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Case Series

Unusual Retroperitoneal Soft Tissue Sarcomas: Giant Masqueraders

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Abstract

Soft tissue sarcomas (STS) in the retroperitoneum are rare and account for a small percentage of adult STS. The most common type is liposarcoma, while fibrosarcoma and extra skeletal Ewing sarcoma (EES) are rarer. Retroperitoneal fibrosarcoma's are extremely uncommon. Diagnosis requires a comprehensive evaluation including clinical, radiological, histopathological, and immunohistochemical examinations to determine the specific subtype of STS in the retroperitoneum. A 76-year-old male presented with a large retroperitoneal tumour. Surgery successfully removed the tumor which was diagnosed as dedifferentiated liposarcoma based on microscopic analysis and positive vimentin and MDM2 markers. We also report a case of 69-year-old male with a retroperitoneal mass that was ultimately diagnosed as adult fibrosarcoma after ruling out other possibilities. The third case was of 55-year-old female who presented with left lumbar pain, backache, and weight loss. Imaging revealed a retroperitoneal mass with hepatic metastasis. Histopathological examination and IHC analysis confirmed the diagnosis of extraskeletal Ewing sarcoma. The importance of accurate diagnosis through histopathological examination and immunohistochemical analysis is emphasized for effective management and prognosis.

Keywords: Retroperitoneum; Fibrosarcoma; Liposarcoma; Extraskeletal Ewing Sarcoma.

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Introduction

Soft tissue sarcoma (STS) comprises less than 1% of all malignant tumors in adults. [1] Approximately 10-15% of adult STS are found in the retroperitoneum. [2,3] STS are commonly classified based on their histological origin [4,5] and exhibit considerable diversity with varying prognosis. The natural behavior and outcome of STS are influenced by factors such as patient age, tumor location, depth, size, resectability, histology, grade, nodal involvement, and distant metastasis [4,7]. The most common type of STS in the retroperitoneum is liposarcoma [6]. Other rare STS found in the retroperitoneum include Ewing sarcoma and fibrosarcoma.[8,9] Liposarcoma is a rare malignant tumor originating from adipose tissue, and it can occur wherever fat tissue is present, with the retroperitoneum accounting for 12 to 40% of all liposarcoma cases.[4] Fibrosarcoma is a malignant tumor derived from fibroblasts and exhibits a herringbone pattern and varying collagen content. Fibrosarcoma's usually affects the deep tissues of the extremities, trunk, head, and neck, and they rarely occur in the retroperitoneum or mediastinum. Consequently, retroperitoneal fibrosarcoma's are extremely uncommon and constitute approximately 0.2% of adult cancers.[10] Extraskeletal Ewing sarcoma (EES) is a rare type of tumor belonging to the ES family of tumors (ESFT), which are characterized by small round tumor cells sharing a common neural histology and genetic mechanism. Retroperitoneal EES accounts for around 14% of all EES cases. To establish a definitive diagnosis, a comprehensive evaluation involving clinical, radiological, histopathological, and immunohistochemical examinations is necessary to determine the specific histological subtype of STS in the retroperitoneum.

Key Rationale: Retroperitoneal STS are uncommon, making it essential to document cases to improve understanding of their clinical features, imaging characteristics, histopathology, and treatment outcomes. This case series helps improve diagnostic accuracy by compiling and analyzing patterns across different cases.

Learning Points: Retoperitoneal STS can present insidiously and may initially be asymptomatic. When symptoms occur, they are often nonspecific, such as abdominal pain, weight loss, or mass palpation. A key learning point is recognizing that large retroperitoneal masses even when they are non-specific, could be soft tissue sarcomas rather than other conditions. Due to overlapping features of retroperitoneal masses, imaging may not be sufficient. A histopathological examination is needed for definitive diagnosis.

