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ORIGINAL ARTICLE

Enchondroma versus low grade cchondrosarcoma in the appendicular skeleton: Clinical-radiological criteria

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KEYWORDS
Enchondroma;
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Abstract
Objectives: To determine the validity of the clinical-radiological characteristics with the biopsy, and contrast the biopsy results with the clinical diagnosis based on the history and radiological tests.
Material and method: The study included 96 patients with cartilage type lesions suggestive of an enchondroma (E) or a low grade chondrosarcoma (LGC) according to the clinical and X-ray data, the anamnesis, physical examination, simple X-ray, computerised tomography (CT), nuclear magnetic resonance (MRI) and a Technetium-99 bone scan of the whole skeleton. The hypotheses were contrasted with the histopathological diagnosis of enchondroma or low grade chondrosarcoma.
Results: Of the 82 patients studied completely, 56 were considered enchondromas (68.29%), 8 as chondrosarcomas (8.33%) and in 18 (18.75%) a definitive diagnosis could not be made and were considered as suspected LGC. Of these, the biopsy showed 3 enchondromas (25%), 9 LGC (50%) and 3 were not definitive (and were treated as LGC).
On the other hand, of the 56 cases diagnosed as enchondromas, 15 were biopsied, with 5 of them being diagnosed as LGC (33.3%). The 8 cases diagnosed as LGC, were also biopsied and only 4 biopsies (50%) confirmed the initial diagnosis.
None of the clinical-radiological characteristics study showed any statistically significant differences that would enable them to be associated with an E or an LGC. Likewise, the correlation analysis between the diagnosis issued initially and the biopsy result gave a value of 0.69 (kappa coefficient), which was considered a good correlation.
Conclusion: The clinical-radiological diagnosis inferred from the clinical picture and the imaging test did not have definitive validity when deciding on simple observation or biopsy and treatment in these patients.

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PALABRAS CLAVE
Encondroma;
Condrosarcoma;
Tumor;
Condral

Encondroma versus condrosarcoma de bajo grado en el esqueleto apendicular. Criterios clínico-radiológicos

Resumen
Objetivos: Determinar la validez de las características clínico-radiológicas con la biopsia y contrastar los resultados de la biopsia con el juicio clínico basado en la historia y las pruebas radiológicas.
Material y método: Se incluyó a 96 pacientes con lesiones de aspecto cartilaginoso indicativas de encondroma (E) o condrosarcoma de bajo grado (CBG) según los datos clínicos y radiográficos, la anamnesis, la exploración física, la radiografía simple, la tomografía computarizada, la resonancia magnética y la gammagrafía ósea con tecnecio 99 de todo el esqueleto. Las hipótesis se constataron con el diagnóstico anatomopatológico de E o CBG.
Resultados: De los 82 pacientes estudiados completamente, se consideró que 56 presentaban E (68,29%), 8 presentaban condrosarcomas (8,33%) y en 18 (18,75%) no se pudo emitir un juicio definitivo y se consideró la sospecha de CBG. En estos casos, la biopsia mostró 3 E (25%), 9 CBG (50%) y 3 no fueron definitivos, por lo que se trataron como CBG.
Por otra parte, de los 56 casos juzgados como E, se biopsiaron 15 y se diagnosticó a 5 de CBG (33,3%). Los 8 casos juzgados como CBG se biopsiaron y solo 4 biopsias (50%) confirmaron el juicio inicial.
Ninguna de las características clínico-radiológicas estudiadas mostró diferencias estadísticamente significativas que permitieran asociarlas al diagnóstico de E o CBG. Asimismo, el análisis de correlación entre el juicio emitido inicialmente y el resultado de la biopsia arrojó un valor de 0,69 (coeficiente κ), lo que se considera una correlación buena.
Conclusión: El juicio clínico-radiológico emitido a partir de la clínica y las pruebas de imagen no ha tenido validez definitiva a la hora de decidirse por simple observación o por biopsia y tratamiento en estos pacientes.

