

Alveolar Soft Part Sarcoma Presenting as Cauda Equina Syndrome

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ABSTRACT

Background: Alveolar soft-part sarcoma (ASPS) is a rare soft tissue sarcoma often affecting adolescents and young adults. Though the tumor has an indolent clinical course, the ultimate prognosis is poor characterized by late metastasis. Histopathological evaluation is crucial to a correct diagnosis.

Case report: A 30-year-old Indian woman presented with paraplegia and a persistent mass over the back. A thorough histological examination alongside imaging techniques shaped a reliable diagnosis.

Conclusion: Alveolar soft tissue sarcoma of the spine is a rare tumor and a very high index of suspicion is required to make an early diagnosis and achievement of complete microscopic resection is critical for successful outcome.

Keywords: Alveolar soft-part sarcoma, Cauda equina syndrome, Immunohistochemistry.

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INTRODUCTION

Alveolar soft-part sarcoma (ASPS) is a rare, vascular soft tissue sarcoma prevalent in adolescents and young adults which rarely occurs in bone.¹ It was described as a separate clinical entity by Smetana and Scott in 1951.² Christopherson a year later coined the descriptive term 'alveolar soft-part sarcoma'.³ It is most commonly described in muscles and deep soft tissue of the trunk and extremity.^{4,5} It can present in any part of the body, having been described in sacrum,⁶ vertebra.⁷ It is a slow growing tumor with an indolent course and usually presents years after its inception and with widespread metastasis.

The literature base for the disease owing to its rarity comprises mostly individual case reports and small

collective series with only a handful of large series. This makes our current understanding and clinical decision-making for the patients of ASPS quite inadequate. We present a case of ASPS presenting as cauda equina in a young Indian lady which is an unusual site of occurrence for this rare tumor.

CASE REPORT

A previously healthy 30-year-old woman was admitted with a 1½ month history of progressive low back pain that radiated to both lower limbs with steady worsening and gradual development of a lump over right side of back. She had no history of trauma or systemic diseases. The patient suddenly became paraplegic 8 days prior to admission. Sphincter dysfunction soon ensued. The patient was also found out to be hypertensive (BP: 160/110) without any significant past history of the same. There was evidence of a 12 × 9 cm oval swelling over the right paramedian region at L1, L2 level, 5 cm from midline which was situated in the subcutaneous plane and was firm and non ballotable. Neurological evaluation revealed flaccid paralysis of both legs with complete loss of power. There was no loss of sensations but tendon reflexes and anal tone was absent. Laboratory data was unremarkable. Magnetic resonance imaging of dorsolumbar spine revealed an 11 × 8.5 cm lobulated mass lesion arising from the posterior element of L1 and L2 vertebra with anterior intraspinal, extramedullary extension and posteriorly invading the paraspinal muscles. It was heterogeneously isointense on T1 and heterogeneously iso to hyperintense on T2 and STIR WI. It also showed restriction of diffusion with low ADC on DWI suggestive of high cellular mass lesion. The lesion was causing significant compression over the conus and roots of cauda equina (Figs 1 to 6). Intraoperatively there was a presence of a highly vascular, poorly circumscribed tumor eroding the posterior elements of L1 and L2 vertebra and invading the spine and canal. Tumor was epidural in location, circumferentially compressing the thecal sac. A large left sided extraspinal extension was observed. Gross total intraspinal and extraspinal component of tumor was removed. Histologically, the lesion was composed of nests of large polygonal cells traversed by fibrous septa

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(Figs 7 and 8). Immunohistochemically it stained negatively with Desmin, MyoD1 and Pan Cytokeratin thereby ruling out a paraganglioma. Postoperatively the patient underwent

an intensive physiotherapy regimen and also demonstrated improvement of anal tone and lower limb power (4/5) upon follow-up at the end of a month.

