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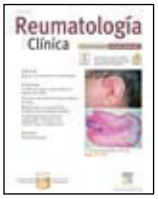

Original article

Synovial sarcomas in Lugo between 2002–2006

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ABSTRACT

Objective: To study the clinical and epidemiological characteristics of all adults patients as having synovial sarcoma in the Hospital Xeral-Calde (Lugo) between 2002 and 2006.
Patients and method: We conducted a retrospective study of the case records of all adults patients diagnosed with synovial sarcoma from January 2002 through December 2006. Patients were considered to be adults if they were more than 18. In all cases a tissue-biopsy sample showing synovial sarcoma was required. The Hospital Xeral-Calde is the only referral center for a population of almost 250 000 people.
Results: Four cases (3 women) met the classification criteria for this study. The mean age was 35 years old (range, 22–41).
The most common presentation was a palpable mass (mean, 6.7 cm) associated with pain in lower extremities. The mean delay for the diagnosis was 17 months, but in one case has been noted as long as 2.5 years. Unlike the neck synovial sarcoma case, a long delay in the diagnosis implied a major tumor size and a higher histological stage.
The mean follow-up was 25.5 months; one patient died 1.5 years after the diagnosis.
Conclusions: The overall annual incidence rate of synovial sarcoma in the Lugo region between January 2002 and 2006 for the population older than 18 years was a minimum estimate 0.32/10.5 Better physician awareness may contribute to the progressive increase in the recognition of this condition, especially in young people presenting with palpable mass. A long delay at the diagnosis implied a poor prognosis.

Sarcomas sinoviales en el área sanitaria de Lugo en el período de 2002 a 2006

Palabras clave:
Sarcoma sinovial
Características clínicas
Pronóstico
Mortalidad

RESUMEN

Objetivo: Estudiar las características epidemiológicas y clínicas de todos los pacientes adultos diagnosticados de sarcoma sinovial (SS) en el período de 2002 a 2006 en el Hospital Xeral-Calde de Lugo.
Pacientes y método: Estudio retrospectivo de todos los pacientes mayores de 18 años diagnosticados mediante estudio de anatomía patológica de SS desde enero de 2002 hasta diciembre de 2006. Este hospital da asistencia sanitaria a 250.000 habitantes.
Resultados: Un total de 4 casos (3 mujeres) cumplían los criterios establecidos para este estudio, con edades comprendidas entre los 22 y los 41 años (media de 35 años).
El motivo de consulta fue tumoración (media de 6,7cm) y dolor predominantemente en las extremidades inferiores. El retraso diagnóstico promedio fue de 17 meses, aunque en algún caso se llegó a los 2,5 años. Excepto para el caso de SS de localización cervical, un mayor retraso al diagnóstico se correlacionó con un mayor tamaño del tumor y un estadio más avanzado.
El seguimiento medio de los enfermos fue de 25,5 meses. Un paciente falleció al cabo de un año y medio del diagnóstico.

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Conclusiones: El promedio de incidencia mínima estimada de los SS en mayores de 18 años en el área de Lugo fue de 0,32 por cada 105 habitantes al año. A pesar de su baja incidencia, ante una persona joven que presenta una masa, a veces dolorosa, en las extremidades inferiores, debe incluirse el SS en el diagnóstico diferencial. Un mayor índice de sospecha por parte de los médicos puede evitar un diagnóstico tardío.

Introduction

Soft-tissue sarcomas represent less than 1% of all tumors in adults. In this group, synovial sarcomas (SS) represent between 5% and 10%. They are highly aggressive and 10% of patients die within the first year after diagnosis.[1,2] The common clinical presentation is that of a yuxta-articular palpable mass which is generally painful. Because of its low index of clinical suspicion it can be mistaken for a benign soft-tissue tumor, bursitis, or arthritis, which leads to a delay in the diagnosis. This diagnostic delay can be of more than a year.[3,4,5,6]

The authors of this study set out to describe the epidemiological and clinical characteristics of all of the adult patients diagnosed with SS, seen during a period that went from 2002 to 2006 in the health jurisdiction of the Hospital Xeral-Calde of Lugo.

Patients and method

The clinical histories of all patients over 18 years of age who had been diagnosed through a biopsy study proving SS were analyzed in this health jurisdiction, starting in January 2002 until December 2006. This hospital attends 250 000 inhabitants and, due to its characteristics, offers no pediatric assistance.

