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Clear Cell Sarcoma of the Knee. A Report of Two Rare Cases

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ABSTRACT

Clear cell sarcoma of soft tissue is a rare type of soft tissue sarcoma. It is derived from melanoblast-like cells located within subcutaneous tissue, tendon and aponeuroses. The tumour is also known as malignant melanoma of soft parts because it has similar morphology to malignant melanoma. Unlike malignant melanoma, however, it is not associated with a cutaneous lesion. We report here two cases of this tumour occurring in young adults.

Key Words:
Clear Cell Sarcoma, Soft Tissue Tumour, Malignant Melanoma

INTRODUCTION

Clear cell sarcoma of soft tissue (CCSST) is a rare melanin producing soft tissue sarcoma. Despite its melanocytic differentiation, it is distinct from malignant melanoma (MM). This slow growing sarcoma commonly affects young adults between 20 to 40 years [1]. It invariably arises in deep soft tissue of the extremities, and 70% of those afflicted exhibit chromosomal translocation. This chromosomal translocation is not seen in MM.

CASE REPORT

Case 1

A 38-year-old man presented with a slow growing left popliteal fossa mass for the previous two years. The initially painless mass eventually became tender and firm. The lesion caused him to limp. Physical examination revealed a large popliteal fossa mass with left inguinal node enlargement. Knee flexion was 60 degrees, limited by the mass and pain. The patient was started on 3 cycles of neo-adjuvant chemotherapy of intravenous ifophosphamide and adriamycin in an attempt to salvage the limb. However due to extensive disease, left leg amputation and left inguinal lymph node dissection were subsequently performed. Intra-operatively, the tumour was seen attached to quadriceps tendon and insinuated in between the quadriceps muscle planes. The tumour measured 7 x 4.5 x 3.5 cm (Figure 1). Palliative radiotherapy was administered post-operatively in view of the rapid progression of the disease. The patient passed away five months after the surgery due to lung metastasis and multiple recurrences of the disease both at the amputation site and lymph nodes.

Case 2

A 28-year-old woman presented with a slow growing painless knee mass for one year. Physical examination showed a nodular mass at the medial aspect of her left knee. The mass was fixed to the underlying structure and firm in consistency. The overlying skin was unremarkable. MRI showed an extra-articular soft tissue mass on the medial aspect of the left knee attached to the medial patella retinaculum. Intraoperatively, the tumour was located at the subcutaneous layer lateral to the medial condyle of the femur. The tumour formed a well-defined nodule, which measured 6.5 x 3 x 3 cm (Figure 2). Wide excision of the tumour mass was performed.

Histologically, the tumour showed similar appearance to the first case. This patient underwent 30 fractions of radiotherapy post-operatively. Chemotherapy was not administered as requested by the patient. There was no tumour recurrence at the one year post-surgery follow-up nor were there any complications from radiation therapy. She is currently well and ambulating with a mild limp.

Histologically, both tumours displayed classical CCSST appearance. The cells were composed of spindle-shaped elongated cells with abundant and clear cytoplasm forming fascicles and nesting patterns (Figure 3). Areas of necrosis were noted in the first case. However, there was only minimal necrosis seen in the second case. Panels of antibodies were utilized to confirm melanocytic differentiation (HMB45 and S100) (Figure 4). Chromosomal study was not performed due to practical constraints.

DISCUSSION

CCSST is currently a distinct entity classified World Health Organization as soft tissue and bone tumours. It is a rare

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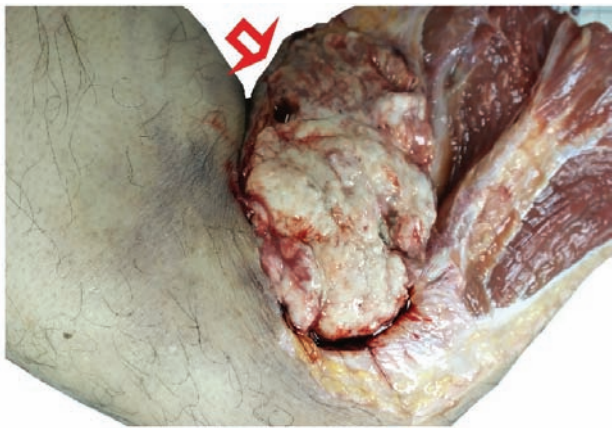

Fig. 1: There was a whitish lobulated tumour with ill-defined border located at left popliteal fossa infiltrating into the quadriceps muscle. There was no area of haemorrhage or pigmentation seen.

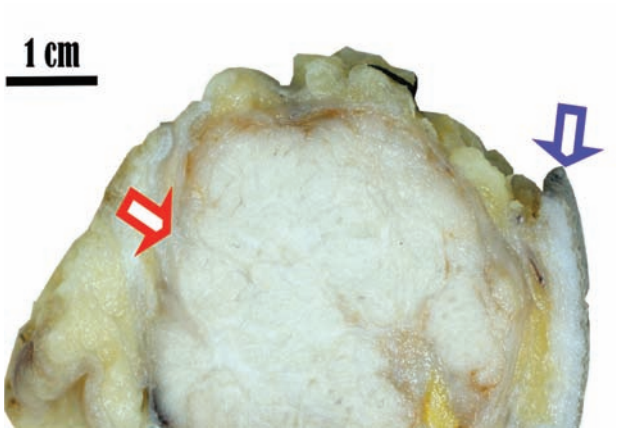

Fig. 2: There was a subcutaneous lobulated and homogenous whitish tumour at the left knee. No area of hemorrhage or pigmentation seen.