Introduction

The diagnosis of bone tumours includes the evaluation of multiple clinical, epidemiological, radiological and pathological parameters. The first normally point the physician more or less towards the final diagnosis, but the last word generally lies with the analysis of the biopsies obtained. However, there are some situations in which the pathology findings do not completely define the nature of the lesion studied. In these cases, clinical-radiological criteria take on special importance in terms of directing the diagnosis and treatment. In the group of cartilaginous tumours, there are 2 entities that lead to confusion when analyzed under the microscope: enchondroma (E), a benign condition, and low grade chondrosarcoma (LGC), a malignant tumour of scant aggressiveness. The difficulties in distinguishing these pose a problem, as the treatment is different (observation and monitoring for E and resection in the case of LGC). The goals pursued in this paper were, on the one hand, to determine the validity of the clinical and radiographic characteristics, based on data from anamnesis, physical examination, simple X-ray, computerized tomography (CT), magnetic resonance imaging (MRI) and full-skeleton bone gammagraphy using technetium (Tc) 99, compared with the biopsy results and, on the other hand, to contrast the results of the biopsy with the physician's clinical judgement based on the case history and the radiological tests carried out prior to knowing the biopsy outcome.

Patients and methodology

We have performed a prospective study in 96 patients, 22 males and 73 females, with a mean age of 51 years, mostly (84.4%) above 35 years of age. The patients had been treated at 4 centres and had been included on the databases of these centres as well as on the databases of the pathology department of one of the centres. The patients studied presented a lesion of cartilaginous appearance indicative of E or LGC depending on the clinical-radiological data reflected on their histories. The hypotheses were contrasted with the pathology department's diagnosis of E or LGC. Patients under 18 years of age were excluded as were those with enchondromatosis or osteochondromatosis, secondary chondrosarcomas on top of prior osteochondromas, cartilaginous lesions localized in the hands and axial skeleton and chondrosarcomas with a degree greater than i according to Evans's classification (Table 1).

A template was completed for each patient with clinical and radiographic information including their personal details, their original centre, the details of the physical examination, symptoms and their progress, with particular emphasis on pain. The group was divided by age between those over 35 and those aged 35 and less. The localization of the lesion was recorded taking into account the laterality, the bone and the part of the bone. As for the radiological images, from the simple X-ray the size and location of the lesion was assessed, together with the

Table 1 Evans's classification

	Enchondroma	Low grade chondrosarcoma
Clinical presentation	• Younger patients (casual finding in adults) • Rarely painful • Appendicular skeleton in general (a cartilaginous tumour in the phalanges is almost certainly an enchondroma) • Generally smaller than 5 cm	• Patients over 25 years of age • Accompanied by pain with inflammatory characteristics • In the axial skeleton, a cartilaginous tumour is a chondrosarcoma until proved otherwise • Normally larger than 5 cm
Radiology	• Normally intra-osteal (except enchondroma protuberans) • No periosteal lesion • No endosteal festoons or very mild • Normally no changes over time • Normally no soft tissue mass	• Generally intra-osteal • It usually presents periosteal lesion and associated micro-fractures • Frequent endosteal festoons • It may present changes, such as the disappearance of calcifications, indicating malignization of the lesion • Soft tissue mass
Biopsy	• Typical "boxed-in" appearance • No endosteal festoons • Generally a multi-nodular appearance • Surrounded by lamellar bone • No infiltration of bone marrow	• Invasion of Havers conduits • Periosteal reaction with endosteal festoons • Occasional foci of necroses and haemorrhage • Invasion of bone marrow and cell obliteration • Generally a single mass

degree of calcification and whether there were any changes in the latter. With the CT scan, the degree of calcification was assessed and whether there were any changes in it, as well as the degree of involvement of the cortical bone and, if so, the presence or absence of soft tissue mass (STM). The MRI also allowed assessment of cortical resorption and the presence of STM. With respect to the Tc 99 gammagraphy, regard was had for the presence or otherwise of uptake and if this was larger than, equal to or less than the physiological uptake of the iliac crests (specifically, the anterior superior iliac spine). For all of these assessments, the basis was the description given in the radiological reports from each centre. For each patient, a clinical-radiological judgement of E or LGC was given on the basis of all this information. Finally, the type and result of the biopsy was included (where this had been performed) according to the reports by the pathologists from each centre, confirming or contradicting the prior suspicion. In the case of patients with suspected E who had not presented any kind of clinical or radiological change in the follow-up over 5 years, these were assimilated to the pathological diagnosis of E.