The epidemiological and clinical characteristics (age at diagnosis, gender, motive for consultation, localization of the tumor, size, diagnostic delay, toxic habits, prior biopsy, histological pattern, immunohistochemistry [IHC], stage, prognosis, mortality, and mean time from diagnosis to the end of the study or death) for each one of the cases was determined.

IHQ techniques included epithelial membrane antigen, S100, and CD99 proteins, among others. With regard to the cell type (epithelial or fusiform) 3 distinct histological patterns were established: *a)* biphasic (coexistence of epithelial and fusiform cells); *b)* monophasic (predominance of a cell linage); and *c)* poorly differentiated (with poorly differentiated areas). For their classification in degrees, as in other soft-tissue sarcomas, we applied FNCLCC (French Federation Nationale des Centres de Lutte Contre le Cancer). This classification combines 3 parameters: degree of differentiation, mitotic activity, and necrosis. In this manner, there are 4 stages, ranging from the most benign (stage I) to stage IV which would be any tumor with lymph node affection or distant metastasis.[7]

For the prognostic evaluation, all of the patients must have had at least a 12 month follow-up. Finally, a PubMed search with the terms "synovial sarcoma," "clinical features," and "follow-up" was performed and as well as in databases that included relevant specialized journals.

Results

In the study period from January 2002 to December 2006 (including both) we found 4 cases of SS (Table), reflecting a minimal estimated incidence average in patients over 18 years of age of 0.32 cases per 100 000 inhabitants.

Of the 4 cases, 3 were female and 1 male, with ages between 22 and 41 years (mean, 35 years of age).

The motive of consultation was tumor and pain in a determined anatomical area, more frequently on the lower extremities. The size of the tumor at the moment of consultation oscillated between 1 and 16 cm (mean, 6.7 cm). From the appearance of symptoms, the average diagnostic delay was 17 months, although in one case it reached 2.5 years. Longer delays correlated with a greater size of the tumor and a more advanced stage. However, it must be pointed out that the SS with a cervical localization caused pain to the patient at least 2 years before and the size of the tumor was smaller than the midfoot SS. All of the patients underwent simple x-rays and magnetic resonance (MR). The x-rays were of help in cases with advanced stages. In the case of the male with a midfoot tumor (stage III), simple x rays showed an increase in soft-tissue opacity between the fourth and the fifth metatarsal bones, and a fracture of the cortical bone of the fourth adjacent metatarsal (Figure). In the case of the thigh SS (stage IV) we observed, apart from the increase in soft tissues, a periosteal widening compatible with periostitis. MR was the technique of choice, both for diagnosis as for deciding how to surgically approach the lesion.

Tissue samples were obtained through a previous biopsy in 2 cases (one through aspiration biopsy with a fine needle and the other one through an incisional biopsy). In the other cases, the biopsy took place along with the excision of the lesion. Half of the patients had a biphasic histological pattern, corresponding to a higher stage (stages III and IV). All of the patients underwent surgery that left tumor-free surgical border (6 to 8 cm) or the amputation of the affected limb at different heights. Two cases also received radiotherapy and chemotherapy. In this center, all of the patients with advanced stages of the disease are included in a protocol of adjuvant chemotherapy.

The mean follow up of the patients was 25.5 months. During follow-up, the patient with the tumor on the thigh and an advanced stage (stage IV) died after a year and a half since diagnosis.

Table
Epidemiological and clinical characteristics of patients 18 and older diagnosed with synovial sarcoma in the Hospital Xeral-Calde of Lugo from January 2002 to December 2006

Age at y	Gender	Localization	Size, cm	Motive of consultation	Diagnostic delay, mo	Histological pattern	Diagnostic	Death	Mean time since diagnosis to the end of the study or death, mo diagnosis
22	F	Median gastrocnemius right leg	0.8	Tumor and pain	2	Monophasic	I	No	54
37	F	Right paravertebral cervical C4-C5	4	Pain	24	Monophasic	II	No	18
41	F	Posteromedial compartment of right thigh	16	Tumor	30	Biphasic	IV	Yes	18
39	M	Left midfoot	6	Tumor and pain	12	Biphasic	III	No	12

F indicates female; M, male.

