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Eosinophilic Granuloma Arising from the Pelvis in Children: A Report of Three Cases

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Abstract

Eosinophilic granuloma (EG) is a benign tumor-like condition which is characterized by a clonal proliferation of Langerhans-type histiocytes and defined as a local form of Langerhans cell histiocytosis (LCH). The radiographic appearances of EG are quite different depending on the phase of the disease and the site of involvement. A status of EG in the bone is divided into acute and chronic phases. Radiologically acute phase of EG is difficult to differentiate from a malignant bone tumor such as Ewing's sarcoma or acute osteomyelitis. Chronic phase of EG may mimic a chronic osteomyelitis or a benign bone tumor. We report 3 children's cases of EG in the pelvis which showed quite different radiological features and clinical courses. A 6-year-old boy (Case 1) had an osteolytic lesion with slightly defined margins in the right acetabulum. A 4-year-old boy (Case 2) had a radiologically similar-looking lesion in the left acetabulum. These lesions resembled radiologically chronic osteomyelitis (Brodie's abscess) or a benign bone tumor and healed spontaneously after biopsy. A 2-year-old boy (Case 3) had an osteolytic lesion with ill-defined margin in the ilium. It was difficult to differentiate from a malignant tumor such as Ewing's sarcoma, or acute osteomyelitis. The lesion became enlarged after needle biopsy. In spite of an additional curettage, the osteolytic lesion remained in the left pelvis in 1 year. Treatment for EG is controversial. Curettage of the affected site and bone grafting is usually accomplished. However, some EG heal spontaneously. It is of great importance to understand the natural course of EG and this knowledge will give us the opportunity to avoid unnecessary treatment. EG with poor osteolytic margins may progress further after biopsy. EG with well-defined margins may heal spontaneously after biopsy only.

Introduction

Eosinophilic granuloma (EG) is a benign tumor-like condition which is characterized by a clonal proliferation of Langerhans-type histiocytes in the bone or lung [1, 2]. The causes and pathogenesis of EG are unknown. In spite of extensive genetic studies or virologic analyses, apparent genetic error or infectious agents have not been found [3, 4]. The radiographic features of EG is quite different depending on the phase of the disease and the site of involvement [3, 5]. A status of EG in the

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bone is divided into acute and chronic phases [5, 6, 7]. The acute phase of EG is a destructive, osteolytic lesion and has poor margins. Therefore it is difficult to differentiate from a malignant tumor such as Ewing's sarcoma, or acute osteomyelitis [5]. On the other hand, the chronic phase of EG is a well-defined lesion, and the radiological features are similar to those of chronic osteomyelitis (Brodie's abscess) or a benign bone tumor [5, 8].

EG is a local condition of Langerhans cell histiocytosis (LCH) and make up 80% of LCH in children [5]. The systemic condition of LCH is a multisystem life-threatening disorder. For example, Hand-Schüller-Christian disease is defined as a triad of exophthalmos, diabetes insipidus and osteolytic lesions of the skull, and Letterer-Siwe disease shows hepatosplenomegaly, lymphadenopathy, skin rash, fever, anemia and thrombocytopenia [1, 4]. Though these three diseases are quite different in disease expression pattern and their prognosis, the histology is similar to each other and indistinguishable [4]. The incidence of EG is estimated at 0.05–0.5 per 100,000 and 90% of EG occurs under the age of 15 years old [3, 4, 5]. Male has twice as high incidence rate as female [8]. Flat bones are involved in 70% of cases and long bones in 30% [8]. Among the flat bones, the skull is most frequently involved, and the pelvis, vertebrae, mandible, and ribs are followed in decreasing order [1, 5]. We report 3 children's cases of EG in the pelvis which showed quite different radiological features and clinical courses.