Case History

Case 1:

We describe a case of a 76-year-old male patient who complained of having a mass in his upper abdomen that had grown to enormous proportion, however, due to a lack of adequate access to healthcare facilities in his geographic location he did not visit a healthcare professional. Various investigations were done, CEA – 3.52ng/ml, LDH – 216 U/ml. On abdominal contrast-enhanced computerized tomography (CT) a huge 40 × 28 × 10 cm encapsulated retroperitoneal tumor with a soft tissue density, and an area containing a calcification noted. At laparotomy, a 40 × 30 × 10 cm reddish soft consistency retroperitoneal mass was. No other masses or lymph nodes were encountered. Grossly we received globular tissue measuring 10x5x4 cm. The cut section was heterogenous with greyish-white areas, yellowish areas, and areas of hemorrhage. The microscopic section studied showed a well-encapsulated tumour with tumour cells arranged in intersecting bundles and a haphazard arrangement of the spindle to oval tumour cells. Few areas of mature adipocyteswere noted. Most of the tumour cells are atypical with few entrapped lipoblasts showing multivacuolated cytoplasm and indented nucleus (Figure1a). So, the diagnosis made was liposarcoma. A few sections showed areas of necrosis and hemangiopericytoma type vascular areas (heterologous sarcomatous area) were noted (Figure 1b). Soon the basis of this a provisional diagnosis was dedifferentiated liposarcoma.

IHC was run for various markers which came out as vimentin with diffuse cytoplasmic positivity, MDM2 showed diffuse nuclear positivity, and beta-catenin with focal nuclear positivity. S100, CD 34, and SMA came out as negative. Histomorphological and IHC features favored the diagnosis of Dedifferentiated liposarcoma (because of focal positivity of beta catenin) (Figures 1c and 1d).

