Giant-Cell Reparative Granuloma of the Hands and Feet

Heather C. Eck, MD
Scott D. Weiner, MD

CASE REPORT

Giant-cell reparative granuloma is a rare, benign, intraosseous lesion first described by Jaffe1 in 1953 believed to be limited to the mandible and maxilla. Since then, giant-cell reparative granulomas have been reported in other skeletal bones. The lesion most commonly occurs in the small tubular bones of the hands and feet.

Giant-cell reparative granuloma must be considered in the differential diagnosis of hand and foot lesions. Some consider giant-cell reparative granulomas “solid” aneurysmal bone cysts due to the histologic similarities without the blood-filled lakes.2-5 Extensive resection is not required as surgical curettage is the treatment of choice.

This article reports four cases of giant-cell reparative granuloma involving the hands and feet and reviews the literature.

CASE REPORTS

Case 1

A 17-year-old boy presented with intermittent symptoms consistent with a stress fracture of the foot. Two weeks prior to presentation, pain became more acute. Medical and family history were insignificant.

On physical examination, an isolated diffuse abdominal wall birthmark was noted but no other stigmata of McCune-Albright syndrome (polyostotic fibrous dysplasia, precocious puberty, and cafe-au-lait spots) or neurofibromatosis were seen. Radiographs revealed a destructive lesion of the third metatarsal head (Figure 1).

Incisional biopsy was performed, and frozen section diagnosis confirmed a benign lesion, most likely an aneurysmal bone cyst or giant-cell reparative granuloma. Curettage without local adjuvant was performed. Iliac crest bone graft filled the defect. Final pathology was consistent with giant-cell reparative granuloma (Figure 2).

At 16 months postoperatively, the defect had consolidated with no recurrence and the patient was asymptomatic. Local recurrence occurred 3 years postoperatively. Repeat curettage, butting and filling of the defect with tricortical/iliac crest was performed. No local recurrence was noted at 1-year follow-up.

Figure 1: Case 1. AP radiograph of the foot reveals a radiolucent lesion of the third metatarsal head. Expansion of the cortex and a poorly defined margin are noted. Figure 2: Case 1. High power histology of clustered giant cells of differing sizes (hematoxylin-eosin, original magnification ×100).

Case 2

A 47-year-old man with insulin-dependent diabetes mellitus presented with moderate pain and swelling of the lateral midfoot. He denied fever, chills, or systemic symptoms. No erythema or fluctuance were noted. Propioception was decreased but sensation was protected.

Radiographs revealed a radiolucent area in the base of the fourth metatarsal. No joint destruction was noted (Figure 3). The remaining regions of the radiograph were normal.

Laboratory results were negative except for a Westergren sedimentation rate of 77 (normal: 0-10). Bone scan showed localized uptake in the region of the radiographic abnormality. The adjacent joints were not involved. Computed tomography (CT) demonstrated a well-defined reactive rim of bone with a continuous periosseous reaction extending distally but no matrix mineralization. A benign process was suspected, but because of discomfort, an inci-
A professional biopsy was performed. Histologic findings were consistent with giant-cell reparative granuloma. Curettage and cementation were performed. At 2-year follow-up, symptoms had resolved.

**Case 3**

A 43-year-old woman presented with an enlarging mass of the right ring proximal phalanx. Medical history was insignificant. Radiographs revealed an eccentric radiolucent lesion with a well-defined rim of bone over the soft-tissue extension (Figure 4). Simple curettage and allograft packing of the lesion was performed. Four months postoperatively, recurrence was noted (Figure 5). Repeat curettage with extended burring was performed, and the defect was filled with methylmethacrylate.

Typical findings of giant-cell reparative granuloma were noted on final pathology. At 28-month follow-up, the patient was asymptomatic with no recurrence.

**Case 4**

An 18-year-old man presented with medial forefoot pain and swelling. He reported no previous trauma, surgery, and systemic signs and symptoms. He had no other bony sites of discomfort, and medical history was insignificant.

Radiographs of the foot showed a radiolucent lesion of the first metatarsal with a poorly defined rim and soft-tissue extension (Figure 6). Bone scan was intensely hot in the area of the radiographic involvement, but demonstrated no other lesions (Figure 7). Magnetic resonance imaging (MRI) showed a lesion of mixed signal intensity with a soft-tissue mass. Preoperative diagnosis was giant-cell tumor or sarcoma.

