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CASE REPORT

Giant cell reparative granuloma of the scapula: report of a case and literature review

Andrea Angelini[1] · Elisa Pagliarini[1] · Elisa Belluzzi[1] · Rocco Cappellesso[2] · Pietro Ruggieri[1]

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Abstract
Giant cell reparative granulomas (GCRGs) are non-neoplastic inflammatory lesions, usually observed in the maxilla, mandible or small bones of the hands and feet. These lesions present a wide range of morphology and the misinterpretation with other giant cell lesions can often occur. We report the case of a 47-year-old woman with GCRG in the left scapula, presenting some uncommon features: the location (scapula) and age at presentation, the lack of underlying bone disease such as Paget's disease or fibrous dysplasia, the large aggressive expansile aspect of the lesion. This was a therapeutic study, level IV (case series with no or a historical control group).

Keywords Aneurysmal bone cyst · Giant cell tumor · Curettage · Hand · Benign tumor · Differential diagnosis · Treatment

Introduction

Giant cell reparative granuloma (GCRG) is a non-neoplastic fibrous lesion with giant cells that seems similar to other benign bone lesions such as giant cell tumor, aneurismal bone cyst (ABC), and brown tumor. Jaffe reported the first case of GCRG in 1953 in a patient with maxillar and mandibular involvement [1]. The lesion is also known as a solid variant of aneurysmal bone cyst (s-ABC) [2, 3]. These two definitions have been equally used in the pathology literature up to the recent years. The GCRG is mainly used to describe lesions involving the short tubular bones of the hand and feet or craniofacial skeleton, whereas lesions occurring within the appendicular long bones are referred to as s-ABC. In the most up-to-date WHO classification, these two lesions have been included in the group of giant cell lesions of bone [4]. These lesions are typically found at the facial bones and skull, but have also been reported in decreasing frequency in the small bones of the hands and feet [5–16], in the long bones [3, 17–21], and in the vertebrae [3, 22]. We present a rare case of GCRG of the scapula treated with surgical resection.

Case report

A 47-year-old woman presented with a 1-month history of swelling of the left shoulder without pain. No previous traumas were reported. Her medical history reveals a previous nasal polyposis and depression. Laboratory findings (complete blood count, prothrombin time, partial thromboplastin time, and serum level of calcium) were within normal limits. Physical examination revealed swelling in the left shoulder with a bony tight mass, adherent to superficial and deep planes, located under the left trapezium muscle. The range of motion of the shoulder, muscle strength, and sensitivity were regular. Radiographs (Fig. 1a) and CT scans (Fig. 1b) of the shoulder showed a lytic lesion with a lobulated aspect, originating from the superior–medial angle of the left scapula. Magnetic resonance (MR) images (Fig. 1c, d) showed an expansile multinodular lesion (6 × 5 cm in the axial plane and with a 4-cm craniocaudal extension) that was isointense on T1-weighted contrast-enhanced images with focal low signal intensity. A guided trocar biopsy was performed, revealing a GCRG. Subsequently, a marginal resection of the lesion

✉ Andrea Angelini
andrea.angelini83@yahoo.it

[1] Department of Orthopedics and Orthopedic Oncology, University of Padova, Via Giustiniani 3, Padova, Italy