For the statistical analysis, the Excel and SPSS programmes were used to calculate the value of p in each comparison and the correlation coefficient in order to determine the validity of the initial judgement with the biopsy result.

Results

In both the group of those aged more than 35 and that of those under 35, the pathological diagnosis of E (50% and 50%) and of LGC (41.4% and 58.6%) were well distributed, so age was not statistically significant. Most of the patients with a biopsy result of E were women (92.9%) as were the patients with a biopsy result indicating LGC (88.9%), so gender was not statistically significant.

The most frequent localization was in the femur, with a little over half of the cases (52.1%), and there was no marked trend in terms of laterality (48.3% on the right and 50.5% on the left). Quite a marked predominance was found, however, for metaphyseal locations, whether proximal (28.1%), mostly in the humerus, or distal (25.8%), mostly in the femur. None of these characteristics was statistically significant for either of the final diagnoses. Of the lesions studied, 71.2% measured less than 5 cm, whereas the rest were 5 cm or more. All of the biopsies with a result of E measured less than 5 cm and, with regard to LGC, half were smaller than 5 cm and the other half were larger. These findings were not statistically significant ($p>0.05$ in Fisher's exact test). Identification of the lesion was casual in 44.7% of cases, while in 55.3% of cases the diagnosis was triggered by the patient's visit. Neither of these situations was found to be statistically significant for one or other of the diagnoses. Of the patients with pain, 40% were found to have E and 60% LGC, and only 14.3% of patients biopsied did not suffer from pain. Pain showed no statistical significance. Mechanical pain was present in 69.2% of the patients with E and 61.1% of the patients with LGC, so this detail was not statistically significant. As for the physical examination, all the patients found to have E on the biopsy and 94.4% of patients whose biopsies revealed LGC had pain on palpation. This detail too was lacking in statistical significance.

All the lesions studied presented some percentage of calcification. In two cases, calcification presented alterations during evolution (fig. 1). In 60% of cases of E, cortical resorption was seen in the CT scan and in 70.6% of those diagnosed as having LGC. Most corresponded to resorption of one third or less of the thickness of the cortical bone (30% of the cases of E and 64.7% of cases of LGC).

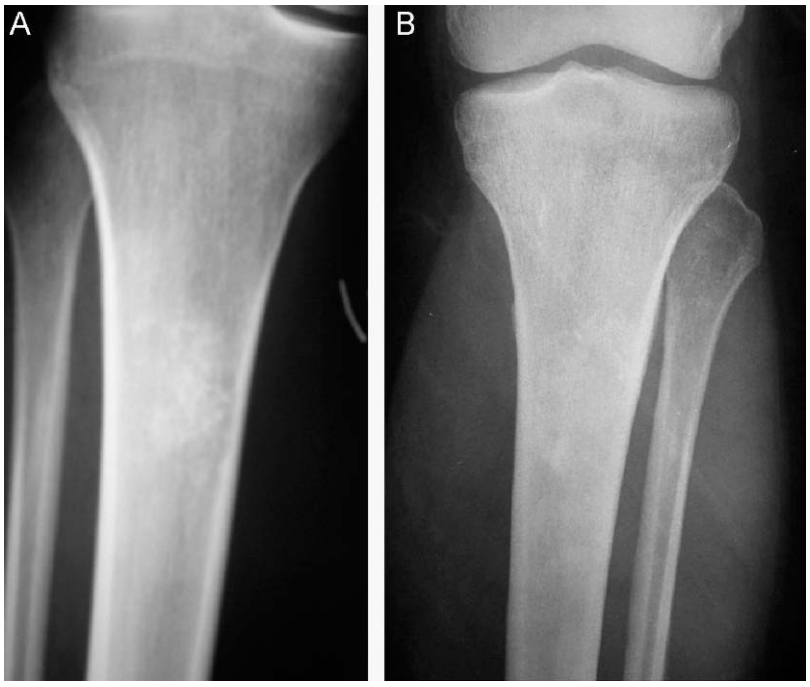

Figure 1 Images of chondral lesion in the proximal tibia, where the calcifications change over time. A) Image from 1994. B) Image from 2000.

