Disseminated Peritoneal Leiomyomatosis: Description of a Case, Radiologic Semiotics and Differential Diagnosis

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AIM: Leiomyomatosis peritonealis disseminata or disseminated peritoneal leiomyomatosis (DPL), is a rare nosological entity characterized by multiple leiomyomas growing within the abdominal region. It is one of the uncommon manifestations of extra-uterine leiomyomas and an eventuality that can lead to diagnostic difficulties, especially in neoplastic patients. This pictorial review aims to illustrate the multimodal characteristics of DPL, providing at the same time relevant information regarding pathogenesis, clinical presentation, and treatment. Furthermore, as DPL may enter in differential diagnosis with other atypical smooth muscle tumour localization or abdominal malignancies, such as retroperitoneal leiomyosarcoma or peritoneal carcinomatosis, the review provides a concise description of each condition: the main epidemiological and pathogenetic aspects are summarized, along with essential information on clinical presentation and radiological imaging, closing with some notes on possible treatment options.
CASE PRESENTATION: A case of incidental detection of DPL in a patient undergoing staging of breast cancer is employed as an example to illustrate the diagnostic difficulties that may be encountered in such scenarios: the finding of multiple vascularized nodules in the abdomen aroused the suspicion of carcinomatous localizations, and the patient underwent in-depth investigations with multiple imaging techniques by ultrasound, computed tomography and magnetic resonance.
RESULTS: Using imaging methods with better contrast resolution in the definition of soft tissues made it possible to orient the diagnostic suspicion over DPL, subsequently confirmed by histological evaluation after laparoscopic excision of bigger nodules. Once the possibility of peritoneal localization of breast cancer was excluded, the patient was treated with neoadjuvant therapy, surgery and adjuvant therapy. Follow-up imaging showed no signs of breast cancer recurrence nor significant changes in the remaining DPL nodules.
CONCLUSIONS: Knowledge of the atypical presentation patterns of leiomyomas, the related imaging characteristics and the differential diagnosis allows both the clinician and the radiologist to formulate more accurate diagnostic hypotheses, thus ensuring better patient management from the view of the subsequent possible invasive diagnostic and therapeutic options.

Keywords: gynaecological imaging; disseminated peritoneal leiomyomatosis; smooth muscle tumors; differential diagnosis

Introduction

Leiomyomatosis peritonealis disseminata, also named disseminated peritoneal leiomyomatosis (DPL), is a rare condition characterized by the presence of multiple solid vascularized leiomyomas in the abdominopelvic region, more specifically localized within the submesothelial layer of the peritoneum or in sub-peritoneal spaces. It constitutes one of the unusual manifestations of leiomyoma, alongside the parasitic leiomyoma, metastatic leiomyoma, intravenous leiomyomatosis and retroperitoneal leiomyomatosis [1].

The case described below focuses on the incidental finding of DPL in a patient undergoing staging for a recent diagnosis of breast cancer, who also was affected by multiple uterine leiomyomas and had a history of previous adnexectomy surgery for ovarian leiomyoma.

The finding of DPL in a neoplastic patient can be a diagnostic challenge for both the clinician and the radiologist. Knowledge of the radiological semiotics of the lesions that characterize this rare condition may facilitate the correct diagnosis, benefitting the patient's quality of life.

Case Presentation

This case was prepared in accordance with the CARE guidelines (Case Report Guidelines) to ensure transparent and accurate reporting (**supplementary material**) [2].

The case is centred on a 41-year-old Caucasian woman recently diagnosed with cT2 cN0 triple negative breast cancer following the analysis of a bioptic sample taken on a lesion identified by screening mammography. The patient was nulliparous, reported menarche at the age of 10 years, was in the pre-menopausal phase and reported regular men-

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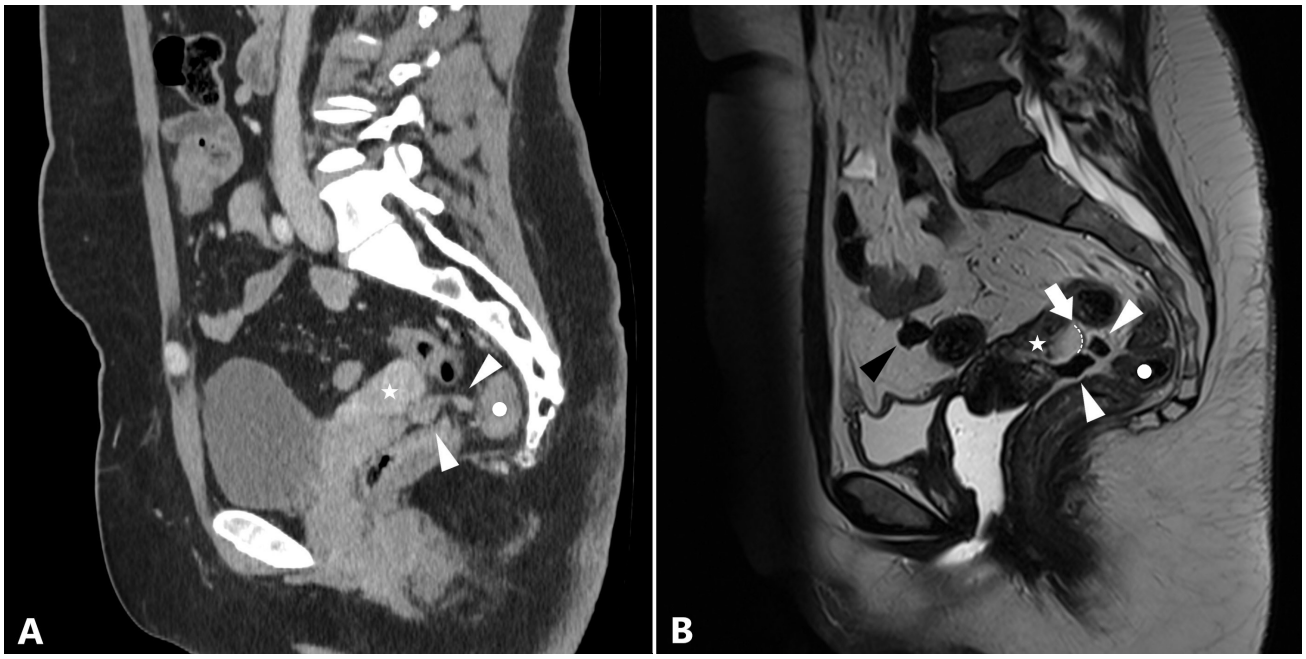

Fig. 1. Imaging features of disseminated peritoneal leiomyomatosis. (A) Pelvis computed tomography scan with intravenous contrast medium on sagittal plane (venous phase): two soft tissue formations with overall size of 30 × 10 mm and characterized by mild contrast enhancement are appreciable in the rectouterine pouch (arrowheads), the anterior one close to the posterior wall of the uterine body (star); it is also appreciable a thin cleavage space with the anterior wall of the rectum (dot). (B) Pelvis magnetic resonance imaging (MRI) scan on the same plane (T2-weighted sequence), showing the same two aforementioned formations, both characterized by markedly hypointense signal, compatible with disseminated peritoneal leiomyomatosis (DPL) nodules (white arrowheads). The MRI study allows for greater definition of anatomical relationships, better representing the contact between the more anterior lesion with both the posterior wall of the uterine body (star) and the peritoneal reflection in the rectouterine pouch (white arrow and dashed line). The posterior formation is completely retroperitoneal, being clearly separated from the peritoneal reflection, and has no relationships with the anterior wall of the rectum (dot). The MRI sagittal plan also show another hypointense DPL nodule between two bowel loops, cranially to the upper bladder wall (black arrowhead), which is better described in Fig. 2.

strual cycles; she also underwent right adnexectomy for an ovarian leiomyoma in 2008.

