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Eosinophilic granuloma: MRI manifestations

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Abstract. The appearance on magnetic resonance imaging (MRI) of 16 cases of pathologically proven eosinophilic granuloma were reviewed retrospectively and correlated with the radiographic appearance of the lesion. The most common MR appearance (ten cases) was a focal lesion, surrounded by an extensive, ill-defined bone marrow and soft tissue reaction with low signal intensity on T1-weighted images and high signal intensity on T2-weighted images, considered to represent bone marrow and soft tissue edema (the flare phenomenon). The MRI manifestations of eosinophilic granuloma, especially during the early stages, are nonspecific, and may simulate an aggressive lesion such as osteomyelitis or Ewings sarcoma, or other benign bone tumors such as osteoid osteoma or chrondroblastoma.

Key words: Eosinophilic granuloma – MRI bone lesions

Eosinophilic granuloma is a relatively rare disease typically presenting in children before the age of 10 years. Early radiographic features include osteolysis, sometimes with poorly delineated margins, and laminated periosteal reaction. In later stages, the lesion is more benign in appearance with sharp margination, well-defined sclerotic borders, and thick or absent periosteal reaction. Less common manifestations of eosinophilic granuloma include button sequestrum, beveled lesions of the skull, vertebra plana, and soft tissue mass [10, 12].

The clinical and radiographic features in the early stages of eosinophilic granuloma are often suggestive of a malignancy and the differential diagnosis commonly includes malignant round cell tumors such as Ewing's sarcoma and lymphoma. The presence of numerous inflammatory cells may make it difficult to distinguish eosinophilic granuloma from bone infection. Magnetic resonance imaging (MRI) has become a well-established technique for preoperative evaluation of bone and soft tissue tumors, because of its improved soft tissue contrast resolution and multiplanar capabilities [3, 11]. MRI has been shown to be highly sensitive for detection of bone and soft tissue lesions, but one of its drawbacks is the relatively low specificity of the technique. Two consecutive cases of eosinophilic granuloma were erroneously interpreted as Ewing's sarcoma on the basis of their radiographic manifestations and the presence of extensive bone marrow and soft tissue MRI signal intensity changes (the flare phenomenon). To better acquaint radiologists with the MR appearance of eosinophilic granuloma, so that this entity is not mistaken for a malignancy, we review here the radiographic, computed tomographic (CT), and MTI studies of 14 additional cases from our own files or shown to us in consultation from other institutions.

Materials and methods

The MRI studies, radiographs, and computed tomograms when available (7 cases) of 16 patients with a pathologically proven diagnosis of eosinophilic granuloma were reviewed. There were 13 male and 3 female patients, age range 1–33 years, mean age 13.3 years. Plain films and/or CT were evaluated for focal areas of osteolysis, zone of transition, rim of sclerosis, periosteal reaction, and collapse, when the lesion involved the vertebral body. Images were reviewed retrospectively by two radiologists in conference, not blinded to the pathologic diagnosis.

Based on the radiographic and CT findings, the lesions were then classified as incipient, mid-, or late phase, according to the radiographic criteria established by Mirra [10]. A lesion was considered to be incipient when the zone of transition was wide and without a sclerotic rim, and when one or more parallel periosteal lamellations were present. It was classified as midphase when the zone of transition was narrow with a thin rim of sclerosis and periosteal reaction, and it was classified as late phase if the rim of sclerosis was thick and the periosteal reaction was resolved. All vertebrae planae were classified as being in the midphase.

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MRI findings were evaluated for the presence of focal or ill defined areas of low signal intensity on T1-weighted images (T1WI) and high SI on T2-weighted images (T2WI) within the bone marrow and/or in the soft tissues, and for abnormalities in the cortex or periosteum. The correlation between MRI findings of bone marrow and soft tissue reaction and radiographic staging was then investigated.