There were no cases with presence of STM. In MRI, only 25% of the cases of E and 52.4% of those of LGC displayed resorption of the cortical bone. There was also a predominance of less than a third of this in E (16.7%) and in LGC (42.9%). There was only one case of STM in a patient with LGC. None of these CT or MRI findings was statistically significant despite showing some differences. With regard to the gammagraphies, 100% of patients showed images of uptake for both diagnoses. In the case of E, 60% captured the same, 30% captured more and 10% captured less. For LGC, 52.9% captured the same, 41.2% captured more and 5.9% captured less. There was no statistical significance.

Of the 82 patients studied completely, 56 were considered to present E (68.29%) and 8 chondrosarcomas (8.33%) while in 18 (18.75%) it was not possible to reach a definitive decision, so they were included in the group of clinical-radiological suspicion of LGC and were biopsied. In these cases, the biopsy revealed 3 E (25%), 9 LGC (50%) and 3 were not definitive (as in the previous step, doubtful cases were treated as if they were LGC). On the other hand, of the 56 cases classed as E, 15 were biopsied. The reason for the biopsy in a lesion initially considered to be E was a change in clinical presentation or in the follow-up radiology, and 5 were diagnosed as LGC (33.3%). The 8 cases diagnosed as LGC were biopsied and only four biopsies (50%) confirmed the initial impression. Finally, the Î coefficient gave a value of 0.69 between the initial judgement and the biopsy, implying a moderate degree of concordance (figs. 2-6).

As for the types of biopsies performed, a total of 42 were carried out, of which there was one FNP, 7 percutaneous biopsies with tru-cut, 8 incisional biopsies and 22 excisional biopsies. In 3 cases, it was necessary to use an excisional biopsy to confirm a doubtful tru-cut result. In one case, an incisional biopsy was confirmed with an excisional one.

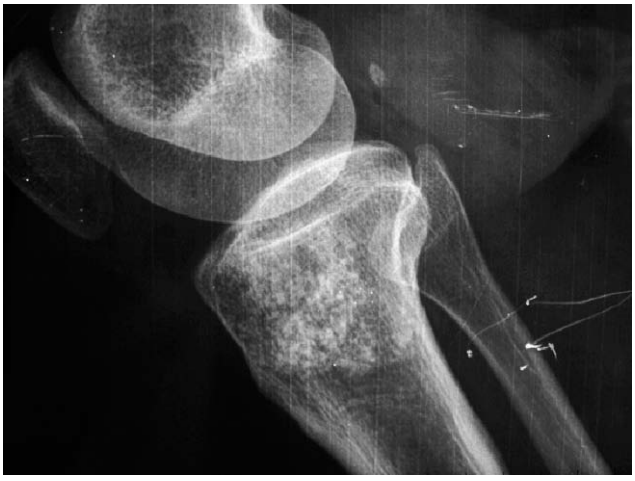

Figure 2 Cartilaginous lesion in the proximal tibia. Malignancy was suspected due to the size. It turned out to be an enchondroma.

There were no significant differences in the correlation coefficient on stratification of the outcomes by type of biopsy effected, which we have attributed to the scant number of patients in each category, except that of incisional or excisional biopsies.

Discussion

The distinction between enchondroma (E) and low grade chondrosarcoma (LGC), when a patient presents with a cartilaginous lesion of non-aggressive or only slightly

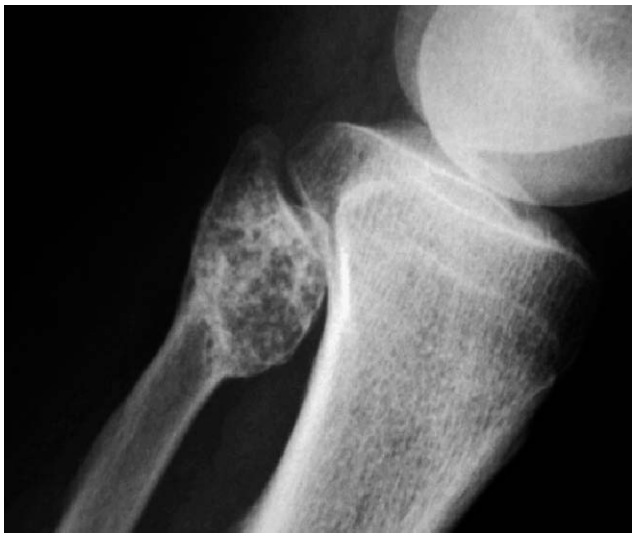

Figure 3 Cartilaginous lesion occupying the diaphysis, metaphysis and part of the diaphysis. Pathology reported it to be a low grade chondrosarcoma.