Case reports

Case 1

A 6-year-old boy was referred to our hospital with pain in the right thigh and limping for 2 months. Physical examination indicated tenderness over the right hip joint without swelling. The motion of the joint was slightly restricted due to pain. Plain radiographs of the pelvis showed a slightly defined osteolytic lesion in the right acetabulum (Figure 1A). Blood test demonstrated normal white blood cell (WBC) count (7,800 /μl), eosinophils (4.7%), and slight increased erythrocyte sedimentation rate (ESR) (21 mm/h). Computed tomography (CT) showed a 3.0 × 2.0 cm osteolytic low density lesion in the right acetabulum with a slightly defined margin (Figure 1B). Magnetic resonance imaging (MRI) revealed that the mass had lower signal intensities on T1-weighted images and higher signal intensities on T2-weighted images than the bone marrow (Figure 1C, D). The right ilium also had lower signal intensities on T1-weighted images (Figure 1C). The mass extended into the lateral soft tissue of the pelvic bone on T2-weighted images (Figure 1D). Based on these examinations, an initial radiological diagnosis was acetabular osteomyelitis and an open biopsy was performed through the anterior approach. Histological examination revealed mixed cellular infiltrate with histiocytes, eosinophils, lymphocytes, and macrophages, which led to the diagnosis of EG (Figure 1E). Because pain was relieved in a week after the biopsy, no further treatment was performed. The plain radiograph showed the signs of healing in 3 months after the biopsy (Figure 1F), and complete healing was observed in a year.

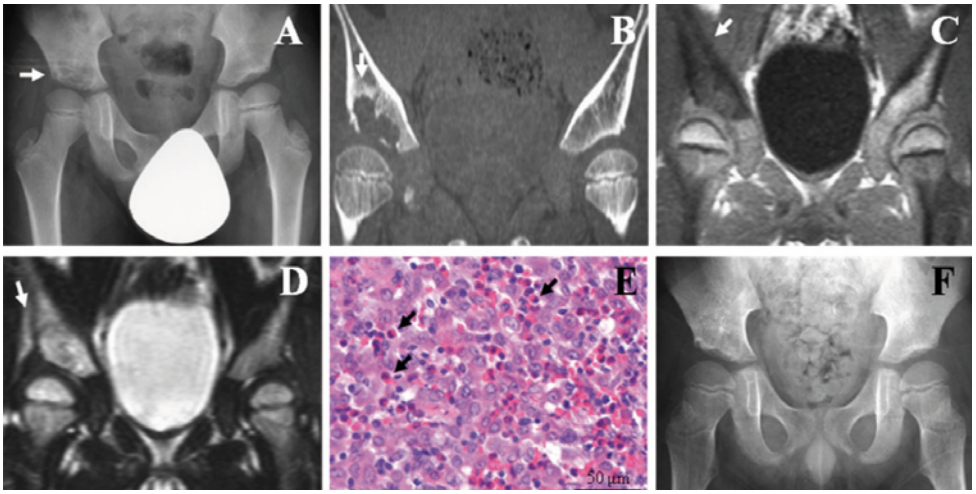

Figure 1 Case 1, a 6-year-old boy of EG in the right acetabulum. **A:** Anteroposterior radiograph of the pelvis showing a slightly defined osteolytic lesion in the right acetabulum (arrow). **B:** Coronal CT demonstrating an osteolytic lesion with well-defined margins (arrow). **C:** Coronal T1-weighted images. The lesion and the right ilium (arrow) showed lower signal intensities. **D:** Coronal T2-weighted images. The lesion and the lateral soft tissue of the pelvic bone (arrow) demonstrated higher signal intensities. **E:** Histological examination indicating a mixed cellular infiltrate with histiocytes, eosinophils, lymphocytes, and macrophages. Arrows show eosinophils. **F:** Three months after the open biopsy. Radiographic signs of healing appeared.

