CASE REPORT Libri Oncol., Vol. 32 (2004), N^{o} 1 – 3, 53 – 58

CLEAR CELL SARCOMA – A CASE REPORT

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Summary

The report covers the first case of clear cell sarcoma (malignant melanoma of soft tissue) recorded in the Croatian medical literature.

It is a rare soft tissue tumor, constituting less than 1% of all soft tissue neoplasms, first reported by Enzinger in 1965. The tumor presents most often in adolescents and young adults, with its peak incidence in the third and fourth decade and slight female predominance.

The tumor produces melanin, but it differs from melanoma in several important respects. The proper name for this neoplasm should be clear cell sarcoma of tendons and aponeuroses in order to prevent confusion with clear cell sarcoma of the kidney and other clear and spindle cell neoplasms.

A 23-year-old female patient presented to our hospital with a 10 cm large, painless, lower right leg mass, and few palpable lymph nodes in the ipsilateral inguinum. Clinical examination (NMR, ultrasound) showed an expansive tumor mass and few suspicious inguinal lymph nodes. Surgical treatment was indicated because of cytologically suspicious diagnosis of clear cell sarcoma or malignant melanoma .

Histopathological and immunohistochemical analysis confirmed the origin of tumor cells and showed melanoma/melanocytic differentiation including clear cell sarcoma (malignant melanoma of soft tissue).

This case report provides evidence that the preoperative definitive diagnosis of primary CCSSP can be rendered if immunocytochemistry is used in addition to cytomorphology in a suitable clinical setting.

KEY WORDS: *clear cell sarcoma, FNA cytology*

SARKOM SVIJETLIH STANICA – PRIKAZ SLUČAJA

Sažetak

U radu je prikazan prvi slučaj sarkoma svijetlih stanica (malignog melanoma mekih tkiva) zabilježen u hrvatskoj medicinskoj literaturi.

Taj rijedak tumor mekih tkiva, koji čini manje od 1% svih novotvorina mekih tkiva, prvi je puta opisao Enzinger 1965. godine.

Tumor se najčešće pojavljuje u adolescenata i mlađih odraslih osoba, s najvećom incidencijom u trećoj i četvrtoj životnoj dekadi i nešto je češći u žena.

Tumor proizvodi melaninski pigment, ali se ipak razlikuje od melanoma u više važnih značajki. Pravilan naziv za tumor trebao bi biti sarkom svijetlih stanica tetiva i aponeuroza kako bi se izbjegla zamjena sa sarkomima svijetlih stanica bubrega i drugim novotvorninama svijetlih i izduženih stanica.

23-godišnja pacijentica došla je u našu ustanovu s tumorskom masom na desnoj potkoljenici i nekoliko palpabilnih ingvinalnih čvorova. Klinički pregled (NMR i UZV) potvrdio je ekspanzivnu tumorsku masu i povećane ingvinalne limfne čvorove. Citološki se postavi sumnja na sarkom svijetlih stanica ili maligni melanom te se učini kirurški zahvat.

Histokemijska i imunohistokemijska analiza potvrdila je melanocitnu diferencijaciju, tj. dijagnozu sarkoma svijetlih stanica (malignog melanoma mekih tkiva).

Prikazani slučaj potvrdio je mišljenje da je preoperativna definitivna dijagnoza sarkoma svijetlih stanica mekih tkiva moguća ako se uz citomorfologiju i kliničke podatke učini i dodatna imunocitokemijska analiza.

KLJUČNE RIJEČI: *sarkom svijetlih stanica, aspiracijska citodijagnostika*

INTRODUCTION

Clear cell sarcoma or clear cell sarcoma of soft parts (CCSSP) was first reported by Enzinger in 1965 (1). Earlier reports emphasized the presence of melanin, placing this tumor in the same group as malignant melanoma of the skin and mucosa - hence, the alternative designation of malignant melanoma of soft parts. Thanks to the introduction of immunohistochemistry in everyday diagnostics proving unidirectional melanocytic differentiation, the reassessment of former clear cell sarcoma into malignant melanoma of soft parts was possible (2). Although it produces melanin, it differs from the conventional melanoma in several important respects(3-5).