Open incisional biopsy represented giant-cell tumor on frozen section. Extended curettage and burring was performed and methylmethacrylate was used as a local adjuvant. Final pathology was consistent with giant-cell reparative granuloma.

The patient was lost to immediate follow-up. At 1 year postoperatively, worsening pain and swelling occurred. A repeat radiograph showed extensive recurrence around the cement (Figure 8). Although the initial concern was for a missed giant-cell rich osteosarcoma, final pathology was consistent with giant-cell reparative granuloma. Repeat extended curettage and cementation was performed. No recurrence was noted 20 months postoperatively.

**DISCUSSION**

In 1953, Jaffe first described a benign bone lesion with intraosseous hemorrhage limited to the maxilla and mandible as “giant-cell reparative granuloma.” In 1962, Ackerman and Spjut reported the first two cases of giant-cell reparative granuloma in the small tubular bones of the hands.5,6 Since then, isolated case reports of giant-cell reparative granuloma have involved the femur, tibia, pelvic bones, vertebrae (cervical and thoracic), ribs, clavicles, humerus, and the small tubular bones of the hands and feet.5-9 Although numerous case reports exist, this entity is not well known and often is confused with more aggressive processes.

The etiology of giant-cell reparative granuloma is unknown. Some speculate that a hemorrhagic episode linked to trauma triggers a reactive granulomatous process.1,10 This is debatable because many reported cases were not linked to a traumatic event. Kenan et al11 believe giant-cell reparative granuloma is caused by intraosseous hemorrhage from trauma because hemorrhage and hemosiderin are found in the medullary cavity.

Due to the microscopic characteristics of this lesion (ie, the irregular granulomatous areas and mixed cellular composition), Hirschl and Katz10 theo-
rize that giant-cell reparative granuloma may be an end result of chronic inflammation or infection.

In most cases, these lesions occur in individuals who have no other pre-existing bone conditions; however, giant-cell reparative granulomas have been reported in association with Paget’s disease and fibrous dysplasia. Giant-cell reparative granuloma usually is a unifocal lesion, but one multifocal lesion has been reported. To date, metastasis has not been reported; the final outcome is always benign.

These benign lesions usually present between the first and third decades of life. Most studies report a female predominance, with some reporting a higher male to female ratio. The most common symptoms are pain and swelling, although some patients do not experience pain. Other symptoms depend on the location of the lesion, and include palpably enlarged bone, tenderness, radiolucent, pathologic fractures, and headache. Symptom duration prior to diagnosis ranges from 6 weeks to 10 years. The combination of clinical features and histology is used to make the diagnosis.

Radiographically, giant-cell reparative granuloma appears as round or oval radiolucent abnormalities. Most lesions involve the meta- and diaphysis within the lesion itself. Most lesions involve the meta- and diaphysis. Some bone expansion may occur, and the bone cortex may be thinned or eroded, but the tumor does not completely penetrate the cortex. Typically, no periosteal reaction (unless a pathologic fracture occurred) or surrounding reactive bone exist. Giant-cell reparative granuloma may extend into the subarticular bone, but not the articular cartilage. When giant-cell reparative granuloma affects a vertebral, the posterior column tends to be the area involved.

Histologically, giant-cell reparative granuloma has giant cells that are grouped together around areas of new and old hemorrhage, giving the appearance of a granuloma, from which it gets its name. The giant cells are small and irregularly shaped and have few nuclei. Osteoid and reactive new bone formation is noted around the areas of hemorrhage within the lesion. The stroma is composed of spindle cells, fibroblasts, histiocytes, areas of abundant collagen formation (fibrosis), and lymphocytic infiltrates. Mitotic figures are rare. Small blood-filled sinusoids and empty cystic spaces may be noted, which differentiate it from other giant-cell lesions. Hemosiderin deposits also are in the narrow cavity.

