RARE CASE OF AGGRESSIVE CLEAR CELL SARCOMA IN A YOUNG FEMALE

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INTRODUCTION

Clear Cell Sarcoma of Tendon and Aponeuroses (CCTA) which is derived from neural crest cells is a highly malignant soft tissue tumor and one of the rarest tumors between all soft tissue sarcomas. CCTA was first described in 1965 by Enzinger in 21 patients and during the past 40 years there have been almost 300 case reports of this unique yet enigmatic entity

CASE PRESENTATION

HISTORY OF PRESENTING ILLNESS:

A 27 year old female without any significant past medical history presented to her primary care physician due to mild to moderate pain at the posterior aspect of the left knee for almost 6 months without a major impact on her daily activities.

PHYSICAL EXAMINATION:

Demonstrated thickened soft tissue on posterior aspect of the left knee extending superiorly without restriction in range of motion. Motor strength, sensory function, and reflexes were normal.

DIAGNOSTIC WORKUP:

Ultrasonography of the Popliteal Fossa:

a complex popliteal cystic mass with irregular wall and internal debris measuring 2.1 x 3.7 x 1.9 cm

MRI of the knee:

A cystic mass located lateral to the tendon for the semimembranosus muscle measuring 3.8 X 2.3 cm in transverse diameter and extending superiorly into the distal thigh

Immunohistopathology and Cytogenetic studies:

The primary morphologic appearance was compatible with a malignant neoplasm with plasmacytoid features, however EMA and CD138 staining were negative. These findings primarily were compatible with malignant melanoma.

The following immunoperoxidase and cytogenetic studies demonstrated:

Lack of staining of the neoplastic cells for Cam 5.2, AE1/AE3 (Epithelial differentiation)
Lack of staining of the neoplastic cells for myogenin/desmin (Muscle differentiation)
Lack of staining of the neoplastic cells for chromogenin/synaptophysin (Neuroendocrine differentiation)
Positive staining for S100 and melan A staining,
Presence of t(12;22)(q13;q12) translocation

SURGICAL INTERVENTION AND STAGING WORKUP:

MRI of thigh and leg to evaluate the extent of disease:

Demonstrated a 34 cm heterogeneous mass with high signal intensity on T2 weighted sequences within gracilis muscle extended locally into and around the tendon and, inferiorly from mid-thigh to knee

Whole body PET scan to evaluate metastases:

Demonstrated central necrosis within the tumor and metastatic involvement of three lymph nodes in the left hemipelvis only.

Eleven weeks after initial presentation the patient underwent complete surgical resection. Popliteal, superficial, and deep inguinal nodes were positive for metastasis (N1), tumor size was > 5 cm(T2b), and histologic examination demonstrated a poorly differentiating tumor(G3)

FINAL DIAGNOSIS:

Clear Cell Sarcoma of Tendon and Aponeuroses; T2bN1M0G3

IMAGING STUDIES

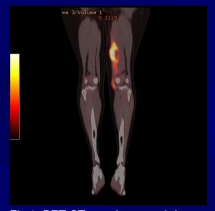

Fig 1- PET-CT scan in coronal view showes increased FDG uptake within the left gracilis muscle

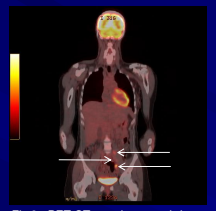

Fig 2 - PET-CT scan in coronal view demonstrates increased FDG uptake in 3 left hemipelvis lymph nodes, without any lung metastasis

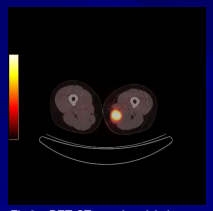

Fig 3 – PET-CT scan in axial view demonstrates increased FDG uptake in medial aspect of left thigh abutting the adductor longus muscle

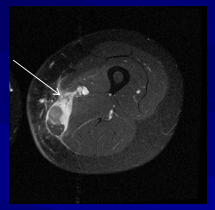

Fig 4 - MRI of thigh using gadolinium demonstrates increased signal in the gracilis muscle on a Fat Saturation sequence. The mass is surrounded by fluid in the fascia which extends laterally to the femoral artery and vein

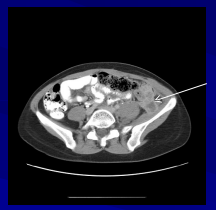

Fig 5 - CT scan of abdomen and pelvis with contrast 3 months after starting chemoradiotherapy demonstrates metastasis in left retroperitoneum

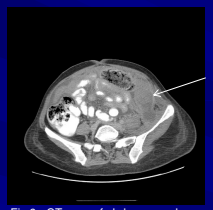

Fig 6 - CT scan of abdomen and pelvis with contrast demonstrates enlargement of the same lesion in left retroperitoneum one month later

ADJUVANT THERAPY:

