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CLEAR CELL SARCOMA MIMICKING A BREAST TUMOR IN AN ELDERLY MAN: A RARE CASE REPORT AND A LITERATURE REVIEW

E. ZAPPETTINI[1], S. CASTILLA[2], B. VALENTE[3], A. CUCCI[4], S. FERNÁNDEZ[5]

[1]Surgery Department, Magdalena´s Hospital, National University of La Plata, Magdalena, Buenos Aires Province, Argentina
[2]Radiologist Department, Magdalena´s Hospital, National University of La Plata, Magdalena, Buenos Aires Province, Argentina
[3]Surgery Department, Magdalena´s Hospital, National University of La Plata, Magdalena, Buenos Aires Province, Argentina
[4]Internist Clinician, Magdalena´s Hospital, National University of La Plata, Magdalena, Buenos Aires Province, Argentina
[5]Head of Surgery Department, Magdalena´s Hospital, National University of La Plata, Magdalena, Buenos Aires Province, Argentina

Abstract – *Objective:* *Clear Cell Sarcoma (CCS) is a rare tumor of mesenchymal origin accounting for 1% of soft tissue sarcomas (STS)[1]. Often misdiagnosed as malignant melanoma[2] (MM), it has only one curative treatment: radical surgery and an extensive postoperative follow-up program2. Herein, we present a case of CCS mimicking a right breast tumor, where the patient´s age, gender, growth and localization of the neoplasm render it uncommon.*

Case presentation: *A 70-year-old male was admitted to the Surgery Department complaining about a 3-month right breast tumor. Ultrasound evidenced a nodular formation (2.29 cm-1.91 cm) and mammography showed a hyperdense image, projected 35 mm from the nipple, surrounded by calcifications. No signs of systemic disease were present. Core needle biopsy expressed histological characteristics compatible with both MM and CCS.*

Results: *After multidisciplinary team meeting, a wide resection surgery was performed followed by lymphadenectomy. The immunohistochemistry and pathology report led to the diagnosis: CCS.*

Conclusions: *CCS is a rare sarcoma with poor prognosis. This case is exceptional due to its epidemiology, unusual clinical manifestations and appearance, setting CCS up as a new differential diagnosis to keep in mind regarding breast tumors. Its extreme rarity could help other colleagues deal with this infrequent presentation.*

KEYWORDS: *Clear cell sarcoma, Soft tissue, Breast, Surgical treatment, Epidemiology, Malignant melanoma.*

INTRODUCTION

CCS is a rare[1] and aggressive[2] STS. This condition is so unusual that there is a lack of strong scientific evidence to support it, which is why the information available[3-12] arises mainly from case reports and reviews.

This tumor usually affects children and young adults[2], especially around the lower extremities[1,2]. It often appears as a small mass[2] with slow

Corresponding Author: Emmanuel Angel Zappettini, MD; e-mail: eazappettini@med.unlp.edu.ar

growth[4,6], but this indolent aspect is not consistent with its bad prognosis[2,5-7]. It is, therefore, not surprising that, by the time of diagnosis, CCS has affected lymph nodes[4,9] and also developed distant metastases[2,5].

The final diagnosis[4], only achievable with Fluorescent *In Situ* Hybridization or Reverse Transcription Polymerase Chain Reaction (RT-PCR), is difficult to obtain regarding the similarities with another neoplasm, malignant melanoma[2]. Wide surgical resection[1,4,8] surrounded by a rim of healthy tissue[2,9] remains the most effective treatment up to date associated with radiotherapy[2,9] and, sometimes, with chemotherapy[2,9]. An accurate follow up program[2,6,9] is mandatory, guided by images and clinical exam during the first three years.

The aim of this work is to report a case of CCS mimicking a breast tumor, presenting it through an epidemiological, clinical and therapeutic approach, highlighting the value of its differential diagnoses. This case suggests a management standard, but also emphasizes the difficulties of investigation and diagnosis in a rare presentation of a strange disease. Surgical oncologists should be aware of this rare pathology and emphasize the importance of and early involvement of the multidisciplinary team[8,9], in order to avoid patient morbidity and mortality.

CASE REPORT

A 70-year-old farmer was admitted to our Department with a 3-month mass on the right breast, complaining about local itching and burning pain. His pathological history evidenced cholecystectomy (2007) and Parkinson's disease (levodopa 1 gram per day). Physical examination revealed a rounded and painful mobile mass in the right breast with increased consistency (Table 1).