According to some authorities, the proper name for this particular neoplasm should be clear cell sarcoma of tendons and aponeuroses (it is a deeply situated tumor that is nearly always intimately associated with tendons or aponeuroses) in order to prevent confusion with clear cell sarcoma of the kidney and other clear and spindle cell neoplasms (6). CCSSP is a tumor with unique genetic rearrangement (t12,22; q13, q12-3) (7-9). Such genetic rearrangement has not been seen in other tumors, including malignant melanoma (10). This rare soft tissue tumor, constituting less than 1% of all soft tissue neoplasms, presents most often in adolescents and young adults, with its peak incidence in the third and fourth decade and slight female predominance (2, 11). Thus, 75% of CCSSPs occur in the lower extremity and 25% in the upper extremity, favoring the tendons and fascia of the distal portions at both sites. The head and neck and the trunk are rarely the primary site of involvement (12).

The earliest stage is a slowly growing, painful nodule in the distal extremities which is the primary site (90-95%), although the overall range of age and anatomic location is wide (13). As exceptional locations appear visceral organs, retroperitoneum, bone, penis and spinal nerve roots (14-19). Most tumors measure 5 cm in diameter closely associated with fascial or tendoaponeurotic structures with often extension into subcutis (20), but cases of visceral locations could be found, although rarely, in literature (14,15).

Non-radical surgery with wide margins is a method of treatment, but in many cases it cannot prevent repeated local recurrence. Therefore, amputation should be performed which is in the same time prevention of developing metastasis in almost half of patients with predilection to lymph nodes, lung or bone (20). The question of prophylactic regional lymph node dissection has not been answered yet (13). There is still an uncertain role of chemotherapy or radiotherapy (20).

Prognostic determinants correlating with impaired outcome are size greater than 5 cm, necrosis and local recurrence (11,21) imply twenty-year survival prospect unlikely to be more than 20% (20). The Mayo Clinic series showed the survival at 5, 10 and 20 years to be 67%, 33%, and 10% respectively (24). Nevertheless, patients with big tumors frequently deteriorate rapidly, as in this case.

PATIENT AND METHODS

A 23-year-old female patient presented to our hospital complaining of a 10 cm painless mass on the lateral lower right leg of 10-month duration (Fig 1). She had also a red, painless tumor formation on the anterior thigh. Enlarged lymph nodes were present in the ipsilateral femoral triangle. The patient had no history of melanoma. Magnetic resonance imaging (MRI) demonstrated a well-circumscribed tumor with heterogeneous, slightly increased signal intensity on T1-weighted images. Ultrasound detected an expansive tumor mass and a few higher lymph nodes, some of them reactive and some locked infiltrated. The specimens obtained by fine-needle

