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Primary alveolar soft tissue sarcoma of the central nervous system. Case report

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Abstract

Background: Alveolar soft part sarcoma (ASPS) is a rare, slow-growing soft tissue tumor with uncertain etiology; it is considered among the least common sarcomas, representing 0.2-1% of these cases in large studies. These tumors usually appear during childhood or young patients, with predominance in females. Case description: We introduce the case of an ASPS in a 62-year-old man, who presented with 7 months of progressive headache and diplopia. MRI showed an infiltrative lesion in the anterior fossa that extended to the right orbital roof. Metastases were ruled out. The patient underwent resection of the tumor with good visual and neurologic recovery. Histologic characterization showed a pattern of homogeneous eosinophilic cells with a solid and vascularized pattern; cells with large and binucleated nucleoli; vessels with endothelial and myoepithelial hyperplasia; numerous apoptotic bodies and mitotic figures were also present, but no necrosis was found. On immunohistochemistry, cells exhibited positivity to CD56, membranous NSE, and slight myogenin reactivity; vessels were strongly positive for myogenin, myoglobin, CD34, CD31, factor VIII, vimentin, and nestin as well as for HBM45, CD20, GFAP, and S-100; cytokeratin showed fine extracellular and intracellular filaments; GATA and TTF1 were negative. Some clear cells were observed to be positive for CD68. The piece was diagnosed as a non-meningeal alveolar sarcoma of soft tissues with a solid pattern. **Discussion and conclusion:** This case corresponds to the second tumor of this kind presented at our institution, the first one reported, and perhaps, one of the oldest patients to develop it worldwide.

Key Words: *alveolar soft part sarcoma; brain tumors; immunohistochemistry.*

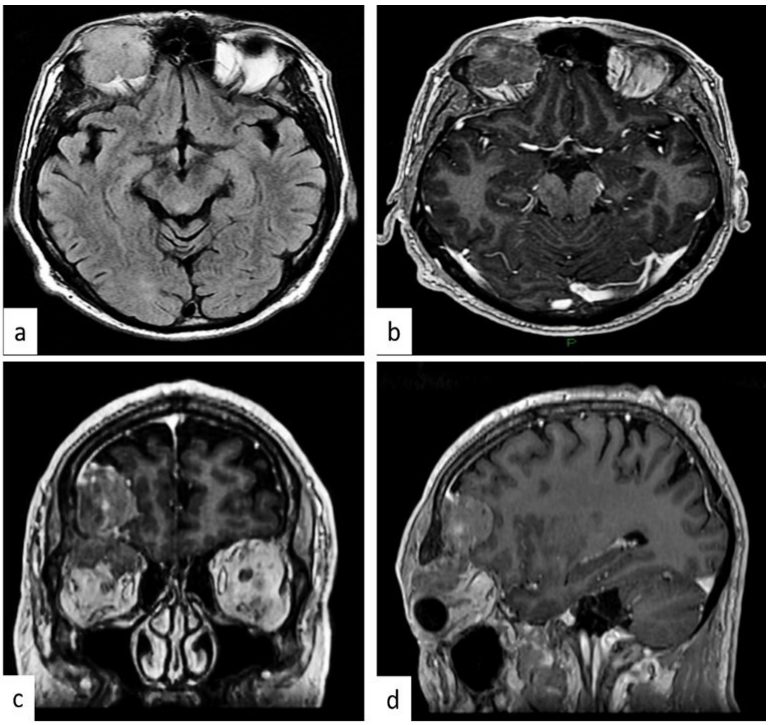
Introduction

Alveolar soft part sarcoma (ASPS) is a rare sarcoma, classically occurring in young patients. It has been previously published under a variety of names,[1] including malignant myoblastoma, granular cell myoblastoma,[2] malignant granular cell myoblastoma, rhabdomyosarcoma,[3] and as malignant tumors of non-chromaffin paraganglia.[4] It has recently been discovered that ASPS are characterized by a tumor-specific deletion (17) t(X; 17) (p11; q25):5 that rages the transcription factor 3 (TFE3) gene at Xp11 to the ASPL gene at 17q25, creating an ASPL–TFE3 fusion protein.[5]

ASPS is a malignant tumor with a slow rate of growth and whose cell of origin is unknown and its presentation and histological features are controversial.[1] It presents in children and young adults. ASPS is extremely rare and accounts for <1% of soft-tissue tumors overall. ASPS represents 10% of cases reported from large sarcoma referral centers, in both adults and children. As much as 60% of ASPS are seen in women, although this female sex predilection may be less pronounced in children.[1,6] The tumor typically occurs in deep soft tissues, although it displays a rather indolent clinical course, the definitive prognosis is poor and is often categorized by metastases. This tumor appears in the extremities, and a smaller number of cases at other soft-tissue locations have been reported, such as arms, chest, retroperitoneal tissues, and lungs.[1] In children, it usually presents in the head and neck, most commonly in the orbit or lingual region.[6] Half of the cases present recurrence. ASPS is histologically characterized by the presence of uniform, organoid nests of polygonal tumor cells, an abundant vascular network separated by fibrovascular septa, a pseudo alveolar proliferation of large, delicate capillary-sized vascular channels, and eosinophilic cells. This work aims to present the case of an intracranial ASPS in a 62 years-old-man.

