis is 53 years [5]. The clinical presentation is usually nonspecific symptoms such as chronic vaginal bleeding, pelvic pain, and dysmenorrhea [1].

Most articles only discuss low-grade extra-uterine ESS in clinical and pathological aspects in our literature search without emphasizing the radiological findings [1–5,8–10]. All the extra-uterine structures involved had solid homogenous masses with intermediate signal on T2-weighted images, restricted diffusion, and variable enhancement relative to the myometrium in our patient. Such features correlate with the pathological description of circumscribed and multinodular solid masses composed of monotonous cells with scant cytoplasm and minimal atypia [7].

The primary differential diagnosis of the right ovarian mass was a metastatic disease, but these frequently tend to be bilateral [8]. Another consideration is the sex cord-stromal tumors, mostly fibroma or fibrothecoma, due to their high frequency. Fibroma/fibrothecomas usually are less 6 cm and have a homogenous low signal on T2-weighted images, and less enhancement to the myometrium [11], not intermediate signal on T2 delineated in our patient. Finally, the most

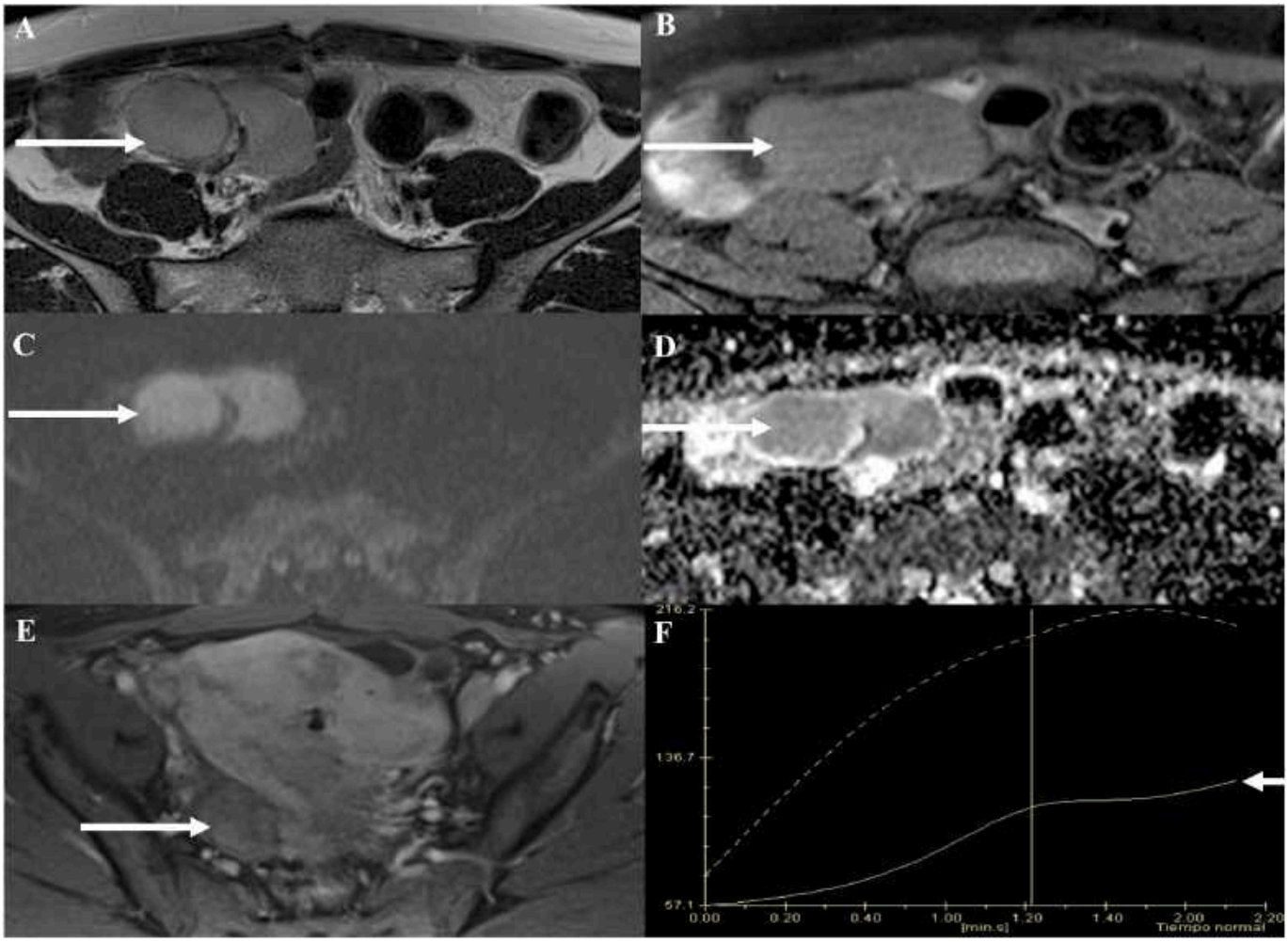

Fig. 2. A bilobed solid mass within the right ovary (long white arrows) demonstrate homogenous intermediate signal on T2-weighted images (A) and low signal on T1-weighted images (B) with restricted diffusion (C, diffusion B value: 1000 mm^3/s; D: attenuation diffusion coefficient). The dynamic contrast-enhanced images (E) demonstrate subtle and delayed enhancement relative to the external myometrium, with type 1 perfusion curve (F).

common cancers associated with endometriosis, such as clear cell or endometrioid cell carcinoma, are usually cystic masses with papillary projections or mural nodules or complex cystic masses [12], not completely solid mass as it was seen in this patient.