[2] Department of Medicine, University of Padova, Padova, Italy

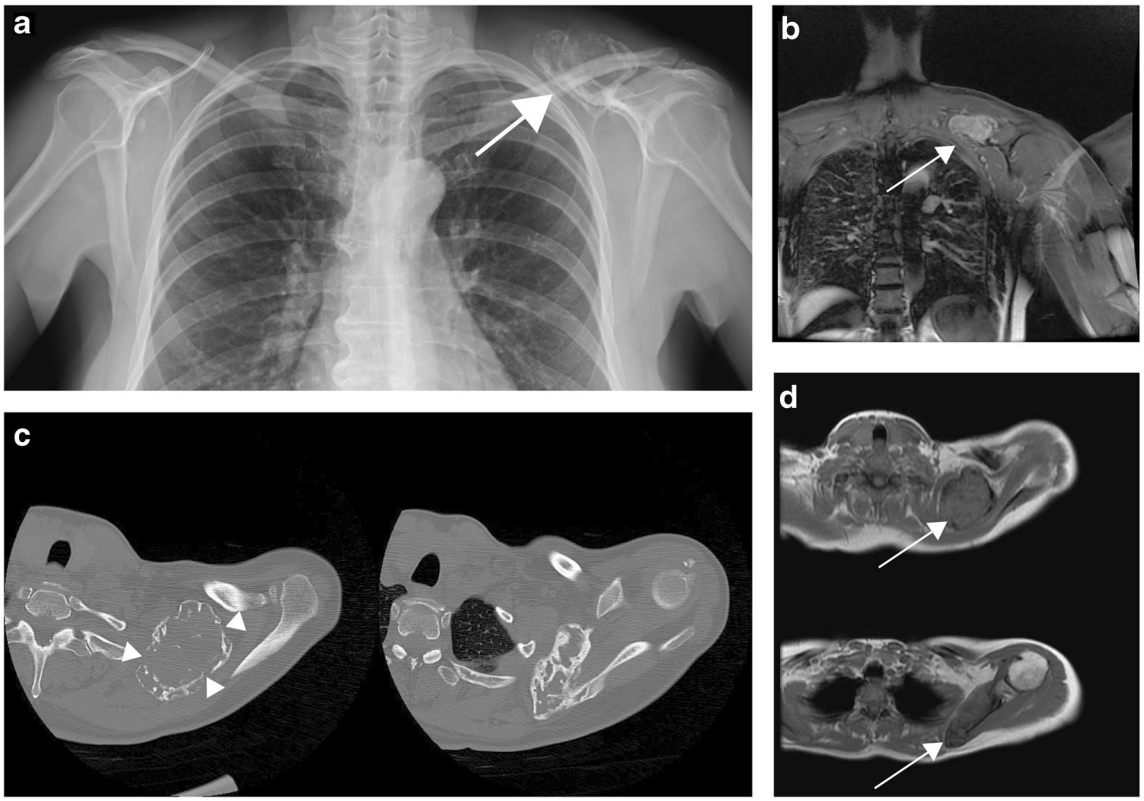

Fig. 1 Giant cell reparative granuloma of the scapula in a 47-year-old woman. **a** Anteroposterior radiographs showing a large lytic expansile lesion of the supero-medial angle of the scapula (*white arrow*). **b** Axial computed tomography scans show a lytic expansile lesion with cortical breakthrough considering the location (*arrowheads*), without soft-tissue involvement. **c** Coronal T2-weighted images show a mass of intermediate to focal high signal intensity (*white arrow*) whereas **d** axial T1-weighted unenhanced spin echo sequences show a low signal intensity lesion with areas of lower signal intensity, corresponding to tumor ossifications (*white arrows*)

was performed. Histological analysis of the specimen showed multiple hemorrhagic areas and reactive osteoid and bone formation (Fig. 2). Multinucleated giant cells were mostly seen around these areas; their nuclei were round, but those of the stromal cells were ovoid or spindle-shaped. The stroma contained abundant collagen, many spindle cells, inflammatory mononuclear cells, hemorrhages, and hemosiderin pigments, and occasional newly formed reactive osteoid or bone trabeculae rimmed with osteoblasts. Atypical mitoses were not seen. Based on these findings, the diagnosis of GCRG was confirmed. No clinical or radiographic evidence for a recurrent lesion was found after 2 years' follow-up (Fig. 3), with normal function of the shoulder.