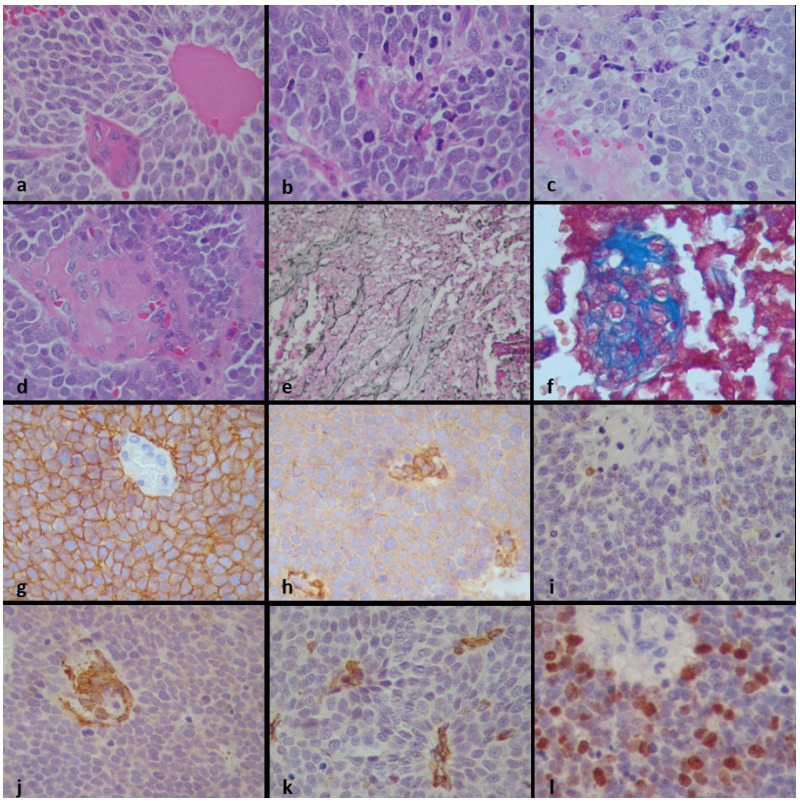
A 62-year-old man with a 7 months history of headache, visual alterations, and diplopia, presented increased volume of the frontal region, which was painful on palpation. CT scan and MRI were performed showing an extra-axial tumor originating from the anterior portion of the sickle with infiltration to the right orbit (Figure 1). A meningioma was initially diagnosed. He underwent surgery, in which total resection was achieved. A soft consistency tumor, with a coloration that ranged from violet to brown, measuring 42x20mm, was macroscopically found.

Figure 1. MRI: T2WI FLAIR axial image at the level of the orbits which depicts an intra and extraconal occupational process that causes destruction of the orbital structures (**A**). Axial (**B**), coronal (**C**), and sagittal T1WI+C in which heterogeneous enhancement with intradural invasion and extension into the orbit and soft parts of the frontal region are observed (**D**).



Histologically, a tumor composed of homogenous eosinophilic cells was identified (Figure 2A), with scarce eosinophilic and clear cytoplasm, as well as abundant mitotic figures (Figure 2B). It did not show a characteristic pattern and occasionally it was distributed in a peri-vascular pattern, as inpseudo-rosettes ; apoptosis bodies are observed (Figure 2C); an abundant vascular network with endothelial and myoepithelial hyperplasia can also be observed (Figure 2D). Inside some vessels there was a positive PAS material, as well as vacuolated clear cytoplasm cells; reticular fibers stain show discrete alveolar edges (Figure 2E), and Masson stain depicts gross septa (Figure 2F). Immunohistochemistry showed two patterns: neoplastic cells that were CD56 positive (Figure 2G), and NSE in the membranous form, as well as mild and focal intracytoplasmic myoglobin and smooth muscle actin (Figure 2H); cytokeratin was negative, however, cellular detritus and focal intracellular filaments can be observed (Figure 2I). Inside vessels, myoepithelial and endothelial cells were positive for myoglobin (Figure 2J), CD34, CD31, Factor VIII, nestin, myogenin (Figure 2K), vimentin, anddesmin; the Ki67 index was >20% (Figure 2L). Based on the histological and immunohistochemical findings, the diagnosis of alveolar sarcoma with a solid pattern was made. After surgery, significant visual improvement and no neurological disturbances were found.