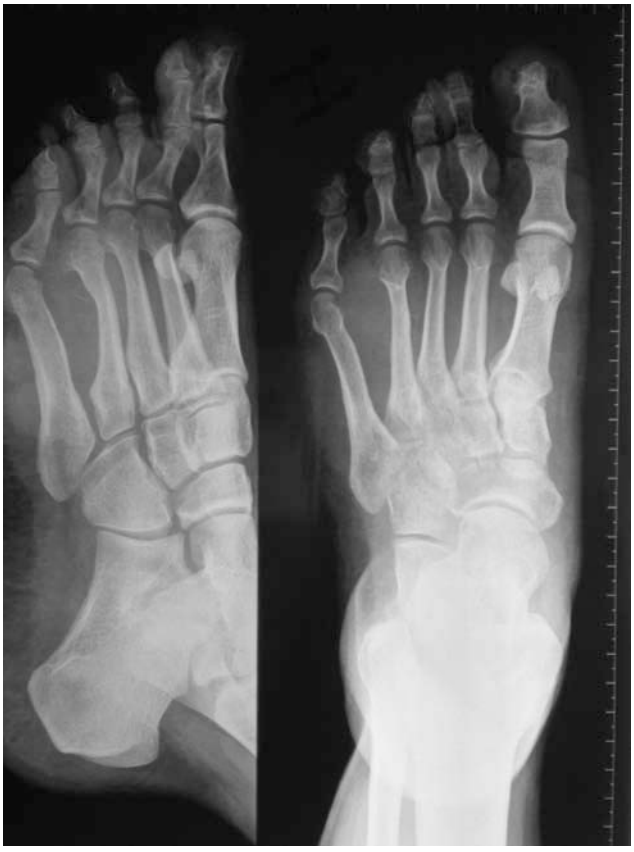

Figure. Simple x-ray of the left foot in 2 projections, showing an increase in soft tissue opacity between the fourth and the fifth metatarsal bones and a fracture of the cortical bone of the adjacent fourth metatarsal.

Discussion

The present study has found 4 cases of SS during 5 years, reflecting an average minimal estimated yearly incidence in adults of 0.32 per 100 000 inhabitants. After excluding patients under 18, the mean age at the moment of diagnosis was 35 years with a predominance of women (3:1). As has been described in the medical literature,[8] initial clinical signs were the presence of an occasionally painful mass, frequently on the lower extremities (3 cases). Its preferred localization was para-articular regions, in association with tendon sheaths, serosal pouches, and joint capsules. The primary intra-articular localization is exceptional.[9]

Its slow growth and benign appearance leads to SS being the soft-tissue sarcoma with the greatest diagnostic delay.[3] Generally, a greater diagnostic delay correlates with a greater tumoral size and a more advanced stage; however, in the present study, the case of a cervical localization was the exception (Table). This finding may be due to the high prevalence of cervical pain in the general population, a fact that may have masked the onset of a later SS.

Simple x-rays were useful in advanced cases and therefore not useful for early diagnosis. In approximately 25% of cases, calcifications have been seen in the interior of the tumor. Between 15% and 20% of cases a periosteal reaction, surface erosion of the bone or its invasion has been seen. Mass destruction of the bone is rare and is only a product of large, poorly differentiated sarcomas with a longer progression.[3] In the present study, MR was the technique of choice for its diagnosis.[10] Synovial biopsy yielded enough material to determine the histological pattern and perform IHC, leading to a diagnosis of certainty. Over 90% of SS contains a characteristic translocation between chromosomes X and 18. Its presence allows for the definite diagnosis, even in cases with atypical clinical and histological findings. This translocation, t(X;18) (p11,2;q11,2), fuses the *SYT* gene of chromosome 18 to one of its homologous genes (*SSX1, SSX2,* and *SSX4*) localized on chromosome X.[1,8] Once the diagnosis of SS is confirmed, the treatment performed was radical surgery, occasionally accompanied by radio and chemotherapy.[1,2,3] The presence of fusion protein SYT-SSX could be useful as a tumor specific therapeutic target or for immunological treatment. Suppression of this target could inhibit the growth of SS cells.[1,8] Long-term survival varies according to tumor size and localization, histological stage and the presence of lymph node affection or metastasis, which can reach 50% to 60% at 5 years.[11] Mortality in the present study was found to be 25%, something that was related to tumor size and histological stage at the moment of diagnosis.

In conclusion, and in spite of its low incidence, when faced with a young patient with a sometimes painful mass son the lower extremities, one must include SS in the differential diagnosis. A greater suspicion index for the physicians may avoid a late diagnosis.

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