Alveolar soft part sarcoma: unusual etiology of mediastinal mass in an adolescent

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Abstract

Alveolar soft part sarcoma (ASPS) is a rare malignancy that usually arises in an extremity. Mediastinal involvement is uncommon, with only two reports of primary mediastinal disease and two reports of metastatic mediastinal disease in the literature, all referencing adult patients. To our knowledge, ours is the first report of ASPS presenting with a mediastinal mass in adolescence. Although ASPS is not generally included in the differential for adolescent mediastinal masses, it should be considered when clinical presentation and imaging appearance are characteristic.

Introduction

Alveolar soft part sarcoma (ASPS) accounts for 0.5-1.0% of soft tissue sarcomas and occurs primarily in the second and third decades of life.[1-3] Almost all cases arise in or adjacent to skeletal muscle, most often in thigh and buttocks.[1,3,4] When ASPS occurs in infants or children, it favors the head and neck.[3,4] Mediastinal involvement is uncommon, with only two reports of primary mediastinal disease and two reports of metastatic mediastinal disease in the literature, all referencing adult patients.[4-6] Because growth is indolent and symptoms are few, the primary tumor may be present for years before it is brought to medical attention.[1] Large primary masses are typical,[3,7] and metastases are reported in 20-70% of patients at diagnosis, most commonly in lung, bone and brain.[1-3,7] Lymph node metastases occur in approximately 10% of cases.[3]

Wide surgical excision of the primary tumor is the treatment of choice.[1,3] Metastasectomy has also been shown to enhance median survival.[1,3] There is no proven survival advantage to chemotherapy or radiotherapy.[1,3,7] Median survival in the absence of metastatic disease is 5-6 years.[3] Because early resection may extend survival, prompt diagnosis and treatment are of paramount importance.[2]

Case Report

A previously healthy 13-year-old girl presented with a five-day history of headache that was unresponsive to non-steroidal anti-inflammatory drugs. Other than a new mediastinal bruit, her physical examination was unremarkable. Chest radiograph revealed a large left mediastinal mass.

On contrast computed tomography (CT) (Figure 1), the 9.6x8.6x8.6 cm anterior mediastinal mass appeared hypervascular, with large vessels, dense peripheral enhancement, and central non-enhancement, consistent with necrosis. No fat or calcifications were seen in the mass, and no vascular invasion, osseous destruction, or adenopathy was evident. Numerous well-defined pulmonary nodules suggested metastatic disease.

Contrast-enhanced head CT also revealed an avidly and homogeneously enhancing left parietal mass, measuring 3.3x3.0x 3.7 cm, with large feeding arteries from the left middle cerebral artery. Circumferential vasogenic edema and mass effect on the left lateral ventricle were present. Brain magnetic resonance imaging (MRI) showed the well-circumscribed left parietal mass to be minimally T1 hyperintense, T2 hyperintense, and homogeneously enhancing, without necrosis, hemorrhage, or diffusion restriction. Large vessels were present both in the mass and radiating from its lateral margin. On MRI perfusion imaging, the mass was hypervascular with increased peripheral blood volume and blood flow. Single voxel MR spectroscopy revealed a highly elevated choline-to-creatine ratio, no lactate peak, and an undetectable N-acetyl aspartate peak, consistent with a non-neuronal, non-necrotic neoplasm with high cell turnover.

The patient underwent wedge biopsies of middle and lower lobe pulmonary nodules. Histopathology was diagnostic of ASPS (Figure 2), with a pseudoalveolar architectural pattern, Periodic acid-Schiff (PAS) positivity, and uniformly positive anti-transcription factor E3 (TFE3) immunohistochemical staining. Due to presence of metastases and the projected difficulty of complete resection, the mediastinal mass was not excised. However, palliative left parietal metastasectomy was performed, again showing histopathology consistent with ASPS.

The patient was referred to the National Cancer Institute for a phase 2 trial of Cediranib. During pre-study evaluation, right thigh MRI revealed an additional 6.7x4.5x2.8 cm soft tissue mass with T1 and T2 hyperintensity, internal flow voids, large peri-tumoral vessels, and avid enhancement (Figure 3). It was centered in the vastus intermedius muscle, abutting right femur. Normal signal intensity was maintained in the right femur, and no right femoral abnormality was seen on technetium-99m bone scan. Bone scan did reveal abnormal radionuclide uptake in right ischium and proximal right tibial metaphysis, potentially representing bone metastases.

Ten months after presentation, the patient has progressive disease. Due to increasing pain, she has undergone palliative resection of her mediastinal and right lower extremity masses. In addition, a new right frontal lobe brain metastasis has been excised, and two smaller brain metastases have been treated with stereotactic radiosurgery.