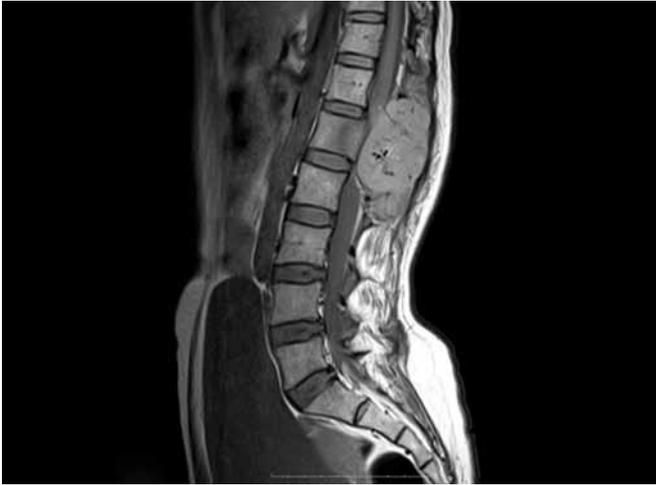


Fig. 1: T1-weighted mid-sagittal section shows an isointense well demarcated lesion at L1-L2 levels with intraspinal extension with severe compression of thecal sac

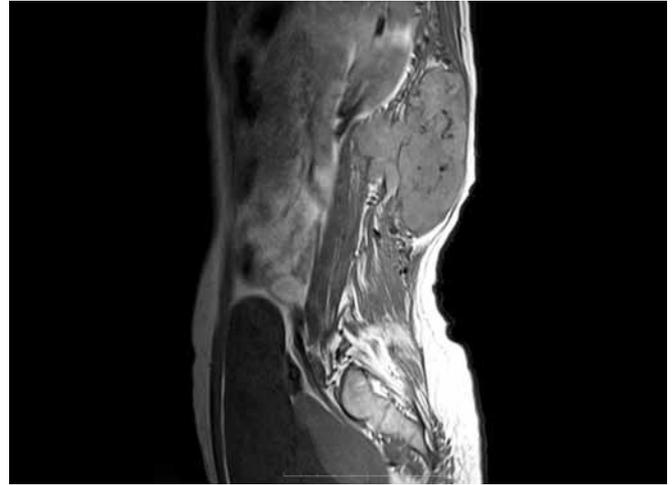


Fig. 2: T1-weighted sagittal section shows an isointense lesion infiltrating the vertebrae and paraspinal muscles



Fig. 3: Mid-sagittal section showing heterogeneous iso to high signal on T2-weighted images with multiple intratumoral signal voids and severe compression of cauda equina



Fig. 4: T2-weighted sagittal section showing heterogeneous signal with intratumoral signal voids infiltrating muscles and bones

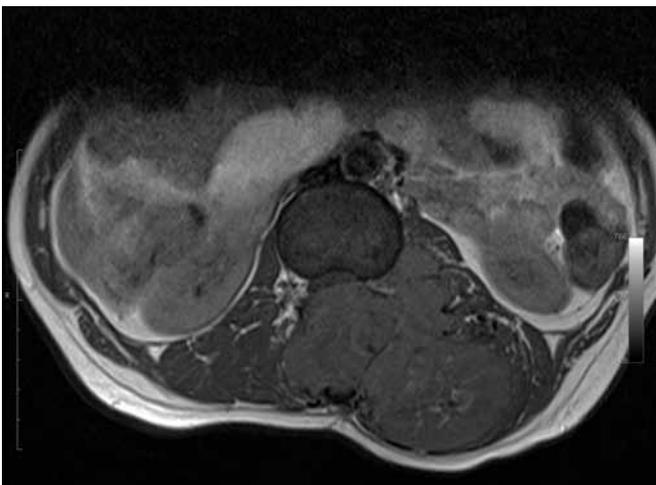


Fig. 5: T1-weighted axial image with isointense lesion compressing the thecal sac and spinal cord



Fig. 6: Postgadolinium sagittal image with tumor enhancement and intratumoral signal voids

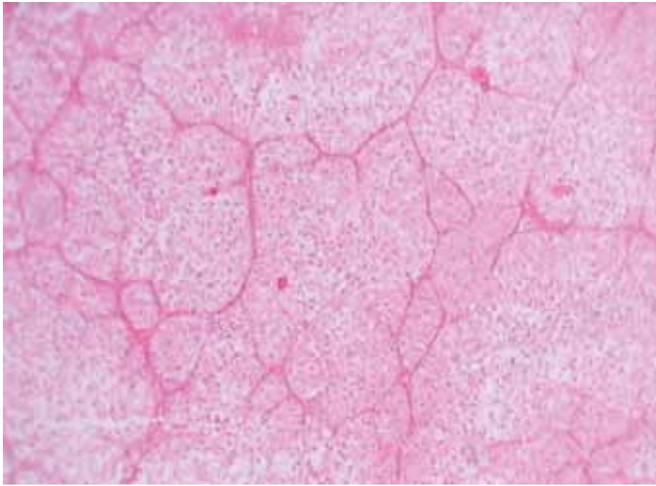


Fig. 7: Light microscopic appearance of the alveolated pattern of the sarcoma, groups of round or polygonal cells circumscribed by connective tissue with capillaries (Hematoxylin-Eosin, $\times 100$)

