Case Report

Retroperitoneal Alveolar Soft Part Sarcoma Mimicking Paraganglioma: A Case Report

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Abstract

Alveolar soft part sarcoma (ASPS) is an uncommon soft tissue malignancy that rarely arises in the retroperitoneum. Its marked hypervascularity on imaging creates diagnostic confusion with paraganglioma, potentially leading to misdiagnosis. We present a case of a 33-year-old male patient with a seven-month history of a progressively enlarging left iliac fossa mass.

Cross-sectional imaging demonstrated a 17×10×8 cm hypervascular retroperitoneal mass arising from the left iliopsoas region and displacing adjacent structures, with intense arterial enhancement, suggesting paraganglioma. Plasma metanephrines were normal. Surgical debulking was performed. Histopathology revealed characteristic organoid-alveolar architecture with nests separated by fibrovascular septa and pseudoalveolar spaces. Tumour cells exhibited abundant eosinophilic granular cytoplasm with PAS-D positive intracytoplasmic crystals. Immunohistochemistry showed strong nuclear TFE3 positivity whilst neuroendocrine, epithelial, renal, myogenic, and melanocytic markers were negative, confirming ASPS. This case highlights that retroperitoneal ASPS can convincingly mimic paraganglioma radiologically. Recognition of characteristic histomorphology and TFE3 immunoexpression is essential for accurate diagnosis. Surgical management and long-term surveillance are crucial given the propensity for late metastases.

Keywords: alveolar soft part sarcoma; TFE3 protein; retroperitoneal neoplasms; paraganglioma; immunohistochemistry; diagnostic imaging

Introduction

Alveolar soft part sarcoma (ASPS) is a rare soft tissue malignancy, comprising less than 1% of sarcomas. First described in 1952, this neoplasm predominantly affects adolescents and young adults.[1] While lower extremity deep soft tissues are most commonly involved, retroperitoneal presentation remains distinctly uncommon.[2]

ASPS characteristically demonstrates marked hypervascularity on imaging, creating significant overlap with other hypervascular retroperitoneal masses, particularly paragangliomas and renal cell carcinomas.[3] This radiological mimicry frequently leads to diagnostic confusion. ASPS is characterized by an unbalanced translocation der(17)t(X;17) (p11.2; q25) resulting in ASPSCR1-TFE3 gene fusion,[4] which underlies strong nuclear TFE3 immunoreactivity—a critical diagnostic marker.

We report a rare case of retroperitoneal ASPS radiologically mimicking paraganglioma, emphasizing the importance of comprehensive immunohistochemistry in establishing the correct diagnosis.

Case Report

A 33-year-old male patient presented to our outpatient department with seven-month history of progressively enlarging, painless left iliac fossa mass. He denied constitutional symptoms including fever, weight loss, or night sweats. There were no alterations in bowel or bladder function. Past medical history proved unremarkable, with no significant illnesses or surgical interventions. Family history revealed no malignancy or genetic disorders.

Physical examination revealed a firm, non-tender mass measuring approximately 15 cm, occupying the left iliac fossa with extension towards umbilical region. The mass demonstrated relative fixity. Overlying skin appeared normal. No lymphadenopathy was detected. Vital signs and systemic examination were unremarkable.

Laboratory investigations including complete blood count and metabolic panel were within reference ranges. Tumour markers showed alpha-fetoprotein 4.6 ng/ml (reference 0–9 ng/ml) and carcinoembryonic antigen 2.3 ng/ml (reference 0–5 ng/ml), both normal. Plasma metanephrine levels were negative.

Radiological findings

Contrast-enhanced computed tomography (CECT) of the abdomen (arterial phase) revealed a large, well-defined lobulated retroperitoneal mass measuring 17 × 10 × 8 cm arising from the left iliopsoas region (Figure 1A). The lesion demonstrated intense heterogeneous enhancement with multiple prominent intratumoral and peripheral vascular channels. Central non-enhancing areas suggestive of necrosis were identified. The mass displaced adjacent bowel loops medially without clear radiological evidence of invasion. No definite vascular encasement or distant metastases were identified at presentation. The left kidney was separately visualized and appeared uninvolved.