Discussion

Although ASPS was first reported as a distinct entity in the early 1950s, its cellular origin remains enigmatic.[1-4,7] A skeletal muscle derivation is favored but has not been proved.[1] Cytogenetic studies of ASPS have identified a specific unbalanced translocation: der(17)t(X;17)(p11;q25).[1] The two fusion tran-

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scripts that result, alveolar soft part locus (ASPL)-TFE3 types 1 and 2, lead to tumorigenesis by transcriptional deregulation.[1]

Because histogenesis is unknown, the descriptive name given to ASPS refers to its histopathology: a pseudoalveolar arrangement of cells within a network of delicate vascular channels and septa.[2,4,8] The cells are large and polygonal in shape with round to oval nuclei, solitary enlarged nucleoli, and copious eosinophilic cytoplasm.[4,8] The majority of tumors contain PAS-positive, diastase-resistant cytoplasmic crystals, composed of monocarboxylate transporter 1 and CD147 proteins.[1,4,8,9] The crystals have a characteristic rhomboid or needle shape on electron microscopy.[4,8] Diagnosis may also be facilitated by identification of ASPL-TFE3 fusion transcripts and by strong anti-TFE3 nuclear immunostaining.[1,8]

Although ASPS usually involves extremities in adolescents and young adults, primary involvement of unusual sites has been reported, including lung, breast, stomach, female genital organs, and bone.[3-4] Primary mediastinal involvement has been reported previously in two young adults.[4] Mediastinal ASPS metastases have also been reported twice in adults.[5,6] To our knowledge, ours is the first report of ASPS presenting with a mediastinal mass in adolescence. Although primary mediastinal ASPS does occur, the mediastinal mass in our patient is almost certainly metastatic, given presence of a concurrent thigh mass. Lower extremity origin and identification of metastases before the primary tumor are common in ASPS.[3] Regardless, our patient's course highlights the importance of considering ASPS in the differential diagnosis of adolescent mediastinal masses when clinical course and imaging findings are characteristic.

On imaging, the appearance of primary and metastatic ASPS reflects rich vascularity, with large vessels being a striking feature, regardless of imaging modality.[2,7] Conventional angiography additionally shows prolonged capillary stain and arteriovenous shunting.[2,7] ASPS is hypodense to muscle on non-contrast CT but enhances avidly with contrast.[7] Tumor invasion of blood vessels and central non-enhancement, indicating necrosis, are frequent; internal calcifications sometimes occur.[2]

On MRI, ASPS has higher T1 signal than muscle and high T2 signal.[2,7] Large, serpiginous intra- and peri-tumoral vessels are characteristic.[2,7] Avid enhancement with contrast is also typical, with or without a non-enhancing, necrotic core.[2,7] When present, hemosiderin staining on gradient-echo sequences indicates prior hemorrhage.[2]

When ASPS occurs in the mediastinum, it must be distinguished from more common mediastinal masses. Lymphomas, germ cell tumors including teratomas, and primary thymic tumors such as thymoma, thymic carcinoma, primary neuroendocrine tumor of the thymus, and thymolipoma generally lack large feeding and draining vessels.[10] In addition, lymph node involvement typical of lymphomas is infrequent in ASPS.[3,10]

T1 hyperintensity on MRI also sets ASPS apart.[7,10] It has been shown to occur in the absence of hemorrhage, melanin, and fat and is hypothesized to be due to slow flow through internal vascular channels.[2] Other mediastinal tumors with T1 hyperintensity include teratomas, thymolipomas, and benign and malignant lipomatous masses.[7,10] T1 hyperintensity due to fat in such masses is distinguishable by fat suppression techniques.[10] Thymic carcino-

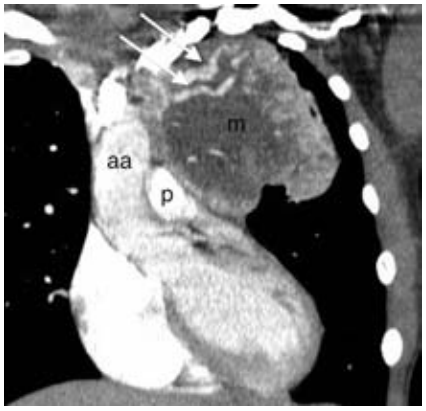

Figure 1. Contrast-enhanced coronal computed tomography image of the chest demonstrates a large, hypervascular mediastinal mass (m), abutting the aortic arch (aa) and main pulmonary artery (p). Also shown are large, enhancing intra-tumoral vessels (arrows), peripheral enhancement, and central low-density, suggesting necrosis. No mediastinal or hilar lymphadenopathy is present.