- The patient was started on "Arm C of ARST- 0332 PROTOCOL" - Adjuvant Chemoradiotherapy treatment in Non Rhabdomyosarcoma Soft Tissue Sarcoma (NRST).
- This protocol consists of 6 cycles of ifosfamide and doxorubicin, along with radiotherapy with adriamycin which starts one month later

FINAL COURSE OF DISEASE:

- Follow up CT scan of abdomen in late stages of chemotherapy demonstrated significant progression of disease including ascites, metastatic lymphadenopathy and obstructive hydronephrosis in spite of treatment.
- Patient continued to deteriorate and 6 weeks later presented with abdominal distention and pain. Repeat CT scan of abdomen demonstrated considerable progression of intra-abdominal malignancy including peritoneal carcinomatosis, omental caking and progressive retroperitoneal lymphadenopathy.
- Patient opted comfort care and deceased 10 days later

References:

1. Clear Cell Sarcoma of Soft Tissues, Sara Sofia Malchau et al., Journal of Surgical Oncology. 2007;95:519–522
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3. Clear Cell Sarcoma of Tendons and Aponeuroses, Daniel C. Dim et al., Arch Pathol Lab Med—Vol 131, January 2007, 152-156
4. The management of clear cell sarcoma, D. R. Kuiper et al., Europian Journal of Surgical Oncology, 2003; 29: 568–570

DISCUSSION

Clear Cell Sarcoma of Tendon and Aponeuroses was first referred to as malignant melanoma of soft parts due to its histologic resemblance to malignant melanoma. Both malignant melanoma and Clear cell sarcoma of tendons and aponeuroses are positive for HMB-45 and S100 protein on Immunohistochemical studies.

Most cases of CCSTA (75%) show a reciprocal cytogenetic translocation t(12;22)(q13;q12) which has never been found in malignant melanoma. This demonstrates a unique chimeric fusion EWSR1/ATF1 gene transcript and can be detected by chromosome analysis, FISH, and reverse transcriptase polymerase chain reaction.

This tumor typically arises in the deep soft tissues of the distal extremities particularly the foot and ankle, and almost always is closely associated with tendons, aponeuroses, or fascial structures.

Clear Cell Sarcoma of Tendon and Aponeuroses rarely awakes suspicion of malignancy in the beginning and usually presents with a typically firm, slowly enlarging, painless or mildly painful mass in the extremities and may be associated with itching or intermittent numbness. It usually presents in young Caucasian adults and demonstrates fairly equal distribution between male and female.

The clinical course of this tumor is very variable and difficult to predict. It can be protracted with metastases appearing after a quiescent period of time, or it can be associated with a rapid and fatal progression.

Local recurrence or metastases may occur as late as 29 years after initial surgical excision so, lifelong follow-up seems to be crucial. The presence of lymph node metastases and its negative impact on prognosis suggests that sentinel node biopsy or even node dissections in some patients is indicated.

This tumor is associated with high local recurrence and distant metastases to lungs, lymph nodes and bones, reported in different studies ranging from 14–26% and 44–83% respectively.

The differential diagnosis of a tumor located in close proximity to tendons and aponeuroses in an extremity includes paraganglioma-like dermal melanocytic tumor, clear cell myomelanocytic tumor, malignant melanoma, malignant peripheral nerve sheath tumor and synovial sarcoma.

The current treatment for clear cell sarcoma is wide local tumor excision. In case of close resection margins, radiotherapy is indicated to improve local control. The benefit of chemotherapy in CCSTA is yet to be established, although doxorubicin-based chemotherapy appears to reduce recurrence rate in localized soft tissue sarcomas and may be effective in patients with metastases.

Different chemotherapy protocols consisting agents such as cyclophosphamide, doxorubicin, ifosfamide, etoposide, vincristine have been tried to reduce recurrence rate in localized soft tissue sarcomas, but the benefit of chemotherapy in CCSTA is not established yet.

The reported 5-year survival ranges from 48% to 55% and adverse prognostic factors includes necrosis, tumor size > 5 cm, local recurrence and metastasis. No correlation between histologic appearance and clinical outcome has been found yet.

CONCLUSION

Clear Cell Sarcoma of Tendon and Aponeuroses is a rare, highly malignant lesion with poor prognosis and unpredictable course. It may easily masquerades as a small benign tumor located in the distal parts of the extremities. CCSTA is a diagnostic challenge due to its benign presentation and histopathological resemblance with malignant melanoma and a therapeutic dilemma because of its poor prognosis secondary to an aggressive nature and early metastasis. Upon diagnosis, this tumor should be taken very seriously and treated vigorously by wide excision and appropriate adjuvant therapy.

This case emphasizes the importance of promptly establishing a correct diagnosis in patients with persistent leg pain so that targeted therapy can be started in order to optimize the potential benefit. The current case also illustrates the aggressive nature of CCSTA. Despite extensive surgical excision and adjunctive chemo-radiation the tumor metastasized to the abdomen and the patient succumbed to death after 8 months.