Case Report

Recurrent epithelioid sarcoma of wrist: A case report and review of literature

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ABSTRACT

Epithelioid sarcoma is a rare variety of soft tissue sarcoma that affects young adults mostly involves forearm and hand. It mainly presents as a painless slow growing mass, but can present as multifocal lesions. It has a high rate of recurrence and metastasis. A 35-year-old male presented to our department in November 2013 with a painful ulcer with bloody discharge in the medial side of left wrist. The patient gave a history of swelling with serous discharge from 11 years. Local excision was done 6 times from 2003 to 2011. The patient also gave a history of falling on an outstretched hand and swelling at same site in July 2013, this time again wide local excision was done. The histopathology report was suggestive of high-grade osteogenic sarcoma. Immunohistochemistry (IHC) showed expression of cytokeratin, epithelial membrane antigen, CD34 and CA-125; tumor cells had lost INI-1 expression. IHC confirmed the diagnosis of epithelioid sarcoma of left wrist. Contrast-enhanced computed tomography thorax was suggestive of lung metastasis. Thus, doxorubicin based chemotherapy was planned.

Key words: Doxorubicin, epithelioid sarcoma, immunohistochemistry, wide local excision, wrist

INTRODUCTION

Epithelioid sarcoma is a rare variety of soft tissue sarcoma affecting 20-40 years of age group.[1] It mainly involves the upper extremities approximately in 60% of cases.[2] The term "epithelioid sarcoma" was given to a group of soft tissue sarcomas with a variety of malignant and benign conditions, by Enzinger in 1970.[1] Epithelioid sarcoma is a rare slow growing sarcoma with high risk of recurrence and metastasis.[3] Due to slow growth of the tumor, rarity and less symptoms, the diagnosis of epithelioid sarcoma is very difficult and challenging.[4] Because of this, it is almost impossible to perform a large number of clinical trials to evaluate different treatment modalities. Gender, involved site, age at diagnosis, tumor size, and pathology are the prognostic factors.[5] Female patients show a more favorable outcome. Proximal lesions show worse prognosis as compared to the distal lesions.[3] Tumors show a better outcome if presented in earlier age group.[5] Tumors >2 cm in diameter and tumors with necrosis, vascular invasion have been correlated with worse outcome.[3]

This article reviews the epidemiology, prognostic factors, clinical features, pathogenesis, diagnosis and treatment of epithelioid sarcoma.

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CASE REPORT

A 35-year-old male presented with a painful bleeding ulcer in the medial side of left wrist. The patient was giving history of swelling with serous discharge from last 11 years. Patient gave history of local excision performed 6 times from 2003 to 2011 at periphery. The patient also gave a history of falling on an outstretched hand in July 2013 and this time again wide local excision was done. Biopsy report was suggestive of high-grade osteogenic sarcoma [Figures 1 and 2]. Immunohistochemistry (IHC) showed expression of cytokeratin, epithelial membrane antigen (EMA) [Figure 3], CD34 and CA-125; tumor cells had lost INI-1 expression. IHC confirmed the diagnosis of epithelioid sarcoma of left wrist.

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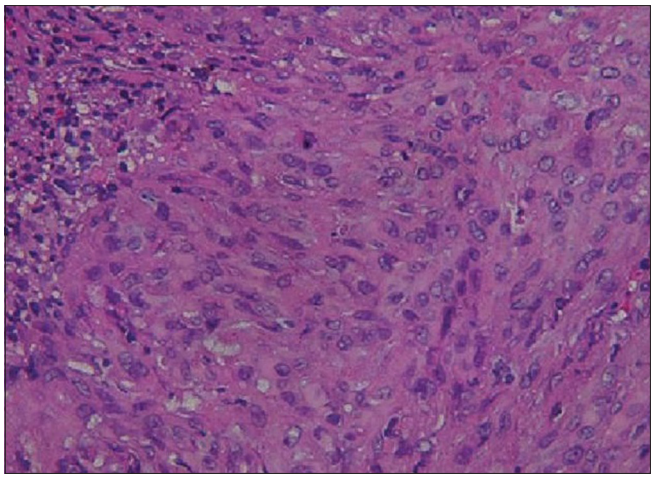