MRI studies were performed at four different institutions using 0.5-tesla and 1.5-tesla field strength magnets. All studies were considered to be satisfactory from the technical point of view. In all cases T1WI with short TR/TE (500–800 ms/20–25 ms) and proton density and T2WI with long TR/short and long TE (1500–2000 ms/20–100 ms) were available. Images were obtained in at least two orthogonal planes using a section thickness of 5–10 mm.

Results

Radiographic/CT findings

The femur was involved in four cases, the spine in three cases, the humerus and the skull in two cases each, and the radius, fibula, tibia, iliac bone, and scapula in one case each. Periosteal reaction was present on plain films or CT in seven cases. In 14 cases there was a focal lucency with a narrow zone of transition, and in two a permeative pattern was present. Beveled edges were present in the two cases involving the skull. There was vertebra plana in the three spine lesions. On the basis of the radiographic and CT findings, seven lesions were classified as incipient, six as midphase, and three as late phase (Table 1).

MRI findings

The most frequent MRI finding was a diffuse, ill-defined hypointesity of the bone marrow on T1WI with hyperintensity on T2WI (Figs. 1, 2). This was present in all but two cases, both in the late phase and located in the skull. The focal lesions were seen as areas of higher signal intensity than the surrounding bone marrow reaction on T2WI (Fig. 3). A low signal intensity rim was present around the focal lesion in seven cases (four in midphase and three in the late phase; Table 1).

In ten cases, the soft tissues surrounding the lesion demonstrated extensive signal changes with hyperintensity on T2WI. These were ill-defined in seven cases, and focal or "mass-like" in three cases, causing displacement of the adjacent muscle groups (Fig. 4). The soft tissues surrounding the lesions were normal in six cases (Fig. 3). The soft tissue changes were present in seven incipient and in three midphase lesions. The combination of bone marrow and soft tissue reaction was present in ten lesions (seven incipient and three midphase).

The three lesions involving the spine presented with vertebral collapse (vertebra plana). Abnormal signal intensity was present in the region of the vertebral collapse and two cases showed soft tissue involvement with mass effect extending into the spinal canal (Fig. 5). The two lesions involving the calvaria were focal, without signs of associated bone marrow or soft tissue edema (Fig. 6).

Discussion

Eosinophilic granuloma is a disease of unknown etiology, grouped under the term Langerhans cell histiocytosis (histiocytosis X, idiopathic inflammatory histiocytosis, or reticuloendotheliosis) along with Hand-Schüller-Christian syndrome and Letterer-Siwe syndrome. These disease are characterized by an abnormal proliferation of histiocytes in various parts of the reticuloendothelial system such as the bone, lungs, central nervous system, skin, and lymph nodes. Cultures are consistently negative. Eosinophilic granuloma is more common in male subjects and about three-fourths of all cases present during the first decade of life, most commonly involving the long bones, pelvis, ribs and spine. Aching pain, swelling, low grade fever, elevated sedimentation rate, and peripheral eosinophilia are common clinical manifestations of the disease. The clinical course of the solitary lesions is benign in most instances, and treatment with curettage leads to complete healing in most cases. Geographic or permeative areas in the bone with associated periosteal reaction are usual radiographic manifestations when there is long bone involvement. Especially during the incipient phase, the radiographic and clinical manifestations may be ominous. It is therefore not unusual that osteomyelitis and Ewing's sarcoma are among the most frequent considerations in the differential diagnosis.

In our series, bone marrow reactive changes were present in all cases classified radiographically as incipient or midphase, and only in one in the late phase. The only two cases that did not show marrow abnormality were located in the skull. Soft tissue changes were also more frequent during the early phases (see Table 1).

