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Case Report

Recurrent clear cell sarcoma and its responsiveness to chemoradiation

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ABSTRACT

Clear cell sarcomas are rare tumours accounting for less than 1% of all soft tissue tumours. They are aggressive lesions with extremely poor prognosis. The clinical diagnosis of this tumour is challenging, requiring histopathologic examination for definite characterization. The treatment protocol for this tumour is not well-established, with most studies showing no clear cut role of chemoradiation. This is a case of clear cell sarcoma of soft tissue in a 57-year-old male who presented with a solid-cystic mass on the thigh and was diagnosed as hematoma clinicoradiologically. Post-operative residual tumour was treated successfully with radio/chemotherapy, in a manner similar to melanoma. This article, thus, also highlights the role of chemoradiation in the treatment of clear cell sarcoma, suggesting that it can be better treated like melanoma rather than like a soft tissue sarcoma.

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1. Introduction

Clear cell sarcoma of soft tissue is a rare malignant tumour of tendons and aponeurosis, believed to originate from neural crest cells. First described by Enzinger in 1965, it was named “malignant melanoma of soft parts” in 1983, owing to its histologic resemblance to malignant melanoma.[1,2] It usually occurs in extremities in young individuals and appears benign on radiologic examination, requiring histopathologic examination for definite diagnosis.[3] We report a case of a 57-year-old male with clear cell sarcoma of soft tissue presenting with solid- cystic thigh mass, which was managed successfully with combination of radiotherapy and chemotherapy.

2. Presentation of the Case

A 57-year-old male presented with a swelling in right thigh for six months. Patient gave history of trauma around the same time. USG showed a large heterogenous lesion of size 8.5 x 5.7 cm in right upper medial thigh in close relation to right common femoral artery. The lesion exhibited internal echoes with clot formation suggestive of a diagnosis of hematoma/ pseudoaneurysm. CECT showed a septated cystic collection with enhancing thick wall measuring approximately 8.3 x 5.2 x 6.2 cm below the right inguinal region on medial aspect of right thigh, anterior to right common femoral artery and vein. Subtle subcutaneous fat stranding with mild soft tissue thickening over cystic lesion was noted. Per-operatively, the tumour was found to be adherent to femoral vessels and nerve. The mass was excised and sent for histopathologic examination.

Grossly, a soft tissue mass covered with skin ellipse was received, measuring 10 x 7 x 6 cm. The tumour was predominantly cystic with a solid, grey white area

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measuring 2.5 x 2.5 cm. Cysts were filled with hemorrhage and necrosis (Figure 1). Microscopic examination showed nests of tumor cells with round to oval pleomorphic nuclei, conspicuous eosinophilic nucleoli and moderate amount of eosinphilic cytoplasm. Brisk mitotic activity was noted in addition to large areas of hemorrhage and necrosis. Multiple sections examined did not show any melanin pigment (Figure 2). On immunohistochemistry, the cells were positive for vimentin, S-100 and HMB-45; and negative for desmin, SMA, cytokeratin, EMA and CD99 (Figure 3). Extensive evaluation of the patient revealed no evidence of cutaneous melanoma. Thus, a final diagnosis of clear cell sarcoma (malignant melanoma of soft parts) was rendered.

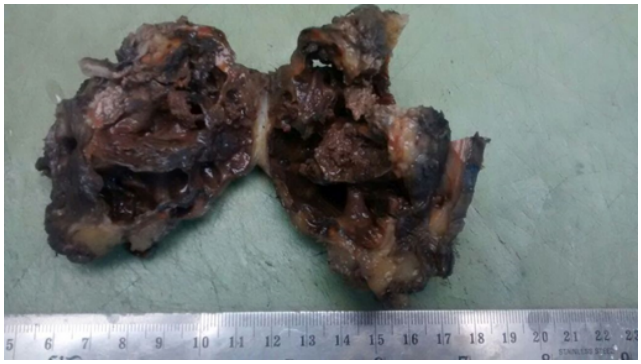

Fig. 1: Gross examination showed a predominantly cystic soft tissue mass having cysts filled with hemorrhage and necrosis along with a solid, grey white area

A postoperative CT angiography of the right lower limb was suggestive of residual/recurrent tumour, showing two well-defined hypodense, multiloculated cystic areas, one measuring 4.2 x 3.2 x 5 cm with peripheral enhancement in anteromedial aspect of thigh and another measuring 3.5 x 3.2 x 6.5 cm at right inguinal region extending along the inguinal canal up to the root of the scrotum (Figure 4 a). Patient was treated like melanoma with a hypofractionated regimen of radiotherapy in which he received a total dose of 60 Gy in 24 fractions. He was then put on adjuvant chemotherapy with single agent dacarbazine. After 3 cycles of chemotherapy, the patient is now in complete remission. A CECT scan performed post chemoradiotherapy showed no residual tumor (Figure 4 b). Further, plan included completion of total 6 cycles of chemotherapy with single agent dacarbazine and to keep the patient on close follow up.

