Abstract:
Clear cell sarcoma is an extremely rare, slow growing and aggressive soft tissue sarcoma with melanocytic differentiation. We report a case of recurrent clear cell sarcoma treated at our Institute for its rarity and need for appropriate diagnosis and treatment. A 26 year old male presented to our Institute with recurrent swelling in the right popliteal fossa for 1 month duration. He had previous excision of the right popliteal fossa lesion and reported as alveolar rhabdomyosarcoma outside and he came to our Institute for further treatment. On evaluation he was diagnosed with non-metastatic recurrent clear cell sarcoma of the right popliteal fossa. He had right popliteal fossa exploration and underwent right above knee amputation in view of popliteal vessel and nerve involvement. He had an uneventful recovery and is receiving ifosfamide and doxorubicin based adjuvant chemotherapy. Clear cell sarcoma is a rare melanin producing soft tissue sarcoma with diagnostic challenge. Complete surgical excision is the optimal treatment for local control.

Keyword: Sarcoma, clear cell, melanoma

Case Report
A 26 year old male was evaluated for swelling in the right popliteal fossa and underwent excision of the swelling elsewhere which was reported as alveolar rhabdomyosarcoma. He presented to our Institute with recurrent swelling and pain in the right popliteal fossa one month after the previous excision. He had limping gait. Examination revealed a swelling of 10x8 cm occupying the right upper calf and medial portion of the scar in the popliteal fossa with no significant popliteal or inguinal nodes. Histopathology review with IHC correlation of the previous excised specimen was suggestive of clear cell sarcoma and MRI local part revealed soft tissue lesion in the right popliteal fossa and upper calf involving medial head of gastrocnemius muscle abutting the popliteal vessels with normal underlying bone and knee joint (Figure 1). He was planned for wide local excision with flap cover. During surgery, popliteal fossa exploration revealed encasement
Popliteal vessels and nerve with satellite nodule in the knee joint cavity compromising R0 resection. Hence he underwent right above knee amputation and the postoperative recovery was uneventful. Histopathology confirmed the diagnosis of clear cell sarcoma measuring 11x8x5 cm with extensive degeneration and positive satellite nodule 1.5 cm at knee joint cavity. He is receiving ifosfamide and doxorubicin based adjuvant chemotherapy.

Discussion

Clear cell sarcomas, a rare soft tissue sarcoma entity, was first described by Enzinger in 1965. (1) It is a melanin producing sarcoma which is clinically, genetically and biologically different from cutaneous melanoma. It was also termed as malignant melanoma of soft parts by Chung and Enzinger in 1983 since histologically similar to cutaneous melanoma. (2) It is an extremely rare soft tissue sarcoma and only few cases are reported in the literature. Between 1980 and 2000 in the Italian and German registry (3) only 28 cases and 32 cases from Hongkong and 52 cases from France are reported. Clear cell sarcoma are seen in young adults with median age of 30 and range from 20 to 40 years. It arises from the deep soft tissue part and lower extremity is the most common site with foot 40%, knee, thigh and hand 30%, head & neck rarely involved. Montogmery et al reported the site distribution with lower extremity 75 %, upper extremity 22%, trunk 2 % and head & neck 0.8 % in their study. (4) It is a deeply seated, slow growing high grade sarcoma occasionally presents with pain and 2 to 5 years elapsed at the time of diagnosis. Occasionally very large lesions may involve the skin otherwise always free. Lymph node involvement and distant metastasis is one of characteristic feature of clear cell sarcoma and reported nodal metastasis incidence are 33% and 53% in Eckardt and Enzinger series respectively.(5) Size and necrosis were independent prognostic factor with size more than 5 cm tumor have worse outcome. Multivariate analysis have proved that size is the most significant factor which prognosticate the outcome.(6) Other factors like age, site, depth and proliferation index are investigational. Clear cell sarcoma macroscopically appears lobulated or multinodular grey white mass firmly attached to tendons or aponeurosis and average size being 2 to 6 cm. Cut surface shows focal haemorrhage, necrosis, cystic changes and dark brown or black discoloration. Histologically tumor shows compact nests or fascicles of fusiform or spindle cells with clear or eosinophilic cytoplasm containing intracellular glycogen (Figure 2). Multi-nucleated gaint cell up to 10-15 peripherally placed nuclei is the characteristic feature and melanin can be demonstrated by special stains (Fontana or warthin starry stain) or IHC and not by routine hematoxylin & eosin stain. These cells stain positive for S-100, HMB 45, melan A, mel CAM, MITF, NSE, Leu 7, LN 3 on Immunohistochemistry. The genetic aberration seen in clear cell sarcoma is the reciprocal translocation t(12;22)(13q;12q) which produces a gene fusion of Activating Transcription Factor 1 (ATF1) and Ewing Sarcoma Breakpoint Region 1 (EWSR1). This chromosomal translocation was first described by cytogenetic karyotyping in the early 1990s by Bridge et al. (7) It is specific and seen in more than 90 % of the clear cell sarcoma which can be utilized for diagnostically challenging cases. In our case it was diagnosed outside as alveolar rhabdomyosarcoma which is a differential diagnosis if the tumor cells are poorly preserved or
degnerated but IHC confirmed the diagnosis of clear cell sarcoma without much diagnostic problem. If the tumor cells are well preserved fibrosarcoma, synovial sarcoma, MPNST, blue nevus and nodular malignant melanoma are the differential diagnosis. Melanin producing tumors(Malignant melanoma) are cutaneous origin, rarely deep, epithelial cells with BRAF mutation that are different from clear cell sarcoma which is deep seated, rarely involve skin with spindle cells and characteristic translocation t(12;22). Clear cell sarcoma is locally recurrent in 14 to 39% with metastasis to nodes and lung develop in 2 to 8 years (50%). Repeated local recurrence is a harbinger of late distant metastasis even after 10-20 years. Eventually all patients develop distant metastasis after local recurrence or nodal involvement. Hence adequate local control is essential for reducing the local recurrence and metastasis. Complete surgical excision with adequate margins is the optimal treatment. Late recurrence and metastatic nature of the tumor mandates long term follow. Lymphadenectomy is not routine unless nodes are positive and SLNB had been reported in literature but insufficient data to recommend for routine standard of care.(8) Adjvant radiotherapy or chemotherapy are investigational and not an established standard. But chemotherapy had proven little efficacy since these sarcomas are slow growing tumors. Ifosfamide and doxorubicin are FDA approved drugs for clear cell sarcoma. (9) Other recent investigational approaches are targeted therapy with TKI inhibitors Crizotinib (10) for metasatic or locally advanced tumor and epigenetic therapy targeting the histone deacetylase enzyme. (11) Clear cell sarcoma or malignant melanoma of soft part was an extremely rare tumor with diagnostic challenge. Hence recognition of the entity and application of appropriate diagnostic armamentarium solve the diagnostic dilemma, for early diagnosis and prompt treatment.

Bibliography


