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Key principles for the initial management of primary retroperitoneal tumours in adults

Walter S Nardi[1], Sergio D Quildrian[1], Victoria Scasso Rebzda[2], Dimitri Tzanis[3] and Sylvie Bonvalot[3]

[1]Sarcoma and Melanoma Unit, Department of General Surgery, British Hospital of Buenos Aires, Perdriel 74, CABA, Buenos Aires 1280AEB, Argentina
[2]Department of General Surgery, British Hospital of Buenos Aires, Perdriel 74, CABA, Buenos Aires 1280AEB, Argentina
[3]Department of Surgical Oncology, Institut Curie, 26 Rue d'Ulm, 75248 Paris, France

Abstract

Background: Primary retroperitoneal tumours (RPTs) encompass a wide range of diagnostic possibilities. Failure to recognise them appropriately may lead to suboptimal management, particularly in non-specialised centers. A structured diagnostic pathway is therefore essential to support appropriate treatment planning and timely referral to specialised teams.

Objective: To review key points of the diagnostic workup of primary RPTs, with special emphasis on those of mesenchymal origin.

Results: Primary RPTs represent a broad and heterogeneous group, with mesenchymal tumours accounting for approximately half of cases. Cross-sectional imaging plays a central role in the initial characterisation. Percutaneous core needle biopsy with histological and molecular analysis is recommended in most cases where imaging is not diagnostic. Serum tumour markers may provide valuable diagnostic clues in selected clinical settings.

Conclusion: Accurate diagnosis relies on a structured diagnostic pathway integrating imaging, biopsy when indicated and expert pathological review. Early referral to specialised multidisciplinary teams is essential to optimise management and improve oncologic outcomes.

Keywords: *retroperitoneal tumour, soft tissue sarcoma, diagnosis, biopsy, imaging*

Review

Introduction

Retroperitoneal tumours (RPTs) arise within the retroperitoneal space. Primary tumours originate independently of retroperitoneal organs and are predominantly of mesenchymal origin, although lymphoid neoplasms, parasympathetic tumours and extragonadal germ cell tumours may also occur. Secondary lesions are usually metastatic carcinomas [1].

According to guidelines from the European Society of Medical Oncology, National Comprehensive Cancer Network and the Trans-Atlantic Retroperitoneal Sarcoma Working Group [2–4], image-guided percutaneous core needle biopsy (CNB) is recommended in

Correspondence to: Walter S Nardi
Email: nardi.ws@gmail.com

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most cases where serum tumour markers and imaging do not provide a precise diagnosis. Histopathological evaluation by a certified expert pathologist is essential, as expert pathology review can modify the initial diagnosis in up to 20% of cases. Finally, a multidisciplinary tumour board (MDTB) defines the global strategy thereafter based on the results obtained.

Despite these recommendations, many patients are still initially managed in non-specialised centers. In some countries, such as France and the UK, sarcoma care is centralised in designated high-volume reference centers [5, 6]. However, this is not the standard of practice in most regions. Confusion remains in the primary care setting regarding the diagnostic algorithm and the importance of early referral of RPTs.

We discuss the initial diagnostic workup of adult patients with suspected primary RPTs, focusing on imaging evaluation, biopsy strategy and referral pathway. We also highlight key diagnostic considerations and common pitfalls that may lead to misdiagnosis and adversely impact patient care.

Methods

This narrative review is based on a non-systematic literature search performed in PubMed and supplemented by major international oncology guidelines [2–4]. Priority was given to recent clinical practice guidelines, key retrospective series and relevant review articles. The selection of studies was guided by clinical relevance and the authors' expertise in sarcoma management.

Diagnostic approach to RPTs

The diagnostic evaluation of RPTs should follow a structured sequence. This sequence typically progresses from initial imaging recognition to characterisation, differential diagnosis, use of serum biomarkers and histological confirmation when required. The following sections summarise key diagnostic considerations within this framework, organised by major tumour groups. Table 1 integrates imaging features, biomarker evaluation and biopsy indications and can be used as a simplified clinical algorithm.

- **Mesenchymal tumours**

Mesenchymal tumours account for approximately half of primary RPTs. The WHO 2020 classification categorises them into different subgroups according to the tumour differentiation line and biological behaviour (benign, intermediate or malignant).

Overall, almost 30% of RPTs are sarcomas. Liposarcoma (LPS), leiomyosarcoma (LMS) and solitary fibrous tumour (SFT) account for nearly 90% of retroperitoneal (RPS) soft tissue sarcomas (STS). Generally, anterior displacement of normal anatomical structures (colon, adrenal glands, kidney and pancreas) in cross-sectional imaging is suggestive of a tumour arising from the retroperitoneal cavity.

When an RPT is identified and imaging does not establish a secure diagnosis, adequate tissue sampling is required, particularly when sarcoma is suspected, because treatment planning depends on histologic subtype and grade. Preoperative biopsy can identify patients who do not require surgery, for example, in lymphoid neoplasms. Image-guided percutaneous CNB, preferably by a ≥14–16 G needle through a posterior retroperitoneal approach and using a coaxial technique when feasible, is generally recommended in most cases. This approach provides high diagnostic accuracy, with a low rate of minor complications (3%), a reported needle track seeding of less than 0.4% and no adverse impact on oncological outcomes [7]. Once the sample is obtained, histologic and molecular biology tests are essential for a correct diagnosis and should be analysed by an expert pathologist in a reference center.

Following diagnosis, resectability should then be assessed. In RPS, staging should include a chest computed tomography (CT) to assess the presence of metastatic disease. This is particularly important for LMS as pulmonary metastases are present in 40% of cases at diagnosis [8, 9]. Assessment of liver metastasis, particularly in LMS, should also be performed on abdominal CT. Finally, following diagnosis and staging, management is typically guided by histology subtype for localised RPS once resectability is established [10]. Currently, it is recommended that specialised multidisciplinary sarcoma units carry out the treatment of sarcoma patients after MDTB meeting discussions in reference centers. Several studies have already shown the benefits of this management approach [11, 12].

Table 1. Comparative summary of main RPT.