Literature review

A systematic search of the literature was performed to identify studies reporting patients with GCRG of the bone. English- and non-English-language papers were searched in PubMed using a combination of terms or MeSH "giant cell reparative granuloma," "giant cell," "granuloma," "aneurysmal bone cyst," and all synonyms. The search was carried out using the literature from 1985 to date. The focus of each reference varied, including series of patients with GCRG regardless of location, case reports, and articles investigating imaging appearance. All cases involving skull and facial bones were excluded. The data of the available papers are summarized in Table 1. We were able to find 71 patients with a slight female prevalence (39 female vs 33 males). Most of the patients were young (mean 22.5 years, range 8 years to 67 years), with the second decade mainly involved (39%) followed by the fourth (19%), first (15%), and third decades (14%). Small bones of the hand and feet were the most frequently reported sites (28 cases, 40%: 7 phalanx of the hand, 6 metacarpal, 3 carpal bones, 5 phalanx of the feet, 5 metatarsal, 1 calcaneus, and 1 cuneiform), followed by femur (11 cases, 18%), tibia (10), ulna (7), humerus (4), vertebrae (3), clavicle (2), radius (2), fibula (2), and rib (1). Patients were studied for clinical, radiological findings and for the type of treatment, except for 30 cases discussed mainly on imaging features. Clinically, most of the patients presented

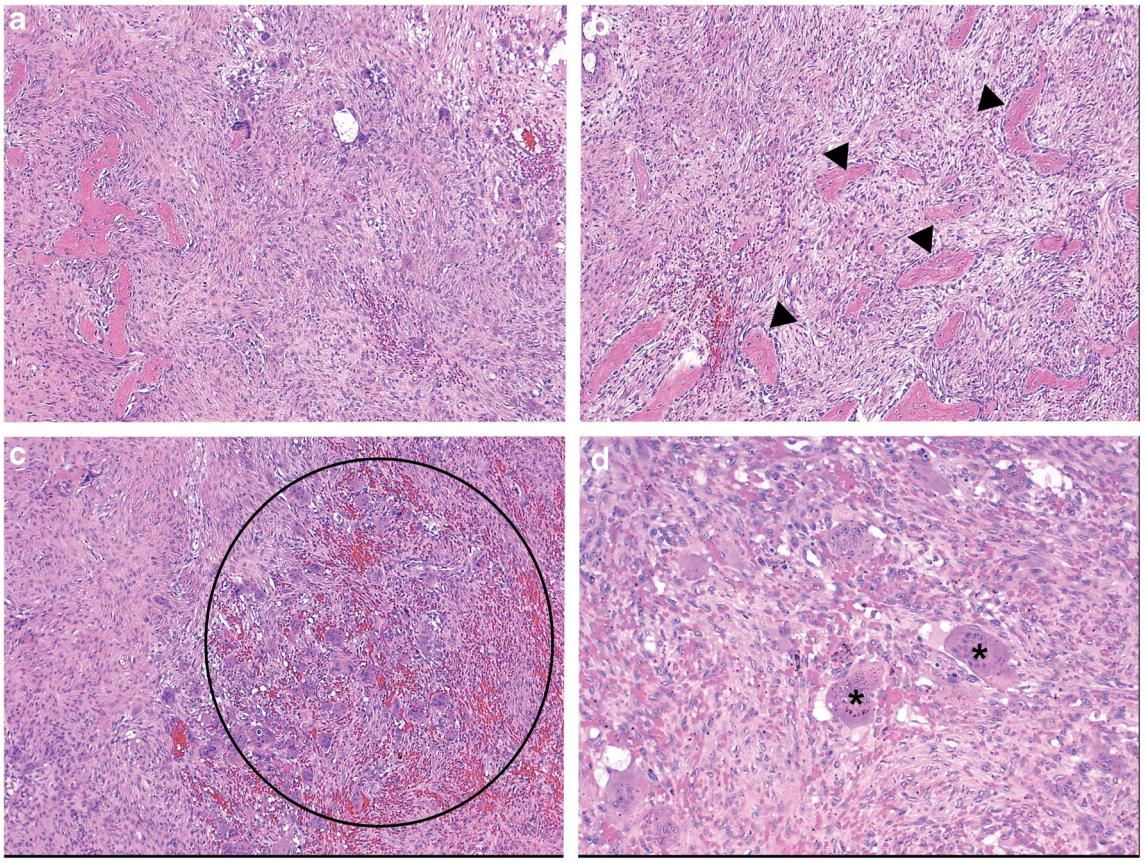

Fig. 2 Photomicrographs show peculiar features of the giant cell reparative granuloma. Original magnification ×100 in **a**, **b**, and **c**, ×200 in **d**. Hematoxylin and eosin stain. **a** Fibrous stromal tissue with spindle-shaped fibroblasts with reactive bone formation, foci of hemorrhage, and unevenly distributed multinucleated giant cells. **b** Reactive bone formation with prominent osteoblastic rims (*black arrowheads*). **c** Area of fresh hemorrhage with a cluster of multinucleated giant cells (*black circle*). **d** Multinucleated giant cells with hemosiderin granules within their cytoplasm (*asterisks*)

