Clear cell sarcoma (CCS), (malignant melanoma of soft tissues) is an aggressive, rare soft tissue tumor that occurs predominantly in the extremities of young adults. The treatment of CCS includes surgical excision, adjuvant radiotherapy or chemotherapy according to tumor dissemination. Here we present a 31-year-old male with an advanced stage of CCS that was located in the deep of the sole of right foot. Since CCS is extremely rare, there doesn’t exist any standard of care for advanced stage disease. For the treatment, a review of the literature was done and subsequently we decided to perform a bioimmunochemotherapy protocol for the patient which has been thought to work better in these tumors compared to conventional chemotherapeutics alone, and he received a combination treatment of cisplatin, dacarbazine, interleukin-2, interferon-α-2b. After three cycles of treatment, he showed partial response. Although the regimen is quite toxic, it seems to be effective for advanced CCS.

**Key words:** Bioimmunochemotherapy; clear cell sarcoma.

Malignant melanoma is a relatively rare skin cancer accounting for only 4% of all skin cancers. Clear cell sarcomas (CCS) account for less than 1% of all melanomas. CCS is an anaplastic tumor originating from melanoblasts and usually arise from subcutaneous tissues, tendons and aponeuroses. CCS is first described by Enzinger in 1965, as a distinct type of soft tissue sarcoma. Since it is extremely rare, there doesn’t exist any standard of care, except for surgery which is only suitable for limited cases. Here we describe a case of CCS with advanced stage of disease.

**CASE REPORT**

A 31-year-old male who is a miner, has applied to orthopedist on September 2008 for his right ankle which was twisted and then swollen. He underwent magnetic resonance imaging (MRI) that didn’t show any pathologic changes except for soft tissue oedema of the right ankle. After a short period of time, he noticed a painful mass in his right inguinal region. Once again MRI of inguinal area was performed which showed multiple lymphadenopathy, and the largest of them was 4 cm in...
A lymph node biopsy was performed to determine the histopathological diagnosis. The specimen revealed tumoral infiltration of the lymphnode and immunocytochemical staining showed positivity for HMB45 and was negative for CD3, CD20, CD30, pancytokeratin. Pathologist reported that it could most likely be the metastasis of malignant melanoma to lymph nodes, however they suggested to search for a primary lesion because morphological properties of the cells make them think that the diagnosis might be CCS. For this aim, positron emission tomography (PET) scan of the whole body was scheduled for searching the primary lesion. PET scan showed a 14x11 cm hypermetabolic soft tissue mass in the sole of right foot (maximum SUV: 17.8) which stood for primary malignancy and also multiple foci of metastases in soft tissues (dominantly right-side location bilateral leg, thigh, gluteal, dorsal side), left lung (maximum SUV: 2.1), lymph nodes (hilary, right external iliac, inguinal) (maximum SUV: 13.1), as well as lesions in the bone (maximum SUV: 6.4) were detected. In malignant melanoma local committee which is held once in a month at Ege University Medical School, these results were evaluated and discussed in details, and because of the suspicious pathologic evaluation of the excised lymphnode and the detection of origin of the primary lesion on PET scan, the diagnosis of CCS was needed to be verified. Before the treatment decision, a trucut biopsy was performed from the primary lesion which was located in the deep of the sole of right foot. Histopathologic examination revealed a tumor characterized with ambiguous fascicular to nested pattern delineated with thin fibrous septa. Tumor cells were polygonal to fusiform shaped with large pale eosinophilic to clear cytoplasm and vesicular nuclei with prominent nucleolus (Fig. 1).

Immunohistochemically, tumor cells were positive for HBM45, S100 and melan A where melan A was focal, others were diffusely stained. In the light of clinical and radiologic data, together with morphologic and immunohistochemical findings, tumor was evaluated as clear cell sarcoma (Fig. 2 and 3). Since there wasn’t any standart of care...
Clear cell sarcoma originating from the sole of right foot which is in deep settling