RPT	Demographics	Diagnostic Key-imaging features	Approach Biopsy
Mesenchymal origin tumours			
Adipocytic tumours			
WDLPS	LPS is the most frequent RPS. Typically asymptomatic until mass effect symptoms due to large size.	Homogeneous large-sized fatty mass (eventual solid/nodular areas that represent sclerosing component).	MDM2-amplification on FISH.
DDLPS	Idem.	Well-differentiated component + dedifferentiated component (non-fatty or nodular areas).	MDM2- and CDK4 amplification on FISH (helpful to distinguish DDLPS from other dedifferentiated sarcomas).
Lipoma	Exceedingly rare (few cases reported in literature).	Homogeneous fat density mass.	Absent MDM2-amplification on FISH.
Angiomyolipoma	Benign. Renal origin.	Fatty mass with internal vessels and notch to the renal hilum.	Co-expression of myogenic and melanocytic markers (HMB45 and/or Melan-A) + MDM2-negativity.
Myelolipoma	Benign. Rarely outside the adrenal cell.	Fatty mass with 'frosted glass' effect.	Mature adipocytes and hematopoietic components.
Smooth/striated muscle tumours			
LMS	Second most common RPS. Mostly extraluminal.	Lobulated and well-circumscribed mass with necrosis and heterogeneous enhancing.	Spindle cells with smooth muscle differentiation (stain for desmin, h-caldesmon and smooth muscle actin).
Alveolar RMS	Exceedingly rare (more common in children and adolescents).	Soft tissue mass with large necrotic areas. Can spread to lymph nodes.	High smear cellularity with poorly cohesive (*pseudoalveolar*) arrangement. t(2;13) translocation.
Fibrous tumours			
SFT	Third most common RPS.	Well-defined hypervascular mass (large peri-tumoural veins).	Monomorphic spindle cells arranged in hypo- and hyper- cellular areas. CD34 and nuclear STAT6 positivity. Distinctive vascular network (diagnostic hallmark).
DT	Young to middle-aged adults, F > M.	Homogeneous mass. Marked hypointensity on MRI T2-weight signal.	Benign appearing monoclonal fibroblastic cells. CTNNB1 gene mutation present.
Neural tumours			
MPNST	Malignant transformation of pre-existent neurofibroma (50% in NF1). Can be sporadic or radioinduced. Rapid onset of symptoms.	Hypodense mass with early peripheral enhancement. Occasional cystic degeneration.	Increased and variable cellularity with high mitotic activity. Perivascular accentuation. SOX10 and S-100 expression.
Schwannoma	No risk of malignant transformation.	No radiological features to distinguish from MPNST.	Antoni-A growth pattern. Diffuse S-100 expression and peripheral EMA positivity

Continued

Table 1. Comparative summary of main RPT. *Continued*

Others **UPS**	Rare.	Well-circumscribed heterogeneous tumour (necrosis, foci of hemorrhages and myxoid areas). Typically contained within the ilio-psoas muscle.	Yes. Is a diagnosis of exclusion.
SS	Rare. Middle-ages adults. Commonly monophasic.	Solid hypodense mass with cystic-necrotic degeneration.	Spindle cells with epithelial differentiation markers (EMA and cytokeratin). t(X;18) translocation.
Cystic lymphangioma	Young adults, F > M. No risk of malignant transformation.	Hypodense cystic tumour with defined borders and capsular enhancement.	Not necessary if clear imaging diagnosis.
Aggresive angiomyxoma	More common in women. Typically arising in pelvis, perineum or labia major.	On MRI: well-defined mass with swirled aspect and avid enhancement.	Yes.
Lymphoma	Represent almost 25% of RPT. Constitutional 'B symptoms'.	Well-circumscribed, lobulated confluent masses encasing vasculature without occlusion nor infiltration ('floating aorta sign'). Supra-diaphragmatic or peripheral lymph nodes may be present.	Yes, mainstay of diagnosis.
PGL	Associated with VHL, NF1, MEN syndromes. Symptoms if catecholamine secretion. Elevated urinary/plasma free metanephrines = Diagnostic.	Midline mass with high-contrast enhancement close to great vessels.	Not recommended if positive biochemical testing.
EGGCT	Youngs > adults. AFP, LDH and Hcg may be elevated.	Indeterminate poly-lobulated mass along the great vessels usually under the renal hilum ('floating aorta sign').	Yes. Confirms diagnosis and EGGCT subtype.

Adipocytic tumours

Fatty tumours are the most frequent retroperitoneal histotype. Well-differentiated liposarcoma (WDLPS) and dedifferentiated liposarcoma (DDLPS) are the main malignant entities, whereas lipomas, myelolipomas and angiomyolipoma represent the benign tumours.

Contrast-enhanced CT is the imaging modality of choice to evaluate adipocytic RPTs. WDLPS typically presents as a large-sized mass with homogeneous fatty content (Figure 1a). In DDLPS, gross findings usually include the coexistence of non-fatty or nodular areas of different density (dedifferentiated component) surrounded by well-differentiated fatty mass (well-differentiated component) (Figure 1b). However, imaging overlap with benign lesions is common [13]. Therefore, although imaging findings may suggest malignancy, preoperative percutaneous biopsy is recommended. Both WDLPS and DDLPS are MDM2 amplified tumours that can be identified by fluorescence in-situ hybridisation (FISH). Biopsy should target the solid areas of the tumour systematically to avoid under-grading. This has been shown to improve sensitivity, particularly for the detection of grade 3 DDLPS [14]. Accurate diagnosis is a key step to personalise the multidisciplinary management, as WDLPS and DDLPS differ in their biological behaviour and recurrence patterns. In this setting, preoperative strategies can be considered and may include radiotherapy [15]. Currently, the STRASS 2 trial is evaluating neoadjuvant chemotherapy versus surgery alone

for LMS and G3 DDLPS (ClinicalTrials.gov Identifier: NCT04031677). Its results could add new options for the peri-operative management of these patients.

Differential diagnosis between WDLPS and lipoma remains challenging. Generally, lipomas have homogeneous fat density without internal septa. Nevertheless, MDM2 gene amplification status in a biopsy specimen confirms LPS (Figure 2). Angiomyolipomas and myelolipomas are also fat-containing tumours. Angiomyolipomas show internal vessels and usually a notch or point of entrance to the renal hilum, suggesting their origin in the kidney. Myelolipomas have bone marrow within the fat (mature adipocytes), making a 'frosted glass' effect on enhanced CT scan. This part can be mistaken for a dedifferentiated component of an LPS [13, 16, 17]. They typically present in the adrenal lodge, rarely found outside.