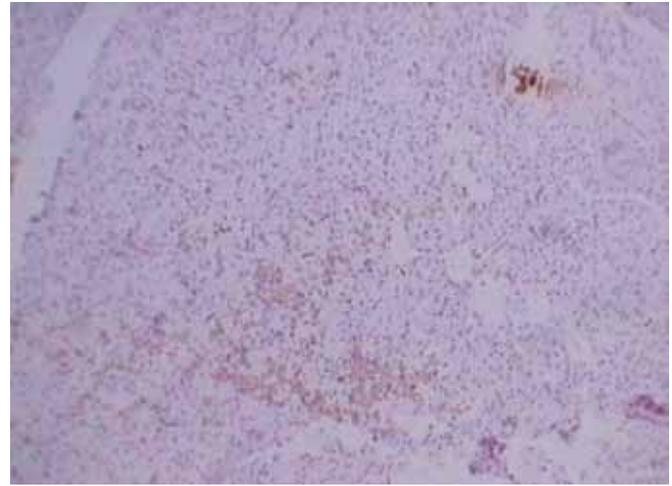


Fig. 8: Immunohistomicrograph of alveolar soft-part sarcoma showing a negative staining with PAN cytokeratin (IHC) (PAN Cytokeratin, $\times 100$)

DISCUSSION

Alveolar soft-part sarcoma is a rare soft tissue malignancy accounting for 1% of all soft tissue sarcomas,^{8,9} and 5% of pediatric nonrhabdomyosarcoma soft tissue sarcomas.⁵ The lesion generally occurs in adolescents and young adults between 15 and 35 years of age with a predilection towards females.^{5,9,10} Pathogenesis of ASPS, as for most soft-tissue sarcomas, is unknown, although the risk factors include irradiation, genetic factors and chemical carcinogens.¹¹ The disease in adults typically involves the deep soft tissues of extremities, trunk, retroperitoneum, head and neck. In children and adolescents its affliction localizes mostly in head and neck regions.^{9,12,13} As a result of its indolent and relentless course this lesion presents mostly with late onset coexistent metastasis and an extended clinical course. The most common sites of metastasis are lungs, bone and 1 to 8% cases lead to brain metastasis.^{8,14,15} Intracranial metastasis has been the most common site for metastatic ASPS.^{14,16} Kayton et al reported 10% metastasis to lymph nodes.¹⁷ Fortunately our patient did not present with any metastatic lesion although the primary tumor invaded the vertebrae.

Grossly the tumor is soft, poorly circumscribed, grey to yellow in color with areas of necrosis and hemorrhage. The most characteristic light microscopic feature is the organoid or nesting pattern separated by thin fibrovascular septa. The tumor owes its name to its pseudoalveolar, histological appearance, with a cluster like polygonal cellular disposition and loss of cell cohesion and central cell necrosis. It is highly vascular with small vascular spaces interdigitating between nests of cells signifying vascular invasion.^{18,19} Cells often have rhomboid or rod-shaped crystalline inclusions markedly demonstrated in periodic acid Schiff stain in 80% of cases. These represent complexes of proteins monocarboxylase transporter 1 (MCT1) and CD 147.^{9,20} At present, the WHO classifies ASPS in the category of

'tumors of uncertain differentiation'.¹² These tumors have a fairly broad differential diagnoses which revolves around Adrenal cortical carcinoma, Renal cell carcinomas, Malignant melanomas, Giant cell tumors, Clear cell sarcomas, Alveolar Rhabdomyosarcoma and Paragangliomas.⁸ In our case the close histological and anatomical resemblance of tumor to paragangliomas prompted us to subject the tissue to immunohistochemical analysis which ruled out our differential.