3. Discussion

Clear cell sarcoma accounts for less than 1% of all soft tissue tumours. It mainly affects young adults in third to fourth decade of life, with no gender predominance. Most common sites of predilection include the extremities

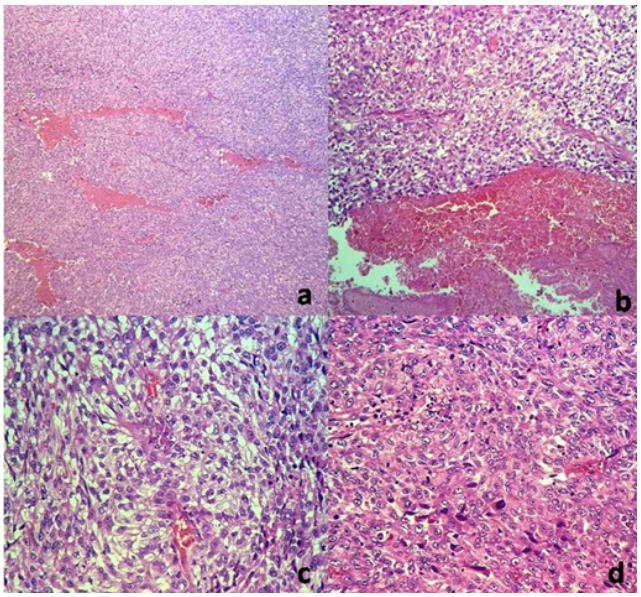

Fig. 2: a): Microscopic examination showed nests of tumor cells (H&E, x100); **b):** Tumour showed large areas of hemorrhage and necrosis (H&E, x200); **c):** Tumour cells showed pleomorphic nuclei with conspicuous eosinophilic nucleoli and clear toeosinophilic cytoplasm (H&E, x400); **d):** Tumour cells showed brisk mitotic activity and did not show any melanin pigment (H&E, x400)

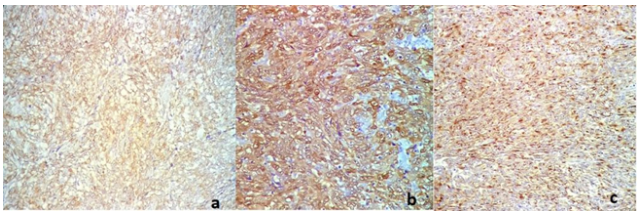

Fig. 3: a): On immunohistochemistry, the tumour cells were positive for vimentin (x200); **b):** Tumour cells were positive for S-100 on immunohistochemistry (x400); **c):** Tumour cells were positive for HMB-45 on immunohistochemistry, (x200)

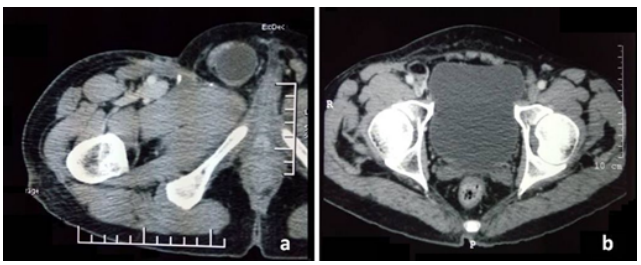

Fig. 4: a): Postoperative CT angiography of right lower limb showed well-defined hypodense, multiloculated cystic area 4.2 x 3.2 x 5 cm with peripheral enhancement in anteromedial aspect of thigh; **b):** Post chemoradiotherapy CECT scan showed no residual tumor

particularly the foot and ankle (40%), followed by knee, thigh, and hand (30%). It has also been reported in unusual locations like head and neck, trunk, gastrointestinal tract, kidney and bone.[2,4,5] Clinically, the tumour presents as a painful slow growing mass involving the deep soft tissue.[2,5] Some patients have a history of trauma as was provided in the present case. This may be misleading, as traumatic hematomas have a similar presentation.[6]

