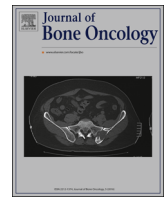




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Journal of Bone Oncology

journal homepage: www.elsevier.com/locate/jbo

Research Paper

The epidemiological and clinical features of primary giant cell tumor around the knee: A report from the multicenter retrospective study in china



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ARTICLE INFO

Article history:

Received 20 October 2015

Received in revised form

9 February 2016

Accepted 9 February 2016

Available online 11 February 2016

Keywords:

Giant cell tumor

Knee

Clinical

Epidemiology

Retrospective study

ABSTRACT

Objectives: We aimed to determine the demographic characteristics of giant cell tumor around the knee in China.

Methods: Between March 2000 and June 2014, patients with primary giant cell tumor around the knee were recruited from 6 institutions located in different regions of China, and were reviewed retrospectively the clinical features according to gender and age.

Results: 334 qualified patients were included in this study. The sex ratio was 1.14:1 (178/156), with mean ages of 36.9 years in men and 33.1 years in women, constituting a significant difference ($P=0.007$). The prevalence of pathological fracture was 32.9% overall (28.7% in men and 37.8% in women). The prevalence of simple fracture was significantly higher in women (26.3%) than in men (15.2%), $P=0.042$. Tumor location and staging did not differ significantly according to sex ($P>0.05$). However, comparing with >40 years old, those patients aged ≤ 40 were more likely to have a right knee tumor (56.7% vs. 44.7%, $P=0.042$), less likely to have Enneking stage 3 disease (18.6% vs. 35.0%, $P=0.005$), and less likely to have both soft-tissue extension and a mass (18.6% vs. 34.0%, $P=0.009$).

Conclusions: Giant cell tumor around the knee was more common in men than in women, although female patients were younger on average. Further, cases among patients ≤ 40 years old were observed to be milder than cases among older patients. The results suggest that efficient treatment and preservation of function should both be valued for young patients with giant cell tumor around the knee.

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1. Introduction

Giant cell tumor (GCT) is a primary intramedullary bone tumor that is composed of mononuclear and giant mononuclear cells, resembling osteoclasts [1]. It usually involves the end of a long bone. The World Health Organization has classified GCT as an aggressive, potentially

malignant lesion [2]. GCT accounts for 3–8% of primary bone tumors in Western nations, but it is more common in Asia, accounting for 20% of primary bone tumors [3–8]. GCT is most commonly diagnosed among 20–40 year olds, more likely to locate many sites of body, but half of GCTs occur around the knee [3,4,9–12]. About 10% of GCTs undergo malignant transformation, and pulmonary metastases occur in 1% to 4% of cases [13]. It has been reported that the postoperative recurrence rate is 10%–65% [5,6,14–16]. Therefore, GCT is one of the most controversial and widely discussed bone tumors [1,17,18].

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Previous, large retrospective studies from a single institution have indicated that GCTs predominantly occur among women, with a male-to-female gender ratio of 0.8:1 [5,19,20]. However, some studies have not shown this predominance [1,17,18]. Further, other studies have shown that most cases in Asia occur in men, with a gender ratio of 1.27–1.77 [21–24].

Recently, several studies from one institution have documented the characteristics of GCT in China. However, there has been an absence of large, multicenter, and representative studies of patients with GCT in China. In this study, we recruited the GCT patients from The Giant cell tumor Team of China, a multicenter nationwide GCT registry system, to explore the epidemiological characteristics of primary GCT around the knee, focusing on improving its diagnosis and treatment in China.

2. Materials and methods

2.1. Patients' selection

Between March 2000 and July 2014, patients with primary GCT around the knee were recruited from this multicenter nationwide GCT registry system, which included 6 centers of Orthopedic Oncology from different regions in China: Tianjin, Shandong, Shanxi, Zhejiang, Jiangsu, and Inner Mongolia. All patients had received their first histologically confirmed diagnoses of benign GCT and underwent surgical treatment. We excluded all patients with a preoperative diagnosis of GCT that was postoperatively determined to have been incorrect (i.e., patients with a non-GCT postoperative diagnosis). We further excluded all cases of GCT recurrence and all patients who were not treated surgically. Clinical and imaging data of the primary GCTs around the knee were reviewed retrospectively.