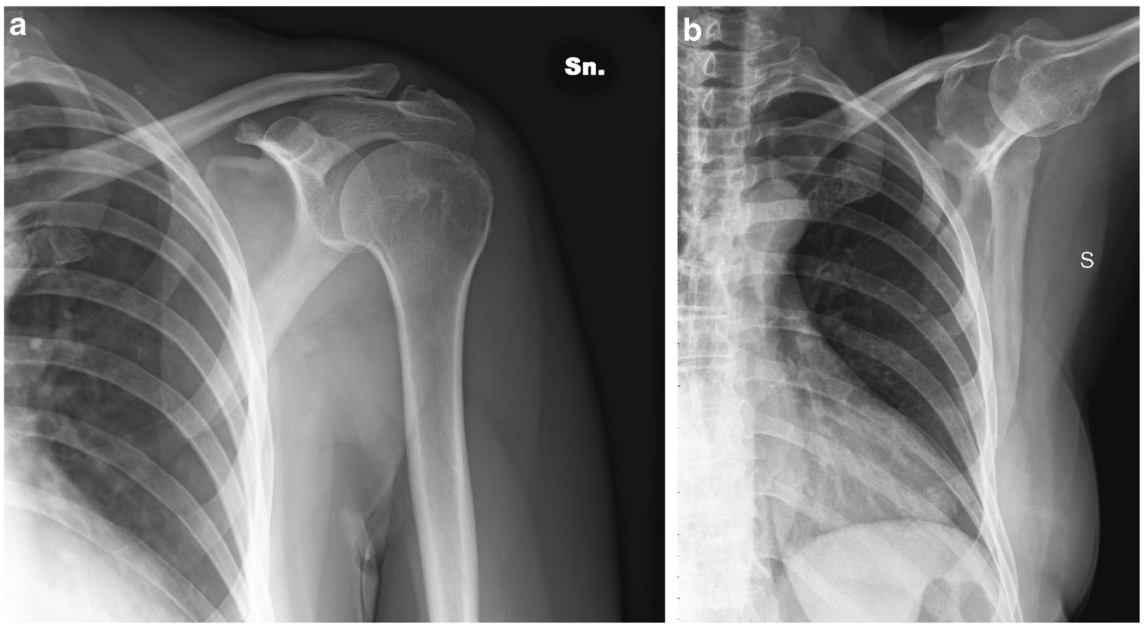

Fig. 3 Follow-up evaluation. **a** Anteroposterior radiographs at 10 months' follow-up. **b** Radiograph of the scapula shows no local recurrence at 20 months' follow-up

Table 1 Giant cell reparative granuloma of bone. Systematic review of the literature from 1985 to 2017