The radiologic appearance in the present case showed a septate cystic collection with thick wall. Such a finding leads to a broad list of differentials which include postoperative seromas, posttraumatic cysts, epidermoid inclusion cysts, lymphoceles, and lymphangiomas. When the enhancement is thick or irregular, diagnoses to be considered are inflamed or infected ganglia, abscesses, hematomas, and necrotic tumor masses.[7] Due to close proximity of the lesion with the femoral artery, a provisional diagnosis of hematoma was given radiologically. Typically, clear cell sarcoma appears as a benign looking, well defined, homogenous mass on computed tomography (CT) and magnetic resonance (MR) scans. On T1-weighted MR images, it is usually homogeneous and isointense or slight hyperintense to muscle due to the paramagnetic effect of intralesional melanin. On the other hand, on T2-weighted MR images, it is usually more heterogeneous with low signal intensity.[8]

Grossly, the tumour usually ranges in size from 2-6 cm, with an average of 4 cm. Tumours more than 5 cm in size are known to behave more aggressively than smaller ones, making tumour size the most important predictor of biologic behaviour.[2,9] Cut surface is grey white with a lobulated or multinodular appearance. Areas of hemorrhage, necrosis and cystic degeneration may be prominent, requiring extensive grossing for identification of the tumour, as in the present case. Some cases may have brown discoloration due to prominent melanin pigment.[2,5,9] In the present case, the mass was predominantly cystic in nature containing hemorrhage and necrosis. Extensive grossing revealed focal solid grey- white areas.

Microscopic examination shows tumour arranged in nests and fascicles with an infiltrative pattern. The cells show prominent nucleoli and moderate amount of eosinophilic to clear cytoplasm, thought to be due to glycogen accumulation. Presence of giant cells and areas of hyalinisation is also known. In some cases, marked degeneration results in a pseudo-glandular appearance reminiscent of alveolar rhabdomyosarcoma. Areas of necrosis may be prominent as in our case.[2] In a study of 52 cases of CSS of soft tissue, Hocar et al have found tumour necrosis more than 50% to be associated with a worse outcome.[9] On immunohistochemistry, the tumour cells show positivity for S-100 and HMB-45.

The differential diagnosis includes other sarcomas occurring in this region such as fibrosarcoma, synovial sarcoma, alveolar rhabdomyosarcoma and malignant peripheral nerve sheath tumour. The distinctive appearance of tumour cells along with the immunohistochemical profile helps in establishing the correct diagnosis.

Although being synonymously known as malignant melanoma of soft parts, because of cytologic and immunohistochemical similarities, they are genetically distinct from melanoma. Distinction from cutaneous melanoma is important and is based on histologic and molecular features. In contrast to melanoma, clear cell sarcomas occur in deep tissue and rarely involve the dermis. Also the arrangement of cells in a fascicular pattern is not seen in melanoma. Most of the cases of clear cell sarcoma (70%) harbor balanced translocation t(12;22)(q13;q12) which is believed to be an early event in tumourigenesis and is not found in melanoma.[10]

Treatment consists of wide excision of the tumour. Early diagnosis and surgery are essential for a favorable clinical outcome. The role of chemo/radiation has not been well established, most studies showing these to be of no benefit. Postoperative radiotherapy is indicated in case of positive and close margins, to decrease local recurrence.[3] Some studies have advocated the role of sentinel lymph node biopsy because of the high incidence of regional lymph node metastases. Presence of lymph nodal or hematogenous metastases to lung, bone, liver and brain is associated with a grave prognosis.[2,5,9] Chemotherapy is mainly employed in metastatic disease.[3] Unlike other soft tissue sarcomas doxorubicin is not effective in this entity, cisplatin based chemotherapy may have potential benefit.[11] According to some reports in the literature, intralesional injection of interferon- alpha has some role in treatment.[12]

4. Conclusion

In the present case, residual tumor was found after surgery. So the patient was then treated like malignant melanoma with chemoradiation and response was significant after hypofractionated radiotherapy and chemotherapy with dacarbazine, which suggests that clear cell sarcoma of soft parts behaves more like a melanoma than a soft tissue sarcoma.

5. Source of Funding

None

6. Conflict of Interest

The authors declare no conflict of interest.

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