Suspecting a breast tumor and following the breast cancer protocol of the Rural Hospital "Santa María Magdalena", the patient underwent triple assessment with X ray, ultrasound and mammography: breast biomarkers were negative and chest x ray was normal. Breast ultrasound showed a solid nodular formation with defined edges (2.29 cm-1.91 cm). Abdominal ultrasound revealed no signs of oncological disease. Finally, mammography (Figure 1) evidenced a hyperdense nodular image at the right upper quadrant with irregular margins, projected 35 mm from the nipple, surrounded by isolated calcifications. Core needle biopsy was performed, showing histological characteristics compatible with both malignant melanoma and clear cell sarcoma.

After a multidisciplinary team met and considered the uniqueness of this patient (elderly, with Parkinson´s disease, living alone in the countryside, no relatives known, with threats to patient follow-up and possible low adherence to adjuvant treatment), it was decided to perform a wide resection surgery (Figure 2), and the tumor was fully dissected (Figure 3). Due to the finding of a palpable lymph node, a sentinel lymph node mapping was performed, followed by lymphadenectomy.

The tumor was encapsulated and well demarcated from all surrounding structures. Characteristic nested growth pattern and fibrous bands were present. Cells were of epithelioid habit, multinucleated, with palely eosinophilic cytoplasm and increased nucleus-cytoplasm ratio. The resection margin was free of neoplastic injury, no necrotic area was present and very few mitosis existed. Only one of the 9 lymph nodes was positive for cancer. Cells stained positive for Vimentin, S-100 and Ki67 with low proliferative index (Figure 4). Reverse Transcription Polymerase Chain Reaction (RT-PCR) made in Buenos Aires confirmed the final diagnosis: Clear Cell Sarcoma (CCS).

The postoperative period was normal, and the patient was discharged on the 3rd postoperative day. The multidisciplinary team indicated adjuvant radiotherapy and chemotherapy, with an active follow-up including magnetic resonance imaging every three months.

TABLE 1.

Epidemiology	*Clinical presentation of the mass*	*Signs and Symptoms*
• Age: 70 • Gender: Male • Comorbidities: 1. Cholecystectomy 2. Parkinson's disease.	• Pain (burning) • Itching • Mass • Evolution time: 3 months	Shape: rounded • Size: less than 5cm • Consistency: increased • Mobility: mobile • Margins: irregular • Calcifications: yes • Biopsy: yes (Core Needle Biopsy)

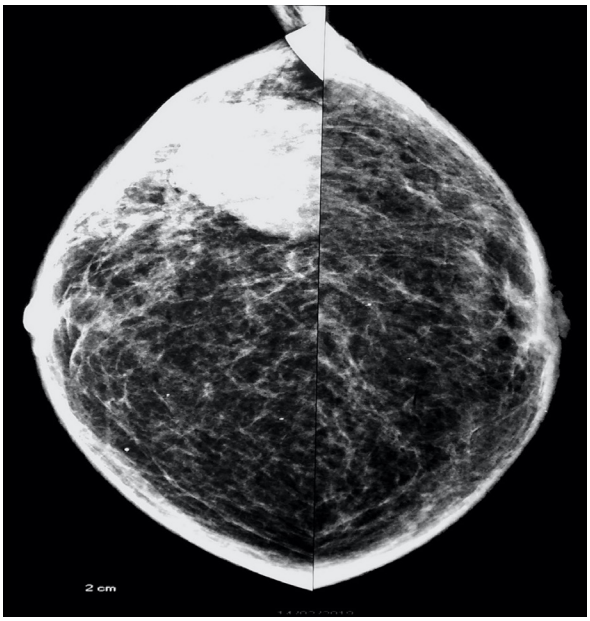

Figure 1. A hyperdense nodular image with irregular margins, projected 35mm from the nipple, surrounded by isolated calcifications.

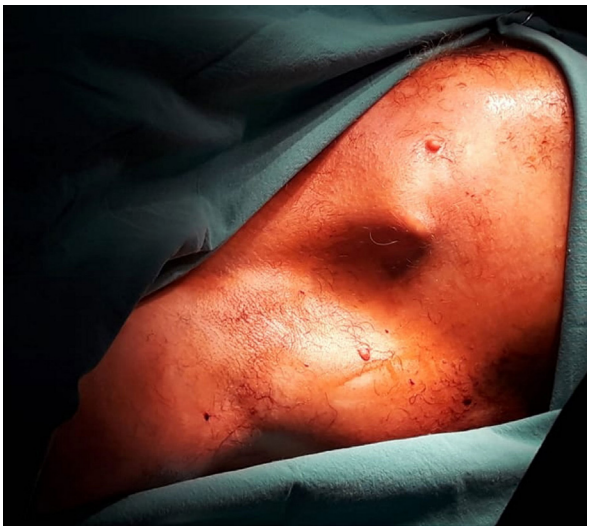

Figure 2. The tumor arising from the right upper quadrant close to the nipple.