Figure 2. Alveolar soft part sarcoma showing an alveolar nesting pattern with tumor cells containing abundant eosinophilic cytoplasm and discohesive nature (**A**), numerous mitotic figures (**B**), and apoptotic bodies were observed (**C**). (**D**) Hyperplastic endothelial and myoepithelial cells in blood vessels were observed (H&Ex40). (**E**) Histochemical reticulin (silver) framework surrounding the tumor nests (reticulin, ×40). (**F**) Masson stain shows gross septae (x40). Tumor cells showing membranous immunoreactivity to CD56 (× 40) (**G**), fine intracytoplasmic membrane with positivity to myogenin (**H**), and delicate filaments of cytokeratin (**I**). Strong positivity in the vessel wall with smooth muscle actin (× 40) (**J**). CD34 showed delicate vascular channels (**K**); immunohistochemistry staining at x400 showed Ki-67 positive nuclear cells (**L**).



Discussion

ASPS is a rare tumor. Most of these lesions correspond to metastases,[7] whilst the minority are in the CNS.[1] Features associated with improved prognosis include younger age at diagnosis, small tumor size, and the presence of localized disease. Adjuvant chemotherapy does not seem to be effective in the treatment of ASPS, while there may be some role for adjuvant radiotherapy in reducing the risk for local recurrences.[1] Histologically, ASPS cells are typically round, regular, and large, composed mainly of eosinophilic tumor cells with eccentrically placed nuclei win which vesicular chromatin and a prominent central nucleolus are apparent. Multinucleation may be present in a few cells,[1] and an organoid to pseudoalveolar pattern may be seen. An abundant vascular network is usually seen. Mitotic activity is usually low and necrosis is infrequent or lacking. Our case presents abundant mitotic figures, without necrosis, and with apoptotic bodies. Anaplastic features, spindle cells or pseudoglandular components, sheet-like growth, xanthomatous changes, myxoid changes, cystic change, hemorrhage, and a prominent lymphocytic infiltrate have also been observed in ASPS.[1] Trichrome stain show ethnophilic and cyanophilic inclusions,[1] the latter presenting as a crystalline structure.

On immunohistochemistry, a new antibody directed against the C-terminus portion of TFE3 has emerged as a highly sensitive and specific marker of ASPS. Usually ASPS are

negative for epithelial markers, such as cytokeratins and epithelial membrane antigen. They also tend to be negative for specific neuroendocrine markers such as chromogranin A and synaptophysin, and negative for specific melanocytic markers, such as HMB45 and Melan-A. In some cases, non-specific markers such as neurone-specific enolase (NSE) and vimentin have been reported. Our case showed a strong membranous immunoexpression of CD56, delicate intracellular filaments of cytokeratins and mild cytoplasmic expression of myogenin. Actin, MyoD1 and myogenin expression in smooth muscle is by no means specific for myogenous differentiation, and the ASR-1 antibody to skeletal-muscle actins is problematic to understand because of high levels of non-specific staining.[1,9] Desmin expression has been reported in around 50% of cases of ASPS. Desmin expression is not limited to myogenous tumors and can be seen in a wide variety of other lesions, including tenosynovial giant-cell tumor, melanoma (Melan A+, HMB-45+-, s-100+), Ewing's sarcoma (CD99+) and angiomatoid malignant fibrous histiocytoma (vin+, fascin+, lisosin+), paragangliomas (NSE+, chromogranin+).[9] Ki-67 expression may assist in distinguishing benign from malignant tumors, higher Ki-67-li may be a prognostic indicator for the development of metastases in ASPS.

The differential diagnosis of ASPS is wide, and revolves around neoplasms that may show nested or organoid patterns of growth and cells with abundant eosinophilic cytoplasm; renal cell carcinomas, adrenal cortical carcinomas and hepatocellular carcinomas may mimic ASPS by feature of their abundant eosinophilic to clear cytoplasm.[9] Alveolar rhabdomyosarcoma, despite its somewhat similar name, appears as an entirely different "small blue round cell tumor", which strongly expresses desmin and myogenin nuclear proteins,[9] and are TFE3-negative. Perivascular epithelioid cell neoplasms, such as epithelioid angiomyolipoma, coexpress smooth-muscle actin and melanocytic markers, and are almost always TFE3-negative.1 In most instances, granular cell tumours lack the striking cytological atypia seen in ASPS and show strong S100 protein expression. We observed strongly positive myogenic markers with perivascular distribution, an abundant vascular network, as well as CD31, CD34 and factor VIII, nestin and vimentin.

On electron microscopy, the characteristic rectangular to rhomboid crystalline inclusions electron-dense granules resembling peroxisomes have been observed in association with elongated granular structures having a periodic, lattice-like arrangement, those tumors also expressing CD68.[10] We observed some clear cells which were positive for CD68.

Conclusions

We presented a rare ASPS originated on meningeal structures with orbital invasion. Histological features showed a solid pattern with abundant mitotic figures, pseudorosettes formation and an abundant vascular network. Endothelial vascular hyperplastic vessels with strong membranous neurogenic, and myogenic positive immunoreaction.

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