Clear Cell Sarcoma of the Axilla (Soft Tissue Malignant Melanoma)

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Abstract

A case of clear cell sarcoma of the axilla (malignant melanoma of soft tissues) is reported. The tumor was ressected and the initial diagnosis was liposarcoma. Two months after operation another nodule was found in the patient lumbar region. Ressection of this second nodule was done. The diagnosis of clear cell sarcoma was very difficult by uncomom clinical picture and the tumor's rarity. Rapid evolution to generalized methastatis occurred.

The literature was reviewed and the main points of clinical and histological findings were presented.

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Introduction

Clear cell sarcoma of tendons and aponeuroses is a rare tumor first described by Enzinger[3] in 1965. The tumor was so named of uncertainty as to its histological origin. Its similarity malignant melanoma was recognized at the time but the progress of the twenty one patients described seemed to indicate that this was a separate entity.

In 1983, Chung and Enzinger[2] carried out a retrospective study on 141 patients with this type of tumor and they suggested that these be known as "soft tissue malignant melanomas" since they detected intracellular melanin in 2/3 of cases. This finding suggests that the tumor arises from cells that migrated from the neural crest during embryonic life and which had retained their capacity for melanin production.

Clear cell sarcoma is a malignant epithelioid neoplasm that affects primarily young adults with an average age of 30 years. Sex distribution is equal[2,4]. To date, less than 180 cases have been reported in the literature.

The tumor usually arises in the tendons, aponeuroses or other fascial structures of the limbs, particularly around the knees and feet, although there have been reports of the tumor arising in the abdominal wall, the neck, back, pharynx[6], penis[5,9] and perineum[11].

The tumor typically presents as a slowly growing, firm, rounded or multilobulated mass adherent to adjacent connective tissue. Pain is uncommon although

it may be present[2]. Overlying skin is usually free of tumor and pigmented skin lesions are not found even when tumor contains melanin[1].

The cut surface of the tumor has a whitish-grey fish-like appearance with brown or black areas visible in 1/4 of cases. On light microscopy, bundles of fusiform or polygonal cells with granular eosinophilic cytoplasm and vesicular nuclei with large nucleoli are observed. These bundles are separated by fibrous septa of variable thickness. Occasional giant cells are also found. Cytoplasmic granules containing melanin, which can be seen using Fontana or Warthin-Starry preparations, are present in 3/4 of cases. Mitotic figures are rare[2].

Under the electron microscope, clusters of cells separated by delicate collagenous septa are seen.

Cytoplasmic bodies resembling melanosomes at various stages of development may be observed[1].

Immunohistochemical techniques serve to differentiate the tumor from soft tissue epithelioid sarcomas, and metastases from clear cell adenocarcinomas. The more important reagents include HMB-45, vimentin, epithelial membrane antigen (EMA), S-100 protein, cytokeratins AE1-AR3 and CAM 5.2. Clear cell sarcomas are positive for the first three while soft tissue epithelioid sarcomas and metastases from clear cell adenocarcinomas are positive for the last two. Since malignant melanoma has an identical immunophenotype to clear cell sarcoma, the presence of a cutaneous or occult visceral melanoma must be excluded[10].

Recurrence rates after treatment are very high reaching 80% in some series. Re-recurrences are also common requiring repeated surgery for treatment[5]. Average 4-year survival is only around 55% despite advances in diagnostic techniques and the use of various modes of treatment. Due to the rarity of this tumor and the difficulty in obtaining the correct diagnosis, we decided to report on a case in our practice.

Case Report

J.A.R.F., a 34 years old white male first complained of apainless lump in his right axilla that had been present for 40 days. He denied any other symptoms. The patients father had had a facial malignant melanoma removed.

On examination the patient looked well and had a diffuse swelling in the axillary region with no inflammatory signs. The overlying skin was normal. On palpation, there was a 4 centimeters long, firm, rubbery, subcutaneous nodule that was not attached to the skin or deep tissues. No other nodules were palpable in the axilla and the patient was then seen at a nother hospital and the lump was removed and a pathological diagnosis of a metastasis from a clear cell adenocarcinoma was made. The most likely primary sites were thought to be the kidneys, lungs, salivary glands and thyroid gland.