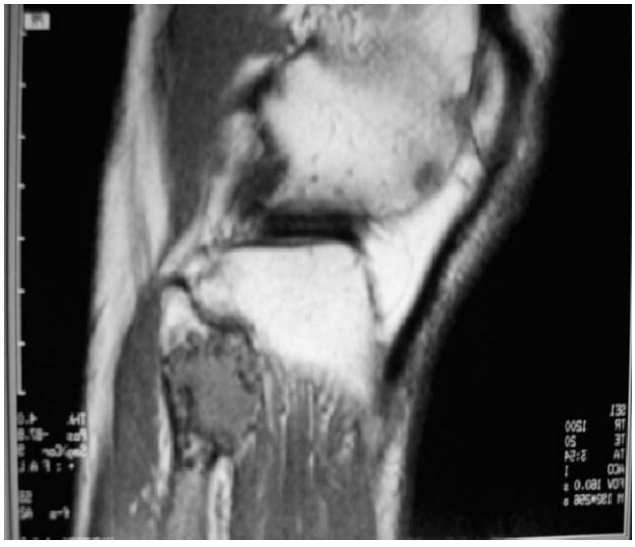

Figure 4 Image of the same mass by magnetic resonance presenting cortical erosion and soft tissue mass.

aggressive appearance, continues to be a controversial topic among specialists dedicated to Musculo-skeletal Oncology.[1-3] Although the differential diagnosis must include other entities, such as osteomyelitis, bone infarct or aneurysmatic bone cyst, E and LGC top the list. There is not a lot of scientific literature on the subject, despite the challenge it poses for the care given to these patients in order to take the correct decisions for their diagnosis and treatment. Orthopaedic surgeons can opt between clinical and radiographic monitoring if it is felt that the original clinical and radiographic findings offer no doubt as to benignness at the time, a percutaneous or incisional biopsy if there are doubts about the aggressiveness of the lesion, or else surgical treatment by means of excisional biopsy and

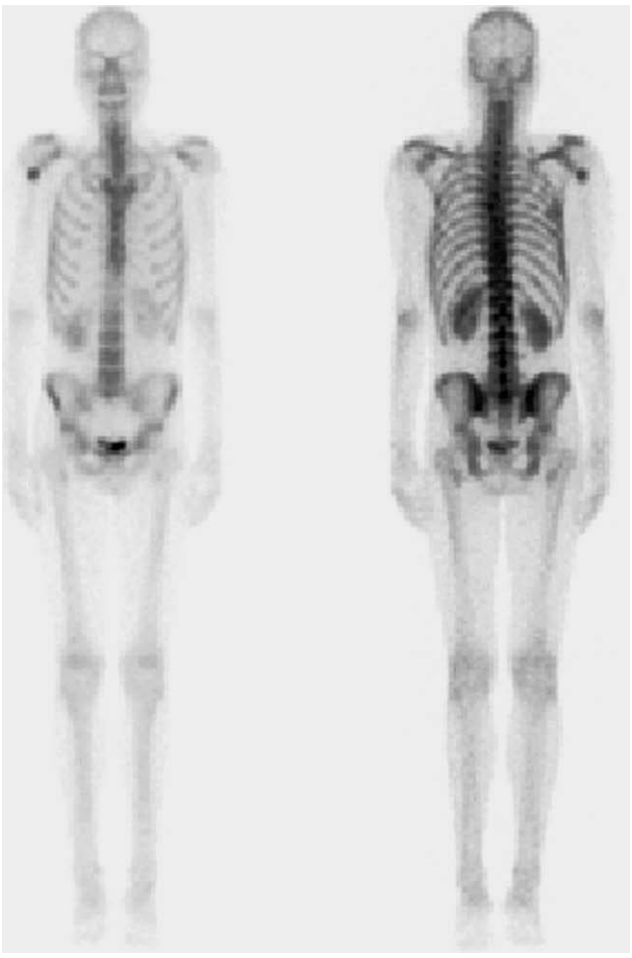

Figure 5 Bone gammagraphy image of cartilaginous lesion in proximal humerus showing higher than physiological uptake in iliac spines. It turned out to be a low grade chondrosarcoma.