DISCUSSION

CCS is a rare tumor of mesenchymal origin accounting for 1% of STS[1]. Firstly described by Enzinger[1,2] in 1965, it is related to a few known risk factors[2], such as radiation, lymphedema, foreign body implants, and exposure to arsenic or vinyl chloride.

CCS mostly affects children[3] and young adults[4], with a female predominance[5] and slow growth[4,6]. It presents as a small mass that involves lower extremities[2] (adjacent to tendons, aponeuroses, or fascial structures), with localized pain[1] or near tumor site[5]. The principal diagnostic imaging is Magnetic Resonance Imaging[2,6] (MRI), which can identify the tumor and its relations to blood vessels, nerves, periosteum and fascia. Also, a PET scan might be used to evaluate the patient´s status and plan radical surgery[2].

In 81-97% of the cases, CCS and MM share[2] some melanocytic markers: S-100, Human Melanoma Black-45, Melanoma antigen and microphthalmia-associated transcription factor, but a peculiar feature of CCS is the presence of the EWSR1-ATF1 oncogene[7]. The final diagnosis can be obtained by Fluorescent *In Situ* Hybridization or RT-PCR[4], which can identify that gene and provide a differentiation between the two diseases. Differential diagnosis[2] includes malignant peripheral nerve sheath tumor, synovial sarcoma, dermal melanocytic tumor, melanoma metastasis and melanotic schwannoma.

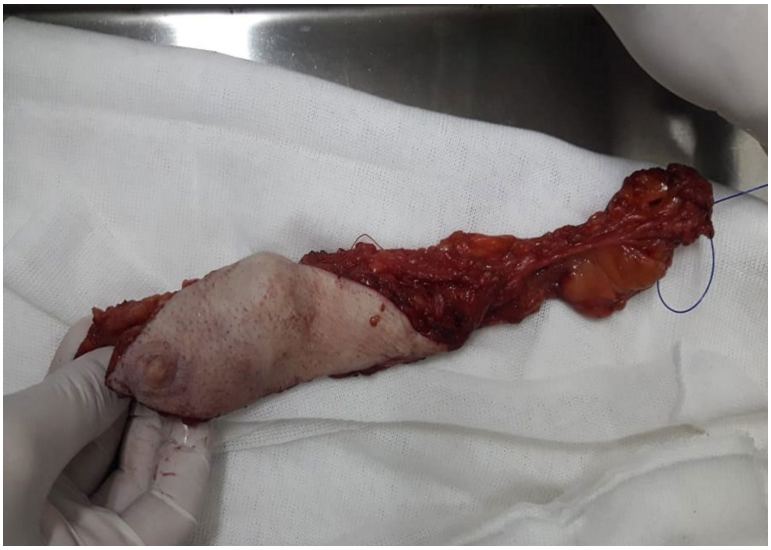

Figure 2. The resected tumor with the axillary lymphadenectomy.