Finally, surgical management principles depend on histologic subtype and are beyond the scope of this diagnostic-focused review [18, 19].

Smooth/striated muscle tumours

LMS (primary vascular sarcoma) is the second most common RPS in the adult (≅ 15%) and originates from smooth muscle cells in the wall of retroperitoneal vessels, mainly in women. It commonly arises from the inferior vena cava (IVC), but it can also originate from the renal (Figure 3), adrenal, gonadal or iliac veins. Uterine location, which is the predominant origin of all LMS, must be ruled out, especially in women with a previous history of resected uterine leiomyoma (occasionally misdiagnosed) [20]. They are mostly extraluminal and typically present as large, lobulated, well-circumscribed masses with necrotic content and heterogeneous enhancing on CT, contiguous to a vessel. Histologically, LMS shows spindle cells with smooth muscle differentiation expressing desmin, h-caldesmon and smooth muscle actin. Genetically, as well as undifferentiated pleomorphic sarcoma (UPS), LMS exhibit heterogeneous complex karyotypic abnormalities. Differential diagnosis includes benign leiomyoma (they generally do not present nuclear atypia and lack necrosis and high mitotic activity) and DDLPS in case of high-grade pleomorphic LMS. The latter can be excluded by confirming the absence of MDM2 amplification on FISH.

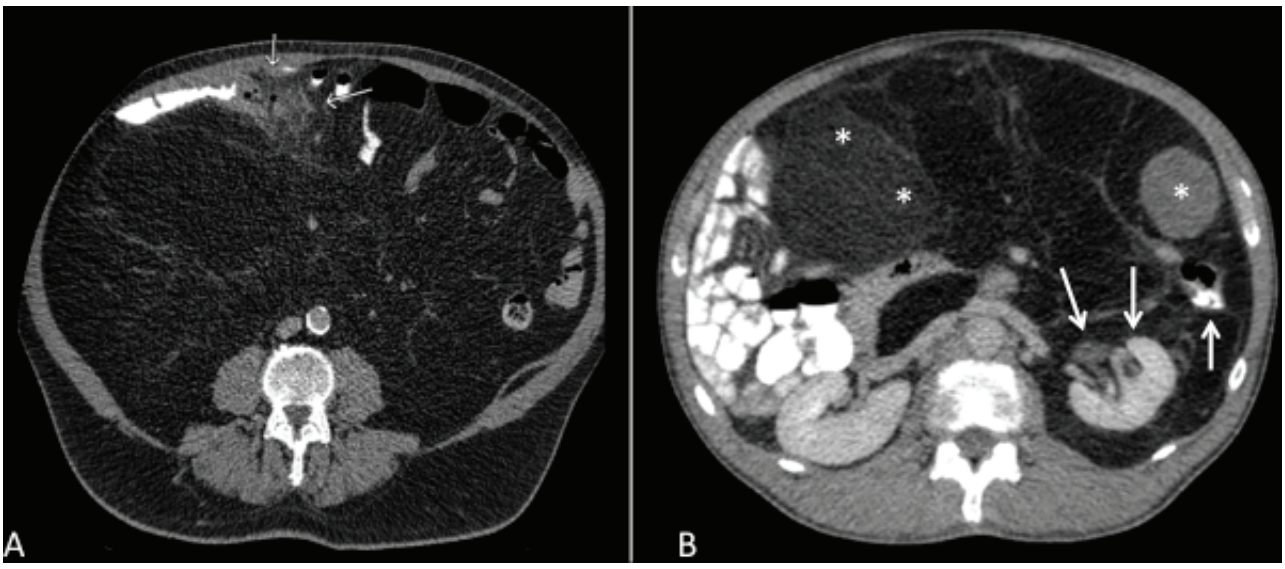

Figure 1. (a): WDLPS. (b): DDLPS. The two components of the tumour can be seen: the well-differentiated part surrounding the kidney and colon *(arrows)* and the dedifferentiated solid part within *(asterisks)*.

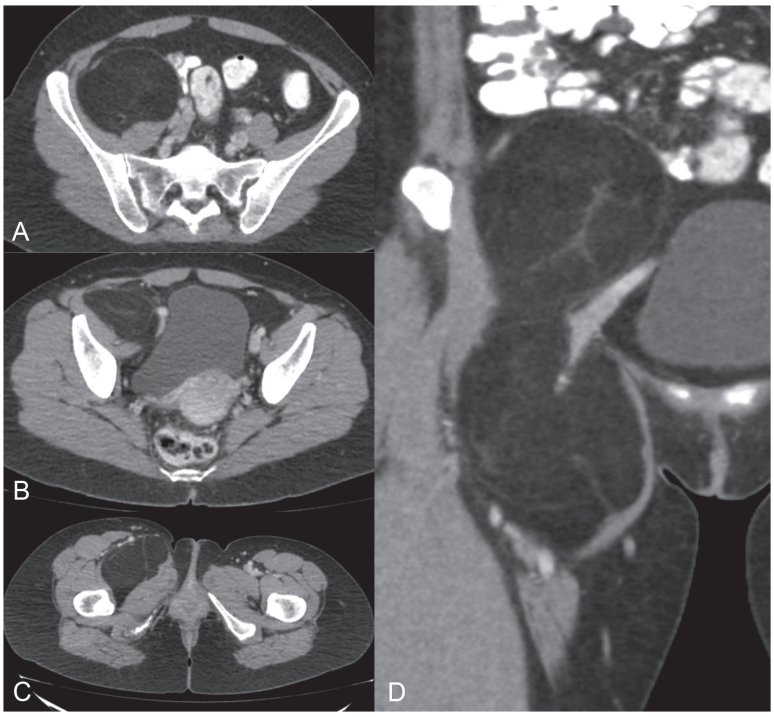

Figure 2. (a): CT scan axial-view showing a right retroperitoneal soft-tissue tumour in contact with the iliopsoas muscle and medially displacing ipsilateral iliac vessels. (b and c): Images showing herniation through inguinal canal into the thigh and displacing forwards the femoral vessels. (d): Coronal view of the tumour with a 'dumbbell appearance'. Biopsy: lipomatous tumour without MDM2 amplification on FISH.