directly performing an extended intralesional resection (curettage, high-speed milling, phenolization, pulse lavage and cementation) if it is felt that the lesion offers no doubts as to the low degree of malignancy. In order to choose one of these options, the diagnosis must be approached using the case history, the physical examination and the imaging tests requested.

The article by Murphey et al.[4] analyzes the clinical and radiological characteristics of 187 patients (92 with E and 95 with LGC). Regarding the differences between these 2 entities in multiple respects, the author concluded that the most definitive characteristics of LGC were as follows: greater age and size, non-mechanical pain, endosteal festoons of two thirds or more (bearing in mind the degree of depth affected but not the extent of the festooning), presence of STM, breakage of cortical bone or periosteal reaction on the CT and MRI, and greater than physiological uptake on the anterior superior iliac spine on the bone gammagraphy with Tc. For their part, the studies by Weiner[5] and Gitelis et al.[6] refer to the treatment of this kind of patient and propose an algorithm to rule out possible malignancies. By following the model in the first publication, we have tried to verify the data in our series with those of Murphey et al.[4]

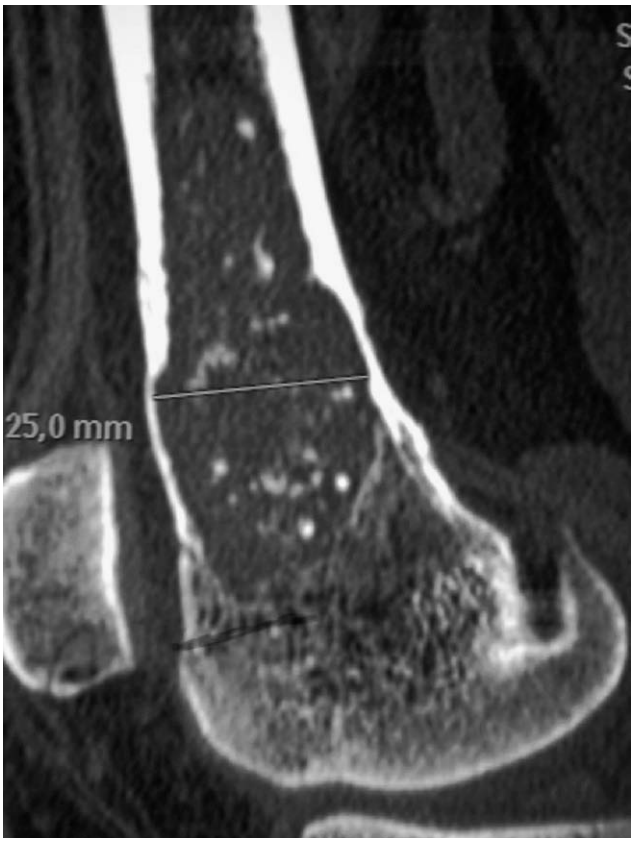

Figure 6 Computerized tomography image of internal cortical erosion in a cartilaginous lesion of the distal femur. After biopsy it was diagnosed as low grade chondrosarcoma.

The clinical presentation of these tumours is generally asymptomatic and their identification is a casual finding in most cases. The localization of the lesion showed a metaphyseal predominance in our series. Pain as a symptom has always been associated with malignancy, at least with a certain degree of aggressiveness, so in principle this symptom would automatically suggest an LGC. However, in their revision article[2] Kendrell et al. recall how essential it is to rule out other sources of pain in the corresponding anatomical region before thinking about malignant processes. In other words, lesions of the rotor cuff, calcifications in the shoulder, or tendonitis or sprains in the case of the distal femur. The mechanical characteristics of the pain may guide the surgeon towards a non-tumoral aetiology. In our paper, pain did not present any significant association with either of the final diagnoses in terms of their presentation nor in their characteristics during the physical examination. The study by Murphey et al.[4] did observe statistical significance between pain and LGC.