Magnetic resonance imaging showed the mass to be heterogeneously hyperintense on T2-weighted sequences with internal flow voids consistent with high vascularity (Figure 1B). On T1-weighted imaging, it appeared iso to hypointense relative to skeletal muscle. Post-contrast sequences demonstrated avid enhancement with patchy necrotic areas. Based on marked hypervascularity and imaging characteristics, a provisional diagnosis of paraganglioma was suggested.

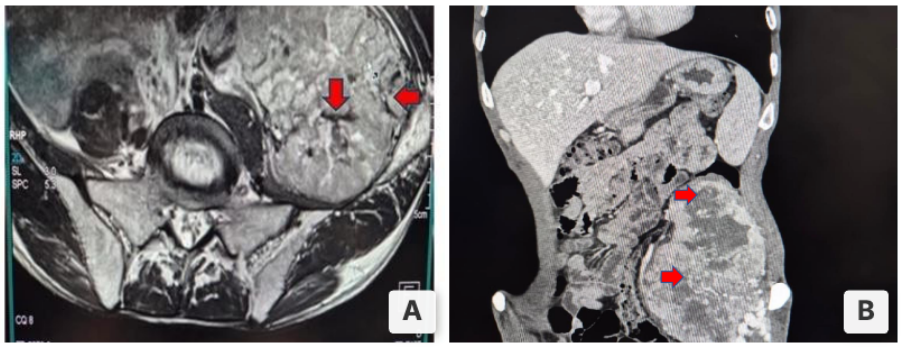

Figure 1: CECT (arterial phase) showing intensely enhancing retroperitoneal mass arising from left iliopsoas region with prominent vascular channels (arrows). B. MRI T2-weighted axial image demonstrating heterogeneous hyperintense lesion with internal flow voids (arrows indicate vascular channels).

Staging chest computed tomography revealed no pulmonary metastases. No distant metastatic disease was identified at presentation.

Exploratory laparotomy revealed a large lobulated retroperitoneal mass intimately adherent to the left iliopsoas muscle, left common iliac vessels, and left ureter, with dense fibrotic adhesions to surrounding retroperitoneal fat. These anatomical constraints, particularly the intimate relationship with major vascular structures and the extensive retroperitoneal adherence, rendered complete surgical resection with clear margins unfeasible; debulking surgery was performed. The specimen measured 17×10×8 cm with bosselated external surface.

Gross examination revealed grey-white to grey-brown parenchyma with extensive necrosis (approximately 40%), haemorrhage, and cystic spaces (Figures 2A, B). Surgical margins were involved by tumour, consistent with the debulking nature of the procedure.

Microscopic examination demonstrated characteristic organoid-alveolar architecture (Figure 3A). Tumour nests separated by delicate fibrovascular septa showed central discohesion creating pseudoalveolar spaces. Rich sinusoidal vascular network was evident. Tumour cells were uniform, large, polygonal with distinct borders and abundant granular eosinophilic cytoplasm. Nuclei showed vesicular chromatin and prominent nucleoli. Moderate pleomorphism with occasional multinucleated forms was present. Mitotic activity remained low (1–2 per 10 high power fields). Ki-67 proliferation index was approximately 5%, consistent with the characteristically low proliferative activity of ASPS. Periodic acid-Schiff with diastase (PAS-D) staining