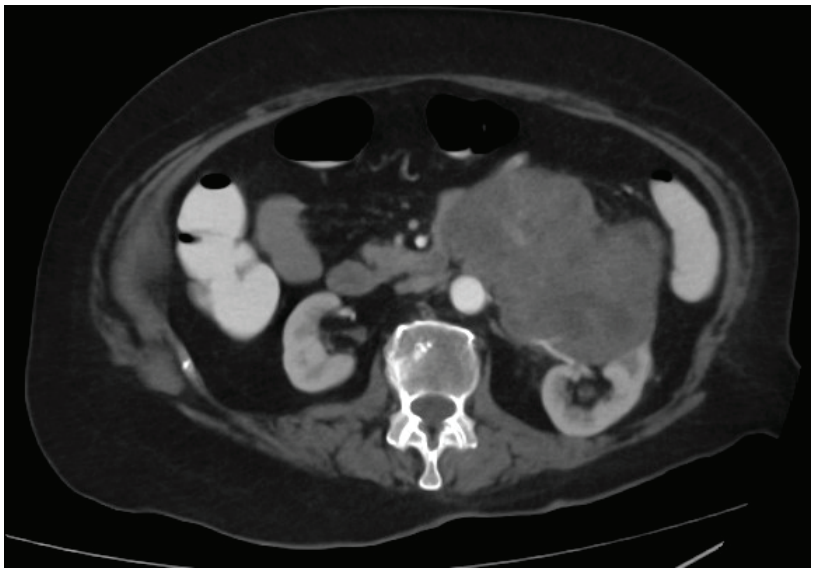

Figure 3. LMS of left renal vein.

Alveolar/Embryonal rhabdomyosarcomas (RMS) (striated muscle differentiation) are exceedingly rare in adults and common in the pediatric and adolescent population. However, pleomorphic RMS is considered a high-grade adult-type STS that can appear (although rarely) in the retroperitoneum. It has a high metastatic risk and poor prognosis. Moreover, despite sarcomas almost never metastasize to the lymph nodes, exceptionally, RMS does. Based on its chemosensitivity at other sites, neoadjuvant chemotherapy may be considered following MDTB discussion.

Fibrohistiocytic tumours

In the retroperitoneum, this group of tumours accounts mostly for desmoid tumours (DT) (unpredictable and locally aggressive potential behaviour) and SFT (variable metastatic potential).

SFT are the third most common subtype of RPS (approximately 6%). They are well-circumscribed hypervascular masses due to large peritumoural veins and intense contrast enhancement in delayed phases of CT scan or magnetic resonance (MRI), denoting the fibrous stroma component. Presumptive diagnosis can be confirmed with a percutaneous CNB. Histologically, they have hypocellular areas (occasionally with hypercellular components) of monomorphic spindle cells and a vascular network of thin-walled and branched vessels (this vascular pattern is called 'stag-horn'). Immunohistochemistry shows tumoural cells with strong CD34 positivity and nuclear expression of STAT6 due to NAB2::STAT6 fusion (molecular hallmark) [21].

DT shows a wide range of T2 signal intensities on MRI [22], but usually, images do not show characteristic features that may suggest a possible diagnosis. Nonetheless, a diagnostic biopsy should be performed. Three European prospective observational trials have demonstrated that active surveillance as a first-line strategy is safe and effective for newly diagnosed DT [23–25] (Figure 4). CTNNB1 gene mutation is required to confirm the diagnosis and is present in 95% of tumours. It remains uncertain whether the mutational profile has a true impact on event-free survival (regardless of the first-line therapy chosen) [26, 27]. The DT Working Group recently published an updated consensus recommending surgery only in cases of tumour-related bowel complications (bleeding, obstruction or perforation) occurring in up to 10% of cases [28]. The main goal should be to solve the complication with resection of the tumour, but only when feasible, without excessive bowel resections that may lead to considerable morbidities. This is particularly relevant for sporadic mesenteric DTs, while for FAP-associated DTs the main objective should be symptom relief and control of the main complication rather than resection of the tumour [29, 30].

Neural tumours

Benign (schwannoma/neurofibroma) and malignant peripheral nerve sheath tumour (MPNST) are tumours arising from the nerves that can also occur in the retroperitoneum and are the most frequent entities of this subgroup.

MPNSTs can arise de novo but are more frequently seen as a malignant transformation of pre-existent plexiform neurofibromas (50% of them occurring in patients with neurofibromatosis type 1, NF-1) [31]. In fact, some studies have shown that NF-1 status is a negative predictor of overall- and distant metastasis-free survival [32, 33]. Differential diagnosis with neurofibromas or schwannomas can be challenging since there are no radiological features that reliably distinguish one from another. On CT scan, lesions appear hypodense with early peripheral enhancement after intravenous contrast and occasionally presenting cystic degeneration (Figure 5). On MRI, peritumoural edema, intratumoural heterogeneous masses or invasive margins are suggestive, although not specific, of MPNST. Moreover, rapid onset of neurologic pain (which is a classic presenting symptom) or interval tumour growth may suggest malignancy. Microscopically, increased and variable cellularity with high mitotic activity and perivascular accentuation is a typical morphologic feature. Instead, schwannomas exhibit a characteristic Antoni-A growth pattern with diffuse S-100 expression and peripheral epithelial membrane antigen (EMA) positivity on perineural cells. Schwannomas do not have a risk of malignant transformation (Figure 6).

Ganglioneuroma is a rare, benign, differentiated neurogenic tumour that arises in neural crest cells. The retroperitoneum is the second most common site after the posterior mediastinum and typically presents in children or young adults. Characteristically, they present well-defined, rounded, homogeneous masses with fibrous shapes, low pre-contrast attenuation on CT scan and occasional punctate calcifications (Figure 7). Definitive diagnosis is made by histopathologic examination. Features include mature ganglion cells admixed with clusters of spindle cells (positive for S-100). Active surveillance is an option [34].