During the initial phase of the staging protocol, the oncologist prescribed a PET scan using 18F-FDG, which recalled attention to a focal slight increased uptake in the left adnexal region, which on the first hypothesis was attributed to a luteal body, but was deemed worthy of clinical and ultrasound correlation, in order to exclude the eventuality of malignant nature.

CEA, CA 15.3, CA 19.9 and CA 125 markers were within limits in multiple consecutive measurements and other blood tests did not reveal any significant anomalies.

The patient was then referred to the gynaecology department for further examination by transvaginal ultrasound (US), which highlighted the presence of some uterine leiomyomas and a small retro-uterine peritoneal effusion in which two iso-echogenic under-centimetric formations were seemingly vegetating, thus raising the suspicion of peritoneal metastatic implants.

Hence, the patient was subjected to a computed tomography (CT) abdomen-pelvis scan with intravenous (IV) iodate contrast medium in order to obtain a better characterization of the aforementioned formations. The CT scan confirmed the presence of two closely spaced solid vascularized nodules of approximately 30 × 10 mm in total, the first one adherent to the right postero-lateral wall of the uterus and the peritoneal fascia of the rectouterine pouch, the second one into the perirectal fat but with an evident, albeit thin, cleavage with the rectum itself (Fig. 1). A further analogue nodule of approximately 20 × 13 mm was detected in the peritoneal reflection between the sigmoid colon and the posterior wall of the bladder, with a thin cleavage plane with both of them (Fig. 2). In conjunction with an enlarged lymph node with axial diameters of 24 × 18 mm along the right iliac lymphatic axis, the nodules described above raised the suspicion of metastatic peritoneal implants.

Therefore, the patient underwent further diagnostic investigation by magnetic resonance imaging (MRI) pelvis with IV paramagnetic contrast medium, as it is an imaging technique with higher contrast resolution in the assessment of soft tissues, compared to US and CT. The MRI exams confirmed the pelvic nodules previously reported, all distinguished by the same signal characteristics: hypointensity in T1-weighted (T1w) sequences, marked hypointensity in

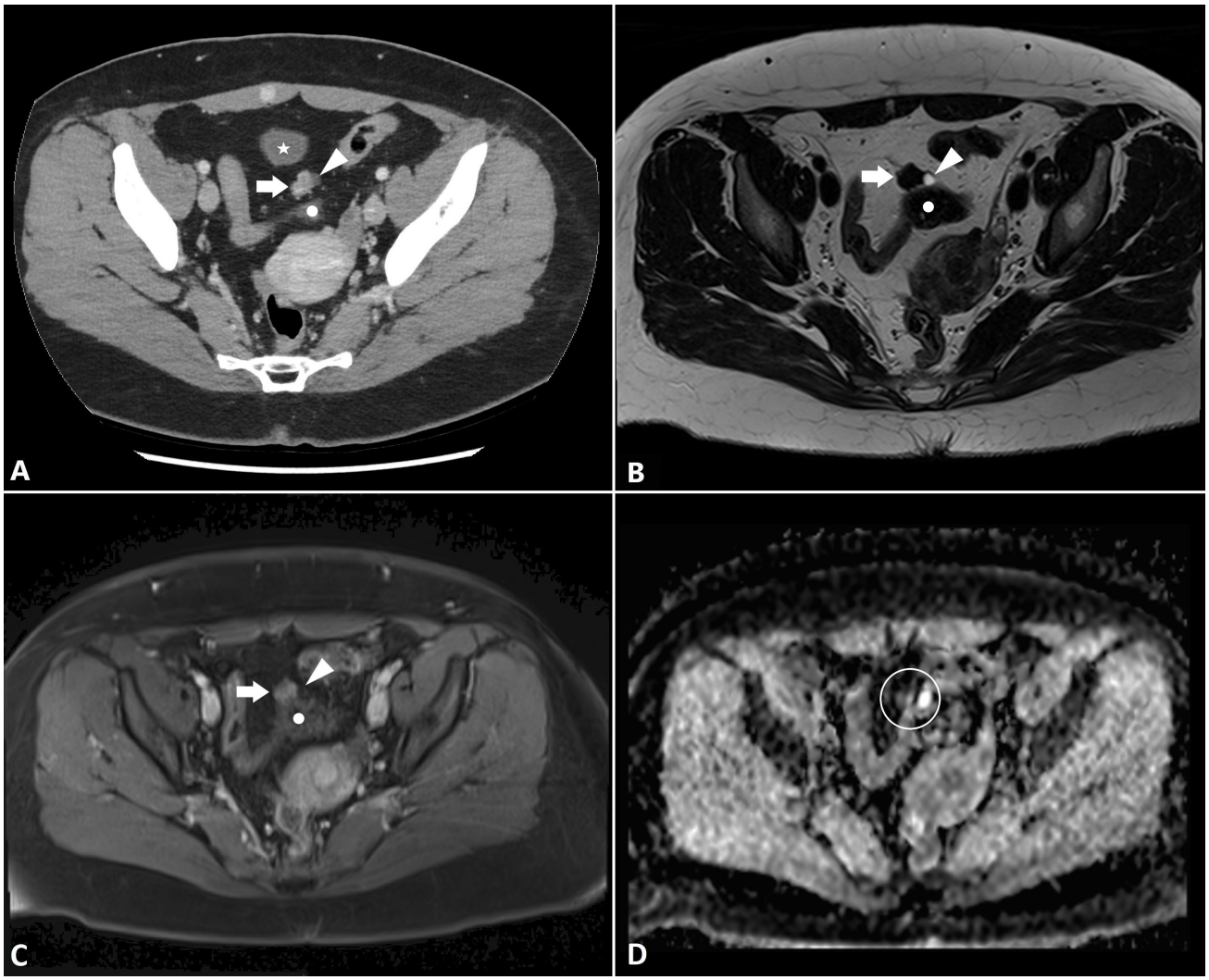

Fig. 2. Imaging features of disseminated peritoneal leiomyomatosis. (A) Pelvis computed tomography scan with intravenous contrast medium on sagittal plane (venous phase): a soft tissue formation of 20 × 13 mm characterized by mild contrast enhancement (white arrow) and a sub-centimetric cystic component (white arrowhead) localized between the bladder roof (star) and the sigmoid colon (dot). (B) Pelvis MRI scan on the same plane (T2-weighted sequence), better representing the marked hypointensity of the nodule (white arrow) and the contextual thin-walled cyst (white arrowhead), both of which are still clearly separated by the sigmoid colon (dot). (C) During dynamic contrast-enhanced MRI sequences, the disseminated peritoneal leiomyomatosis (DPL) nodule shows mild early enhancement (arrow), while the cystic component remains completely avascular (arrowhead), and both the nodule and the cystic component show different enhancement from the nearby sigmoid colon (dot). (D) Apparent diffusion coefficient map of the same section highlights the absence of increased restriction of water diffusion in the DPL nodule (circle).