Reference	Year	Number of patients	Age (years)/ gender	Site	Symptoms	Treatment	Local recurrence	Follow-up (months)
Caskey et al. [5]	1985	1	24/male	Metacarpal, capitate	n.a.	n.a.	n.a.	n.a.
Picci et al. [6]	1986	11	Mean 22/ mostly males	Phalanx (6) Metacarpal (1) Carpal bones (2) Tarsal bones (2)	n.a.	Curettage + grafts (9) Resection (2)	n.a.	n.a.
Inoue et al. [22]	1986	1	16/female	Vertebra	n.a.	Curettage	Yes[a]	38
Thomas et al. [17]	1988	1	14/female	Humerus	n.a.	Curettage	n.a.	n.a.
Robinson et al. [16]	1989	1	17/male	Calcaneus	6 months of pain, pathological fracture	Curettage + grafts	n.a.	n.a.
Herman et al. [18]	1990	1	57/male	Femur	3 months of pain	Resection	–	18
Oda et al. [3]	1992	1	36/male	Humerus	Pain	Curettage + grafts	–	228
		1	34/female	Clavicle	Pain	Resection	–	22
		1	32/female	Tibia	Pain	Curettage + grafts	–	26
		1	17/female	Vertebra	Radiculopathy	Curettage + grafts	–	12
		1	16/female	Vertebra	Back pain	Curettage + grafts	–	100
		1	16/male	Rib	–	Research	–	204
		1	8/male	Clavicle	Pathological fracture	Curettage + grafts	–	24
Panico et al. [7]	1994	1	41/male	Metacarpal	n.a.	Resection	Yes	65
		1	16/male	Phalanx	n.a.	Curettage	–	27
		1	17/male	Metatarsal	n.a.	Curettage	–	33
		1	31/female	Metatarsal	n.a.	Curettage	–	32
		1	34/female	Phalanx	n.a.	Resection	–	30
Giza et al. [8]	1997	1	67/female	Metacarpal	1 month of pain	Resection	–	36
Cook and Braunstein [9]	1998	1	33/male	Cuneiform	3 months of pain	n.a.	n.a.	n.a.
Ugwonali et al. [10]	1999	1	45/female	Metacarpal	Pathological fracture	Curettage + grafts	Yes	150
Forouhar et al. [11]	2000	1	15/female	Metatarsal	1.5 months of pain	Resection	n.a.	n.a.
		1	12/female	Phalanx	2 months of pain	Curettage + grafts	n.a.	n.a.
		1	8/female	Phalanx	4 months of pain	Curettage + grafts	n.a.	n.a.
Subasi et al. [19]	2003	1	60/female	Tibia	2 months of pain	Resection + grafts + intramedullary nailing	–	24
Macdonald et al. [12]	2003	1	25/male	Metacarpal	8 months of pain	Resection + grafts	–	7
Ilaslan et al. [20]	2003	30	Mean 18/ mostly female	Femur (10) Ulna (7) Tibia (7) Humerus (2) Radius (2) Fibula (2)	n.a.	n.a.	n.a.	n.a.
Hori et al. [21]	2008	1	45/male	Tibia	2 months of pain	Curettage + grafts	–	24
Mavrogenis et al. [13]	2010	1	34/female	Hamate	2 months of pain	Curettage + grafts[b]	–	12
Kamoun et al. [14]	2015	1	13/male	Hallux	Several months	n.a.	–	12
Huan and Norzila [15]	2016	1	21/female	Phalanx	2 years of swelling	Curettage + grafts + intramedullary K-wire	n.a.	n.a.
Angelini et al. (current study)	2018	1	47/female	Scapula	1 month of pain	Resection	–	24

n.a. not available

[a] Treated with new curettage

[b] With adjuvant chemoablation with phenol

with pain (17 cases), pathological fractures (3 cases), swelling (2 cases), and back pain with radiculopathy (2 cases), and the duration of symptoms ranged from 1 to 8 months. Previous trauma has been rarely reported. Surgical treatments consisted of curettage ($n = 26$) associated with bone grafting in 81% of the cases ($n = 21$), or resection/amputation (12 cases) followed by reconstruction with bone graft in 2 cases.

Discussion

The reported case has three remarkable teaching points:

1. Scapular localization and age at presentation.
2. Absence of underlying bone disease such as Paget's disease or fibrous dysplasia.
3. Large expansile aspect of the lesion.

Through our literature research, we were able to find 71 cases of extragnathic GCRG (Table 1) and most of these involved long bones (including short tubular bones of the hand and feet). Although GCRG may potentially affect each bone, only a few cases in uncommon sites have been reported. To date, no lesions affecting the scapula have been reported. Multiple involvement was reported in only two papers in the literature [5, 16].