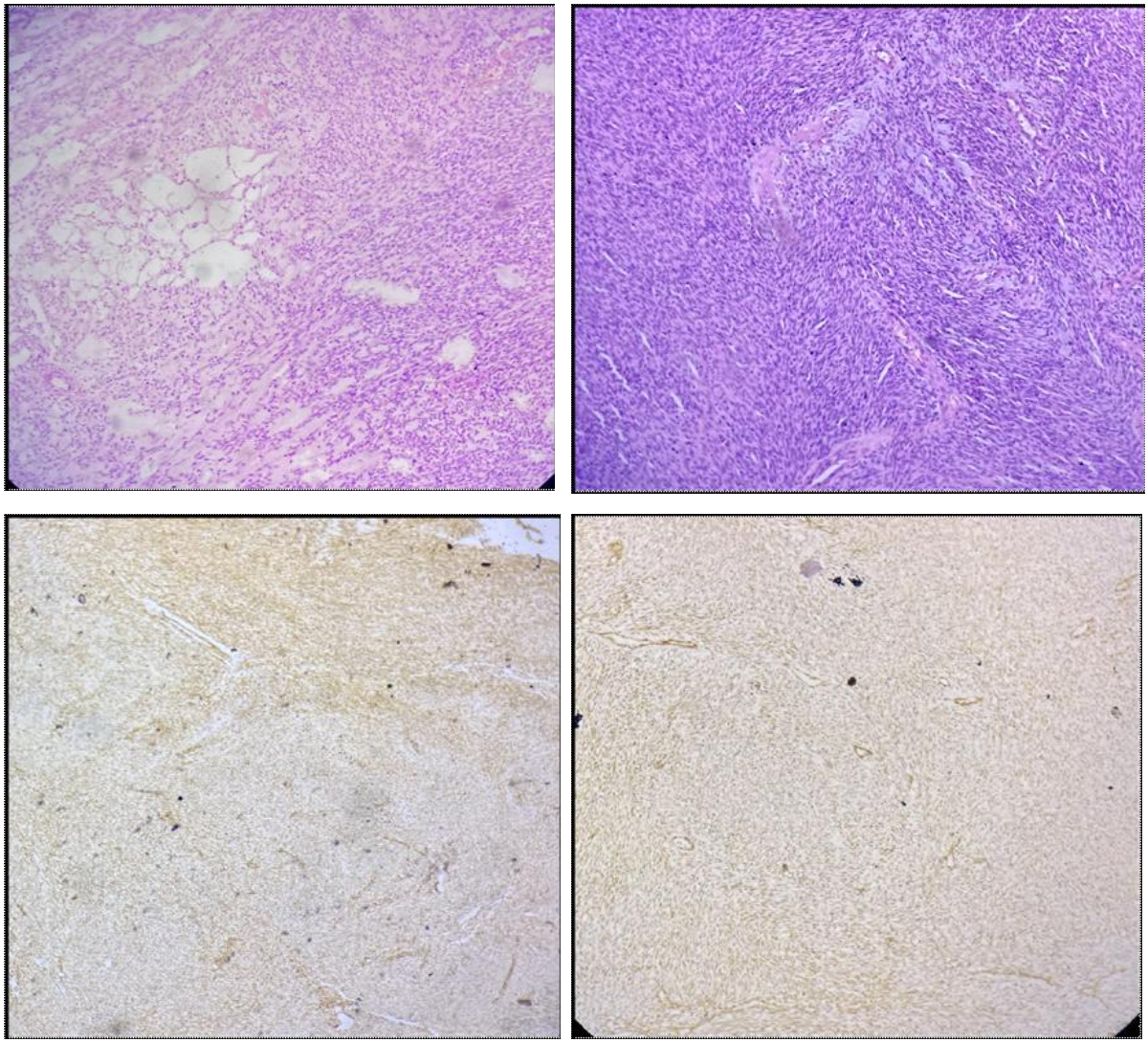

Figure 1a Shows well encapsulated tumour with tumour cell comprising of intersecting bundles and haphazard arrangement of spindle to oval tumour cells. few areas show areas of mature adipocytes. Most of tumour cells are atypical with few entrapped lipoblasts showing multivacuolated cytoplasm and indented nucleus characteristic of a liposarcoma. Figure1b shows a hemangiopericytoma like area (dedifferentiated area). 1c and 1d shows MDM2 diffuse nuclear positivity and beta catenin focal nuclear positivity respectively.

Case 2:

A 69year old male presented to the Surgery Department of IGIMS Patna with a huge swelling over the anterior abdominal wall and vomiting after solid meals. Physical examination revealed a 10 × 10cm sized lump in the right hypochondrium and lumbar region. Radiological findings confirmed a 15 x 10 x 9 cm well-circumscribed, heterogeneously enhancing soft tissue mass with a central non-enhancing area in the right pararenal region, abutting and displacing the right kidney, inferior surface of the liver and ascending colon. The patient underwent surgery, and we received a large globular soft to firm mass measuring 16 x 10 x 10cm in our Pathology department. The tumour was well-circumscribed, and had a smooth outer

surface, with a greyish-white homogenous appearance on the cut section. Histomorphological examination revealed a well-circumscribed tumour comprising spindle-shaped tumour cells arranged in a herringbone pattern. The individual tumour cells had a scant to moderate amount of cytoplasm with vacuolation in a few cells and dark elongated tapered nuclei with indistinct nucleoli. Mitosis was found to be 10-12/10 HPF (Figures 2a and 2b). Foci of necrosis were seen which was less than 50%. Area of mature adipocyte not seen on sections examined.

Special stain with reticulin showed strong and diffusely positive pericellular staining of the tumour cells (Figure2d). Immunohistochemical analysis was done with Vimentin showed strong cytoplasmic positivity in the tumour cells, and p53 showed diffuse nuclear positivity (Figure2c). S-100, c-KIT, and MDM2 were negative. Ki 67 index was 14%.

The stated histomorphological and immunohistochemical findings and features were consistent with a Fibrosarcoma, Adult type, with a French Federation of Cancer Centre Sarcoma Group (FNCLCC) histological grading of Grade 2.