The most frequent combination of MRI findings in our series, particularly in long bones, was the presence

Table 1. Correlation between radiographic classification and MRI findings in eosinophilic granuloma

Radiographic phase	No. of cases	MRI findings			
		Bone marrow reaction	Ill-defined soft tissue reaction	Mass-like soft tissue reaction	Rim of low signal intensity
Incipient	7	7	6	1	0
Mid	6	6	1	2	4
Late	3	1	0	0	3
Total	16	14	7	3	7

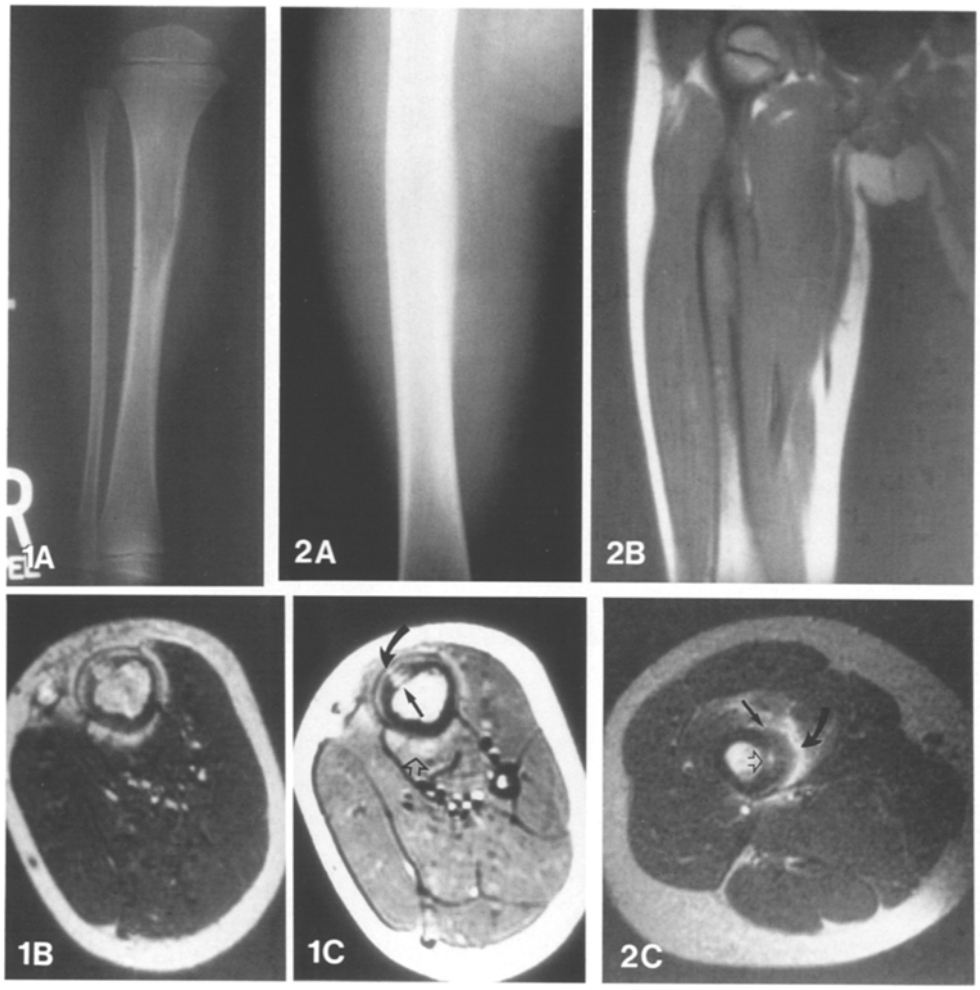


Fig. 1A–C. Eosinophilic granuloma (incipient phase) of the tibia in a 3-year-old boy. **A** The plain films demonstrate a permeative pattern with periosteal reaction. **B, C** T2 and spin density axial images demonstrate relative hyperintensity of the bone marrow space of the proximal tibia, a focal lesion (*straight arrow*), and periosteal reaction (*curved arrow*). A halo of hyperintense edema is also noted surrounding the tibia posteriorly (*open arrow*)