T2-weighted (T2w) sequences, early contrast enhancement (CE) and hypointensity in diffusion weighted sequences (DWI) (Figs. 1,2); moreover, an additional formation characterized by a contextual minute cystic component with fluid content and thin walls was identified along the right iliac vessels at the level of the pelvic inlet, misrecognized as a right iliac enlarged lympnode on the CT. The MRI characteristics of the suspect peritoneal lesions were deemed compatible with the hypothesis of DPL, as the patient had two factors associated with this condition, namely the history of adnexectomy for ovarian leiomyoma and multiple uterine leiomyomas.

Given the oncology team's need to exclude the possibility of metastatic localizations with certainty, the patient underwent an exploratory laparoscopy, during which the surgical team confirmed the presence of multiple faintly pink, well-demarcated nodules loosely adherent to the pelvic peritoneum, corroborating the hypothesis of DPL. The largest nodules were removed and sent to the pathological anatomy laboratory for further histological and immunohistochemical evaluation, during which it was reported that all specimens have taut-elastic consistency with a whitish and compact cut surface and were mainly composed of smooth muscle cells in fascicles; no significant atypia or mitosis was

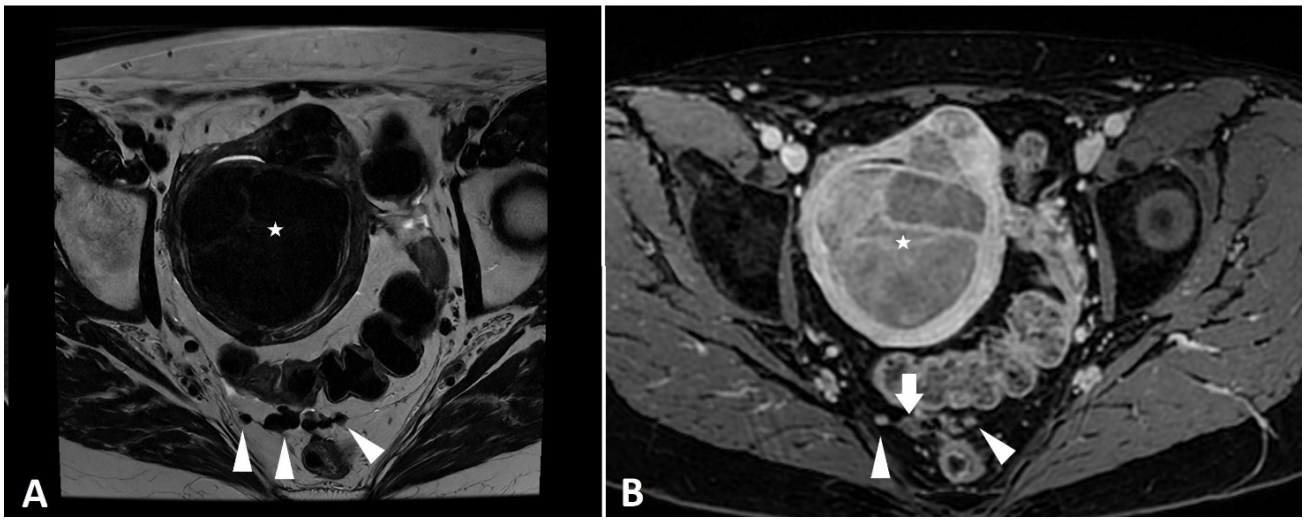

Fig. 3. Another case of disseminated peritoneal leiomyomatosis. (A) Pelvis magnetic resonance imaging scan on axial plane (T2-weighted sequence) showing multiple small disseminated peritoneal leiomyomatosis (DPL) nodules partially confluent with each other and adherent to the peritoneum (arrowheads) in a patient with greatly enlarged uterus due to multiple large leiomyomas (star). (B) After intravenous administration of contrast medium the aforementioned DPL nodules either show homogeneous enhancement (arrowheads) or bland mainly peripheral enhancement (arrow), with a pattern not dissimilar to the larger uterine leiomyomas in the same section (star).

described, and cells were positive for desmin phenotypic characterization while being negative for pan-cytokeratin (pan-CK), thus being referable to leiomyomas with minimal hyaline degeneration, confirming the diagnostic hypothesis formulated during the MRI evaluation.

The exclusion of metastatic breast disease allowed to proceed with neoadjuvant therapy, which was followed by excision of the sentinel lymph node, the analysis of which was negative for tumour infiltration, and by subsequent left quadrantectomy. The patient had no post-surgical complications, has undergone adjuvant therapy, and is currently on regular follow-up. At subsequent total-body CT scans, no mammary disease recurrence or changes in the non-resected DPL nodules were detected.

Discussion

DPL is a rare condition characterized by multiple solid nodules composed of smooth muscle cells in the abdominopelvic region, distributed in adhesion to the peritoneal sheets and in the subperitoneal spaces [1,3].

The precise epidemiology of DPL remains to be defined, although current evidence indicates that it is more frequently found in pre-menopausal women, even if cases have been reported in post-menopausal women and in men [3,4].

Several theories have been proposed to explain the genesis and development of this disease. As some cases showed familiar inheritance, the presence of a genetic substrate has been hypothesized, although there is currently no evidence of a specific phenotypic arrangement correlated to the onset of the pathology [4]. The hypothesis that DPL may spontaneously derive from a proliferation of mesenchymal stem cells has more substantial support, albeit with different interpretations regarding the specific differentiation patterns [5,6]. Despite these divergences, the hormonal influence on these processes is widely recognised: *in vivo* tests on animals have demonstrated the induction of DPL-like lesions following combined estrogenic and estrogenic-progestinic exposure [3–5], and receptors for this class of hormones on the spindle-shaped cells of DPL lesions have been reported [3–5]. The influence of increased hormonal stimulation in the pathogenesis has been recognized in humans as well, namely in the form of association with hormone producing ovarian tumours (i.e., fibrothecoma or granulosa cell tumour) [3,7–9], intake of oral contraceptives and with pregnancy [3,5–9], the latter associated both with cases of rapid dimensional growth of DPL nodules and with relapse of DPL [7]. Nevertheless, cases in nulliparous women who were not taking contraceptives suggest the involvement of some other predisposing factors [5,6]. Furthermore, post-menopause hormone replacement therapy and tamoxifen treatment of breast cancer have been reported as risk factors for DPL [10]. Finally, iatrogenic forms of DPL are extensively described in association with laparoscopic uterine myomectomy or hysterectomy, especially if morcellation is employed [3,7,8,11,12].

DPL is generally asymptomatic and in most cases is identified incidentally in patients undergoing diagnostic investigations for other pathologies or during caesarean section or laparotomy [13–15]. When symptomatic, DPL may cause non-specific symptoms like abdominal pain, genital or rectal bleeding, dyspareunia or pollachiuria [14–16]; in rare cases, an DPL nodule may prompt mechanical bowel obstruction [4,15].