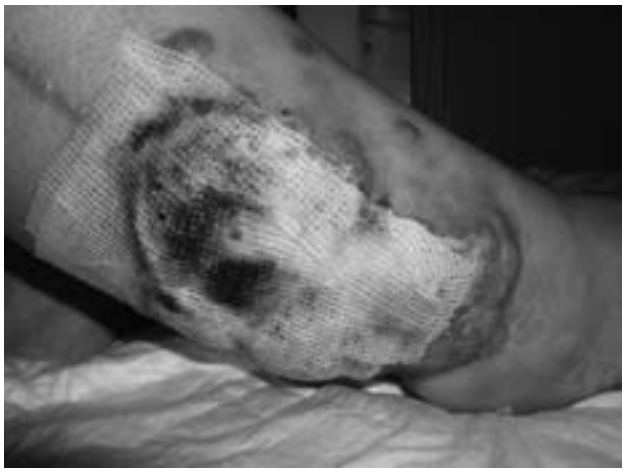

Figure 1. Clinical photograph

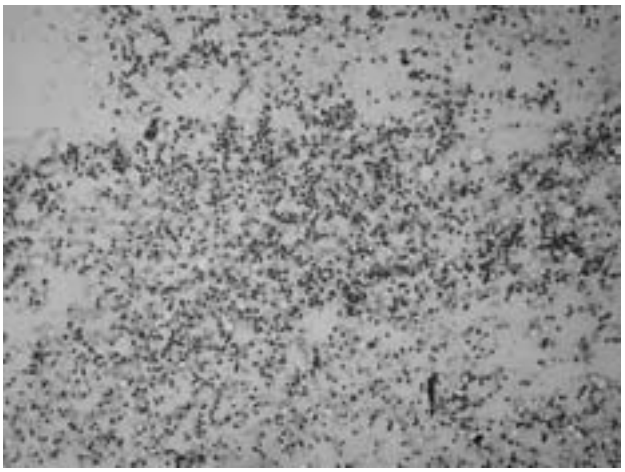

Figure 2. Clear cell sarcoma (MGGx100)

aspiration from the primary tumor, second suspicious mass of the anterior tight and from lymph nodes of the right inguinum. Smears were stained with MGG and additionally immunocytochemicaly analyzed for HMB-45, and S-100 was done. The differential cytologic diagnosis was clear cell sarcoma versus metastatic melanoma. Prompt surgical treatment was indicated. Paraffin-embedded tumor samples were sliced into 5 μm sections and standard stained with H&E. In order to achieve a definite diagnosis, the sections were subsequently analyzed by NSE, S-100, HMB-45 and Melan –A.

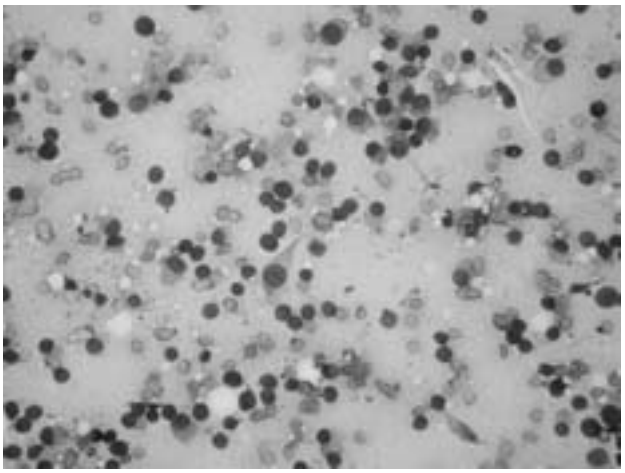

Figure 3. Clear cell sarcoma (MGGx400)

RESULTS

Cytologic findings

The aspirates were very cellular in a relatively clean background. The cells were dispersed, discohesive predominantly single cells and very rare in small clusters. The cells didn't vary much in size and were polygonal with a delicate cytoplasmic process in most of the cells (Fig. 2). There were some spindle cells. Most of the nuclei were round, hyperchromatic, excentrically placed with finely granular chromatin (Fig. 3). Occasional mitotic figures were noted. In a few cells, melanin pigment was seen. Immunostains S-100, HMB-45, EMA and Vimentin were performed. The cells were weakly positive for S-100, HMB-45 and Vimentin, and negative for EMA. Smears from the red, painless tumor formation

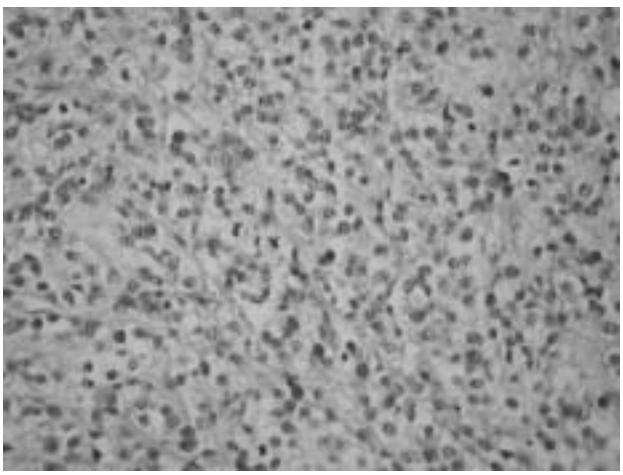

Figure 4. Clear cell sarcoma (H&Ex400)