Figure 1: Epithelioid tumor cells in granuloma-like fashion around areas of necrosis and central hyalinization (H and E, ×10)

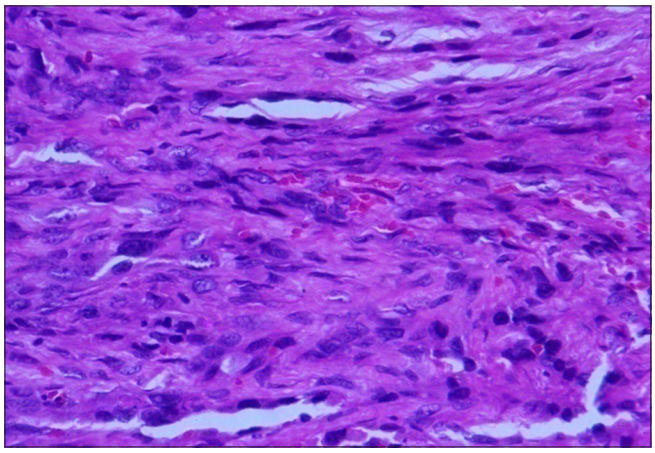

Figure 2: Striking acidophilic tissue due to cytoplasmic staining and desmoplasia (H and E, ×40)

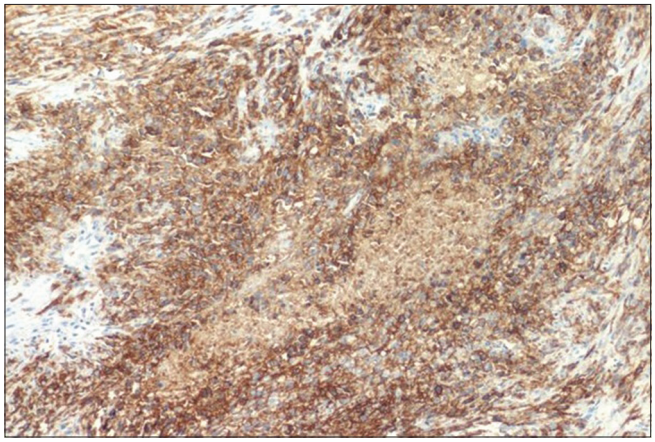

Figure 3: Tumor cells showing positive epithelial membrane staining

Preoperative magnetic resonance imaging (MRI) of left wrist was showing cortical erosions and marrow edema in distal ulna including its styloid process, triquetral, pisiform, capitates and base of 5th metacarpal, with evidence of marked synovial thickening, mild joint effusion and small thick collection (30 × 15 mm) medially. Contrast-enhanced computed tomography (CECT) scan of thorax showed a nodular lesion with central cavitation in anterior aspect of apical segment of right lower lung, measuring 12 × 18 × 11 mm (AP × TD × HT). Subcentimeter hypo dense lymph node was seen in pretracheal region, measuring 9 mm in short axis. CECT thorax was suggestive of lung metastasis. Wide local excision is the primary modality of treatment. The patient was presented with lung metastasis, so doxorubicin based chemotherapy was planned.

DISCUSSION

A recent study based on surveillance, epidemiology, and end results database, showed that the incidence has been increasing with 5.2% per year since 1973 and in 2005, the incidence was 0.4 case per million.[3] It has been shown to be the second and the sixth most common soft tissue sarcoma in the hand and upper extremity respectively.[2,4] This tumor commonly affects 20-40 years of age group (mean age 27 years) and affected male-female ratio is 1.8:1.[4] Females carry a favorable prognosis in epithelioid sarcoma.[5] Studies have failed to reveal any geographical or racial predisposition for the rare disease.[2,5] Epithelioid sarcoma of other sites like lower extremities, vulva, penis and spine also have been reported.[5-8]

Epithelioid sarcoma mostly presents as a firm or hard swelling arising from dermis or deep tissue at the origin site. This may be misdiagnosed as ganglion cyst or giant cell tumor of the tendon sheath. Sometimes, it can present as a superficial ulcer mistaken as traumatic wound. In most of the cases, the swelling or lesion is painless or nontender but in about 20% cases it may be painful or tender.[5] About 13% of cases have multifocal tumors at presentation, while 13% have distant metastasis.[9] The average duration of presenting symptoms before initial surgical procedure was 29 months in a retrospective study, indicates the slow growing nature of the tumor.[5]