Fig. 2A–C. Eosinophilic granuloma (incipient phase) involving the proximal femoral diaphysis in a 6-year-old boy. **A** Plain film demonstrating periosteal reaction involving the diaphysis of the right femur. **B** Coronal T1-weighted image (SE 500/20) showing diffuse hypointensity of the bone marrow. **C** Axial T2-weighted image (SE 2000/80) showing hyperintense bone marrow, periosteal reaction (*straight arrow*), soft tissue edema (*curved arrow*), and a small cortical focal lesion (*open arrow*)

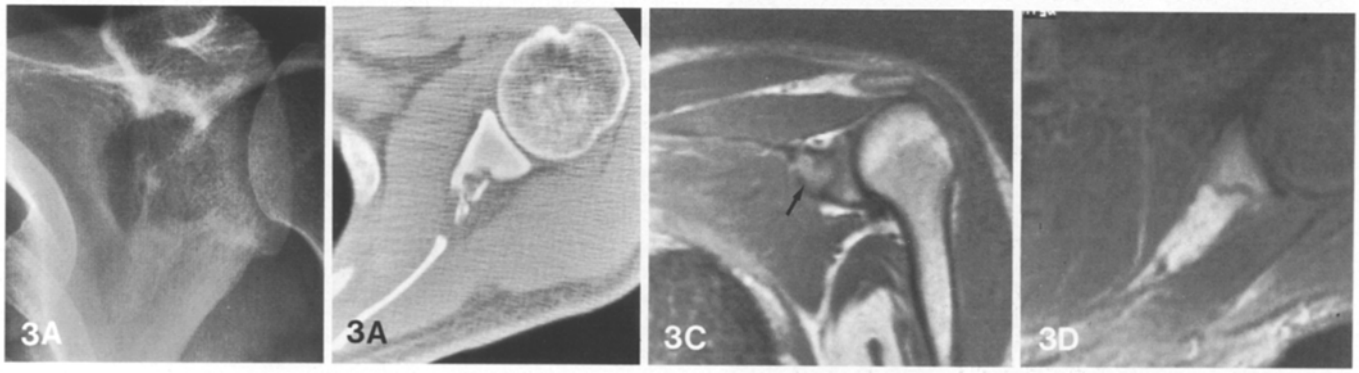
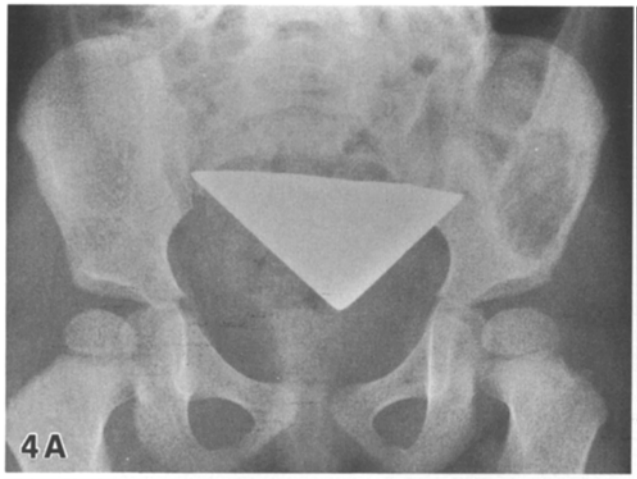
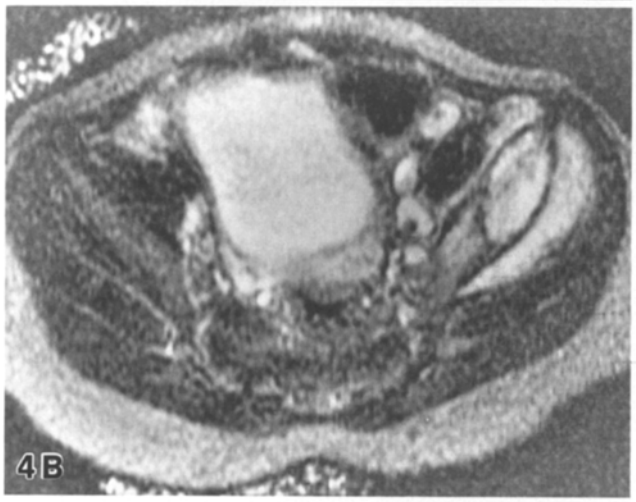