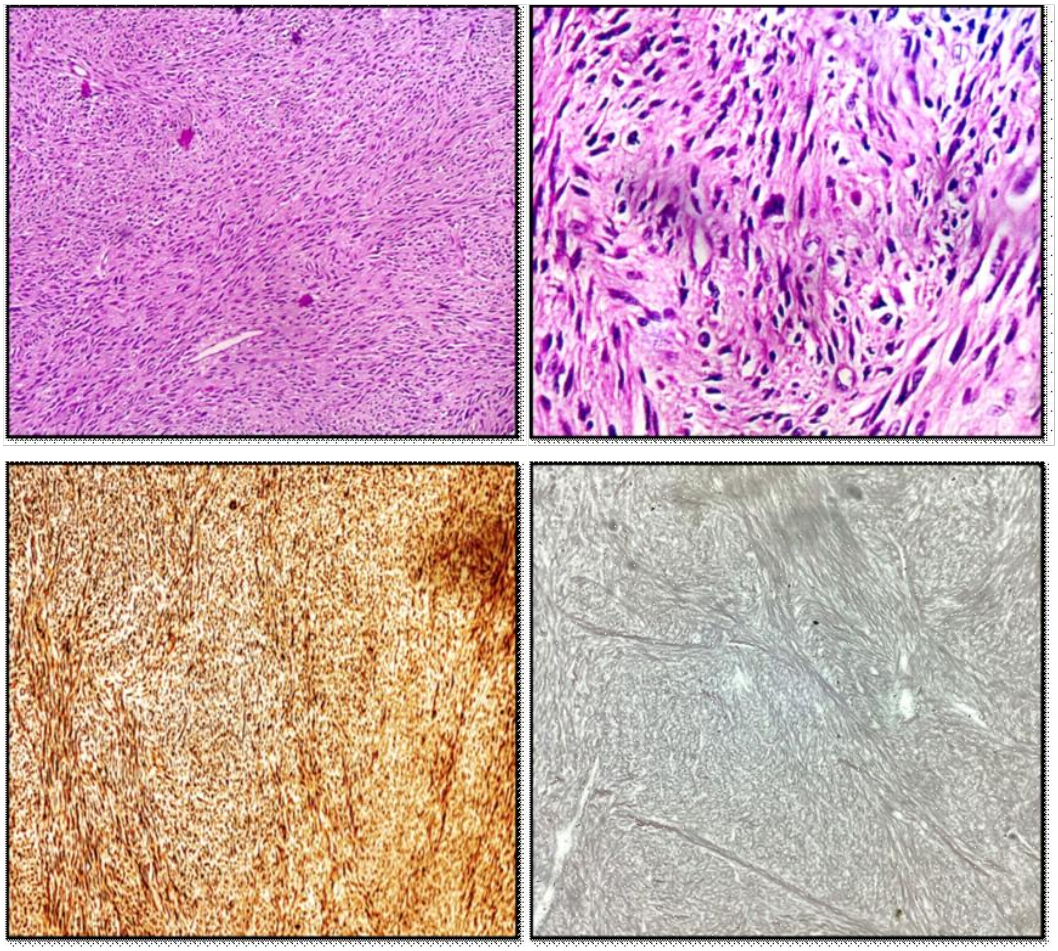

Figure 2a and 2b. Histomorphological examination revealed a well circumscribed tumour comprising spindle shaped tumour cells arranged in herringbone pattern. The individual tumour cells were having scant to moderate amount of cytoplasm with vacuolation in few cells, and dark elongated tapered nuclei with indistinct nucleoli. Mitosis was found to be 10-12/10 HPF. Figure 2c and 2d p 53 showed diffuse nuclear positivity and Reticulin shows diffuse positivity in stromal fibres respectively.

Case 3:

We present a case of an elderly female aged 55 years who came to the regional cancer center, IGIMS, Patna with the complaint of left lumbar pain and backache for 1 year along with significant weight loss. Various investigations were done, CEA – 2.46ng/ml, CA -19-9 – 2.44ng/ml, CA-125 – 22.8 UI/ml and LDH – 334.2 U/ml. On ultrasound of the abdomen, a well-defined heterogenous hypoechoic soft tissue mass lesion measuring 11.6x 8.6 cm in left lumbar region with vascularity within, the diagnosis of likely neoplastic retroperitoneal mass with hepatic metastasis. CT imaging features suggest neoplastic etiology likely retroperitoneal sarcoma with lung and liver metastasis. USG-guided trucut biopsy from the abdominal mass was sent for histopathological examination. Grossly we received tiny grey, white tissue bits all amounting to 0.3cc. Microscopically section studied shows sheets of round cells with minimal nuclear pleomorphism, inconspicuous nucleoli, and scant cytoplasm in dispersed population. These cells surround the blood vessels. Hemorrhage was also identified in the section studied. IHC was run for various markers which came out as vimentin and CD 99 was strongly positive (+++), S 100 was moderately positive (++), FLI 1 showed diffuse positivity(+), CD 34, CD31, LCA, CD117, and synaptophysin came out as negative. Histomorphological and IHC features favour extra skeletale wing sarcoma – retroperitoneal mass.