An important variation from the rest of the sarcomas is the tendency for lymph node metastasis. Other sarcomas with lymphatic spread include synovial sarcoma, clear cell sarcoma, angiosarcoma, rhabdomyosarcoma and embryonal sarcoma. In a long-term clinical study, 45% patients of epithelioid sarcoma developed metastasis in the lung (51%), lymph nodes (34%) and scalp (22%).[5] In our report also, patient was presented with recurrent epithelioid sarcoma with metastasis to lung.

Epithelioid sarcoma rarely can cause demineralization or cortical thinning of the adjacent bone.[5] Soft tissue swelling can be visualized in some cases by conventional X-ray. Rarely, speckled patterns of calcification are

seen. MRI is the imaging modality of choice prior to biopsy and histopathologic diagnosis. The role of MRI is primarily determining the extent of the tumor and in differentiating doubtful cases of recurrence from postoperative changes due to multiple excisions.[10] One study on 160 soft tissue sarcomas, based on positron emission tomography (PET) - computerized tomography imaging showed 3 cases of epithelioid sarcomas, and all three were PET positive.[11]

Tissue biopsy is the diagnostic modality of choice to diagnose sarcoma, and immunohistochemical analysis differentiates the different types of sarcomas including epithelioid sarcoma. INI1, located on the chromosome 22 (22q11.2), is a member of SWI/SNF multi subunit chromatin remodeling complex. The loss of this tumor suppressor gene is associated in more than 80% epithelioid sarcoma.[12] Vimentin reactivity is present in almost all cases.[5,12] Pankeratin AE1/AE3 and EMA were positive in 96% and 98% of the cases respectively.[12] CA-125 can be used as a serum marker to monitor metastasis. S100 and p63 are typically negative. CD34 is expressed in 50-60% of epithelioid sarcomas,[13] but is negative in carcinoma.

In gross appearance, a white nodule with infiltrating margins is one of the basic features of epithelioid sarcoma. Microscopically, the tumor consists of ovoid or polygonal epithelial cells well blended with fusiform eosinophilic cells with intracytoplasmic vacuoles.[5] Distinct sheets of polygonal cells with spindle cells as seen in biphasic synovial sarcoma are not visualized in the traditional variant. Pseudogranulomatous proliferation of cells is seen around a necrotic acellular central zone. Multinuclear giant cells can be present in a small number of tumors.[5]

Wide local excision is the primary treatment modality in epithelioid sarcoma. Some studies showed up to 77% recurrence rate after marginal resection in epithelioid sarcoma.[5] Thus, most authors recommend wide resection or tumor bed resection despite the dysfunction and morbidity associated with it.[9,10] However, epithelioid sarcoma tend to spread proximally in the same limb (distant to the original tumor) leading some to consider less radical treatment for local control. Amputation can be considered in case of multiple recurrences or if there is not a significant loss of function. However, it does not decrease the risk of local metastasis.[5] Since lymphatic spread can occur in epithelioid sarcoma, sentinel lymph node biopsy and regional lymph node dissection has been proposed by some authors.[14] However, further research is needed as outcome literature of this technique for sarcomas is lacking.

Because of slow growing nature and rarity of epithelioid sarcoma, it is very difficult to have long-term follow-up to compare and evaluate different adjuvant treatment modalities. Adriamycin based chemotherapy has been used for multifocal, large (>5 cm), or metastatic tumor. It has not been shown to improve overall survival,[15] but there are not large published trials. External beam radiotherapy was also tried in some institutes for primary and recurrent cases[16] for limb salvage, but it has not shown to increase overall survival as compared to amputation.[15] The late effects of radiotherapy like scarring, stiffness or neuropathy can be debilitating in the hand.[4] 5-year survival in epithelioid sarcoma is approximately 50-70%.[14]

CONCLUSION

Epithelioid sarcoma is a rare slow growing sarcoma with high risk of recurrence and metastasis. Due to slow growth of the tumor, rarity and less symptoms, the diagnosis of epithelioid sarcoma is very difficult and challenging.

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