The ethics committee of Tianjin Hospital approved the study, and written informed consent was obtained from all patients during recruitment.

2.2. Tumor location

The patients with primary GCT around the knee were classified in three ways, according to the locations of their tumors. The first method of classifying location included the distal femur, proximal tibia, and other sites (the fibula and patella). The second method of classifying the tumor provided information on laterality (whether the tumor was located in the left or right knee). In the third method of grouping the tumors, tumors were classified as having grown centrally or eccentrically.

2.3. Staging

GCT is staged according to the Enneking staging system for benign bone tumors [25]. Under this system, stage 1(T₀) includes latent lesions that are biologically static; stage 2(T₁) includes active, slow-growing lesions that are confined within the bone; and stage 3(T₂) includes locally aggressive lesions with soft-tissue extension. GCTs can also be stratified according to the Campanacci system, which is based on plain radiography [26]. Under the Campanacci system grade I are the least common, and show features of latent or slow-growing tumors. The lesion is small, with a mild amount of sclerosis delineating the tumor. Bone contour is not affected, although the cortex can be thinned. The tumor does not extend to the articular cartilage. Symptoms are absent or minimal and of long duration. Grade II show features of an active lesion with ill-defined borders and without sclerosis. The cortex is thinned, if not breached and deformed with expansion, and the periosteum is elevated. The tumor often extends to the articular

cartilage from within the marrow. Grade III show features of extreme aggressiveness, with a tumor that has a large volume, destroys bone, and invades the surrounding soft tissues.

2.4. Soft-tissue extension and mass

Depending upon whether soft-tissue extension and/or mass were present, all patients were divided into 3 groups: patients with neither soft-tissue extension nor mass, patients with soft-tissue extension alone, and patients with both soft-tissue extension and mass.

2.5. Pathologic fracture

Pathologic fracture was confirmed based on radiological and surgical data. The types of pathologic fracture included (i) the absence of any pathological fracture, (ii) simple pathological fracture, and (iii) complex pathological fracture. Simple pathological fracture was defined as the presence of pathological fractures located extra-articular, or the presence of intra-articular fracture with a complete articular surface, no or mild shifting, a gross tumor volume < 200 cm³, a distance of > 3 mm between the tumor and subchondral bone, and no soft-tissue extension or mass. Complex pathological fracture was defined as the presence of pathological fractures located in the intra-articular with a destructive articular surface, obvious shifting, a gross tumor volume > 200 cm³, a distance of < 4 mm between the tumor and subchondral bone, and soft-tissue extension and mass.

2.6. Surgical treatment

Surgical techniques were based on the severity of the tumor and included intralesional curettage, curettage combined with resection, and en bloc marginal resection [27].

Intralesional curettage was indicated for patients with a localized lesion. With this procedure, a window in the cortical bone is made, followed by resection of the mass using a series of curettes of various sizes; the residual tumor cavity is then polished with a high-speed burr until the normal cortical bone is reached and is filled with allogeneic particle bone graft to fill the window.

Curettage combined with resection was performed in patients with an extensive lesion. With this procedure, the cortical bone and soft tissue mass impossible reserved are removed, and the tumor cavity is disposed using curettes and a high-speed burr; cavity bone defects are then filled with allogeneic particle bone graft, and an anatomical bone plate is used for internal fixation.

En bloc marginal resection was indicated for patients with severe involvement lesions. With this procedure, an osteotomy plane is confirmed based on preoperative magnetic resonance imaging, and the tumor is resected en bloc; an articulated prosthesis is used to reconstruct the knee.

2.7. Follow-up and outcome

The patients were followed-up every 3 months for the first 2 years post-operation, every 6 months until 5 years post-operation, and every 12 months until 10 years post-operation. Telephone interviews were allowed only after 5 years of follow-up. Information of local recurrence and metastases was obtained by face-to-face interview or telephone follow-up.

2.8. Statistical methods

All patient data were analyzed according to gender and age group. Because cases of GCT most commonly occur among patients 20–40 years old, age was categorized to two groups: ≤ 40 years

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