Table 1. Summary of the main characteristics of disseminated peritoneal leiomyomatosis and related differential diagnoses for each imaging method.

Differential diagnosis	Imaging key findings		
	Ultrasound	Computed tomography	Magnetic resonance
Disseminated peritoneal leiomyomatosis Typical lesion location: ● Peritoneal cavity	Multiple nodules or single isolated mass with complex B-mode pattern	Single or multiple circumscribed nodules: ● Native images: soft tissue attenuation ● Post-contrast images: some degree of enhancement	Single or multiple circumscribed nodules: ● T1w sequences: hypointense to muscle ● T2w sequences: hypointense to muscle ● Post-contrast images: variable enhancement
Metastasizing benign leiomyoma Typical lesion location: ● Lungs	Not employed for lung parenchyma evaluation	Multiple circumscribed round nodules: ● Native images: soft tissue attenuation ● Post-contrast images: no significant enhancement or homogeneous enhancement * May show cavitation or calcifications	Not routinely employed for lung parenchyma evaluation
Intravenous leiomyomatosis Typical lesion location: ● Uterine veins ● Other systemic veins	Intravenous thrombus with vascularized Doppler pattern	Intravenous filling defect: ● Native images: soft tissue attenuation ● Post-contrast images: some degree of enhancement	Intravenous filling defect: ● T1w sequences: isointense or hypointense to muscle ● T2w sequences: hypointense to muscle ● Post-contrast images: enhancement
Parasitic leiomyoma Typical lesion location: ● Uterine broad ligament ● Omentum ● Lower retroperitoneum	Single or multiple circumscribed nodules/masses with no identifiable pedicle	Should be avoided in favour of MRI as second level imaging	Single or multiple circumscribed nodules/masses with no identifiable pedicle: ● T1w sequences: hypointense to muscle ● T2w sequences: hypointense to muscle * May show myxoid, hyaline or necrotic degeneration
Retroperitoneal leiomyomatosis Typical lesion location: ● Lower retroperitoneum	Not routinely employed for retroperitoneum evaluation	Single or multiple circumscribed nodules: ● Native images: soft tissue attenuation ● Post-contrast images: some degree of contrast enhancement	Single or multiple circumscribed nodules/masses: ● T1w sequences: hypointense to muscle ● T2w sequences: hypointense to muscle * May show myxoid, hyaline or necrotic degeneration
Retroperitoneal leiomyosarcoma Typical lesion location: ● Upper retroperitoneum ● Lower retroperitoneum ● Systemic arteries or veins of retroperitoneum	Large solid mass or Intravenous thrombus with vascularized Doppler pattern or Combination of the two * May show cystic and haemorrhagic components	Large mass and/or Intravenous filling defect: ● Native images: soft tissue attenuation ● Post-contrast images: some degree of contrast enhancement * May show cystic and haemorrhagic components * Often infiltrates surrounding structures	Large mass: ● T1w sequences: isointense or hypointense to muscle T2w sequences: variable signal ● Post-contrast images: heterogenous or marked enhancement * May show cystic or haemorrhagic components ● Black blood sequences: intravascular filling defect (if intravascular growth)

Table 1. Continued.

	Imaging key findings		
Differential diagnosis	Ultrasound	Computed tomography	Magnetic resonance
Peritoneal carcinomatosis Typical lesion location: ● Peritoneal spaces ● Sub-peritoneal spaces	If some degree of ascites is present hypoechoic nodules or thickening of peritoneal surface *Ascites loculation as indirect sign	Irregular nodules and/or infiltrative masses (omental cake) and/or thickening of peritoneal surface ● Native images: soft tissue attenuation ● Post-contrast images: some degree of contrast enhancement * Often associated with ascites	Not routinely employed to assess peritoneal carcinomatosis: useful problem-solving tool in complex cases involving small lesions

T1w, T1-weighted; T2w, T2-weighted.