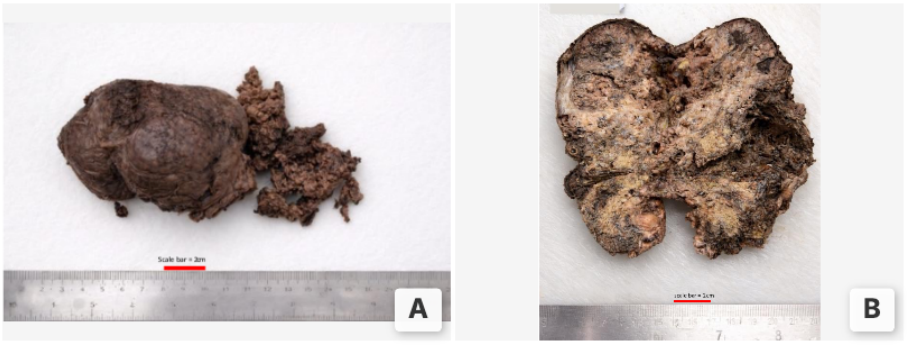

Figure 2: A. Gross specimen with lobulated surface (scale bar = 2 cm). B. Cut surface revealing grey-white parenchyma with necrosis and haemorrhage (scale bar = 2 cm).

demonstrated intracytoplasmic crystalline material (Figure 3B).

Immunohistochemistry performed on formalin-fixed paraffin-embedded tissue sections cut at 4 μm thickness using an automated immunostainer (Ventana BenchMark ULTRA) revealed strong, diffuse nuclear TFE3 positivity (clone MRQ-37, Cell Marque) (Figure 3C). The tumour was negative for synaptophysin (clone SP11), chromogranin (clone LK2H10), cytokeratin AE1/AE3, PAX8 (clone MRQ-50), carbonic anhydrase IX (clone M75), desmin (clone D33), HMB45 (clone HMB-45), and S100 (polyclonal). The complete immunohistochemistry panel with antibody clones and results is summarized in Table 1. This immunoprofile confirmed alveolar soft part sarcoma and excluded neuroendocrine, epithelial, renal, myogenic, and melanocytic differentiation.

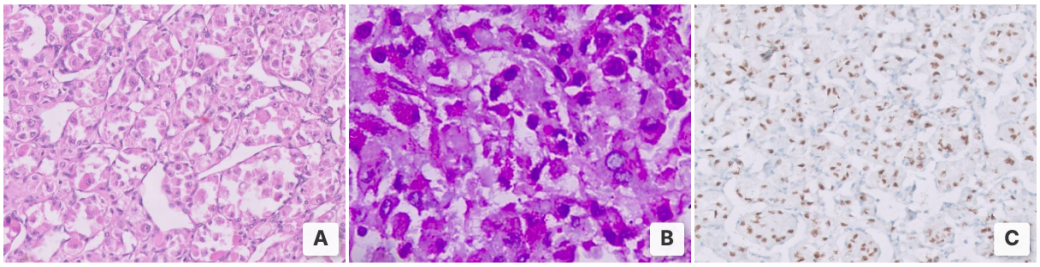

Figure 3: A. H&E ($\times$100) showing classical organoid-alveolar architecture with delicate fibrovascular septa and central discohesion. B. PAS-D stain demonstrating intracytoplasmic crystalline material ($\times$600, oil immersion). C. TFE3 immunohistochemistry (clone MRQ-37) showing strong nuclear positivity ($\times$200).

Table 1: Immunohistochemistry panel: antibody clones, dilutions, and results. All immunohistochemistry performed on 4 μm formalin-fixed paraffin-embedded tissue sections using Ventana BenchMark ULTRA automated immunostainer.