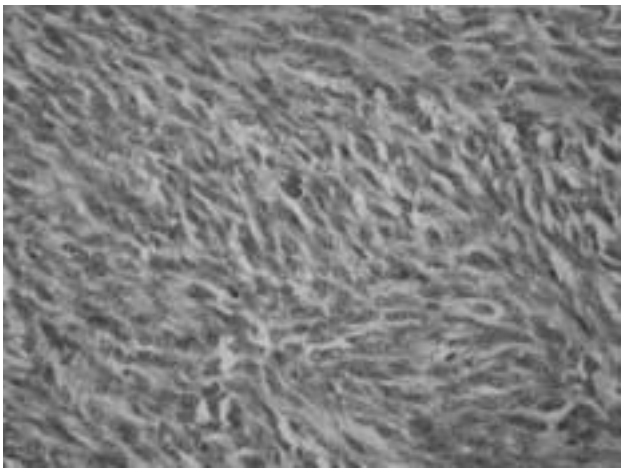

Figure 5. Clear cell sarcoma (H&Ex400)

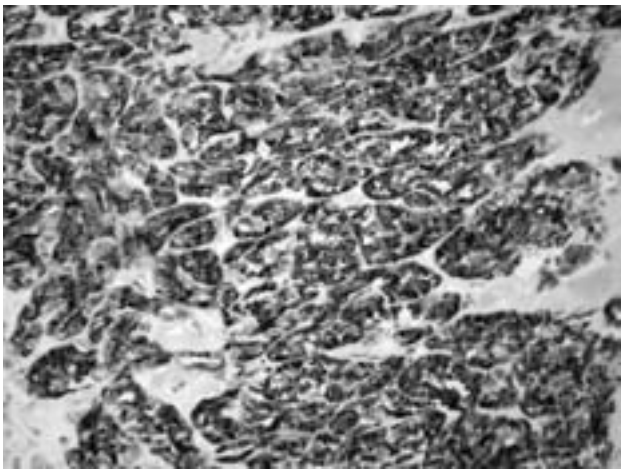

Figure 6. Clear cell sarcoma (HMB-45x400)

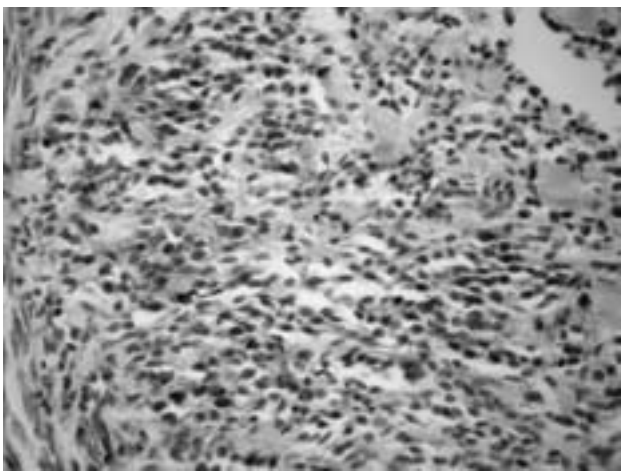

Figure 7. Clear cell sarcoma (Melan-Ax400)

Table 1.

RESULTS OF IMMUNOHISTOCHEMICAL ANALYSIS OF CLEAR CELL SARCOMA

Antibody	Semiquantitive analysis	Descriptive analysis
HMB-45	+++	diffuse, granular
Melan-A	++	focal, fine
S-100	+++	diffuse, granular
NSE	++	focal, fine

on the anterior thigh and from the lymph nodes aspirate were cellular and showed malignant cells with similar features as described before.

Macroscopic examination

The material consisted of a muscle portion and a portion of the fibula. The muscle portion showed knot-shaped tumor tissue, 4x2 cm in diameter, whitish-rosy, firm and partly confined in cross section. There were some areas of necrosis and hemorrhage.

