Fine Needle Aspiration Cytology Diagnosis of Angiosarcoma of the Rib bone. Report of a Case and a Brief Review of the Literature

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Abstract

Angiosarcoma is a rare malignant neoplasm arising from lymphatic or vascular endothelial cells with an annual incidence of approximately 2 in 1,000,000. Angiosarcomas are commonly found in the skin, soft tissue, bone and viscera. Angiosarcomas are usually metastatic at presentation with an average survival of 6-16 months. The risk factors associated with developing angiosarcoma are radiation exposure, longstanding lymphoedema, environmental carcinogens and genetic syndromes. Angiosarcoma present with non-specific findings making it difficult to diagnose. Imaging studies may aid in diagnosis of angiosarcoma however histology is required for definitive diagnosis. Histologically, angiosarcoma appears as spindled, polygonal, epithelioid and primitive round cells staining positively for vascular and endothelial antigens such as CD31, CD34 and VEGF. Angiosarcoma can be treated with surgery, radiotherapy, chemotherapy, and targeted immunotherapy. We present a case of 62-year-old man diagnosed with angiosarcoma of the rib by fine needle aspiration.

Keywords: Angiosarcoma; Bone; Malignant; Metastasis

INTRODUCTION

Angiosarcoma is a malignant neoplasm arising from lymphatic or vascular endothelial cells (1). They are most commonly found in the skin (60%), soft tissue, bone and viscera but can also be located anywhere in the body (2). Angiosarcomas are a rare malignancy, roughly accounting for about 2% of all sarcomas with an annual incidence of approximately 2 in 1,000,000. Angiosarcomas invade local structures with approximately 16-44% of cases presenting with advanced/metastatic disease. Therefore the average survival is about 6-16 months with a 5 year survival rate of approximately 31% (3). Clinically those most commonly affected will present in the 6th to 7th decade of life with a high proportion being male (4). While the pathogenesis of angiosarcoma remains unclear, some of the risk factors include radiation exposure, longstanding lymphoedema, environmental carcinogens and genetic syndromes (1). Diagnosing angiosarcoma is challenging due to the rarity of this malignancy as well as the non-specific presenting symptoms. Imaging techniques such as ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) can be utilized however these have their limitations (5). Thus, histology with immunohistochemistry (IHC) studies is required to confirm the diagnosis of angiosarcomas. Histologically, angiosarcoma appears as a spindled, polygonal, epithelioid and primitive round cells. They stain positive for vascular and endothelial antigens such as CD31, CD34 and VEGF (6). The most effective treatment for angiosarcoma is radical surgery followed by adjuvant radiotherapy while chemotherapy is used for inoperable or metastatic malignancies (7).

We present a case of 62-year-old man who presented with a mass arising from the 7th rib that was diagnosed as primary epithelioid angiosarcoma. We also provide a brief review of the literature.

CASE PRESENTATION

A 62-year-old man presented with recent weight loss and abdominal pain, with swelling on the right side of the chest wall. Patient provided no significant medical history or family history of malignancy however he reported chronic occupational exposure to Vinyl Chloride. He also gave history of remote severe trauma in motor vehicle collision to the right side of his chest. Physical examination was significant for the presence of large mass at the right upper chest wall. An X-ray of the thoraco-lumbar and sacral spine revealed focal degenerative change and scattered spurs formation. The chest X-ray showed a bony defect at upper border of the right 7th rib. A subsequent chest CT scan showed bony erosions and destructive osteolytic right rib lesion along with adjacent pleura involvement.

Fine Needle Aspiration Cytology (FNA) sampling of the mass was performed and an adequate sample was obtained, which was
sufficient for cellblock preparation. Microscopic examination of cytology preparation and cellblock showed irregular complex anastomosing vascular channels lined by malignant spindle and epithelioid pleomorphic cells adjacent to necrotic foci. Tumor cells were arranged as sheets of high-grade pleomorphic epithelioid neoplastic cells with abundant amphophilic and slightly eosinophilic cytoplasm, large vesicular nuclei, and prominent nucleoli. Abundant abnormal mitosis exceeding 15 mitosis/10 HPF was also noted (Figure 1A-B). IHC studies were utilized for definitive diagnosis. The malignant tumor cells were positive for CD31, factor VIII, and vimentin (Figure 1C). Additional IHC studies were performed and the tumor cells were negative for S-100, HMB-45, cytokeratin AE1/AE3, TTF-1, Thyroglobulin, and chromogranin. The cytomorphology and the IHC studies were diagnostic of epithelioid angiosarcoma. The tumor morphology was consistent with a high grade angiosarcoma. Ki-67 was high with 35% nuclear staining and molecular studies showed MYC gene amplification. Skeletal and body survey showed no evidence of angiosarcoma at other sites, so the tumor was diagnosed as primary Angiosarcoma of the rib bone.