On gross examination, giant-cell reparative granuloma is a soft, spongy, gritty, friable tissue reddish in color. This tissue can range in color from pinkish tan to gray to brown. Some authors have reported the lesion to be solid. Giant-cell reparative granuloma tumor is devoid of the large blood-filled sacs seen in aneurysmal bone cysts. Some lesions have an eggshell thick layer of reactive bone surrounding the tumor.

The differential diagnosis of giant-cell reparative granuloma includes aneurysmal bone cyst, giant-cell bone tumor, and brown tumor of hyperparathyroidism. On radiographs, giant-cell reparative granuloma and aneurysmal bone cyst are radiolucent lesions, but aneurysmal bone cyst has a typical eccentric cystic “blow-out” appearance. Disruption of the cortex exists, which does not typically occur with giant-cell reparative granuloma. Fluid-fluid levels on CT or MRI are missing in giant-cell reparative granuloma. Despite these differences, these two entities overlap. Therefore, an accurate diagnosis cannot be made solely on the basis of radiographs.

On histological examination, both lesions have common features, such as spindle-shaped stromal cells mixed with reactive multinucleated giant cells, giving rise to the term solid variant of aneurysmal bone cyst. One distinguishing characteristic is the blood-filled vascular spaces found in aneurysmal bone cysts, compared with the small blood-filled spaces and noncystic appearance of giant-cell reparative granuloma.

Histologically and radiographically, giant-cell reparative granuloma and brown tumor of hyperparathyroidism are indistinguishable. However, it is rare that a brown tumor would be the only skeletal manifestation of hyperparathyroidism, since generalized osteopenia and subperiosteal resorption of the cortex usually accompany multiple lytic lesions. On hyperparathyroidism histological examination, hemorrhage, increased osteoclastic activity, marrow fibrosis, and signs of reactive repair are present. Serum calcium, phosphorus, alkaline phosphatase, and parathyroid hormone levels can be obtained to differentiate between the two disorders. Work-up for hyperparathyroidism usually is deferred unless multiple bone lesions or significant osteopenia is present.

Another condition that must be differentiated from giant-cell reparative granuloma is giant-cell bone tumor. Giant-cell bone tumor is a more aggressive lesion, and metastasis to the lung has been reported. Compared to giant-cell reparative granuloma, where the giant cells are present in clusters around areas of hemorrhage, the giant cells in giant-cell bone tumor are found uniformly throughout the lesion.

Giant-cell bone tumors rarely produce osteoid or new bone compared to the reactive new bone formation in giant-cell reparative granuloma. Also, the giant cells in giant-cell bone tumors are larger, more numerous, rounder, more evenly distributed, and contain more nuclei. The stromal cells of giant-cell bone tumor are plump and oval-shaped. Giant-cell bone tumors have a less cellular fibrous stroma than giant-cell reparative granulomas. In contrast to giant-cell reparative granuloma, lymphocytes are not usually found in giant-cell bone tumor.

On radiographs, the lesion is eccentric, lytic, and expands into the bone.
Giant-cell bone tumors are found in the epiphysis and occasionally extend into the metaphysis. The cortical destruction may occur, and a soft-tissue mass may be noted.

Initial treatment is curettage with bone grafting, if needed. If the lesion is not amenable to surgery or if it was not completely removed through surgery, small doses of radiation therapy can be used. Radiotherapy should only be used in these rare instances because of the risks it carries to the patient, such as secondary sarcoma development. Radiation should only be used for inaccessible lesions where continued growth would lead to unacceptable morbidity.

Recurrence rates between 33% and 75% have been reported after curettage. These can be treated by repeat curettage and bone grafting, ray amputation, or excision and bone grafting. Dahlin found that recurrences did not occur if more aggressive therapy, such as wide resection, was performed initially. The benign nature of a local recurrence does not seem to support a wide resection unless located in an expendable bone.

Although rare, second recurrences have been reported. These can also be treated with curettage, although amputation or resection may be necessary if the lesion is large. Repeated curettage rather than extensive resection is indicated due to the benign nature of the lesion.

The three recurrences in the current patients were believed to be due to incomplete initial curettage. Extending the intraosseous margin with a high-speed burr or adding cement may decrease the risk of local recurrence. The authors have no experience with phenol or liquid nitrogen as local adjuvants for giant-cell reparative granuloma.

REFERENCES