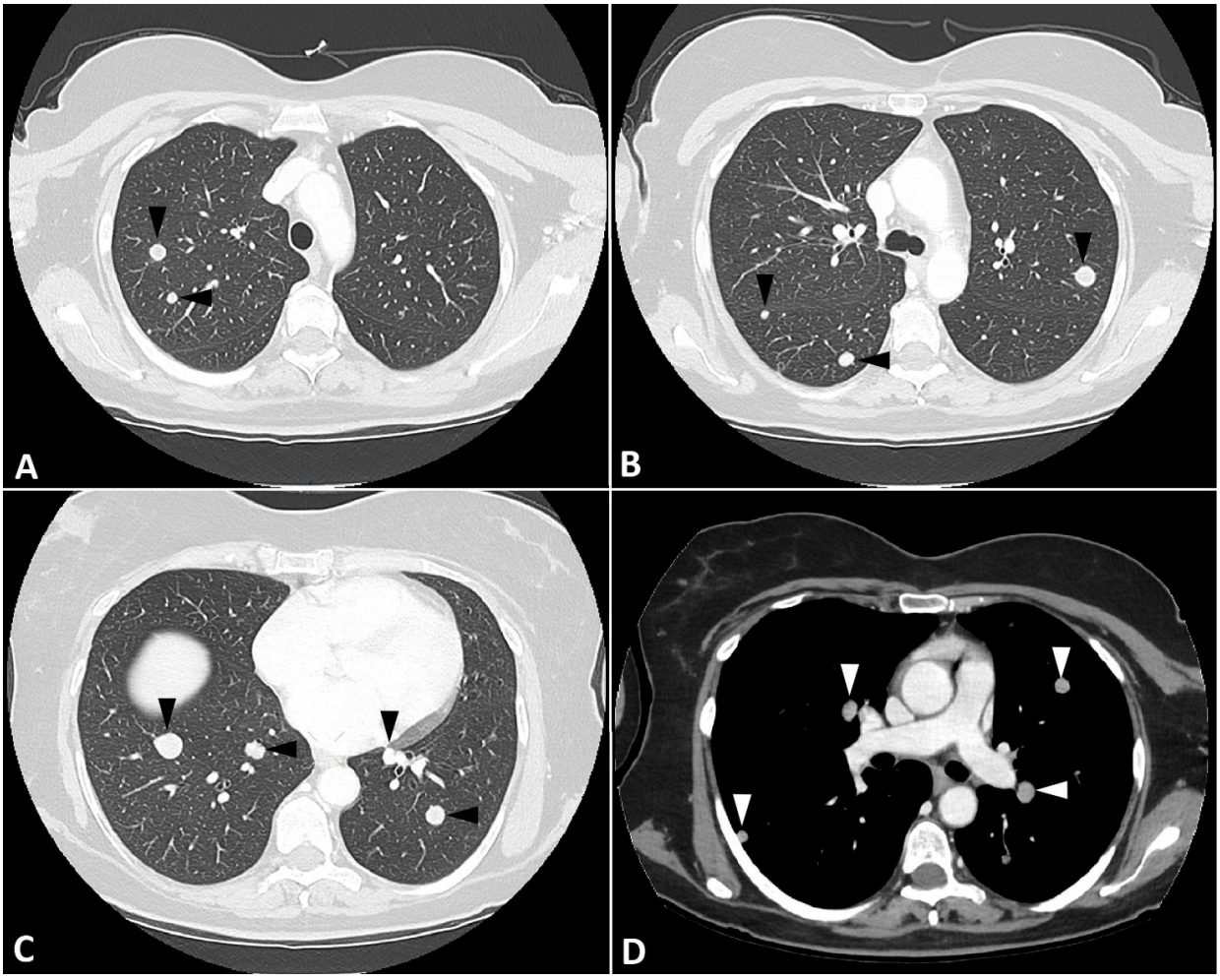

Fig. 4. Metastasizing benign leiomyoma. (A–C) Chest computed tomography (CT) scan on axial plane of superior (A), medium (B) and lower lungs (C) of another patient affected by benign metastasizing leiomyoma, which shows multiple round nodules with clear margins (black arrowheads). (D) Chest CT scan on axial plane with contrast medium (venous phase) on the same patient: the soft tissue window highlights how the nodules have a fairly homogeneous contrast enhancement and no central necrosis (white arrowheads) and constitute a non-specific finding that is difficult to characterize with the CT imaging alone.

DPL on US may have variable appearance, ranging from multiple small abdominal-pelvic nodules to a single isolated mass [1] which may exhibit complex characteristics [17]. On CT, DPL appears as a single or multiple well-circumscribed solid masses of variable size localized in the peritoneal cavity and characterized by solid tissue attenuation with contrast enhancement usually similar to that of uterine leiomyomas [1,17,18]. On MRI, DPL lesions are

typically isointense relative to muscle on T1w sequences, hypointense to muscle on T2w sequences and characterized by variable enhancement after IV administration of gadolinium [1,10,18–20] (Fig. 3).

Differential diagnosis of DPL typically requires the exclusion of other atypical localizations of smooth muscle lesions, namely metastatic leiomyoma, intravenous leiomyomatosis, parasitic leiomyoma and retroperitoneal leiomyomatosis. It is also paramount to consider possible malignancies, such as leiomyosarcoma if dealing with a single large mass, or metastatic peritoneal disease when DPL manifests as multiple small nodules [1,10,21] or is associated with ascites [22].

Primary differential diagnoses are described in more detail in the following dedicated paragraphs, while the main findings for each imaging technique are summarized in Table 1.

Regarding the pathological diagnosis, from both a macroscopic and microscopic point of view, the localizations of DPL appear comparable to conventional leiomyomas. DPL nodules are solid, well-circumscribed formations with whorled tan-white surfaces after cutting. Cells are arranged in intersecting fascicles and have spindled morphology, eosinophilic cytoplasm and elongated nuclei, showing no significant cytologic atypia or mitotic activity [7].

Once correctly identified, DPL can be treated with a medical or surgical approach: the choice of treatment should take into consideration the number and location of the lesions, the patient's symptoms, and comorbidities. Patients with reproductive desire may be treated conservatively by medical castration, although the possibility of malignant transformation should be taken into account. A more aggressive approach by surgical adnexectomy, either with or without removal of the DPL nodules, may be adopted in symptomatic patients or to avoid the risk of malignancy [7,20,21,23].

Benign metastasizing leiomyoma (BML) is a condition characterized by the presence of well-differentiated leiomyomas localized distant from the uterus, typically in the lungs, but also in the brain, heart, lymph nodes, bone and skin [1,24,25]. It is a rare entity, and it has been suggested that only uterine leiomyomas with a peculiar genetic profile may exhibit metastatic potential [7,26]. However, like DPL, an iatrogenic factor may be involved, as BML is associated with hysterectomy in patients with uterine leiomyomas and it is hypothesized that surgery may facilitate the hematogenous distant spread of smooth muscle cells [24,27]. Nonetheless, other theories support the spontaneous multifocal proliferation of estrogen and progesterone sensible smooth muscle cells in different tissues [1,24].

BML typically grows slowly [28], mainly with an indolent behaviour, and patients are usually asymptomatic, although lung nodules may cause respiratory symptoms [1,24,29].

At imaging, both in CT and MRI, BML is typically a pulmonary finding and it is characterized by multiple round nodules, usually well-defined, without significant contrast enhancement or homogeneously enhanced, which may occasionally present signs of cavitation of calcifications [1, 21,29–31]. These nodules are usually non-specific, making them difficult to distinguish from infectious granulomas, sarcoidosis, rheumatoid and amyloidosis nodules and metastases (Fig. 4); thus, a histologic exam on a bioptic sample is required to obtain a definite diagnosis [1,27,30, 32].

The management of BML is not standardized [31]: the lesions may regress spontaneously after menopause or during pregnancy [29,33,34], but if treatment is required, the approach is centred around the removal of the resectable symptomatic lesions, possibly in association with bilateral adnexectomy in order to reduce the hormonal stimulus; when this is not possible, hormone therapy may be employed [7,24,34].

Intravenous leiomyomatosis (IVL) is a rare disease characterized by the intraluminal growth of smooth muscle cells in uterine and other systemic veins, mainly in patients with coexisting uterine leiomyomas or a history of leiomyoma excision [21,35–37], although it is hypothesized that spontaneous growth of smooth muscle cell of the vessel wall may be involved [35–40]. Despite being denoted by benign lesions, this condition may be clinically aggressive as tumours may reach the inferior vena cava, the heart and even pulmonary arteries, thus having significant haemodynamic effects [24,36,37,41,42].

As far as imaging is concerned, the first diagnostic step is usually an US evaluation, which may evidence an intraluminal thrombus with a vascularized Doppler pattern [1,39], a finding that CT may confirm, as it can demonstrate hypoattenuating intraluminal filling defect [35,38], which may show contrast enhancement [37], thus distinguishing it from the typical bland thrombus [1,43]; CT may also identify associated lung nodules, as IVL may be associated with BML [44,45]. MRI is the most helpful tool in providing diagnostic details, as it can better differentiate tissue characteristics: IVL thrombi typically have low to intermediate signal intensity on T1w and low signal on T2w, usually without significant signs of invasion of nearby tissues and with enhancement on post-contrast sequences [1,35,39,45].

Differential diagnosis typically consists of bland thrombus, hepatocellular carcinoma or renal carcinoma with vascular invasion or leiomyosarcoma [35,36,38,39,42,46]. While the first can easily be excluded by imaging and non-responsiveness to heparin and thrombolysis, a definitive diagnosis between the latter hypothesis may require a biopsy [35,36,38,47].