Antibody	Clone	Manufacturer	Result	Interpretation
TFE3	MRQ-37	Cell Marque	Positive	Strong, diffuse nuclear
Synaptophysin	SP11	Ventana	Negative	Excludes neuroendocrine
Chromogranin A	LK2H10	Ventana	Negative	Excludes neuroendocrine
Cytokeratin AE1/AE3	AE1/AE3	Ventana	Negative	Excludes epithelial
PAX8	MRQ-50	Cell Marque	Negative	Excludes renal origin
Carbonic anhydrase IX	M75	Ventana	Negative	Excludes clear cell RCC
Desmin	D33	Ventana	Negative	Excludes myogenic
HMB45	HMB-45	Ventana	Negative	Excludes melanocytic/PEComa
S100	Polyclonal	Ventana	Negative	Excludes melanocytic/neural
Ki-67	30-9	Ventana	$\approx$5%	Low proliferative index

Postoperative recovery proved uneventful. The patient was counselled regarding late metastasis risk and long-term surveillance necessity. Follow-up protocol incorporated periodic chest imaging and abdominal cross-sectional studies at 3–6 month intervals. At nine-month follow-up, patient remains clinically well with no recurrence or metastatic disease.

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Discussion

ASPS constitutes a diagnostically challenging entity amongst soft tissue sarcomas. Originally described in 1952, this neoplasm demonstrates distinctive clinicopathological features distinguishing it from other soft tissue malignancies.[1] The tumour exhibits marked predilection for younger age groups, with peak incidence in second to fourth decades, consistent with our patient's age.

Retroperitoneal localization remains distinctly uncommon. Recent clinicopathological analyses of ASPS have documented only sporadic retroperitoneal presentations, with extremity locations predominating.[5, 6] This rarity contributes to diagnostic delay, as clinicians may not readily consider ASPS in differential diagnosis of retroperitoneal masses. Our case exemplifies this challenge, with initial radiological impression favouring the more common paraganglioma diagnosis.

Reported retroperitoneal cases in the literature have similarly described large hypervascular masses with intense arterial phase enhancement, frequently leading to an initial radiological impression of paraganglioma or renal neoplasm.[5, 6] Tumour sizes in reported cases often exceed 5 cm at presentation, reflecting the deep location and delayed clinical detection. Our case mirrors these observations, with a large lesion and classical imaging features resulting in diagnostic confusion. To our knowledge, retroperitoneal ASPS remains exceedingly rare, and reports highlighting detailed radiologic-pathologic correlation are limited.

Paragangliomas characteristically exhibit intense arterial enhancement with prominent flow voids on T2-weighted MRI sequences, mirroring imaging features observed in ASPS. Current clinical practice guidelines recommend measurement of plasma free metanephrines as the initial biochemical screening test for catecholamine-secreting tumours, given their high sensitivity and specificity.[7] However, approximately 10–20% of paragangliomas are biochemically silent, further complicating diagnosis. In our case, normal plasma metanephrine levels did not exclude paraganglioma, necessitating histopathological confirmation. The absence of renal parenchymal lesion on imaging and negative immunohistochemical staining for renal markers (PAX8, CA IX) effectively excluded renal cell carcinoma in our patient.

The differential diagnosis of TFE3-positive neoplasms warrants careful consideration. Nuclear TFE3 immunoreactivity, whilst characteristic of ASPS, is also observed in TFE3-rearranged renal cell carcinoma (RCC) and TFE3-rearranged perivascular epithelioid cell tumours (PEComas). TFE3-rearranged RCC, now classified as a distinct entity in the 2022 WHO classification, often demonstrates clear cell or papillary architecture with positive staining for epithelial markers (cytokeratin's) and renal tubular markers (PAX8, CD10). In our case, the absence of a renal mass on imaging, negative PAX8 and cytokeratin staining, and characteristic organoid-alveolar morphology excluded this entity. TFE3-rearranged PEComas represent a distinct subset characterised by co-expression of melanocytic markers (HMB45, cathepsin K) and myogenic markers (smooth muscle actin), features absent in ASPS. Our case demonstrated negative HMB45 and S100 staining, effectively excluding PEComa. The combination of organoid-alveolar architecture, PAS-D positive intracytoplasmic crystals, strong TFE3 nuclear positivity, and a negative panel for alternative lineage markers conclusively established the diagnosis of ASPS.[8, 12]