A multidisciplinary tumor board recommended wide surgical excision with wide safe margins to be followed by radiation. The 5 cm mass was completely excised with adequate safe margins. Microscopic examination of the excised tumor confirmed the cytology diagnosis and post-operative radiation therapy was initiated. The patient was followed for 27 months with no recurrence or metastasis, but he developed advanced coronary heart disease. While managing the coronary heart disease the patient developed severe cough and hemoptysis. Imaging studies shows widespread metastatic disease involving the lung bilaterally, the diaphragm, and abdominal organs. FNA of one of the lung masses confirmed the diagnosis of metastatic angiosarcoma. Although chemotherapy was attempted, the patient expired three weeks following the diagnosis of metastatic disease.

DISCUSSION

Angiosarcoma is an aggressive tumor arising from endothelial cells making up less than 2% of sarcomas. While the pathogenesis of angiosarcoma remains unclear, some of the risk factors include radiation exposure, longstanding lymphoedema, environmental carcinogens and genetic syndromes (1). Radiation can lead to gene mutations and is one of the strongest risk factors associated with angiosarcomas. Common sources of radiation include occupational exposure and diagnostic/therapeutic radiation (8). Radiotherapy is a mainstay treatment in sarcomas especially in the breast. Angiosarcomas can also arise secondary to chronic lymphedema. Common causes of chronic lymphedema include lymph node dissection, filariasis, idiopathic, congenital and traumatic (9). Some of the common carcinogens associated with angiosarcomas include vinyl chloride monomer colloidal thorium dioxide (thorotrast) and chronic arsenic ingestion (10).

Angiosarcomas can be found anywhere in the body but are most commonly found in the skin (60%), soft tissue, bone and viscera (2). Angiosarcomas commonly invade local structures with approximately 16-44% of cases presenting with metastatic disease. The average survival is about 6-16 months with a 5 year survival rate of approximately 31% (3). Angiosarcomas most commonly presents in 60–70-year-old males (4).

Angiosarcomas commonly present with non-specific symptoms thereby making a clinical diagnosis challenging. The variability of presentation in different organ systems further complicates the diagnosis. Angiosarcomas in the skin, present as bluish or red nodules, which can often ulcerate (11). In the liver they can present with pain in the right upper quadrant.

Figure 1 Cytopathologic examination of the rib bone mass
1A: High-grade pleomorphic epithelioid and spindle neoplastic cells with abundant amphophilic and lightly eosinophilic cytoplasm, and large vesicular nuclei (Pap stain X60 magnification)
1B: High-grade pleomorphic epithelioid and spindle neoplastic cells with abundant amphophilic and lightly eosinophilic cytoplasm, and large vesicular nuclei (DQ stain X60 magnification)
1C: Tumor cells positive for CD31

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15. Guo T, Zhang L, Chang NE, Singer S, Maki RG, Antonescu CR. Consistent along with jaundice (10). Due to the non-specificity of the presenting symptoms, imaging modalities such as ultrasound, CT and MRI play a crucial next step in diagnosis. Ultrasound is commonly used in hepatic angiosarcoma due to its ability to visualize effusions and identify masses in visceral organs (12). CT and MRI both have high resolutions to identify masses as well as characterizing the tissue type (5). While imaging may identify an angiosarcoma, immunohistochemical examination is necessary to confirm the diagnosis. The most common ways to obtain a specimen from a tumor include resection of the mass, frozen section during surgery, and needle biopsy. Histologically, well-differentiated angiosarcomas form vascular channels lined by endothelial cells. Poorly differentiated angiosarcomas are composed of primitive cells with poorly formed vascular spaces (13). Immunohistochemistry is utilized to diagnose poorly differentiated angiosarcomas. Angiosarcomas stain positively for markers of endothelial cells such as CD31, CD34 and vascular endothelial growth factor (14).

Various vascular specific tyrosine kinases such as TIE1, KDR, TEK, and FLT1 are found to be upregulated in angiosarcomas (15). Additionally, genes involved in angiogenesis are altered in angiosarcomas such as MYC gene amplification, protein tyrosine phosphatase receptor type B and phospholipase C gamma 1 mutation (16). Treatment options for angiosarcomas include surgery, radiotherapy, chemotherapy, and targeted immunotherapy.

A fine needle biopsy was utilized to diagnose angiosarcoma in this case. Fine needle aspiration can be used to diagnose angiosarcomas either by the presence of typical histological findings or positive immunohistochemical staining or both (17, 18). The combination of cytology and radiology has allowed for minimally invasive, safe, accurate, and cost-effective diagnosis of suspicious masses, previously accessible only by surgical biopsy techniques. As a result, cytologists are increasingly called upon to diagnose disease in a specimen procured under image guidance for different organs. Rather than causing delay, cytology facilitates timely diagnosis and management is an integral part of a multimodal approach to various tumor diagnoses. Several reports have already concluded the efficacy of cytology specimens alone, including cellblock preparation, in establishing definitive diagnosis of tumors in different organs before surgical resection (19, 20). The definitive diagnosis of angiosarcoma in our case was solely established utilizing cytology sampling including cellblock preparations.

We report this case and we hope that this will raise awareness of clinicians and pathologists to include epithelioid angiosarcoma in the differential diagnosis of osteolytic bone tumor mass and that continued investigation drives further development of efficacious and safe treatments for improving patient’s outcomes.

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