IVL is usually treated surgically [35–38,42], resorting to vein ligation distally to the growing mass when excision is not possible [24]; in these cases, as the masses are hormone-sensible and usually diagnosed during the premenopausal age, exogenous oestrogens should be avoided [38] and bilateral adnexectomy should be considered [24,35,36,42]. It

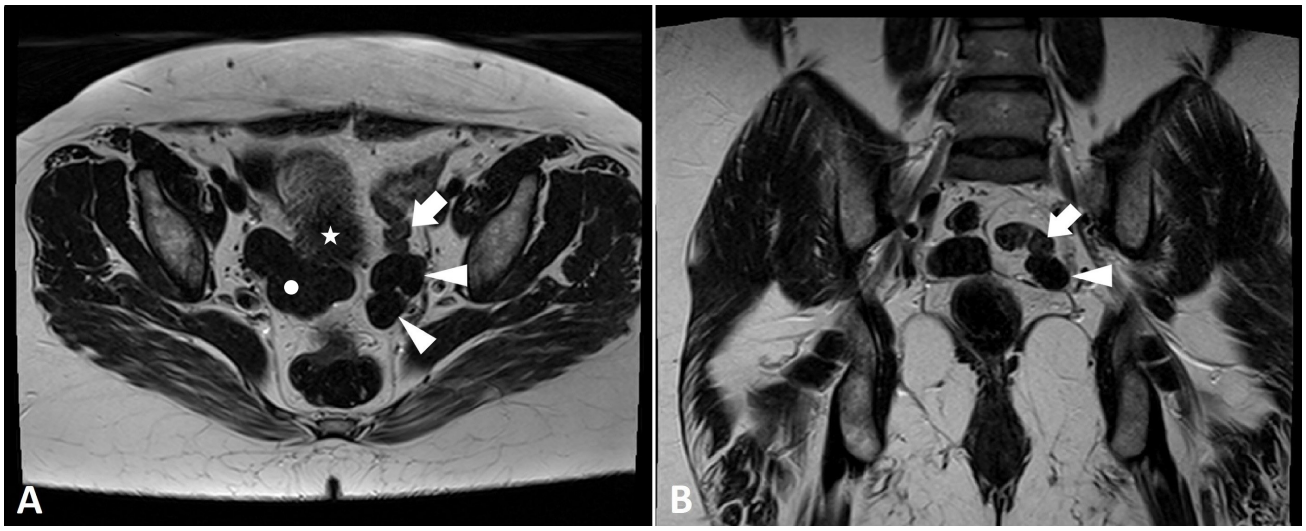

Fig. 5. Parasitic leiomyoma. (A) Pelvis magnetic resonance imaging scan on the axial plane (T2-weighted sequence) showing, in another patient, two intra-peritoneal parasitic leiomyomas in the left iliac fossa (arrowheads), one of which is adherent to a small bowel loop (arrow); both of the aforementioned formations are clearly separated from the uterus (star), which is only partially included in this slice and is affected by multiple conglomerate sub-serosal leiomyomas (dot). (B) A coronal sequence on the same patient better highlights the strict relation between one of the parasitic leiomyomas (arrowhead) and the wall of the small bowel (arrow), from which the myoma probably sustain itself.

is advisable to set up a follow-up to allow identification of disease recurrence [24,41,45], as it is common in case of incompletely excised intravenous masses [35,38,42]: US, CT or MRI may be considered on discretion, as there are no standardized follow-up guidelines [24,36,41,45].

A parasitic leiomyoma (PL) is a smooth muscle cell benign tumour of the uterus which does not have a direct attachment to the uterus [48]. Some sources in the literature describe iatrogenic PL following hysterectomy, making this condition comparable in some aspects to DPL, already discussed earlier in the article. When not associated with surgery, PL occurs when a uterine leiomyoma adheres to an adjacent structure and starts developing an autonomous vascularization from said structures, losing its original attachment to the uterus due to torsion or necrosis of the pedicle [1,21,49–51]. These lesions are usually located on the broad ligament, in the omentum or the retroperitoneal space and, although typically silent, may be symptomatic when interfering with surrounding structures, like ureters, urethra or intestine [1,49,52].

US is a valuable early diagnostic step, primarily if performed with a transvaginal probe, as it can differentiate uterine masses from ovarian or broad ligament ones [1] and can be employed to demonstrate the absence of a pedicle attaching the leiomyoma to the uterus; however, a particularly thin pedicle may not be identifiable [53]. Further diagnostic information can be obtained by MRI, which is capable of demonstrating the typical signal characteristics of leiomyomas, in particular homogeneous low signal on T1w and T2w sequences (Fig. 5), and the eventuality of degenerative components of myxoid, hyaline or necrotic nature, thus granting the ability to differentiate benign leiomyomas from solid pelvic tumours [1,49,54], which are the primary differential diagnosis, as both PL and ovarian carcinoma have been associated with increased CA-125 serum level and pseudo-Meigs syndrome [49]. A biopsy must be performed to obtain a histologic sample if a histologic diagnosis is needed [1].

Given the fact that the typical clinical behaviour of PL is similar to uterine leiomyomas, they can be treated by hormonal therapy or surgically, either to resolve symptoms or to avoid involvement of nearby viscera [21,49,55].

Retroperitoneal leiomyoma (RL) or retroperitoneal leiomyomatosis refers to another pattern of unusual growth of single or multiple smooth muscle cell tumours in the retroperitoneal space, typically in the lower retroperitoneum, but it may occasionally occur in the upper retroperitoneum up to the juxta-renal region [1,47,56]. This condition shares some aspects with DPL as far as aetiology and pathogenesis are concerned: several cases are associated with uterine leiomyomas or uterine leiomyomas excision, while it cannot be excluded that RL may consist of synchronous lesions developing from mesenchymal cells of the retroperitoneum, a process in which hormonal stimulation is supposed to play a role [1,57,58]. Another theory claims that RL may be a form of parasitic uterine tumour developing from the uterus and then losing its connection to it, thus acquiring new vascular sustain from retroperitoneal space [57]. Contrarily to common uterine leiomyomas, RL is not usually associated with abnormal uterine bleeding, being usually asymptomatic or manifesting itself as a palpable pelvic mass which may cause abdominal tenderness, pelvic

pain or weight loss [59]. As retroperitoneal smooth muscle tumours are more frequently malignant than benign, and RL may be associated with increased CA-125 levels, it may be a diagnostic challenge for the clinician and the radiologist [56–58].

As far as imaging is concerned, MRI is considered the best imaging technique for investigating retroperitoneal masses, allowing the characterization of an RL as a mass with an isointense signal compared to muscle in T1w sequences and hypointense in T2w ones with homogeneous contrast enhancement and occasional signs of degeneration [1,60].

Although leiomyosarcoma usually shows signs of necrosis and invasive growth, it is not possible, based on imaging alone, to clearly distinguish an RL from other neoplasms of the retroperitoneal space, for which the differential diagnosis is wide and dependent on the clinical scenario. Therefore, biopsy is needed to obtain a definitive histologic diagnosis, provided the lesion is accessible [1,61,62]. RL typically shares a histologic profile similar to that of common uterine leiomyomas, as they have low mitotic count and not show signs of atypia or necrosis [62,63].

RL is usually treated surgically with complete mass excision through either by laparotomic or laparoscopic approach, while hormonal therapy has been only suggested, and it is not currently a recommended approach [56–58,61, 62,64].