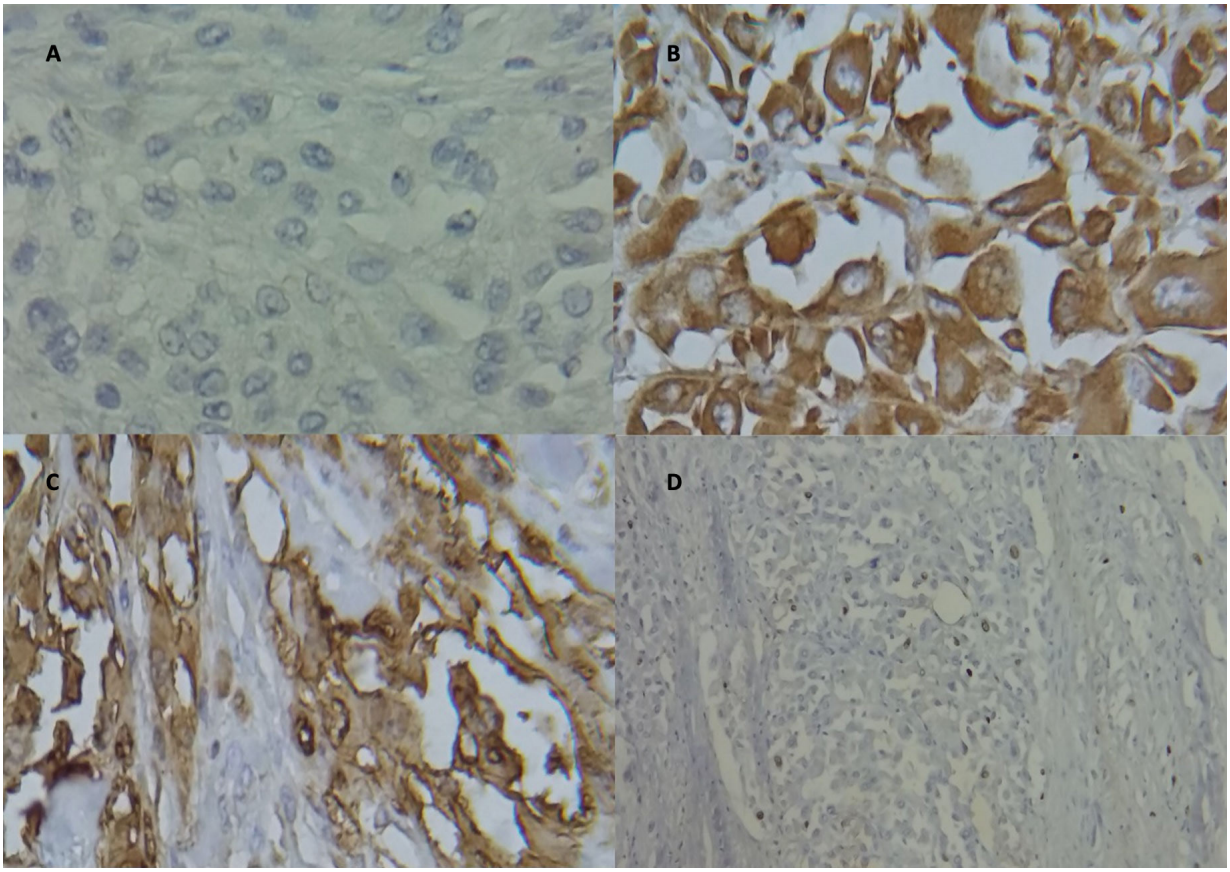

Figure 4. Immunohistochemistry (A: CKAE1AE3 negative 400X; B Vimentin positive 400X; C S-100 positive 400X; Ki67, low proliferative index, 100X).

The main treatment[1,4,8] with curative[2] intention is surgery, consisting in an en bloc excision with R0 margins, removing the tumor in a single specimen with a rim of normal tissue around it[2,9]. The safety margin should be, at least, of 1 cm[2,10]. Amputation[2] of a compromised limb is not recommended, except when blood vessels or nerves have been invaded[1]. CCS involves lymph nodes at an early stage[1], even at the time of first diagnosis[4,9]. Some reports express the advantage of performing sentinel node procedure to achieve a complete oncologic resection, but the accuracy of this method is left to be understood[2]. Haematogenous metastasis usually affects lungs[2] and local recurrence affects 20% to 84% of the patients[2,5]. The role of Chemotherapy[2,9,10] still remains conflicting in CCS, with controversial results in different studies. In essence, CCS is considered primarily a chemo-resistant sarcoma[11]. Some trials were conducted with Immunotherapy[11] (using sorafenib, sunitinib and tinvatinib) with a certain clinical benefit. Radiotherapy is used after surgery as a classical treatment[9], but also when surgery cannot guarantee a free safety margin or when surgery is not feasible[2]. Nowadays, there is an overall shift towards the use of preoperative radiotherapy, mainly when the goal is to protect critical structures[9].

The prognosis[2,5,6,7] is bleak with a low 5 to 10-year survival rate. Negative prognostic factors[2,5] are necrosis under microscopic examination, mitotic index, tumor margins, anatomic location and size[6]. A strict follow-up program[2,6,9] is recommended every 3 months in the first 3 years: clinical examination, chest X-ray, MRI and PET scan might detect metastases and local recurrence. However, just as there are no specific guidelines for the management of CCS[10], there is also no specific follow-up program for this sarcoma[12]. All of the aforementioned must be developed under the supervision of a multidisciplinary team[8-10] (with surgeons, pathologists, radiologists, medical oncologists, radiation oncologists, etc.), sometimes tailoring the approach to each patient and specific histiotype[12], in order to achieve better outcomes. It has been demonstrated that a dedicated tumor board[11] is associated with an improvement of 5% in the 2-year disease-free survival, whereas its absence has been recognized as a novel poor prognostic factor for STS.

CONCLUSIONS

CCS is a rare sarcoma with poor prognosis because of an unpredictable course[5] and a late medical consultation. The characteristics of this case contrast with the evidence that emerges from the cited bibliography, establishing CCS as a new differential diagnosis to take into account in relation to breast cancer. Its extreme rarity could help other colleagues deal with this infrequent presentation.

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ORCID ID:

Emmanuel Zappettini **https://orcid.org/0000-0001-8044-010X**

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The study was approved by the Ethical Committee of our Institutions. The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have gave given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Consent for publication:

The consent to publish had been taken from each participant in this work.

Competing interests:

The authors declare that they have no competing interests.

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