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Case Report

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CLEAR CELL SARCOMA IN A CHILD- A RARE ASSOCIATION.

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ABSTRACT

Clear cell sarcoma, also known as malignant melanoma of the soft parts, accounts for 1% of all soft tissue neoplasms. It has a predilection for the distal extremities. It occurs in the age group of 20-40yrs and is rare in the pediatric population. The tumour is thought to arise from neural crest cells and expresses various markers of melanoma. The tumour also shows a characteristic chromosomal translocation giving rise to the transcript EWS-ATF1 gene which helps to distinguish it from malignant melanoma. Here we present a case of clear cell sarcoma in a 10 year old child, who presented with a swelling over the left knee joint of 6 months duration. Imaging revealed a soft tissue mass without any bone involvement. Histopathology from the mass showed cells with round to oval nuclei and prominent nucleoli arranged in nests and fascicles, surrounded by thin fibrous septa & interspersed with multinucleated giant cells. Immunohistochemistry revealed positivity for HMB-45, thus confirming the diagnosis of Clear cell sarcoma of the tendon sheath.

KEYWORDS: clear cell sarcoma, child, rare, melanoma, translocation, immunohistochemistry.

INTRODUCTION

Clear cell sarcoma of soft parts accounts for 1% of all soft tissue neoplasms.[14] It has a predilection for the distal extremities particularly around the ankle joint.

It occurs in the age group of 20-40 years.[1,11] and is rarely seen in the pediatric and elderly population. Some case reports have shown a female predominance.[12] although gender distribution among males and females is equal.[2]

The tumour shows presence of melanin and immunohistochemically stains for S-100 and HMB-45. The tumour is highly aggressive and readily metastasizes to the lymph nodes Thus, Enzinger and Chung proposed the name "malignant melanoma of soft parts".[2,8] However, clear cell sarcoma unlike melanoma does not express BRAF mutations. Further, clear cell sarcoma shows a specific chromosomal translocation t (12:22)(q13,q:12) giving rise to transcript EWS/ATF1 fusion gene.[19]

Recently, this fusion gene product has been found to be responsible for the melanocytic phenotype of clear cell sarcoma. EWS/ATF1 binds and activates MiTF(microphthalmia – associated transcription factor) in the presence of sox-10 and this results in the expression of melanocytic phenotype.[20]

CASE REPORT

A ten year old female patient presented with a swelling over the lateral aspect of the left knee joint since 6 months. The swelling was insidious in onset and progressive in nature.

Imaging of the left knee joint showed a primary soft tissue mass without any bone involvement The fine needle aspiration from the mass showed ovoid to spindle cells with mild to moderate nuclear pleomorphism , multinucleated giant cells,collagen and calcified material was also noted. This was suggestive of a mesenchymal lesion.

Thereafter an incisional biopsy from the mass was done. The impression was suggestive of sarcomatous lesion. Subsequently, the patient underwent a wide excision of the tumour and the sample was sent for histopathology to our department of pathology at NRSMCH.

Gross inspection revealed a skin covered, well circumscribed, ovoid mass measuring 5.5 X 3.5X 2 cm. The cut surface of which was greyish and fleshy. No foci of any haemorrhage or necrosis were noted.

The light microscopy showed oval to spindle cells with elongated plump vesicular nuclei with prominent central nucleoli and pale staining cytoplasm arranged in nests and sheets surrounded by fibrous septa and interspersed with multinucleated giant cells. The tumour cells showed mild nuclear pleomorphism and 2-3 mitotic figures per 10 High Power Field (HPF). No tumour necrosis was found.

On immunohistochemistry the tumour cells showed strong positivity for HMB-45.
The above lead us to a diagnostic dilemma between malignant melanoma and clear cell sarcoma. However, as there were no epidermal changes or any identifiable primary cutaneous neoplasm, we gave the final diagnosis as clear cell sarcoma of the tendon sheath.

DISCUSSION

Clear cell sarcoma or malignant melanoma of soft parts is a rare tumour with adverse prognosis. The largest determinant in patient survival is the tumour size. Sizes >5cm and presence of tumour necrosis suggest a bad prognosis.[7] The 5year, 10 year and 20 year survival rates are 67%, 33% and 10%, respectively.[16]

Distal extremities are the most common sites although cases have been reported to arise from kidney, gastrointestinal tract, penis and head and neck regions.[17] The tumour is highly aggressive and readily metastasizes to the lymph nodes. Metastasis to lungs and bones have also been reported.[18]

Primary or metastatic malignant melanoma is the closest differential. Clear cell sarcoma unlike malignant melanoma is characterized by presence of hyalinized and reticulated stroma with fascicles of uniform population of tumour cells surrounded by delicate fibrous septa and interspersed with tumour giant cells with characteristically multiple peripherally placed nuclei.[13] Further, clear cell sarcoma lacks the pagetoid spread of atypical melanocytes. In cases with unusual histological findings cytogenetics plays a keyrole.

Here in our case the patient failed to give any history of a prior mole. Further, grossly, the overlying skin of the tumour was found to be apparently normal. In addition, the microscopy did not reveal any involvement of the epidermis and no atypical melanocytes were identified. The above histopathological examination thus, excluded melanoma and so cytogenetics was not sought after.