Case 2

A 4-year-old boy was referred with a month history of pain and limping in the left lower limb. Physical examination revealed tenderness over the left hip joint without swelling. The motion of the joint was not restricted. Blood test showed normal WBC count (8,520 /μl), eosinophils (5%), and slightly increased ESR (35 mm/h). Plain radiographs showed a 3.0 × 2.5 cm osteolytic lesion with slight marginal sclerosis in the left acetabulum (Figure 2A). A complete bone scan with ^{99m}Technetium showed an increased uptake in the left acetabulum (Figure 2B). The lesion and the surrounding area in the pelvic bone had lower signal intensities on T1-weighted images (Figure 2C). The lesion and lateral soft tissue of the pelvic bone had higher signal intensities on T2-weighted images (Figure 2D). A temporary diagnosis was osteomyelitis of the left acetabulum. CT-guided needle biopsy was performed through the posterolateral aspect of the lesion. Histological examination showed characteristic appearances of EG (Figure 2E). His pain rapidly subsided and limping disappeared in a couple of weeks after the biopsy. There was no abnormality radiologically after one year of the biopsy (Figure 2F).

Case 3

A 2-year-old boy was referred with a limping in the left leg for a month. On physical examination, motion of the joint was not restricted and neither swelling nor tenderness was observed. WBC and ESR increased (11,460 /μl and 30 mm/h, respectively). Eosinophils were within the normal range (3%). Plain radiograph

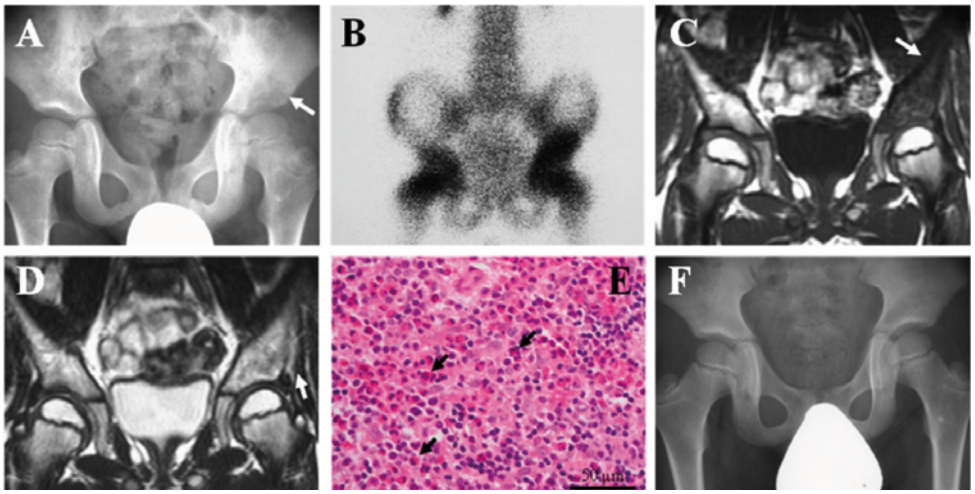

Figure 2 Case 2, a 4-year-old boy of EG in the left acetabulum **A:** Anteroposterior radiograph of the pelvis showing a slightly defined osteolytic lesion in the left acetabulum (arrow). **B:** Bone scan with ^{99m}Technetium demonstrating an increased uptake in the left acetabulum. **C:** Coronal T1-weighted images. The lesion and the left ilium (arrow) showed lower signal intensities. **D:** Coronal T2-weighted images. The lesion and lateral soft tissue of the pelvic bone (arrow) demonstrated higher signal intensities. **E:** Histological examination indicating characteristic appearances of EG. Arrows show eosinophils. **F:** One year after needle biopsy. A radiograph showed normal appearances.