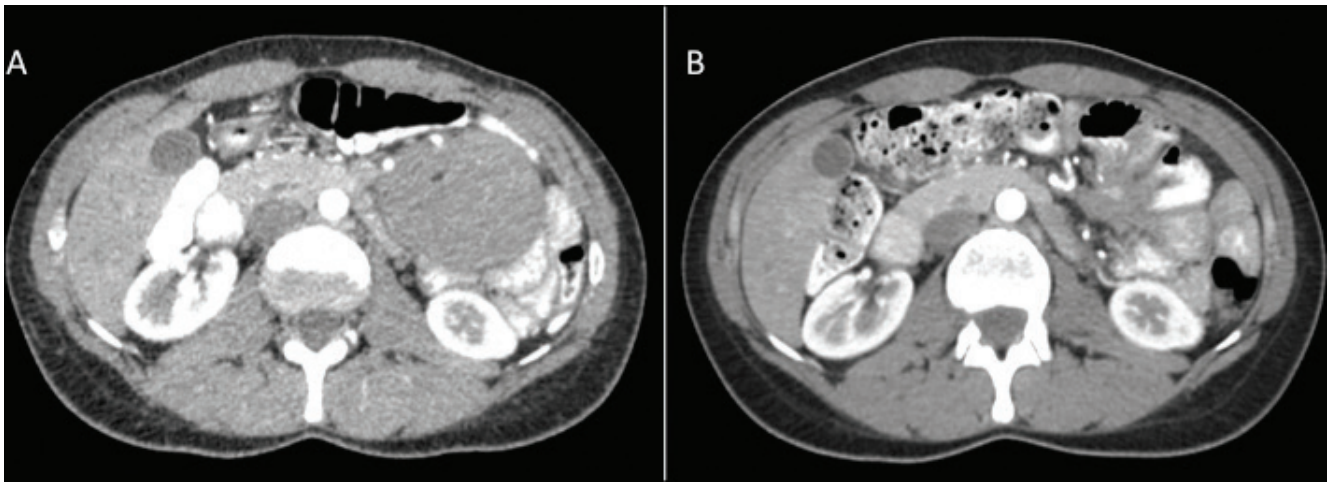

Figure 4. (a): Intra-abdominal asymptomatic mass measuring 9 cm. Biopsy confirmed DT and active surveillance (AS) was decided after multidisciplinary discussion. (b): CT scan after 3 years of AS.

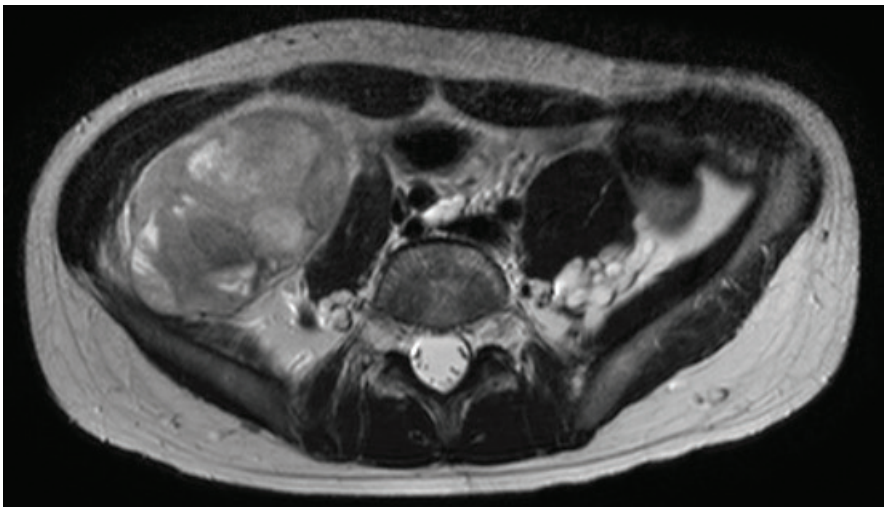

Figure 5. (a and b): MPNST originating in the right crural nerve territory and displacing medially the psoas muscle in a NF-1 patient. Neurofibromas (*arrows*).

Vascular tumours

Cystic lymphangiomas are benign tumours originating from the endothelium of lymphatic vessels with no risk of malignant transformation. They predominantly occur in young patients, mostly females. They most frequently present in the head and neck region or mediastinum, but also can appear in retroperitoneum, mesentery or greater/lesser omentum. Diagnosis is based on imaging findings showing a typical hypodense cystic tumour with defined borders and capsular enhancement on CT scan (Figure 8), and does not require biopsy. They may enlarge slowly until they become symptomatic lesions due to compression of surrounding structures or even encase adjacent organs, which makes surgical resection more difficult.

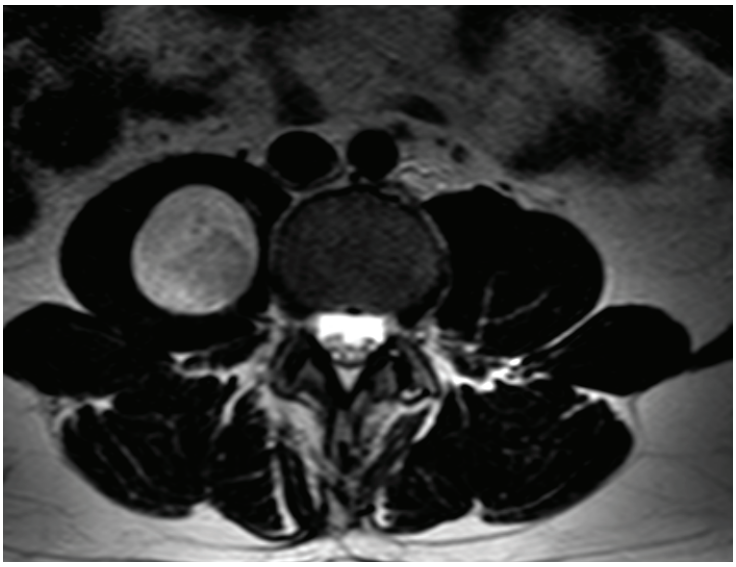

Figure 6. (a and b): Schwannoma with cystic degeneration contained within the left psoas muscle. Percutaneous biopsy showed areas of densely populated spindle cells (Antoni-A) positive for S100 and SOX10 on immunohistochemistry confirming nerve sheath differentiation.