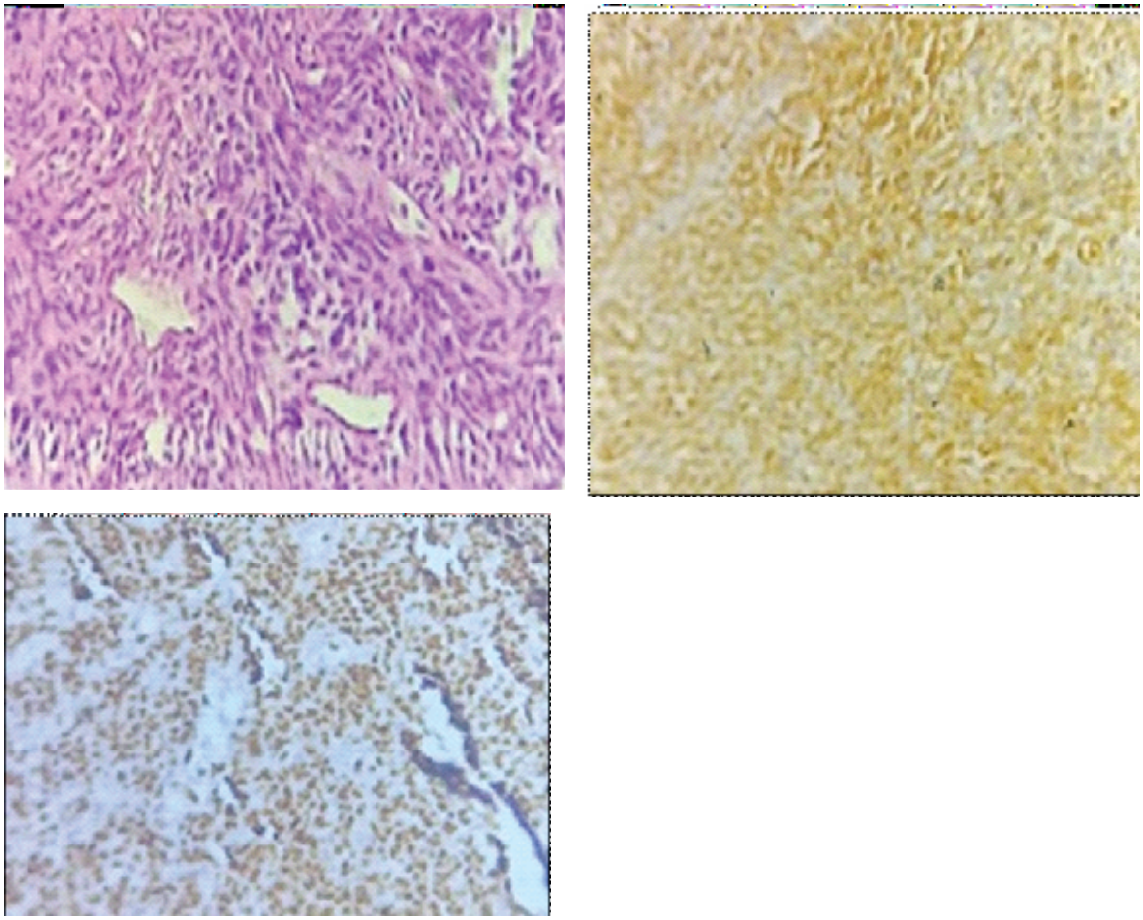

Figure 3a: H&E- Section shows round cells with minimal nuclear pleomorphism, inconspicuous nucleoli and scant cytoplasm in dispersed population. These cells surround the blood vessels. Figure 3b: Tumor cells show strong positivity for CD 99 Figure 3c: Tumor cells are moderately positive for FLI-1

Discussion

Soft tissue sarcomas (STS) are an extremely rare form of cancer, accounting for only 1% of all tumors in adults [11]. Among STS, 15% originate in the retroperitoneum. The most common type of retroperitoneal sarcoma is liposarcoma, which can develop anywhere fat is present but is found in 12-40% of retroperitoneal cases. Liposarcomas exhibit a wide range of behaviors, from well-differentiated tumors that do not metastasize to aggressive tumors with dedifferentiated components, likely caused by genetic defects [12,13]. Approximately 10% of patients experience dedifferentiation, which most commonly occurs in the retroperitoneum [14,16].The differential diagnosis of dedifferentiated liposarcoma includes pleomorphic liposarcoma, lipomatous hemangiopericytoma, non-lipogenic sarcoma, and gastrointestinal stromal tumor. Pleomorphic liposarcoma have a more cellular morphology throughout and are MDM2 and CDK4 negative. The lipomatous hemangiopericytoma on the other hand are circumscribed and cytologically bland and without atypical lipomatous areas. The gastrointestinal stromal tumor is CD117, DOG1 positive while these markers are negative in dedifferentiated liposarcoma. [15,17]