of the pelvis revealed an osteolytic lesion with ill-defined margins in the ilium (Figure 3A). CT showed an osteolytic lesion in the ilium extending into the medial retroperitoneal space (Figure 3B). The left ilium showed lower signal intensities on T1-weighted images (Figure 3C) and higher signal intensities on T2-weighted images which extended into the medial retroperitoneal space and the lateral gluteal muscles (Figure 3D). Bone scan with ^{99m}Technetium showed a massive uptake in the left pelvis (Figure 3E). An initial radiological diagnosis was Ewing's sarcoma and CT-guided needle biopsy was performed through the posterior aspect of the left ilium. The histological examination demonstrated a cellular lesion consisting of numerous histiocytes and eosinophils. The lesion was well-defined after the biopsy, but gradually enlarged in a month (Figure 3F). CT also confirmed enlargement of the lesion, but the adjacent sacrum was not involved (Figure 3G). MRI demonstrated that the mass and soft tissue abnormalities became enlarged (Figure 3H, I). Curettage was carried out immediately. His pain and limping subsided gradually after the operation. However, the plain radiograph taken after 1 year later showed that the osteolytic lesion of the left pelvis remained (Figure 3J).

Discussion

The radiographic feature of EG is completely different depending on the phase of the disease and the site of involvement [3, 5]. A status of EG in the bone is divided