The pathogenesis of GCRG remains unknown. The lesion has been thought to be related to trauma, repair, or faulty development [23]. Some authors reported that GCRG may originate in bones affected by certain underlying bone diseases, such as Paget's disease [24] and fibrous dysplasia [25, 26]. In our case, no underlying bone diseases were observed. Usually, the GCRG appears as a lytic, centrally localized expansile lesion that thinned the cortex without erosion or soft-tissue mass, and without evidence of periosteal new bone formation. Radiographically, GCRGs are indistinguishable from other giant cell lesions, such as giant cell tumors (GCTs) of the bone, aneurysmal bone cysts, brown tumors of hyperparathyroidism, chondroblastomas, and other lytic lesions of the appendicular skeleton as benign and malignant neoplasms [27]. Usually, GCRC does not penetrate the cortex compared with GCTs, which sometimes appear as aggressive, radiolucent, expansive lesions with cortical destruction and extension into the soft tissues [28]. However, some authors reported that GCRG may sometimes erode through the cortex, even if it is always well contained by the periosteum [6, 29]. Moreover, in our literature review, calcified matrix (6 cases), periosteal reaction (3 cases), and soft-tissue mass (7 cases) should be considered rare findings [8, 11, 19, 20, 26]. In our case, because of the location (angle of the scapula) and large tumor volume, cortical breakthrough has been considered an expected finding, without soft-tissue extension from the lesion. The right diagnosis of GCRG is essential for appropriate treatment. The defining histological features include homogeneous moderately to highly cellular stroma, with abundant collagen (fibroblastic or fibro-histiocytic background), many spindle and/or ovoid cells, and multinucleated giant cells. Surrounding areas of intraosseous hemorrhage with areas of reactive osteoid formation are often present [1, 23]. Atypical mitoses are usually absent [21]. The multinucleated giant cells of GCTs contain more nuclei than those of GCRG and less osteoid or bone formation [21, 25]. Histologically, ABC is a bone cyst composed of large, blood-filled vascular spaces, whereas GCRGs contain bare cystic sinuses and small blood-filled spaces only [23]. Osteoid and hemosiderin deposit may be seen in both lesions. The primary and secondary hyperparathyroidism result in the overproduction of parathyroid hormone that causes increased osteoclastic activity, leading to bone resorption and trabecular fibrosis that are not present in GCRGs. Brown tumors can be very similar, both radiographically and histologically, but could be excluded by the evaluation of biochemical abnormalities: in fact, the renal profile is normal in GCRG, without elevation of serum calcium, phosphorus, and alkaline phosphatase. Approximately 80% of ABC/GCRG cases with genetic abnormalities reported in the literature have shown some alterations of chromosome 17, with t(16;17)(q22;p13) as the most frequent rearrangement observed [30]. However, in a large literature review, there was a higher proportion of s-ABC or GCRG of the gnathic or small bones of the hand and feet without chromosome 17 involvement [30].

Complete curettage and bone grafting, especially in nondestructive lesions, is considered the gold standard of treatment for GCRG of bone [3, 6, 7, 10, 11, 13, 15–17, 21, 22, 26], but in some cases surgical resection is required [3, 6–8, 11, 12, 18, 19]. GCRG does not metastasize, but could be locally aggressive, with a reported recurrence rate up to 30%-50% after surgery [5, 7, 10]. In our patient, marginal resection of the scapular lesion was done and no signs of local recurrence were observed at the latest imaging examination.

Conclusion

Giant cell reparative granuloma has a wide range of clinical and radiographic presentations. As in the case reported here, the lesion could appear in an uncommon location and with an aggressive imaging pattern (breakage of the cortex, bony permeation, and soft-tissue extension). Adequate staging and biopsy are mandatory to avoid diagnostic errors and potential mismanagement.

Authors' contributions Conception and design of the study (AA, PR).
Acquisition of data (AA, EP, RC).
Analysis and interpretation of data (EP, EB).
Drafting the article or revising it critically for important intellectual content (AA, EP, RC).
Final approval of the version to be submitted (AA, PR).

Compliance with ethical standards

Conflicts of interest Each author certifies that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements) that may pose a conflict of interest in connection with the submitted article.

Ethical review board statement Each author certifies that his/her institution has approved the reporting of this case and that all investigations were conducted in conformity with ethical principles of research.

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