The differential diagnosis of an infiltrative tissue within the recto-uterine pouch, vesicouterine pouch, and the anterior pelvic wall is deep infiltrating endometriosis, which usually has a low signal on T2-weighted images due to the fibrous component [12]. However, if such tissue has intermediate-to-high signal intensity on T2, it should be correlated with other sequences to evaluate the presence of restricted diffusion and either similar or intense and early enhancement to the myometrium, to suggest possible cellularity [12].

However, with ill-defined margins, the nodular configuration, and especially the intermediate T2-signal intensity, restricted diffusion, and enhancement, a malignant etiology is favored.

Uterine ESS is usually a large mass with myometrial invasion. It has low-T2 signal bands, which represent the myometrium bundles separated by the infiltrating tumoral cells, or marginal nodules, which have worm-like intra-myometrial nodules, due to invasion in the vessels or ligaments [5]. The difference between low-grade and high-grade is primarily made on histopathology, but MRI features can help differentiate them. The presence of finger-like projections invading the myometrium and lymphatics favors low grade [3,7], but if there are necrosis and hemorrhage with a feather-like enhancement, then a high grade is more likely [5].

The definitive treatment for uterine or extra-uterine ESS, either high or low grade, is a hysterectomy with bilateral salpingo-oophorectomy. Regardless of the uterine or extra-uterine localization, patients with low-grade ESS benefit from adjuvant hormonal therapy, patients with high-grade ESS require systemic chemo-radiotherapy [5,7,13].

In conclusion, we aimed to highlight with this case report the importance of analyzing the signal characteristics of an endometriosis tissue carefully. If there is an intermediate-to-high signal on T2, it should be correlated with other sequences to evaluate possibly cellularity. Furthermore, uterine or extra-uterine ESS should always be considered in patients with a history of endometriosis.