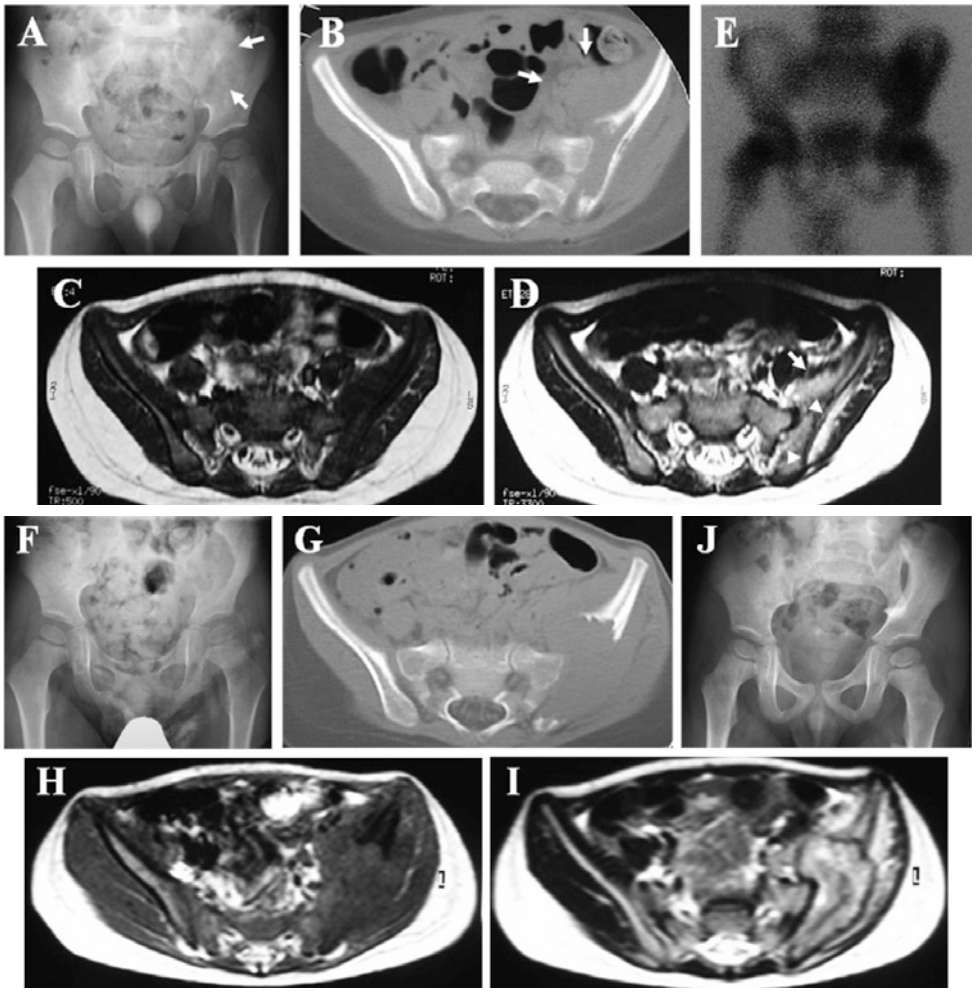

Figure 3 Case 3, a 2-year-old boy of EG in the left ilium **A:** Anteroposterior radiograph of the pelvis showing an osteolytic lesion with ill-defined margins in the ilium (arrows). **B:** Axial CT demonstrating an osteolytic lesion in the ilium extending into the retroperitoneal space (arrows). **C:** Axial T1-weighted images. The left ilium showed lower signal intensities. **D:** Axial T2-weighted images. The medial retroperitoneal space (arrow) and lateral gluteal muscles (arrowheads) showed higher signal intensities. **E:** Bone scan with ^{99m}Technetium demonstrating an increased uptake in the left pelvis. **F:** Anteroposterior radiograph of the pelvis in a month after the needle biopsy. The lesion was well-defined but enlarged. **G:** Axial CT demonstrating the enlarged lesion without extension into the adjacent sacrum. **H, I:** Axial T1 and T2-weighted images. The mass and surrounding soft tissue abnormalities enlarged. **J:** One year after the thorough curettage of the lesion. The osteolytic lesion of the left pelvis remained.

into acute and chronic phases [5, 6, 7]. The acute phase of EG shows osteolysis with poorly defined margins and the chronic phase of EG shows well-defined margins. Case 3 is consistent with the acute phase and case 1 and 2 are the chronic ones. In the pelvis, the lesion may present as poorly defined areas of osteolysis in the acute phase that become progressively circumscribed as they mature in the chronic phase [4].

MRI is a sensitive, but nonspecific modality to detect bone marrow involvement and a soft tissue mass [4, 5, 9]. T1-weighted images are useful for demonstrating bone marrow involvement and T2-weighted images for indicating a soft tissue mass [4, 5, 9]. These changes are considered as edema of bone marrow and soft tissues [4]. Edema of adjacent bone marrow and soft tissue is particularly seen in the acute phase lesions [5]. Chronic phase lesions show decreased signal intensity on T2-weighted images, indicating re-ossification of the osteolytic lesions with resolution of the soft tissue mass [4]. The acute phase is defined as the tumor invading the surrounding soft tissue but the chronic phase is localized as itself [8]. Case 3 showed an extensive, irregular soft tissue mass in the medial retroperitoneal space and the lateral gluteal muscles. On the other hand, the mass in the case 1 and 2 was localized.

Vertebral lesions show a symmetrical flattening of the vertebra with intervertevral disc space preservation, which are called as "vertebra plana", and easily diagnosed only by plain radiographs [4]. However, it is very difficult to diagnose from radiological examinations in the pelvis. Plain radiograph or MRI is a very sensitive modality to detect the lesions, but it is not specific because of the radiological diversity of EG. We could not distinguish EG from malignant bone tumors such as Ewing's sarcoma or acute osteomyelitis in the case 3 and a chronic osteomyelitis or benign bone tumors in the case 1 and 2. Therefore, not only plain radiograph and MRI but also open or needle biopsy is indispensable to arrive at the correct diagnosis of EG.