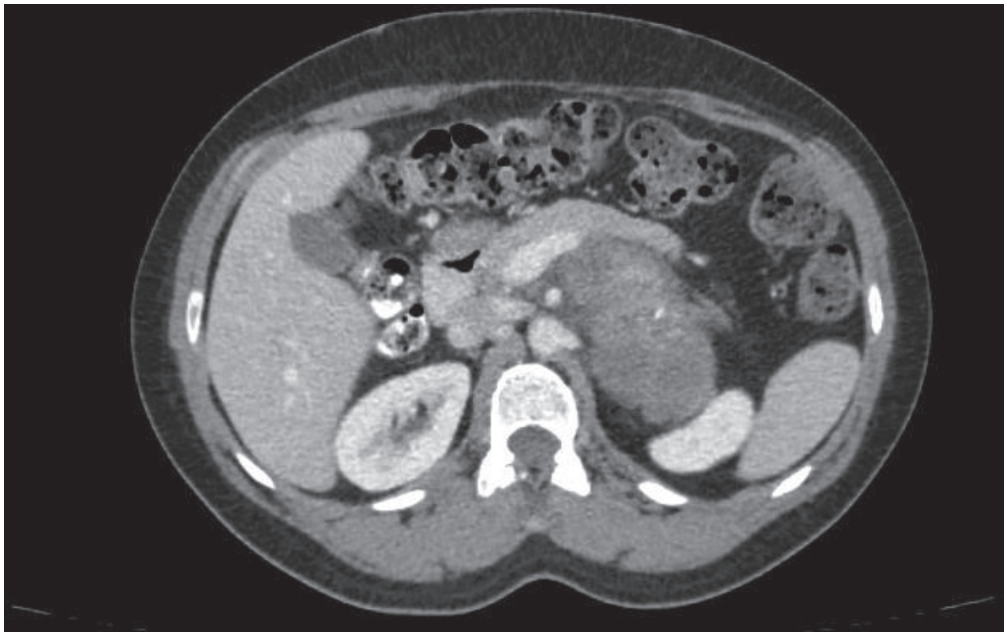

Figure 7. Ganglioneuroma. Well-defined retroperitoneal mass with punctate calcifications. Diagnosis was established by biopsy, as ganglioneuromas lack pathognomonic imaging features.

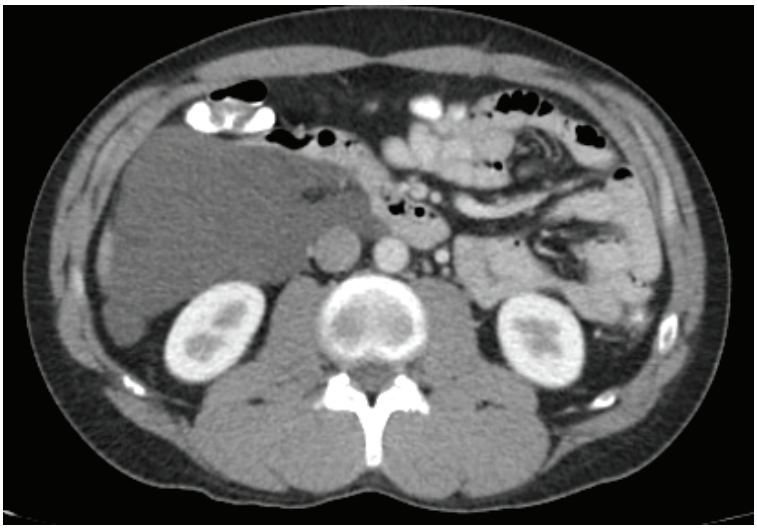

Figure 8. Cystic lymphangioma.

Primary aortic involvement is very rare. It is usually affected by adjacent tumours with a secondary wide encasement or partial infiltration [35]. However, it can also be affected by primary malignant vascular tumours: high-grade angiosarcoma and intimal sarcomas (that generally grow into the aortic lumen). Retroperitoneal angiosarcoma has a dismal prognosis and mortality is usually related to local complications, mainly thrombo-embolic events.

Extra-skeletal osseous/cartilaginous tumours

They are rare in the retroperitoneum. Extra-skeletal Ewing's sarcoma, known for its chemosensitivity, benefits from an already established neoadjuvant chemotherapy. Because the site of origin (bone versus soft tissue) determines the therapeutic strategy, accurate diagnosis through imaging and biopsy is essential to guide therapy.

Others

UPS accounts for approximately 10% of sarcomas in the adult and is rare in the retroperitoneum. It is typically a fast-growing mass contained within the musculature (ilio-psoas muscle), but direct invasion into adjacent organs may be present. Images show a well-circumscribed heterogeneous tumour with necrosis, foci of hemorrhages and myxoid areas. Morphologic, immunohistochemical and molecular findings are non-specific; therefore, UPS remains a diagnosis of exclusion. Cellularity is marked by an extensive pleomorphism without an identified line of differentiation. High mitotic count and abundant necrosis are usually present. Before classifying a tumour as UPS, pleomorphic DDLPS must be ruled out [30].

Perivascular epithelioid cell tumours (PEComas) are a family of mesenchymal tumours with myomelanocytic differentiation, sharing a specific cell type, the PEComas. They exhibit different biologic potential: from benign behaviour (angiomyolipoma), intermediate course (sclerosing PEComa) to malignant behaviour with higher rates of recurrence and mortality (PEComa NOS – not otherwise specified). The latter is composed of a nest of epithelioid and spindle cells intimately arranged around blood vessels walls, expressing both melanocytic and smooth muscle markers. Most are sporadic but can be associated with tuberous sclerosis. They are often large (> 5 cm) heterogeneous infiltrative masses with strong arterial enhancement and small calcifications. However, there are no pathognomonic imaging features, and a biopsy is

needed for diagnosis. Most PEComas do not recur after complete surgical resection, but a subset (malignant subtype) can evolve during follow-up with locally aggressive recurrences or distant metastasis. These scenarios entail a poor prognosis with little or no effective therapy described so far [36].

Synovial sarcoma (SS) is rare. It appears as solid hypodense masses with cystic-necrotic degeneration on CT scan that can be confused with MPNST or LMS. Microscopically, SS are commonly monophasic comprised only of spindle cells, with expression of epithelial differentiation markers (EMA and cytokeratin). Its unique t(X;18) translocation confirms the diagnosis.

Aggressive angiomyxoma is a highly vascularised tumour with intermediate differentiation, usually affecting women. Commonly arising from the perineum (often clinically as a perineal mass) or labium major, can also appear in the sub-peritoneal space. If suspected, an MRI scan should be performed showing a well-defined mass with a swirled aspect and avid enhancement after contrast administration on T2-weighted images (Figure 9). It is a benign lesion with no propensity to metastasize but a historically reported high rate of local recurrence after surgery. After conservative surgery in reference centers, particularly in young patients, a good local control can be achieved [37].