Toguchida et al have reported possibility of p53 gene mutations associated with tumor progression and genetic alterations in ASPS and other types of sarcoma.²¹ Current cytogenetic studies show that ASPS exhibits a conserved abnormality in the form of an unbalanced translocation $\text{der}(17)\text{t}(X;17)(\text{P}11;\text{q}25)$, which fuses the N-terminal region of alveolar soft-part locus gene (ASPL), located at 17q25, to the C-terminal region of the transcription factor E3 (TFE3) located at Xp11. This leads to two alternate fusion transcripts ASPL type 1 and type 2 that result in tumorigenesis by transcriptional deregulation.²² An expression of ASPL/TFE3 fusion protein ensues of which TFE3 protein is overexpressed making its antibody an ideal immunohistochemical agent.^{23,24} As seen in our case, the female preponderance of ASPS has been attributed to the female's extra X-chromosome, which theoretically would increase the risk of developing X:17 translocation.²⁵ Recently, results from a comprehensive study by Stockwin et al identify several targets involved in angiogenesis, cell proliferation, metastasis, and steroid biosynthesis. It also shows elevated expression of muscle-restricted transcripts (ITGB1BP3/MIBP, MYF5, MYF6 and TRIM63), strengthening the case for a muscle cell progenitor as the origin of disease.²⁶

Occasionally, plain film radiography may show a soft tissue mass associated with punctuate calcification.

Upon bone invasion ASPS produces an ill-defined, non-specific, lytic lesion.²⁷ Typical angiographic features are of enlarged feeding arteries, early draining veins, capillary staining, arteriovenous shunting and slow wash out.^{27,28} Ultrasound shows a variable echo pattern with heterogeneous hypogenicity, infiltrated margins and solid content while Color Doppler Ultrasonography shows prominent vascularity within the tumor with a low resistive index.^{29,30} Unenhanced computerized tomography scans of ASPS display an attenuation less than or equal to that of surrounding muscle which is infiltrating. The extent of bony invasion, periosteal reaction cortical erosion and intramedullary extension are also defined. There is dramatic enhancement with contrast administration.²⁷ ASPS on Magnetic Resonance Imaging demonstrate iso or heterogeneous high signal on T1-weighted and T2-weighted images, with or without multiple intra and extratumoral signal voids. The signal voids have been attributed to tortuous feeding vessels. These areas obviously enhance on postgadolinium images. Such signal voids may not be specific for ASPS, but an amalgamation with high signal on T1-weighted and T2-weighted images would clinch the diagnosis of ASPS.^{27,28,30,31}

As focused upon by various case series, an achievement of complete microscopic resection of locoregional disease is of overriding importance.^{5,13,14,17,32} Regional lymph node dissection is performed as part of the primary resection if found to be positive.^{5,17} Re-excisions are warranted if residual tumor is present after primary resection.¹³ The resectable metastatic disease can also be subjected to surgical excision.^{14,17} Alternatively residual tumors and metastatic disease can be subjected to Adjuvant Chemotherapy and/or External beam radiation (XRT).^{5,13,17,32} Chemotherapeutic agents used in various combinations included doxorubicin, ifosfamide, cyclophosphamide, cisplatin, etoposide, gemcitabine and docetaxel.^{13,17,32,33} Brachytherapy has also been administered in a select few cases as an adjuvant modality with intriguing results.^{17,34} Given the small numbers of cases no conclusion can be drawn regarding the role of XRT, brachytherapy or chemotherapy for ASPS.^{13,17,32,33} Response of ASPS to Interferon alpha-2a has been anecdotal.^{35,36} Targeted therapy with antiangiogenic agents like cediranib and sunitinib (VEGF inhibitors) individually or in combination with other agents have shown some promising results.^{32,37,38}

The five year survival overall after tumor resection varied from 64 to 83% in various studies.^{5,13,17,32} A five year progression-free survival of 22% was reported at Memorial Sloan-Kettering Cancer Centre. Tumor size (5 cm or smaller vs larger than 5 cm) had a significant impact on progression free survival rates and metastatic spread.^{5,13,17}

CONCLUSION

This case illustrates several of the recognized characteristics of alveolar soft-part sarcoma and adds on a relatively rare feature, that is, presentation as a vertebral tumor. Not infrequently, reaching a diagnosis in such a presentation can be confusing because of misinterpretation of the biopsy material as paraganglioma. A thorough radiological evaluation, thorough immunohistochemical analysis of tissue sample and a high index of suspicion are the key to a correct diagnosis.

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