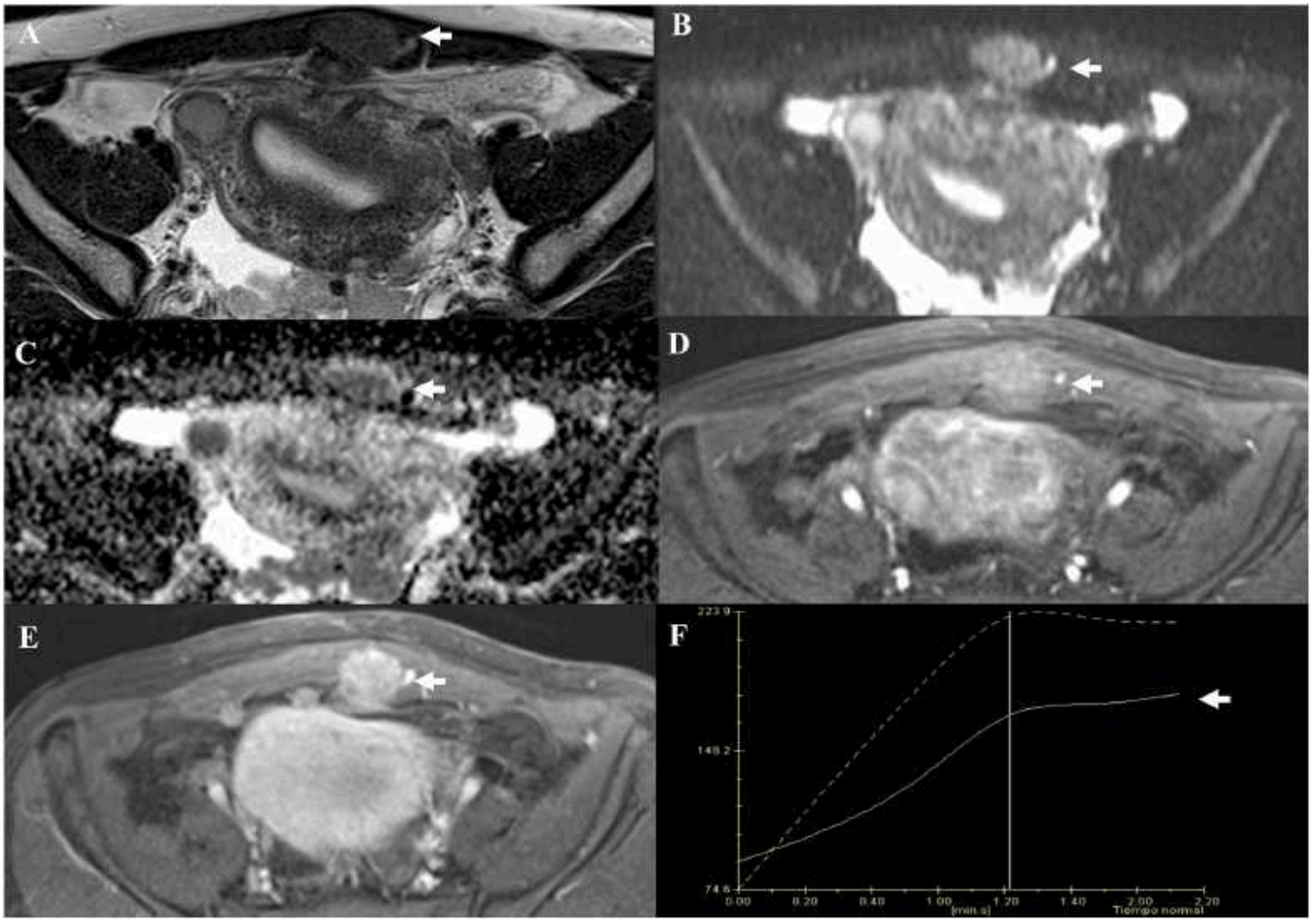

Fig. 3. The abdominal wall implant (short white arrows) demonstrates an intermediate signal on the T2-weighted signal (A) and restricted diffusion (B, diffusion B value: 1000 mm^3/s; C: attenuation diffusion coefficient). On the post-contrast dynamic image (D, 10 s; E, 30 s), it has a similar enhancement pattern to the myometrium, with type 2 perfusion curve (F).