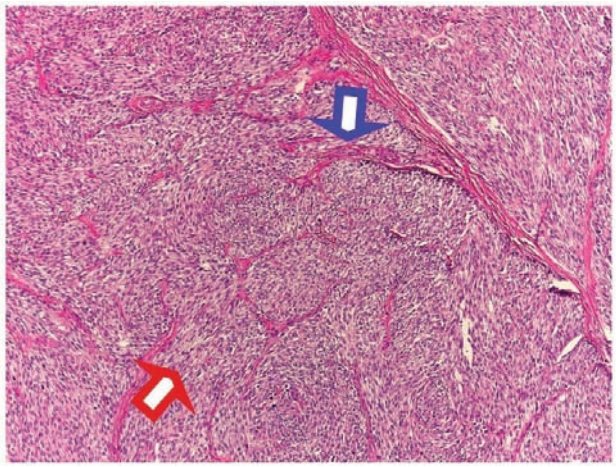

Fig. 3: Photomicrograph shows tumour cells forming nesting pattern (red arrow) and delicate intervening connective tissue (blue arrow). The cells are mainly spindle in shape with pale-staining tumour cells and clear cytoplasm. Low frequency of mitotic figures in this tumour is in concordance with the slow growing nature of the lesion. No pigmentation seen in both cases (H&E 20X).

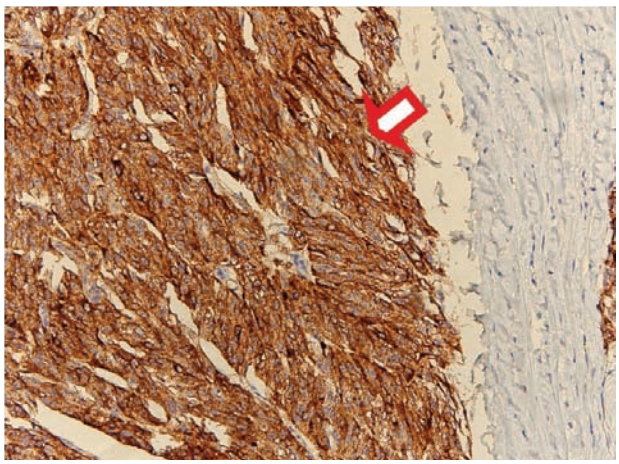

Fig. 4: Photomicrograph of tumour cells with diffuse cytoplasmic immunoreactivity with HMB45 which is a melanocyte marker (HMB45 immunostain 40X).

tumour accounting for only a small percentage of soft tissue tumours [2]. The median age of patients at diagnosis is 32 years [1]. The most common site of involvement is the extremities including the foot and ankle [1]. Others common sites include the knee, thigh and hand[1]. There are reports of CCSST occurring in gastrointestinal tract, kidney and retroperitoneum.

In the present cases reported here, both patients were adults with primary tumour arising from around the knee. CCSST has a propensity for slow progressive invasion [3]. At presentation, the malignancy of the swelling is seldom suspected. Early detection of this tumour is hampered by the fact that typical presentation consists of an innocuously small and non-pigmented swelling that has existed for a long duration prior to presenting to the physician. Deenik *et al* found that in 13 studied cases, the initial clinical diagnosis include epithelial cyst, exostoses, clavus, lipoma, hematoma, neuroma and benign cutaneous adnexal tumour [2]. The tumour typically adopts a quiescent phase for many years without radical growth.

In both case, the mass became painful at a later stage of the disease and they only sought treatment when the lesion hindered their daily activities. The tumours exhibited aggressive behaviour at the time of diagnosis. An important differential diagnoses is metastatic MM. A possible source of primary lesion must be excluded before making a diagnosis of CCSST [2]. In contrast to MM, CCSST is deeply situated and generally located in non-pigmented areas. CCSST arises from neural crest cells and is commonly associated with tendons or aponeuroses. It is genetically associated with translocation of chromosome 12 and 22 [1,4]. A unique chimeric EWSR1-ATF1 fusion gene is formed with this genetic

mutation and is associated with the tumour induction. CCSST shows similar microscopic features to MM. However, since the tumour is located deep in the soft tissue, it may mimic other soft tissue sarcomas when analyzed under routine hematoxylin and eosin staining [1]. Mitotic activity tends to be low despite its poor prognosis [1].

For CCSST, prognostic factors are the tumour size and necrosis. A small tumour of less than 2 cm generally has a better survival rate [3]. Patients are generally subjected to local control through surgery followed by adjuvant radiotherapy. Adjuvant radiotherapy should be considered in incomplete resections, large (>5 cm) tumours and/or high grade lesions[5]. The role of adjuvant chemotherapy is not clear. Some study showed that aggressive multi-agent chemotherapy and radiotherapy have no significant influence on the treatment outcome [3].

This sarcoma has the propensity for lymphatic spread [3]. About one third of CCSST patients develop regional lymph node metastasis during follow-up [2]. Recurrence of the tumour commonly follows inadequate local control. The prognosis is dismal once metastasis occurred. Distant metastasis commonly occurs within two years after lymph nodes metastasis become clinically detectable [2].

Early detection and adequate local control of the lesion are the most important aspects in the management of CCSST. Histological diagnosis requires a high level of suspicion since this tumour may mimic other soft tissue sarcomas. The benefits of adjuvant radiotherapy and chemotherapy have not been fully evaluated due to the rarity of this disease.

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