Eosinophilic granuloma
A DIFFERENT BEHAVIOUR IN CHILDREN THAN IN ADULTS
F. Plasschaert, C. Craig, R. Bell, W. G. Cole, J. S. Wunder,
B. A. Alman
From the Hospital for Sick Children and the Mount Sinai Hospital, Toronto, Canada
and the New England Medical Centre, Boston, USA

Localised Langerhans-cell histiocytosis of bone (eosinophilic granuloma) is a benign tumour-like condition with a variable clinical course. Different forms of treatment have been reported to give satisfactory results. However, previous series all contain patients with a wide age range. Our aim was to investigate the effect of skeletal maturity on the rate of recurrence of isolated eosinophilic granuloma of bone excluding those arising in the spine.

We followed up 32 patients with an isolated eosinophilic granuloma for a mean of five years; 17 were skeletally immature. No recurrences were noted in the skeletally immature group even after biopsy alone. By contrast, four of 13 skeletally mature patients had a recurrence and required further surgery. This suggests that eosinophilic granuloma has a low rate of recurrence in skeletally immature patients.

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The clinical spectrum of Langerhans-cell histiocytosis (LCH) is wide, ranging from a potentially lethal leukaemia-like disorder to a solitary lytic lesion of bone. Localised LCH of bone is a benign tumour-like condition which is characterised by a clonal proliferation of Langerhans-type histiocytes, and is commonly referred to as eosinophilic granuloma. The bones which are the most commonly involved are the skull, the pelvis, and the diaphysis of long bones. The systemic condition includes Hand-Schüller-Christian disease with a triad of exophthalmos, diabetes insipidus and osteolytic lesions of the skull, and Letterer-Siwe disease with hepatosplenomegaly, lymphadenopathy, skin rash, fever, anaemia and thrombocytopenia.

A variety of forms of treatment has been reported for solitary eosinophilic granuloma of bone, including observation, injections of steroid, local excision and curettage with or without bone grafting, chemotherapy and irradiation. All of these treatments are reported to give satisfactory results with a recurrence rate of less than 20%. The age of the patients in these series varies widely. Furthermore, eosinophilic granuloma of the spine in children is known to resolve spontaneously with time and surgery is not usually recommended. Our aim in this study was to examine the effect of skeletal maturity on the rate of recurrence of isolated eosinophilic granuloma of bone excluding that arising in the spine.

Patients and Methods

Patients with an isolated, biopsy-proven eosinophilic granuloma who had been treated at three different institutions between 1990 and 1995 were identified from records and databases. The exclusion criteria were multiple sites of involvement, those arising in the spine, the absence of a histological diagnosis and a biopsy or other treatment at another hospital before being referred to one of the three participating institutions.

The initial clinical presentation was determined from the medical records, and the radiographs and pathology were reviewed for each patient. They had undergone either a bone scan and/or a skeletal survey before treatment in order to identify multifocal lesions. Clinical and radiological outcome data were available for each patient.

There were 32 patients who met the inclusion criteria; 17 were skeletally immature and aged between 3 and 14 years and 15 skeletally mature aged between 16 and 28 years at the time of diagnosis. The lesions involved six different bones: the femur (seven skeletally mature, seven immature), the humerus (three skeletally mature, four immature),
the pelvis (two skeletally mature, three immature), the tibia (two skeletally mature, two immature), the forearm (one skeletally mature) and the clavicle (one skeletally immature).

Six of the skeletally immature patients had undergone biopsy followed by observation alone (open biopsy in three and percutaneous in three). In the other patients the biopsy had been followed by curettage with or without the addition of autogenous bone graft. In all skeletally mature patients the treatment consisted of biopsy, curettage and bone grafting.

The patients were followed at least yearly for a minimum of three years after treatment with clinical and radiological review. Any recurrence and its treatment, if necessary, were recorded. The mean follow-up period was five years for both groups.