Histopathological findings

Diagnosis was established in H&E samples thanks to strongly nested or packed architecture of large, polygonal or spindle tumor cells having clear or palely eosinophylic cytoplasm with vesicular nuclei and prominent brightly eosinophylic nucleoli (Fig. 4 and 5). Very few cells were seen with intracytoplasmatic pigment.

Immunohistochemical analysis without any doubt confirmed the origin of tumor cells showing melanoma/melanocytic differentiation which includes clear cell sarcoma (Table 1). All used markers were positive; predominating ones were HMB-45 (Fig. 6) and S-100 with diffuse granular and dusty intracytoplasmatic staining, respectively, while NSE and Melan- A (Fig. 7) showed focal positive reaction.

DISCUSSION

CCSSP, first reported and named by Enzinger in 1965, was for some time thought to be histogenetically related to MM, owing to the presence of melanin pigment and the ultrastructural finding of melanosomes (1). It is now clear that CCSSP has only a phenotypic resemblance to MM; the characteristic translocation of CCSSP

present in 50-75% of cases, is not seen in cutaneous and uveal MM (2, 9).

FNA of CCSSP usually yields cellular smears with typical malignant cytological features. However, these features are not pathognomonic of CCSSP. FNA cytology findings of about 20 cases have been described in the cytology literature (12,23-28).

The cytologic features described include highly cellular smears containing cohesive groups and dispersed single cells. The cells are round to polygonal or fusiform with abundant cytoplasm (often clear), excentric nuclei, intranuclear inclusion, and either one prominent or two to three smaller nucleoli. The presence of melanin is unusual and has been described in only four of all described cases. In two cases, melanin was seen predominantly in macrophages (24), while in the other two cases (28, 29) melanin was seen in the tumor cells. In the presence of melanin, the differential diagnosis is narrowed to two entities: metastatic melanoma and clear cell sarcoma. Typical cytological features with positive immunoreactivity for S-100 and HMB-45 will be able to distinguish CCSSP from these entities.

The distinction could also be assisted by clinical findings. CCSSP is more deeply located, it is intimately associated with tendons or aponeurosis, and lack epidermal involvement and junctional changes. Metastatic malignant melanoma of soft tissue is located more superficially and rarely involves tendons and aponeurosis; it is common in the head and neck and trunk region, which is an uncommon location for CCSSP.

In the absence of melanin, the diagnosis of clear cell sarcoma by FNA is difficult to suspect. The differential diagnosis would include synovial sarcoma, alveolar soft part sarcoma, epitheloid sarcoma, and other spindle cell sarcomas, such as fibrosarcoma, leiomyosarcoma and malignant schwannoma.

In our case, the cells were dispersed, discohesive predominantly single cells and very rare in small clusters. The cells didn't vary much in size and were polygonal with a delicate cytoplasmic process in most of the cells. There were some spindle cells. Most of the nuclei were round, hyperchromatic, excentrically placed with finely granular chromatin. Occasional mitotic figures were noted. In just a few cells, melanin pigment was seen.

Clonal abnormalities are seen in CCSSP and chromosome 22 is consistently involved in the reported cases (6-10). In these reports reciprocal translocation t(12:22)(q 13:13) appears to be characteristically associated with CCSSP. In our case, there were the same clonal abnormalities.

Detection of this translocation in cytologic specimens would provide an added dimension in the preoperative diagnosis of CCSSP.

CONCLUSION

A definitive diagnosis of clear cell sarcoma of soft parts is possible by FNA despite a lot of difficulties, especially because melanin is usually absent.

Although most of CCSSPs can be easily diagnosed as malignant neoplasm by fine-needle aspiration (FNA), establishing the diagnosis of CCSSP on primary tumors could be difficult in distinguishing them from other sarcomas in similar locations and age groups.

This case report and the literature review provide ample evidence for the belief that preoperative definite FNA diagnosis of primary CCSSP can be rendered, if immunocytochemistry is used in addition to cytomorphology in a suitable clinical setting. Unfortunately, out patient came late and it wasn't possible to make amputation because of the spread of the disease. The patient died one year after.

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Received for publication: October 30, 2004

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