Retroperitoneal leiomyosarcoma (RL) is the most common primitive malignant smooth cell tumour in the retroperitoneum [65]. It is more frequent between the fifth and the sixth decade, with a slight female predominance [66]. It can arise from smooth muscle cells of vascular walls, especially from the inferior vena cava, or from other smooth muscle cells in the retroperitoneal space and, depending on their origin, it may present several growth patterns between extravascular, intravascular or a combination of the two [66]. Extravascular involvement is typically asymptomatic, and the mass may grow to large sizes before being detected as an incidental finding or before becoming symptomatic, while RLS with intraluminal growth may have a significant haemodynamic effect on the venous circulation, either because of infiltration of the inferior vena cava or a renal vein [66]. Occasionally, similarly to IVL, a leiomyosarcoma of the inferior vena cava can reach the heart and even the pulmonary arterial circulation [65]. Metastases are relatively common at the time of the diagnosis, although they are more frequently reported during the follow-up, with most common sites of involvement in the lungs, liver and peritoneum [65,66].

On US evaluation, RLS appear as a solid mass with the frequent presence of cystic and haemorrhagic components, and when intravascular growth is involved, the lesion shares some ultrasonographic aspects with the IVL, being an intraluminal defect with vascularized Doppler. On CT, RLS usually presents as a mass of large dimensions with moderate contrast enhancement and coexistent necrotic and haemorrhagic foci [65,66], frequently showing signs of local invasion of surrounding structures; when intravascular growth is present, it is comparable to IVL as a contrast-enhanced filling defect (Fig. 6). CT is also useful for identify distant metastases, especially pulmonary ones [67]. On MRI, leiomyosarcoma with prevalent vital tissue is characterized by low or intermediate signal on T1w sequences and variable from hypointense to hyperintense signal on T2w sequences [65,66], with heterogenous or marked contrast enhancement [65]. Degenerated components have variable signal intensity based on their characteristics: cystic and necrotic areas are hyperintense in T2w sequences, while haemorrhagic foci are easily identifiable as hyperintense in T1w sequences. Intravascular involvement can be evaluated using black blood sequences, as they can easily differentiate the intraluminal neoplastic mass, while bright blood sequences are helpful in the pre-operative setting to reconstruct vascular anatomy. Histologic evaluation is the key to obtaining a diagnosis: leiomyosarcoma usually shares positivity to smooth muscle markers with leiomyoma while being distinguished by cellular pleomorphism or atypia, necrosis and mitotic activity [68].

The optimal treatment is based on surgical excision of the mass and of all involved organs, aiming to obtain radicality whenever possible, as this is the main prognostic factor [65,66]. Radiation therapy and/or chemotherapy may play a role both with neoadjuvant and adjuvant approach [66]. After treatment, imaging plays a pivotal role in the subsequent follow-up, as every patient requires close serial checks by CT and or MRI [69].

Peritoneal carcinomatosis (PC) is the intraperitoneal secondary dissemination of an epithelial neoplasm that does not originate from the peritoneum itself [70–72]. It is the most common malignant entity with diffuse peritoneal involvement and a frequent manifestation of metastatic malignant tumours, especially gastrointestinal and ovarian ones [71,73].

Neoplastic cells access the peritoneal surfaces and space either by contiguous spread, haematogenous dissemination or lymphatic route; then, they tend to linger where the fluid is subject to stagnation, but they can follow its ascending distribution pattern, thus being able to widely affect the entire peritoneum [71,74,75], causing ascites by obstruction of lymphatic vessels or by influencing capillary permeability [71,73]. PC is a subtle condition, as it can either develop synchronously to the primitive tumour or during the follow-up while being asymptomatic in both cases until progressive involvement of the peritoneum causes signs and symptoms like ascites, abdominal pain, nausea, vomiting, or bowel obstruction.

US may prove a useful initial exam in evaluating patients presenting with ascites, as this exam may directly detect PC implants as hypoechoic nodules or thickening of the peritoneal profile or may highlight ascites loculation as an indirect sign of neoplastic disease CT is the reference

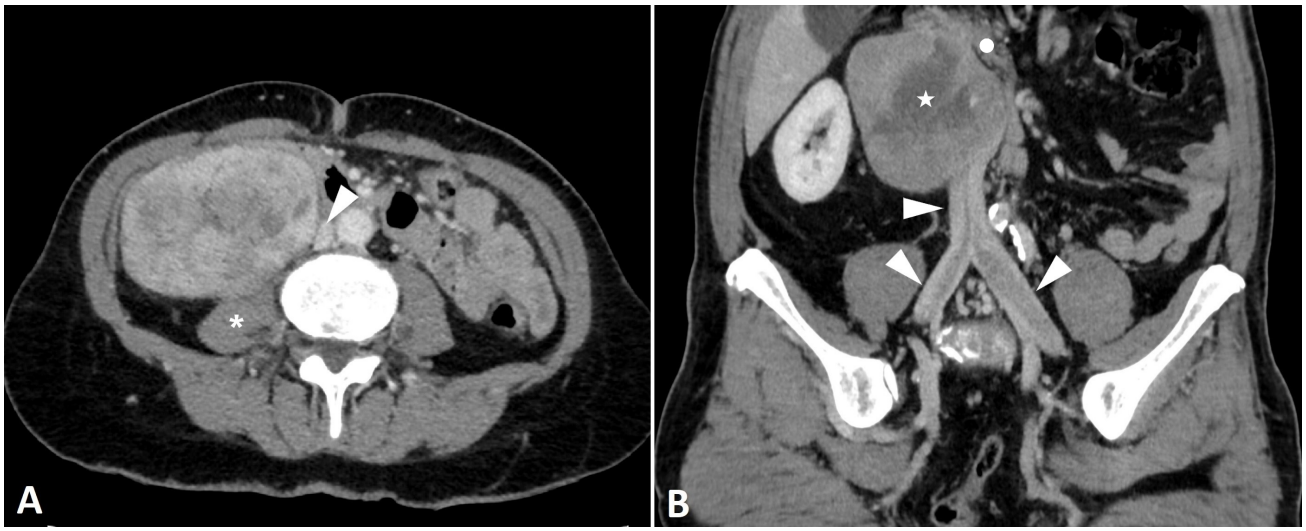

Fig. 6. Retroperitoneal extravascular leiomyosarcoma. (A) Abdominal-pelvic computed tomography (CT) scan with intravenous contrast medium on axial plane (venous phase) in another patient affected by retroperitoneal extravascular leiomyosarcoma: a voluminous inhomogeneously vascularized mass occupies almost entirely the right iliac fossa, dislodging medially the inferior vena cava (arrowhead) and slightly compressing the right psoas muscle (asterisk), but without signs of infiltration. (B) Abdominal-pelvic CT scan with intravenous contrast medium on para-coronal plane (venous phase) in a patient affected by a retroperitoneal leiomyosarcoma with combined extravascular and intravascular growth: a large, mostly necrotic, mass (star) occupies the great vessel compartment of the retroperitoneum, dislocating the pancreatic head (dot), while the intravascular component of the neoplasm consist in a inhomogeneously vascularized filling defect in the lumen of the inferior vena cava and of both iliac veins (arrowheads).