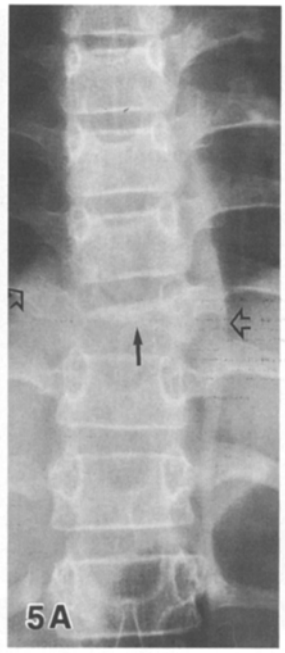
Fig. 3A–D. Eosinophilic granuloma of the scapula (midphase) in a 24-year-old man. **A** Frontal radiograph of the left scapula showing a geographic lesion with minimal sclerotic rim and narrow zone of transition. **B** CT scan also displays a destructive lesion, with cortical breakthrough. **C** Coronal T1-weighted image (SE 400/20) shows a relatively hypointense lesion demarcated by a rim of low signal intensity (*arrow*). **D** Axial T2-weighted image (SE 1800/80) demonstrating hyperintense lesion with low signal intensity rim and surrounding bone marrow reaction. Compare the signal intensity of the scapular bone marrow space with the humeral head. Note the absence of associated soft tissue edema

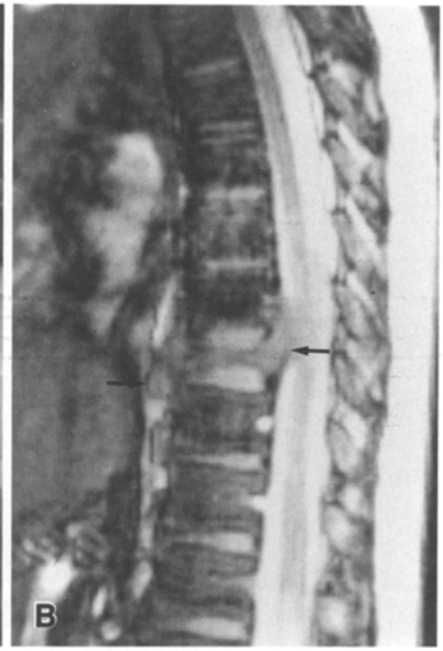
of a focal lesion surrounded by prominent signal intensity changes of both the bone marrow and adjacent soft tissues: this was noted in 10 of our 16 cases. We interpreted these signal changes as reflective of an inflammatory response, probably reactive edema and increased interstitial water.

The MRI findings seen in our series are not specific for eosinophilic granuloma. Bone marrow edema has been detected by MRI in osteomyelitis, trauma, transient osteoporosis, and avascular necrosis [4, 15]. In the soft tissues, its presence has been correlated with malignant bone and soft tissue tumors [2, 7] and with inflammatory