- **Lymphoid tumours**

Lymphomas, represent almost 25% of primary RPTs. A wide variety of subtypes exist and each one of them has its own prognostic and therapeutic considerations. Lymphomas are considered clinic-pathologic syndromes with variable presentations. Constitutional 'B symptoms' (low-grade fever, night sweats, weight loss) as well as multiple peripheral lymph nodes are not always present. On imaging, lymphomas present as well-circumscribed, lobulated, confluent masses along great vessels. These masses typically encase the vasculature without occlusion nor infiltration (Figure 10). Noncontiguous spread (multiple enlarged lymph nodes) along iliac vessels can also be present and favours a diagnosis of lymphoma.

Diffuse large B-cell lymphoma is the most frequent in adults (35% of all non-Hodgkin's lymphomas) and the most frequently associated with HIV infection and immunosuppression. Pathological assessment through CNB remains the mainstay of diagnosis and chemotherapy is the standard of care in this disease [38, 39].

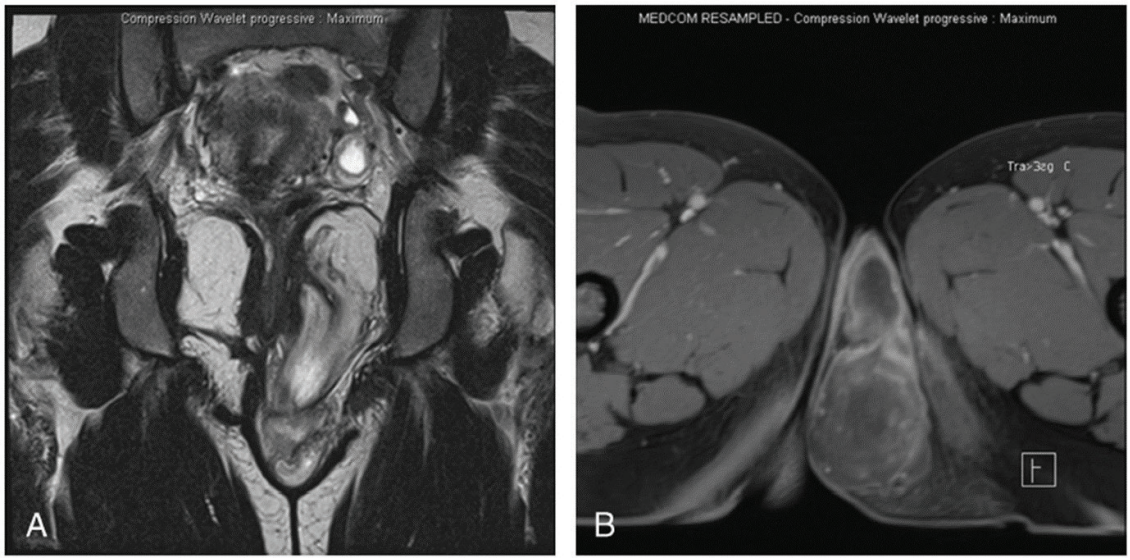

Figure 9. Aggressive perineal angiomyxoma. Coronal (a): and axial (b): views.

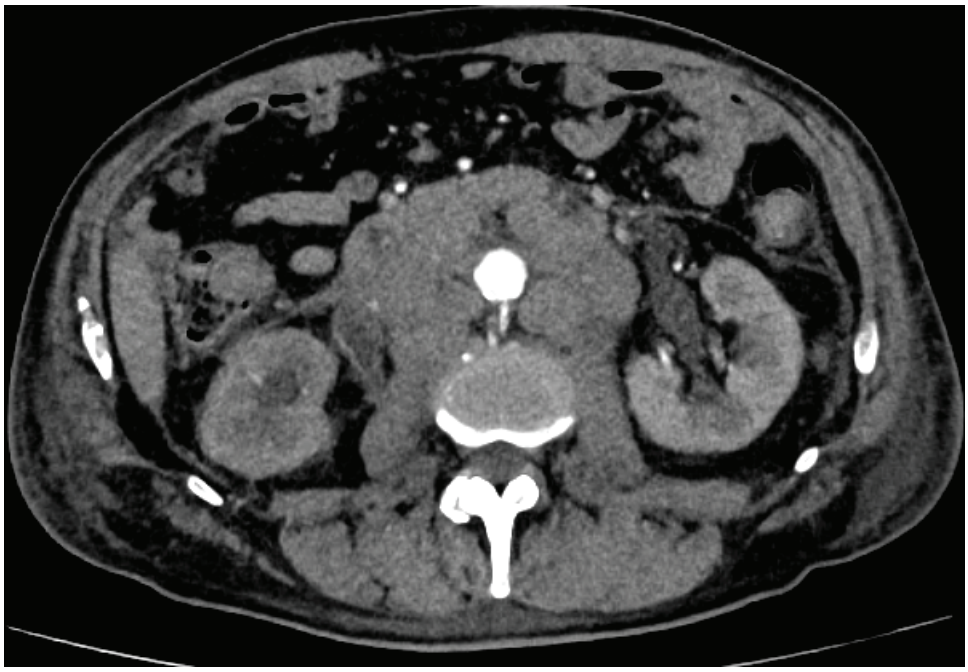

Figure 10. Retroperitoneal well circumscribed confluent and lobulated mass encasing but not infiltrating the abdominal aorta and displacing it away from the vertebral column ('*floating aorta sign*') most commonly suggests a lymphoma diagnosis.