Abdominal and thoracic computer tomography (CT) scans, abdominal and pelvic ultrasound, and a thyroid scan were performed. Clinical examination of the head and neck and rectal examination were also performed. All of these investigations were normal.

At this time the histological sections were sent to two other pathologists for examination. One reaffirmed the diagnosis, while the other diagnosed a liposarcoma having performed histochemical analysis with a positive result for vimentin, and negative results for HMB/45 (melanoma), EMA, and cytokeratin (AE1-AE3). The diagnosis was confirmed at a clinical meeting of the Department of Pathology of the Antônio Prudente Foundation in São Paulo.

In view of these reports the margins of the original excision were extended and examination of the operative specimen showed residual tumor in the central portion, with deep regions and 26 lymph nodes free of tumor.

Two months after the operation a nodule was detected in the patient's left lumbar region which was removed and the pathologist that had originally diagnosed a liposarcoma confirmed the diagnosis stating that this was a case of multicentric liposarcoma.

Slides and paraffin blocks of both specimens were sent to the Sloan Kettering Memorial Cancer Center in New York and the Royal Marsden Hospital in London.

Positive results for vimentin and S-100 were obtained and negative for cytokeratin and EMA. Opinions were different as to HMB-45 which was reported as positive in New York but negative in London. However both centers gave the diagnosis as soft tissue malignant melanoma, the so called clear cell sarcoma. The report from the Royal Marsden stated, "On morphological grounds the appearances are consistent with the so called clear sarcoma (melanoma of soft parts), although the clinical picture is unusual for this. The immunohistochemical profile and morphology are not wholly inconsistent with metastasis from a renal cell tumor which should be excluded by ther means".

The patient consulted the medical department at the Memorial Hospital where no specific treatment was indicated, leaving the patient with the option of using an immunostimulator such as leucocytin, which

he chose not to do.

The general condition of the patient remained good until eight months after the first nodule was noticed, when he developed ascites with liver metastases and died three weeks later.

Discussion

Clear cell sarcoma is a rare tumor with a poor prognosis. In a recent study involving 17 patients, 10 patients died an average survival time of 49 months. Factors such as age, sex, race, site of lesion, duration of symptoms, initial treatment, frequency of mitoses, tumor necrosis, proportion of epithelioid cells and nuclear pleomorphism appeared not to have any bearing on survival time[7].

In the patient we studied, survival was very short. Factors which may have influenced this include the rarity of the tumor and the delay in excising it with sufficient safety margin, during which time the diagnosis of metastatic tumor was being considered and a primary tumor was being searched for. The location of the tumor in the axilla appears to be unique and this may also have led to delay in diagnosis.

The spread of the lesion in this case differs from other reports where spread is by local invasion and lymphatic spread to adjacent lymph nodes. Hematogenous spread is usually to the lungs and the bones[2,3].

Although sarcomas in general only metastasize to lymph nodes in 5-20% of cases, lumphadenectomy was performed since the tumor was initially thought to be a liposarcoma located in a region rich in lymphatics and in addition, the extent of the original excision was not known.

There histological diagnoses were made in all before the final conclusion was reached and each was confirmed by at least two different laboratories. This is consistent with reports that the tumor is difficult to diagnose and easily confused with other tumors, especially sarcomas[2,3,8,10,11].

Histochemical analysis of clear cell sarcoma is usually positive for vimentin, although this is not specific. HMB-45, which is specific may give false negative results. EMA and cytokeratin are invariably negative[10].

The positive result with S-100 obtained at the Memorial Hospital supported the diagnosis of clear cell sarcoma.

Although this is not specific, is positive in over half the cases[7]. The detection of HMB-45 also supported the diagnosis.

The small number of cases in the literature and the various methods of treatment used do not enable conclusions to be drawn as to the ideal method of treatment and the sensitivity of the tumor to radiotherapy and chemotherapy have yet to be fully established. However, the general consensus at present is that surgery is the best method available.

In this case, the extended excision was sufficient to prevent local recurrence but the recurrence at a different site and the presence of large numbers of liver metastases are characteristic of the aggressiveness of this tumor.

It is important to note that the immunohistochemical profile of clear cell sarcoma is identical to that of metastatic malignant melanoma and the two conditions should be differentiated on the basis of the clinical findings.

As clinicians become more aware of this tumor and diagnostic methods improve, better methods of treatment and consequently a better prognosis may result.

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