The other differentials include epithelioid sarcoma, synovial sarcoma, alveolar soft part sarcoma and malignant peripheral nerve sheath tumour.

Epithelioid sarcoma is a rare tumour affecting young adults and predominantly involving the forelimbs though cases have been reported around the knee and ankle joints.[9] Histologically, it simulates clear cell sarcoma. However, occasionally the tumour shows a characteristic central necrosis with palisading tumour cells and perivascular as well as perineural invasion unlike clear cell sarcoma.[9]

Further, synovial sarcoma is also a rare tumour primarily affecting young adults, involving the extremities and histologically simulating clear cell sarcoma. It displays a biphasic and monophasic pattern. It is the monophasic synovial sarcoma that mimics clear cell sarcoma. However, most tumours display a haemangiopericytomatous vascular pattern unlike clear cell sarcoma. Above all it shows a characteristic chromosomal translocation t(X; 18) (p11;q11).

Alveolar soft part sarcoma is yet another tumour which presents with a picture similar to that of clear cell sarcoma both clinically and histologically. Although, the tumor is characterized by extensive areas of haemorrhage and necrosis with scarce mitotic activity. Moreover, the nests of alveolar soft part sarcoma are composed of cells with minimal pleomorphism and PAS+, diastase resistant cytoplasmic granules. These nests are separated by septa containing sinusoidal vessels unlike the fibrous septa seen in clear cell sarcoma. Further, vascular invasion is a common feature of alveolar soft part sarcoma unlike clear cell sarcoma.

Furthermore, the epitheloid variant of malignant peripheral nerve sheath tumour is also difficult to discern from clear cell sarcoma. It is often associated with a large peripheral nerve or neurofibromatosis unlike clear cell sarcoma, and is charcterised by a myxoid stroma, hyperchromatic nuclei and brisk mitotic activity.

So to differentiate these histologically similar tumours immunohistochemistry plays a keyrole. Of the immunohistochemical stains HMB-45 is of prime importance as none of the above mentioned tumours except malignant melanoma are HMB-45 positive.

CONCLUSION

Clear cell sarcoma is a highly aggressive tumour, and requires surgical management at the earliest. Neither chemotherapy nor radiotherapy is much helpful. The largest determinant in patient survival is tumour size. Sizes <5cm in largest diameter are associated with better prognosis. Histopathology with immunohistochemistry is quite conclusive to establish the diagnosis. In cases of unusual presentation, EWS/ATF1 translocation is critical in distinguishing it from malignant melanoma. Hence, early detection by the clinician and diagnosis by the pathologist, can improve patient outcome.

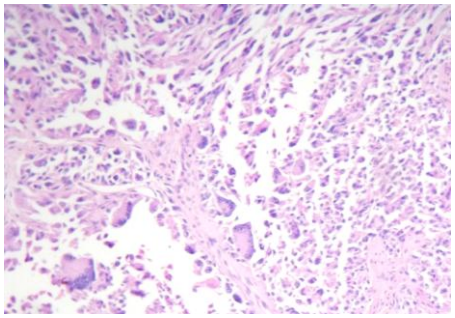

Figure1

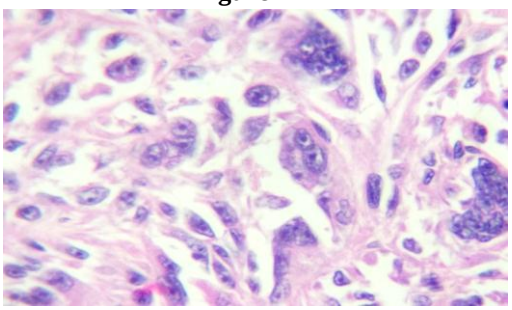

Figure 2

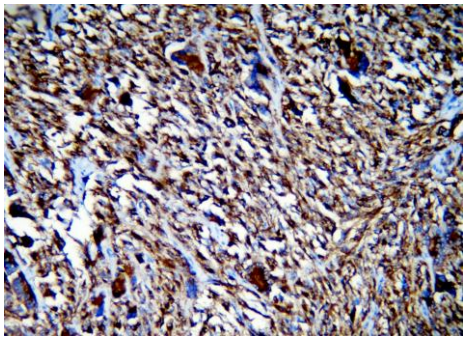

Figure 3

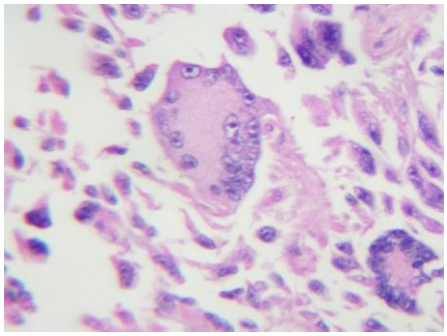

Figure 4

Figure legends

Fig 1: fascicles and nests of round to fusiform cells surrounded by fibrous septa with interspersed multinucleated giant cells. (H&E stain, X40)
Fig 2: nests and fascicles of tumour cells with intervening fibrous septa,(H&E,X 400)
Fig 3: tumour cells showing HMB-45 positivity. (HMB-45 stain,X100)
Fig 4: multinucleated giant cells interspersed amongst tumour cells.(H&E stain, X400)

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