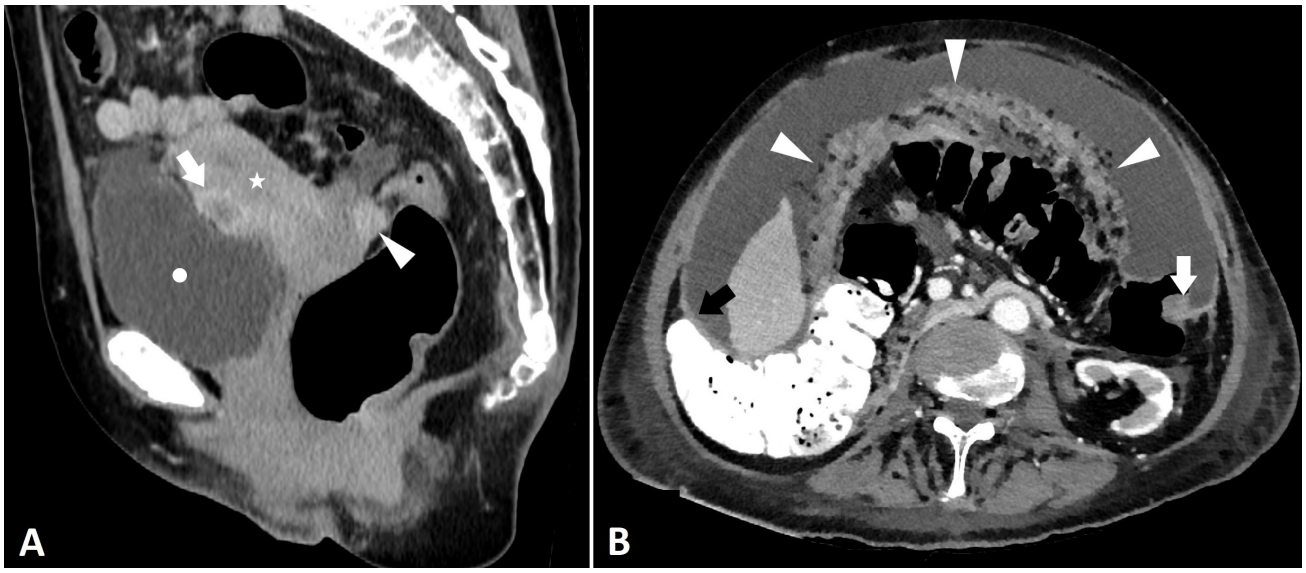

Fig. 7. Peritoneal carcinomatosis. (A) Abdominal-pelvic computed tomography (CT) scan with intravenous contrast medium on sagittal plane (venous phase) in another patient affected by ovarian carcinoma with peritoneal involvement: the scan shows a soft tissue nodule with contrast enhancement in the recto-uterine pouch (arrowhead) that appears in continuity with the uterus (star) and that might mimic a smooth muscle tumour of uterine origin; the presence of another similar nodule in the vescico-uterine pouch (arrow) characterized by a necrotic core and adherent to the upper wall of the bladder (dot) orients the diagnostic suspicion towards the hypothesis of peritoneal metastatic implants, later confirmed by histologic samples. (B) Abdominal-pelvic CT scan with intravenous contrast medium on axial plane (venous phase) which highlights, in a different patient, extensive peritoneal carcinomatosis with coexistent ascites: the entire greater omentum is replaced by a conglomerate of inhomogeneously contrast enhanced soft tissue and fat, also known as "omental cake" (arrowheads), while the parietal peritoneum in both paracolic gutters is thickened and exhibit noticeable contrast enhancement (black arrow), also assuming a focally pseudo-nodular shape (white arrow).

investigation for evaluating PC [73,76], whose appearance varies from soft tissue irregular nodules to infiltrative masses which affect peritoneal and sub-peritoneal spaces and which may or may not be associated with ascites [70–72,75] (Fig. 7); attention should be posed also on thickening and abnormal contrast enhancement of peritoneal surfaces, which are suggestive for malignant infiltration [71,74,75]. When assessing the distribution of the implants, the circulation of the peritoneal fluid in the peritoneal recesses should be considered, especially if ascites is absent, as PC may be more challenging to identify in these cases [71,75]. The widespread infiltration of the peritoneal surface and omental fat outlines the picture called "omental caking", in which omental fat appears replaced by an irregular mass composed of a mixture of multiple minute nodules associated with fibrosis [10,70,71,75] (Fig. 7). MRI is not routinely used to evaluate peritoneal disease; however, like in this case report, it can be a problem-solving complementary tool thanks to its greater contrast in soft tissue evaluation [73] and it is reported as a superior modality compared to CT when assessing sub-centimetric lesions [73,76], which may identifiable by their slow contrast enhancement in delayed post-contrast sequences at 5–10 minutes [73] or as hyperintense foci on DWI sequences [70,73].

Differential diagnosis of PC should consider many other pathologies that cause diffuse peritoneal involvement, either of neoplastic and inflammatory or infective origin, including DPL [71–73]. Compared to DPL, PC is more frequently associated with weight loss, ascites and size progression on subsequent imaging investigations [1,23] and diagnosis may be made easier by patient anamnesis or by identification of a primary neoplasm on imaging.

PC is burdened by poor prognosis as it is not curable, although a combination of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy is a promising approach to improve survivability in selected patients [73,75,76].

Conclusions

DPL is a rare occurrence with a typical benign course that can be a diagnostic challenge for both the clinician and the radiologist. Given that it may mimic some malignant conditions, it requires extensive instrumental diagnostics to be correctly identified, although anamnestic information on the patient may be a useful tool in narrowing down the differential diagnosis options.

In our case, the patient had a history of ovarian leiomyoma, a rare benign ovarian lesion which shares several characteristics with the much more common uterine leiomyoma and, just as uterine leiomyoma itself, has been reported in association with DPL. The previous diagnosis of ovarian leiomyoma and the subsequent laparoscopic adnexectomy is highly suspected to be the primary cause of the dissemination of smooth muscle cells on the peritoneal surface of our patient. However, it is not possible to exclude the eventuality of spontaneous DPL, given the presence of uterine leiomyomatosis and a previous ovarian leiomyoma.

Knowledge of the atypical presentation patterns of leiomyomas and the related imaging characteristics may benefit both clinicians and radiologists. The presenting symptoms and the multimodal radiological characteristics on US, CT and MRI may allow, even in the initial stages of the patient's diagnostic assessment, to differentiate conditions with a predominantly benign course, such as DPL or other atypical intra-abdominal localizations of leiomyoma, from potentially problematic conditions, such as BML or IVL, or frankly malignant ones, such as RLS or PC, thus allowing to reserve invasive diagnostics for selected cases. Despite the high diagnostic potential of modern imaging, subsequent invasive manoeuvres may sometimes not be avoided, as histological characterization of bioptic or laparoscopic samples is needed when dealing with doubtful conditions. Nevertheless, radiology can allow for better patient management, guiding therapeutic choices and supporting subsequent follow-up.

Availability of Data and Materials

All data are included in the article.

Author Contributions

ACP and RB designed the research study; AC, RB, GF and MG performed the research; RB and GF collected and analyzed the data. RB and AC has been involved in drafting the manuscript and all authors have been involved in revising it critically for important intellectual content. All authors give final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki. Ethics approval was waived (Institutional Review Board, Arcispedale Sant'Anna). Written informed consent was obtained by the patient for personal data publication.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.62713/aic.3751.

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