In spite of good prognosis of EG, various therapeutic approaches have been proposed. The effectiveness of curettage and bone grafting, local injection of corticosteroids, irradiation, and chemotherapy has been reported [1, 10–13]. Because the incidence of EG is low (1% of total primary bone tumor) and the trend to spontaneous healing is high, it is very difficult to assess the true efficacy of these therapies. Treatment of EG affecting the pelvis is usually accomplished by curettage of the affected site and bone grafting [4]. On the other hand, spontaneous healing of EG after open or needle biopsy has been reported by several authors [2, 4, 5]. Case 1 and 2 showed a pain relief in a few weeks after biopsy and spontaneous healing in a few months. In this respect, a careful observation after open or needle biopsy is thought to be one of the treatment options for EG. Some of EG may resolve spontaneously, and the other will persist or expand after biopsy [12]. Case 3 showed an osteolysis with ill-defined margins and large soft tissue mass which extended into medial retroperitoneal space and the lateral gluteal muscles. This case did not resolve spontaneously. Howard et al. reported a similar case of EG in the pelvis as the case 3 which showed prominent osteolysis with ill-defined margins and large soft tissue edema extending into both side of the bone on T2-weighted images. This case did not show any tendency to resolve after biopsy, and additional curettage was carried out [14]. EG with acute radiological features such as osteolysis with ill-defined margins and large soft tissue edema on T2-weighted images may progress after open or needle biopsy. The chronic form of EG with well-defined margins and localized soft tissue mass on T2-weighted images may resolve spontaneously. We need further attention for EG especially with acute radiological features.

References

1. Plasschaert F, Craig C, Bell R, Cole WG, Wunder JS, Alman BA (2002) Eosinophilic granuloma: a different behavior in children than in adults. J Bone Joint Surg Br 84: 870–872.
2. Muscolo DL, Slullitel G, Ranalletta M, Aponte-Tinao LA, Ayerza MA (2003) Spontaneous remission of massive solitary eosinophilic granuloma of the femur. J Pediatr Orthop 23: 763–765.
3. Stull MA, Kransdorf MJ, Devaney KO (1992) Langerhans cell histiocytosis of bone. Radiographics 12: 801–823.
4. Hoover KB, Rosenthal DI, Mankin H (2007) Langerhans cell histiocytosis. Skeletal Radiol 36: 95–104.
5. Arouz EM, Saigal G, Rodriguez MM, Podda A (2005) Langerhans' cell histiocytosis: pathology, imaging and treatment of skeletal involvement. Pediatr Radiol 35: 103–115.
6. Kilborn TN, Teh J, Goodman TR (2003) Pediatric manifestations of langerhans cell histiocytosis: a review of the clinical and radiological findings. Clin Radiol 58: 269–278.
7. David R, Oria RA, Kumar R, Singleton EB, Lindell MM, Shirkhoda A, Mandewell JE (1989) Radiologic features of eosinophilic granuloma of bone. Am J Roentgenol 153: 1021–1026.
8. Monroc M, Pointe HD, Haddad S, Josset P, Montagne JP (1994) Soft tissue signal abnormality associated with eosinophilic granuloma: correlation of MR imaging with pathologic findings. Pediatr Radiol 24: 328–332.
9. Schepper AMA, Ramon F, Marck E (1993) MR imaging of eosinophilic granuloma: report of 11 cases. Skeletal Radiol 22: 163–166.
10. Yasko AW, Fanning CV, Ayala AG, Carrasco CH, Murray JA (1998) Percutaneous techniques for the diagnosis and treatment of localized Langerhans-cell histiocytosis (eosinophilic granuloma of bone). J Bone Joint Surg Am 80: 219–228.
11. Camargo OP, Oliveira NRB, Andrade JS, Filho RC, Croci AT, Barros TEP (1992) Eosinophilic granuloma of the ischium: long-term evaluation of a patient treated with steroids. J Bone Joint Surg Am 74: 445–447.
12. Greis PE, Hankin FM (1990) Eosinophilic granuloma: the management of solitary lesions of bone. Clin Orthop 257: 204–211.
13. Sessa S, Sommelet D, Lascombes P, Prévot J (1994) Treatment of Langerhans cell histiocytosis in children. Experience at the Children's Hospital of Nancy. J Bone Joint Surg Am 76: 1513–1525.
14. Howard CB, Nyska M, Porat S, Bessorai R, Anir A, Meller I (1996) Solitary eosinophilic granuloma of pelvis in children: a report of three cases. Arch Orthop Trauma Surg 115: 216–218.

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