Statistical analysis. The differences in outcome and rate of recurrence between the groups were compared using Fisher’s exact test calculated using the SAS/STAT program (SAS, Cary, North Carolina).

Results

In the immature group all 17 lesions healed. This included the six in patients treated by biopsy alone (Fig. 1). There were no clinical or radiological signs of recurrence. All patients had a full range of movement of the affected limb, and returned to unrestricted physical activity.

In the 15 skeletally mature patients, four lesions (26%) recurred all of which produced clinical symptoms or radiological changes within two years of treatment. One had a humeral lesion which required further curettage and grafting and two had a femoral lesion necessitating further curettage, grafting and internal fixation. The fourth patient had a recurrent pelvic lesion which also required further curettage and grafting.

Using Fisher’s exact test, the difference in the rate of recurrence between the skeletally mature and immature patients was significant (p = 0.038).

Discussion

Solitary eosinophilic granuloma of bone can present dilemmas of both diagnosis and treatment. The aetiology is unclear and the therapeutic approach controversial. In our series, all the patients were treated by biopsy or biopsy with autogenous bone grafting alone. No recurrences were found in the skeletally immature group after a mean follow-up of five years. By contrast, four patients in the skeletally mature group required further surgery for a recurrence within two years of the initial treatment.

Since the clinical course of the disease is usually benign,
a simple, minimally invasive form of treatment with a low rate of complications is desirable. In view of the possibility of spontaneous resolution, biopsy alone to confirm the diagnosis\(^9\) could be a strategy for treatment. Our results support this approach for the treatment of solitary eosinophilic granuloma of bone in the skeletally immature.

Intralesional infiltration with corticosteroids, either as an adjunct to treatment or as primary treatment, was recommended by Capanna et al\(^{10}\) as being effective, convenient and safe. Egeler et al\(^{11}\) found that the results of treatment with intralesional steroids were comparable to those of other forms of treatment reported in the literature. Although this treatment seems minimally invasive they reported two complications in 15 patients, one case of femoral osteomyelitis and one of obstructive hydrocephalus. Some lesions fail to respond or are unsuitable for treatment by injection because of their site, impending fracture or soft-tissue invasion. The place of treatment with corticosteroids remains to be determined, although the high rate of healing which we found in children, suggests that the administration of corticosteroids adds little in this age group.

The resolution of symptoms in the skeletally immature after confirmation of the diagnosis is analogous to the previous findings of vertebral remodelling in patients with eosinophilic granuloma of the spine. Raab et al\(^{12}\) showed that, in 14 patients without neurological signs who were aged between 1.2 and 11.3 years, conservative treatment with immobilisation in a brace was sufficient to allow remodelling and reconstitution of the vertebral height.

Previous studies\(^7,8\) show a wide variation in the outcome after different treatments for eosinophilic granuloma. One explanation may be the age variation in the mix of the patients. Since eosinophilic granuloma in skeletally immature patients is more likely to resolve, regardless of the form of treatment, a series with a higher percentage of younger patients should show a better rate of success.

The lesion resolved spontaneously in all patients in our series who were treated by biopsy alone, while there were recurrences in those treated by local resection and bone grafting. This raises the intriguing possibility that resection results in a higher rate of recurrence than less aggressive procedures. Such a concept is at odds with conventional views regarding tumour surgery, but cannot be excluded, using our data. Further study of different surgical approaches in age-matched groups of patients are needed to exclude this possibility.

The discovery of clonality in unifocal LCH does not allow either the biological outcome or the clinical behaviour to be predicted.\(^{13}\) The causes for the age-related differences which we found possibly include factors such as a different pathology in the clone and/or the patient’s age-dependent host response. This is, to our knowledge, the first study which describes a different clinical course for eosinophilic granuloma in the skeletally mature compared with the immature patient. Skeletally mature patients with a solitary eosinophilic granuloma of bone may require more aggressive treatment than the skeletally immature.

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References