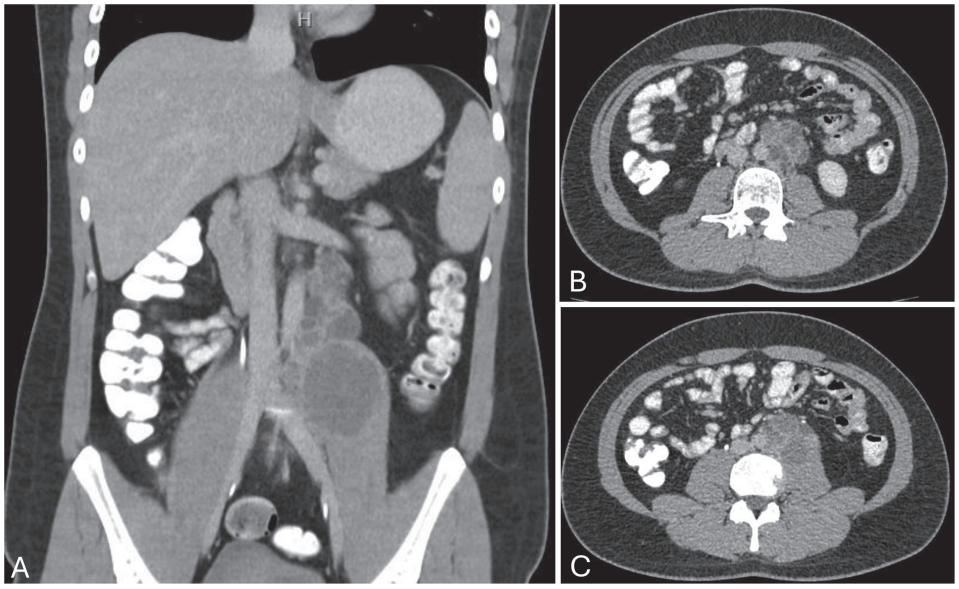

Figure 11. CT scan coronal (a): and axial views (b and c): of an EGGCT in a 24 year-old male with elevated serum tumour markers (mainly β-human chorionic gonadotropin). Percutaneous biopsy confirmed choriocarcinoma.

- **Retroperitoneal paraganglioma (PGL) and adrenal tumours**

PGL is a rare catecholamine-secreting neuroendocrine tumour arising from the sympathetic and para-aortic retroperitoneal sympathetic ganglia. Pheochromocytoma is called when tumour arises in the adrenal gland (by definition, strictly not a primary RPT). Many of them are sporadic but some can be associated with genetic inheritable mutations (mostly MEN2A, Von-Hippel Lindau disease or NF-1). Particular scenarios should raise awareness to ask for genetic counseling [40]. Up to 40% of PGL patients present with symptoms due to active catecholamine secretion such as paroxysmal hypertension, palpitations, hyperglycemia and/or flushing. On imaging, midline masses with high contrast enhancement close to the aorta or IVC with intratumoural vessels are characteristic. If suspected, biochemical testing should be performed. Marked elevation of plasma-free or urinary fractionated metanephrines (2 or 3 times above the upper limit of normal values) is diagnostic [41]. Biopsy is not recommended as it can produce a sudden release of hormones with potential life-threatening hypertension. Definitive treatment for PGL is complete surgical resection. Preoperative alpha-adrenergic blockade is recommended to prevent perioperative hemodynamic instability.

Sometimes, because of the size, tumours arising in the adrenal lodge can raise doubts of the true origin and be confused with a primary RPT. Adrenocortical carcinoma must be suspected if the adrenal gland is not visible.

- **Germ cell tumours**

Primary germ cell tumours originate from the testicles or ovaries. Retroperitoneal lymphatic spread can be present at diagnosis or as disease progression after treatment during follow-up. Extra-gonadal germ cell tumours (EGGCTs) are a heterogeneous group composed by malignant germ cells arising in extra-gonadal locations without the presence of a gonadal primary tumour. EGGCTs are uncommon neoplasms with an overall incidence of 1.8 to 3.4/1 million and retroperitoneum is a common location following the brain and mediastinum [42].

Altogether (primary or secondary), germ cell tumours account for approximately one quarter of all RPT and are an important differential diagnosis when assessing a retroperitoneal mass. On imaging, an indeterminate poly-lobulated mass along the great vessels, usually under the renal hilia may be observed. In the diagnostic process, specific serum tumour markers (α-fetoprotein, β-human chorionic gonadotropin, lactate dehydrogenase) are frequently elevated in EGGCTs [43]. A previous history of disease in a young male patient is highly evocative and if not, a testicular ultrasound should be considered. Percutaneous CNB is encouraged to confirm diagnosis and type of EGGCT (Figure 11). Morphological and immunohistochemical characteristics of gonadal germ cell tumours are the same as the extra-gonadal counterparts. However, a precise diagnosis is important to determine the therapeutic algorithm that often includes chemotherapy, followed or not by surgical resection.

Diagnostic pitfalls and common errors

Awareness of common diagnostic pitfalls is essential to avoid mismanagement and inappropriate therapeutic decisions.

Misinterpretation of imaging findings is common, especially in large or heterogeneous masses. In adipocytic tumours, underestimation of the tumour extent through the natural anatomic spaces of the abdomen (i.e., inguinal ligament, diaphragmatic hiatus and great sciatic notch) and failure to correctly identify well-differentiated areas within DDLPS is also a common mistake [13] (Figure 1b). In addition, many foci of dedifferentiation and/or necrosis can be misinterpreted as multifocal disease. **Misinterpretation of tumour origin** may also lead to misdiagnosis, particularly when large masses arise from adjacent organs (e.g., adrenal or renal tumours) and are mistaken for primary RPT. All this can potentially lead to inadequate surgical planning, incomplete resections with tumour rupture or even unjustified contraindication of surgery.

Inadequate or non-representative biopsies may underestimate grade of differentiation or result in non-diagnostic samples. Hence, it is particularly important to target the solid or more suspicious areas of the tumour. In addition, biopsy should be avoided in specific scenarios, such as PGLs, where it may trigger life-threatening complications.

Failure to consider alternative diagnoses is also a recurrent issue. Lymphoma (Figure 10), EGGCTs (Figure 11) and benign entities may mimic sarcoma on imaging but require different management strategies. In these cases, serum tumour markers and biopsy are important to avoid inappropriate surgery.

Finally, **delayed referral to specialised centers** remains a major issue. Initial management and inadequate surgical resections performed in non-specialised centers adversely affect oncologic outcomes. Early referral to experienced multidisciplinary teams is therefore critical [10–12].

Limitations

Limitations of this review include its narrative design and non-systematic methodology. The available evidence, from which recommendations are drawn, is limited by the usual limitations of retrospective, registry-based and non-randomised data due to the rarity and heterogeneity of most retroperitoneal entities.

Conclusion

Primary RPTs are a heterogeneous group of entities that require a structured diagnostic approach. Accurate imaging interpretation, appropriate use of image-guided biopsy when necessary and expert pathological assessment are essential to establish diagnosis and guide proper management.

Early referral to specialised multidisciplinary centers is critical, particularly for suspected sarcomas, as treatment strategies depend on histologic subtype and expertise in complex surgical management is often required. Avoiding diagnostic and therapeutic pitfalls is key to improving outcomes.

Conflicts of interest

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Ethical approval

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Data availability

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Disclosures

None.

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