for metastatic CCS, a review of the literature was done and subsequently we decided to perform a bioimmunochemotherapy protocol for the patient which has been thought to work better in these tumors compared to conventional chemotherapeutics alone, and he received a combination treatment of cisplatin, dacarbazine, interleukin-2, interferon-α-2b. \[3\] Briefly, it was scheduled as dacarbazine 250 mg/m\(^2\) intravenously on days 1, 2 and 3; cisplatin 25 mg/m\(^2\) on days 1, 2 and 3; interleukin-2 18 million units/m\(^2\) days 6-10 and 13-15 and interferon α-2b 5 million units/m\(^2\) on days 6, 8, 10, 13, 15. But during the first cycle of the treatment, due to interleukin application the patient’s liver enzymes elevated more than 5-times of the upper normal limits; that is why we had to stop the interleukin-2 infusion and reduced the dose of interleukin-2 by 25% for the second cycle. After the administration of the three cycles of treatment, the patient showed partial response of the disease, and his palpable right inguinal lymphadenopathy regressed significantly. Because he was responsive to the treatment, he received two more cycles of the same regimen. After these two cycles, the response was evaluated again and stability of the disease achieved.

We decided to follow him with interferon α-2b 5 million units/m\(^2\) three days/weekly. However, only after two months he was on this schedule of treatment, he developed multiple liver metastases and died due to hepatic failure in the end of June, 2009. Although the bioimmunochemotherapy regimen is quite toxic, it seems to be effective for advanced CCS, since it does not have a standard treatment option.

**DISCUSSION**

CCS, also known as malignant melanoma of soft tissue, is a very rare entity. The diagnosis of the tumor is generally challenging, as it was in our case and needs a experienced pathologist. Specific immunocytochemical markers used to delineate clear cell sarcoma. More specifically, S-100 and HMB-45 are used to differentiate clear cell sarcoma from epithelial tumors, and more specifically, from synovial sarcoma. \[2-4\] Although the absence of keratin with positive S-100 and HMB-45 immunostains is often associated with the primary diagnosis of CCS, faint keratin immunoreactivity has been observed in CCS. Therefore, absence of keratin staining does not rule out CCS. \[4\] More recently, molecular genetic characterization of clear cell sarcoma has shown to be specific for t(12;22) chromosomal translocation which is typically not present in cutaneous malignant melanoma. \[5\] However, the t(12;22) chromosomal translocation may not always be identifiable in some cases. In our case, chromosomal translocation was not studied because of technical impossibility.

The prognosis of clear cell sarcoma of soft parts is not well established. It has an unpredictable course. Metastases occur in 60-70% of patients. \[6\] CCS is a tumor with a propensity for lymphatic and distant spread. Frequent local recurrences and eventual nodal and distant metastasis (usually pulmonary) characterise the disease. Lymph node metastasis has been reported in a high number of cases, so sentinel lymph node biopsy is now indicated with the diagnosis of CCS. \[4\] Once regional lymph node metastasis or haematogenous spread has occurred, the prognosis is very poor. The studies have concluded that SLN status predicts the predictive of additional node involvement at the time of the diagnosis and possible recurrence of the disease. \[7,8\] In a study done by Al-Refaie et al., \[9\] detection of metastatic SLNs in CCS was a predictive factor for developing early bone metastases, also suggesting concurrent nodal and distant metastases for CCS. In concordance with these results, van Akkooi et al. \[10\] reported positive SLNs in two out of five CCS patients that they followed, who presented additional metastatic sites found after lymphoadenectomy. These limited reported observations do not allowed to show us reliable conclusions. However, it does appear from multiple literature reviews, that tumors less than 2 cm and having negative SLN have a generally better long term prognosis.

The most effective treatment of a CCS is the surgical resection of the tumor. Complete tumor resection represents the mainstay of treatment and is the gold standard of treatment for patients with small tumors. Aggressive surgical resection with wide margins is warranted to decrease local recur-
rences. When conservative complete excision is not feasible, mutilating surgery should be considered. In patients with complete excision, adjuvant treatment seems unnecessary and has no evidence up to now.\[11\] Radiotherapy is strongly suggested for close resection margins.\[4-12\] Bioimmunochemotherapy is predominantly employed in case of advanced disease.\[6-12\] The standard sarcoma regimens are not successful in CCS treatment. However, remissions in metastatic CCS after the use of bioimmunochemotherapy combination have been reported in the literature.\[6-13\]

REFERENCES