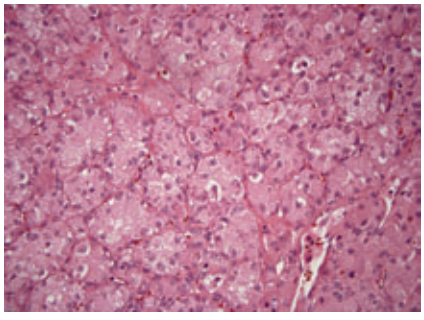

Figure 2. Histopathology of lung metastasis (hematoxylin and eosin stain, x200). As is characteristic of alveolar soft part sarcoma, this specimen has a pseudoalveolar architectural pattern and is composed of large epithelioid cells with abundant eosinophilic cytoplasm, vesicular nuclei, and prominent nucleoli.

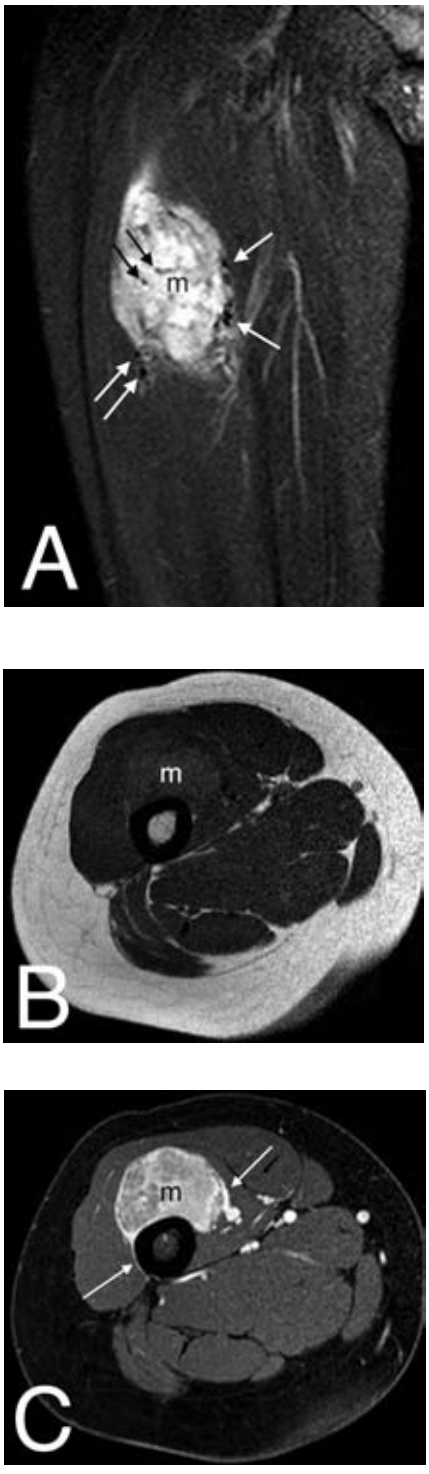

Figure 3. Coronal T2-weighted short tau inversion recovery magnetic resonance imaging (MRI) of the right thigh (A) shows a high signal intensity soft tissue mass (m), with prominent intra-tumoral flow voids (black arrows) and peri-tumoral flow voids (white arrows), reflecting hypervascularity. On axial T1-weighted MRI (B), the anterior compartment mass (m) is mildly hyperintense to adjacent musculature. On axial gadolinium-enhanced T1-weighted MRI with fat suppression (C), the mass (m) and its feeding vessels (arrows) enhance vigorously.

ma may be mildly hyperintense to muscle on T1-weighted images but occurs almost exclusively in older adults.[10] Proteinaceous and hemorrhagic cystic mediastinal masses sometimes have high T1 signal but are differentiated by their lack of enhancement.[10]

Diagnostic confusion has been reported between ASPS and arteriovenous malformations (AVM). Both may result in an audible bruit.[2-3,7] On imaging, ASPS shows a soft tissue mass with slow washout of contrast, whereas AVM has rapid washout of contrast and no soft tissue mass.[2,7] Misdiagnosis of ASPS as an AVM may lead to inappropriate embolotherapy instead of prompt biopsy and excision.[7]

Conclusions

Although ASPS is rare, it should be included in the differential of a mediastinal mass when imaging findings are characteristic. Mediastinal ASPS may represent either primary or metastatic disease and, if metastatic, may present before the primary tumor. Suggestive imaging findings include a large, slowly growing, hypervascular soft tissue mass with large peri-tumoral vessels in an adolescent or young adult.[7] T1 hyperintensity that does not suppress with MRI fat-suppression techniques distinguishes ASPS from lymphoma, teratoma/germ cell tumor, and most thymic neoplasms.[7] Metastatic spread to lung, bone, and brain rather than to lymph nodes also favors ASPS over lymphoma.

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