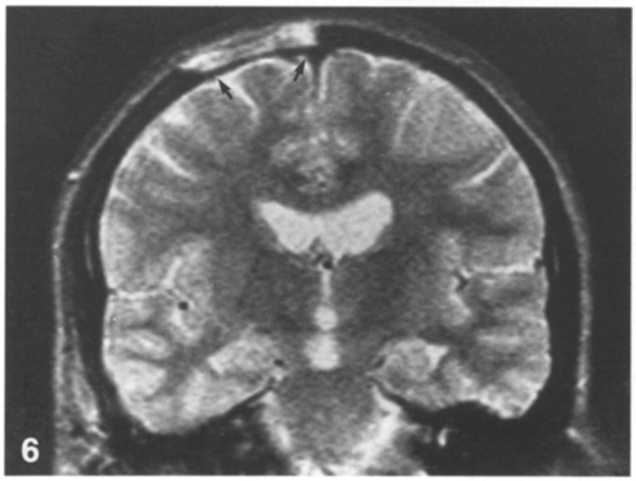


Fig. 4A, B. Eosinophilic granuloma (midphase) of the left iliac bone in a 20-month-old girl. **A** Frontal radiograph of the pelvis shows a geographic lytic lesion of the left iliac bone with a rim of sclerosis. **B** Axial T2-weighted image shows the lytic lesion with a rim of low signal intensity associated with well-demarcated soft tissue and mass-like reaction of the gluteus minimus and iliac muscles

Fig. 5A, B. Eosinophilic granuloma (midphase) of T9 in a 3-year-old girl. **A** Frontal radiograph of the spine showing vertebra plana of T9 (*arrow*) and widening of the perivertebral soft tissues bilaterally (*open arrows*). **B** Sagittal T2-weighted gradient echo image showing hyperintense vertebral body of T9 with mass-like reaction or hemorrhage extending anterior and posterior to the collapsed vertebral body (*arrows*)

Fig. 6. Eosinophilic granuloma (late phase) of the skull in a 23-year-old man. Coronal T2-weighted image (SE 2000/80) showing hyperintense lesion with beveled edges (*arrows*). Note lack of edematous changes in the calvaria or surrounding soft tissues

conditions such as polymyositis [8]. MRI changes compatible with bone marrow edema have also been described in benign bone tumors, including osteoid osteoma [1, 9], chondroblastoma [5], and osteoblastoma [13]. The "flare phenomenon" was first described by Crim et al. [6] in a case of osteoblastoma. Biopsy of the reactive area in their case demonstrated replacement of normal fatty marrow by considerable edema fluid, fibroplasia, and chronic inflammatory cells, predominantly plasma cells. Analogous inflammatory reaction extending to the periosteum was described by Brower et al. [5] in chondroblastoma. In our series, pathologic material from the bone marrow space surrounding the lesion was available for evaluation in only two cases. In one case only a small amount of normal bone was found and in another case there was abundant reactive fibrous and fibrocartilaginous tissue.

Mirra and Gold [10] described three phases in the

evolution of eosinophilic granuloma: incipient, mid; and late phase. During the early phases, the lesions tend to have aggressive patterns with periosteal lamination and poorly marginated or permeated lytic lesions. Histologically, inflammatory cells are usually present along with hemorrhage and necrosis. During the late phase the lesions tend to become more circumscribed and histologically the cellular inflammatory infiltrate clears. This evolution of the radiographic and histologic findings of eosinophilic granuloma could, in part, explain the reactive manifestations in our cases. Patients whose MR scans demonstrate extensive edema are most likely in the early phases of their disease, while those without edema are in the late phase. On the basis of this classification, ten of our cases would be in the incipient or midphase of the disease, given the aggressive radiographic and MRI manifestations. This three-phase classification of eosinophilic granuloma provides some insights into the pathophysiology of these lesions and contributes to the understanding of the radiographic and MRI findings.

All lesions involving the vertebrae were located in the vertebral bodies and presented the characteristic sign of vertebra plana on plain radiographs. On MRI the vertebral bodies demonstrated diffuse low signal intensity on T1WI and high signal intensity on T2WI. In two cases there were reactive changes in the paravertebral area. This finding could be related to soft tissue edema, or it could reflect hematoma due to recent vertebral body collapse.

In summary, eosinophilic granuloma, like other benign tumors of childhood and adolescence, can induce an extensive inflammatory reaction in the host bone, extending into the soft tissues. The MRI signal intensity changes produced by this reaction, however, are nonspecific.

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