Fibrosarcoma is a malignant tumor characterized by spindle cells with a herringbone pattern. [18] It typically affects deep tissues in the extremities, trunk, and head and neck, but rarely occurs in the retroperitoneum. Symptoms often appear late and are associated with organ displacement and obstruction. [19,20] Retroperitoneal fibrosarcoma's are usually large masses, with over 50% of cases having a size greater than 20cm at diagnosis. [21] Complete resection is often challenging due to the involvement of vital structures, resulting in a worse prognosis compared to extremity fibrosarcoma's. The differential diagnosis for retroperitoneal fibrosarcoma's includes fibromatosis, liposarcoma, leiomyosarcoma, malignant peripheral nerve sheath tumor, monophasic synovial sarcoma, and gastrointestinal stromal tumor (GIST). [22,23] Immunohistochemistry and morphological analysis help differentiate these tumors. In the case of retroperitoneal fibrosarcoma, fibromatosis, liposarcoma, leiomyosarcoma, and monophasic synovial sarcoma were excluded based on specific characteristics and immunohistochemical markers. Malignant fibrous histiocytoma (MFH) or undifferentiated pleomorphic sarcoma was also ruled out due to the absence of specific morphological features [23].

Extra-skeletal Ewing sarcoma (EES) in the retroperitoneum is a rare and diagnostically challenging tumor composed of small, round cells. It mainly affects young patients with nonspecific abdominal complaints. The diagnosis is typically confirmed through histologic and immunohistochemical examination. The histology shows sheets of small, uniform round tumor cells with dispersed chromatin, small nucleoli, and scant clear cytoplasm. Immunohistochemistry, particularly positivity for CD99 with membranous accentuation, is characteristic of EES and helps differentiate it from other small round cell tumors such as rhabdomyosarcoma and lymphoma [24,25]. Immunohistochemical markers such as FLI-1 can also aid in the diagnosis of EES. Chemotherapy has significantly improved survival rates for localized EES, with five-year survival increasing from 10% without chemotherapy to 70%-80% with appropriate treatment [26].

It is important to note that molecular confirmation of the cases was not available in this study. However, through a comprehensive approach involving clinical assessment, imaging, histological examination, and an appropriate panel of immunohistochemical markers, a definitive diagnosis was reached.

Conclusion

Retroperitoneal soft tissue sarcomas are extremely rare and have a poorer prognosis compared to sarcomas in other locations. Therefore, early diagnosis is crucial for improving patient survival. Pathologists play a crucial role in the management of differentiated liposarcoma beyond just making a diagnosis. Their expertise and findings contribute to prognostication, selection of treatment strategies, and disease monitoring. Accurate classification by pathologists helps guide therapeutic decisions and contributes to ongoing research and understanding of this rare subtype of sarcoma.

Retroperitoneal fibrosarcoma's are exceptionally rare and pose diagnostic challenges due to their morphological diversity and similarities to other rare tumors such as retroperitoneal gastrointestinal stromal tumors (GISTs). Diagnosis of fibrosarcoma is achieved through a process of exclusion, and early and accurate diagnosis is important due to the poor prognosis and high likelihood of recurrence. Although rare, it is important to consider extraskeletal Ewing sarcoma, which has a bimodal age distribution and presents as a large heterogeneous mass in the trunk, extremities, or soft tissues. Additional factors such as evidence of internal hemorrhage and cystic necrosis, along with the absence of calcification and nodal metastases, may help indicate the diagnosis. Further confirmation of the diagnosis may require additional tests, such as elevated LDH levels and an immunohistochemical panel. Adequate sampling for histological evaluation is necessary, and integrating clinical history, imaging features, histopathological findings, and immunohistochemistry is essential for a correct diagnosis and prompt management of retroperitoneal soft tissue sarcomas.

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