The appearance of these tumours on a simple X-ray is notable for its popcorn aspect with formations of "arches and rings". Although this is one of the first tests requested and already gives us the suspicion of cartilaginous tumouration, it was not useful when it came to assessing the real size of the lesion, the calcifications, their extension (measurements tend to be over-estimated due to the difficulty in establishing the limits of the lesion through having only 2 projections and not axial, coronal and sagittal slices) or the involvement of the internal face of the cortical bone. On this point we coincide with Murphey et al.,[4] in that CT and MRI are much more precise for evaluating these characteristics. Mirra et al.,[7] in their review of cartilaginous tumours, observe that E usually has a more nodular aspect, while LGC presents with an appearance of a single mass. This is due to the fact that E is considered as a "regrowth" of small residual nidi in the epiphyseal plate that for some reason undergo proliferation again, so macroscopic E would stem from several foci. LGC was more common in the metaphysis of the bones, while E predominated in the diaphysis.[4] This was not seen in our study, in which both tumours were almost equally distributed with a metaphyseal predominance.

In MRI and CT, Murphey et al.[1] found a statistical association between LGC and the habitual signs of malignancy: endosteal festoons of more than two thirds of the cortical bone, STM, breakage of the cortical bone or periosteal reaction.[4] In our study, we only assessed the depth of the endosteal festoons, there was no case of breakage of the cortical bone, periosteal reaction or pathological fracture and there was only one case of STM. The endosteal festoons, which in most cases did not exceed one third of the cortical bone, was not statistically significant in our series.

With regard to gammagraphy images with Tc 99, greater metabolic action is expected in malignant lesions, so uptake should be higher in LGC. Nonetheless, a number of circumstances can explain why E could also show increased uptake: pathological fracture, expansion of cortical bones in very small bones (excluded from our study) or a spatial conflict with other adjacent structures leading to inflammation in the area. Murphey et al.[4] analyzed the data from 51 patients. Like ours, their study differentiated uptake into 3 categories: 1) less than the anterior superior iliac spine (ASIS); 2) the same as the ASIS, and 3) greater than the ASIS, and they found that 42 out of 51 patients with LGC had increased uptake, a statistically significant result. We did not find any statistical association for this variable in our study.

The correlation between the initial suspicion and the outcome of the biopsy gave a Î coefficient of 0.659, interpreted as good/ moderate. Our reading is that, although the definitive characteristics have not been defined for each entity in this paper, the surgeon's experience (the 2 observers in the study had respectively spent 15 and 30 years on Musculo-skeletal Oncology) and the information provided by radiologists and specialists in Nuclear Medicine continue to furnish a very valid criterion for taking a decision.

We feel that one of the weaknesses of the study is that, out of 96 patients, it was possible to drawn on complete information for only 82, for whom pathology results were available for 40. In our opinion, the prospective, multi-centric nature of the study provides a good basis for continued data collection so as to give greater statistical weight for the results in future.

Chondrosarcomas are difficult lesions to diagnose and therefore pose problems when decisions need to be taken

regarding their treatment. Both LGC and E represent a challenge for radiologists, oncological orthopaedic surgeons and pathologists. Our study has not managed to define any clinical or radiological characteristic that can be associated more with E or LGC. It has been able to show a good correlation between the surgeon's initial impression based on all the tests and clinical assessment and the final biopsy result, which highlights the importance of professional expertise and teamwork among specialists dedicated to these illnesses. A larger number of patients would be needed to be able to state this on a more solid basis.

Studies must be continued into the differentiation of these 2 entities. Treatment must be multi-disciplinary and must include in the team specialists in bone tumours, radiology and pathology. Inexperience may lead to serious diagnostic errors and, therefore, therapeutic failures. The future of this controversy may, as in other fields of our speciality, lie in the identification of tumoral entities by means of their genetic and cytological characteristics.[8]

Conflict of interest

The authors declare they have no conflict of interest.

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