The histopathological features of ASPS are highly characteristic. The organoid-alveolar architecture remains the defining microscopic feature. The cytological features—large polygonal cells with abundant granular eosinophilic cytoplasm and vesicular nuclei with prominent nucleoli—differ markedly from smaller cells with finely granular cytoplasm characteristic of paraganglioma. PAS-positive, diastase-resistant intracytoplasmic crystalline inclusions, when present, provide strong supportive evidence for diagnosis.[3]

Immunohistochemical demonstration of nuclear TFE3 expression serves as a reliable surrogate marker for the underlying ASPSCR1-TFE3 gene fusion.[8] Strong, diffuse nuclear staining effectively confirms diagnosis when encountered in appropriate morphological context. The comprehensive negative immunohistochemical panel in our case excluded neuroendocrine tumours (synaptophysin, chromogranin), renal cell carcinoma (PAX8, CA IX), epithelial neoplasms (cytokeratin), myogenic tumours (desmin), and melanocytic lesions (HMB45, S100), reinforcing the diagnosis of ASPS.

Despite relatively indolent local growth and low mitotic activity, ASPS demonstrates aggressive metastatic potential. Metastatic disease occurs in a substantial proportion of cases, with lungs representing the most frequent site, followed by brain and bone.[5] Notably, metastases may manifest years or even decades after initial diagnosis, necessitating prolonged surveillance. Large tumour size, retroperitoneal location, and incomplete resection, all present in our patient, have been associated with poorer outcomes.[5] The patient was counselled regarding these adverse prognostic factors and the importance of adherence to surveillance protocols.

Complete surgical excision with negative margins, when anatomically feasible, remains the primary treatment modality for localized ASPS. Conventional cytotoxic chemotherapy has demonstrated limited efficacy. However, recent studies have shown encouraging responses to targeted therapies including sunitinib and pazopanib in patients with advanced disease.[9, 10] These agents, through inhibition of vascular endothelial growth factor receptors and platelet-derived growth factor receptors, capitalize upon the tumour's dependence on angiogenic signaling. Moreover, atezolizumab, an anti-PD-L1 immune checkpoint inhibitor, received FDA approval in December 2022 for unresectable or metastatic ASPS, representing a landmark therapeutic advance for this rare sarcoma.[11]

Long-term surveillance is mandatory given the documented propensity for late metastases, which may manifest years or even decades following initial treatment. A structured follow-up protocol should incorporate clinical examination with periodic chest computed tomography and cross-sectional imaging of the primary tumour bed. Initial surveillance at 3–4 month intervals during the first two years, extending gradually to 6-month intervals thereafter, represents a reasonable approach.

Given reports of delayed metastasis, extended long-term follow-up is advisable.[5, 6]

Limitation: The relatively short follow-up duration of nine months in our case represents an inherent limitation, particularly given that ASPS is well recognised for late metastases occurring years to decades after initial diagnosis. A nine-month disease-free interval is clinically inadequate to comment on prognosis, especially in the context of surgical debulking without clear margins. This patient requires extended surveillance with vigilant monitoring for potential late metastatic disease, particularly to lungs, brain, and skeletal system. We acknowledge that meaningful prognostic assessment will only be possible with prolonged follow-up, and the patient remains under active surveillance.

Conclusion

This case underscores the diagnostic challenges presented by retroperitoneal ASPS, which may convincingly mimic paraganglioma on radiological grounds. The characteristic organoid-alveolar histological architecture, coupled with strong nuclear TFE3 immunoexpression and negative staining for other lineage markers, establishes the diagnosis.

A comprehensive differential diagnosis including TFE3-rearranged RCC and PEComa should be considered in TFE3-positive neoplasms. Surgical resection, when feasible, coupled with structured long-term surveillance for late metastases, remains essential for optimal patient management. Awareness of this rare entity is essential to prevent diagnostic pitfalls and guide appropriate management.

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