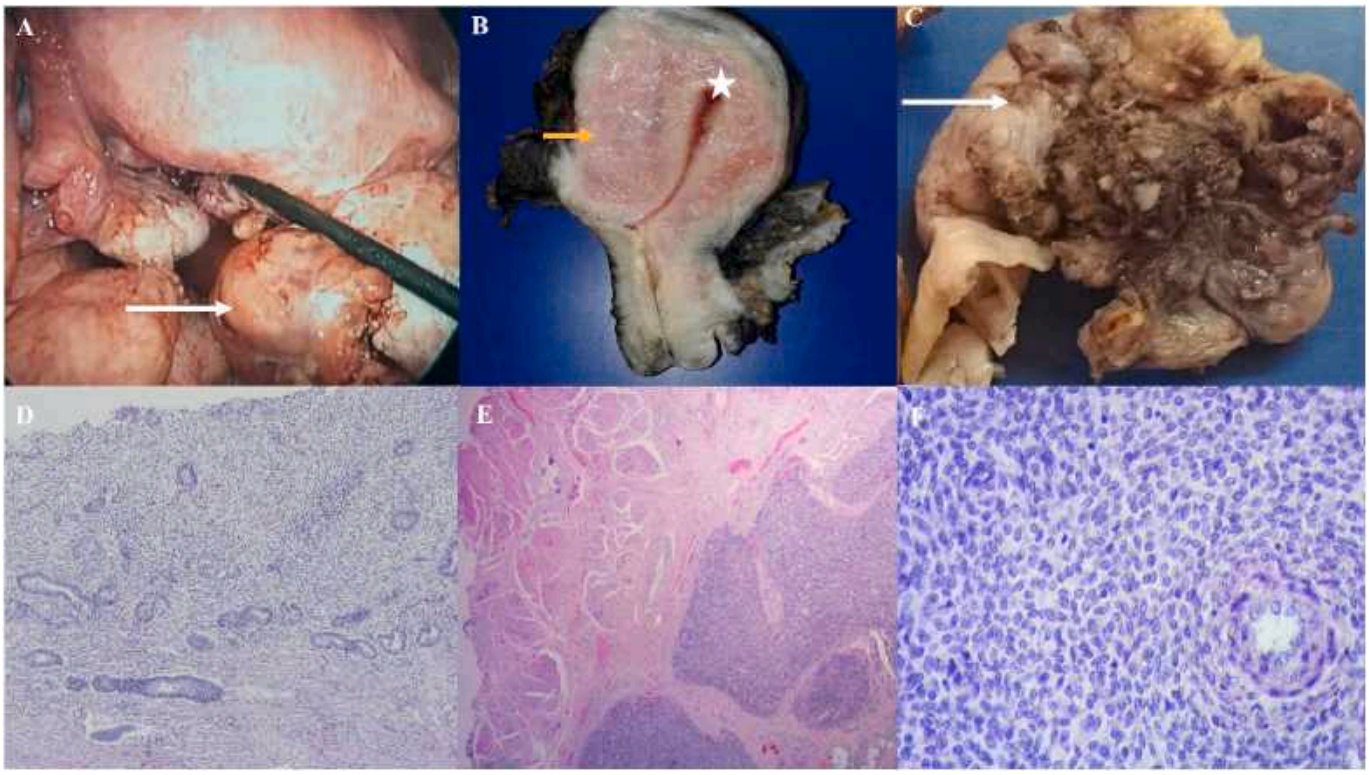

Fig. 4. Intraoperative images (A) demonstrate a mass within the right ovary (long white arrow). Macroscopic specimen (B) delineating infiltration of the external myometrium (short orange arrow), without a well-defined endometrial mass (star). The macroscopic examination of the right ovary (C) demonstrates a solid mass within the right ovary. Histopathology on H/E 10× of the endometrium (D) shows normal endometrial proliferative cells without atypia, correlating with the gross specimen and MRI findings. On the contrary, there is tumoral infiltration in the outer third of the external myometrium (E). Finally, the histopathological image of the right ovary using H/E 100× demonstrate characteristic round cells (F).

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