

## CASE REPORT

# Malignant transformation of a Giant Cell Tumor: a case report

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## ABSTRACT

**Introduction:** the knee is the anatomical region where most benign and malignant tumors affecting the human skeleton are found, including giant cell tumor.

**Patient information:** male, 28 years old, white, with no morbid health history, who came to the Orthopedics and Traumatology outpatient clinic for presenting a tumor at the level of the right knee accompanied by pain that appeared two years ago, but has increased in size rapidly in the last two months. Imaging tests and incisional biopsy were performed to confirm the diagnosis. The multidisciplinary team decided to amputate the limb.

**Conclusions:** giant cell tumor is a disease that occurs more frequently from the third to the fifth decade of life; its main complications are recurrence, pulmonary metastasis and malignant transformation. Patients with the latter complication require procedures such as limb amputation.

**Key words:** giant cell tumor; malignant transformation; amputation

## RESUMEN

**Introducción:** la rodilla es la región anatómica en la que asientan la mayor cantidad de tumores benignos y malignos que afectan el esqueleto humano, entre ellos el tumor de células gigantes.

**Información del paciente:** masculino, de 28 años de edad, blanco, sin antecedentes mórbidos de salud, que acudió a la Consulta externa de Ortopedia y Traumatología por presentar una tumoración a nivel de la rodilla derecha acompañada de dolor que apareció hace dos años, pero ha incrementado su tamaño de forma rápida en los últimos dos meses. Se le realizaron exámenes imagenológicos y toma de biopsia incisional para confirmar el diagnóstico. El equipo multidisciplinario decidió la amputación de la extremidad.

**Conclusiones:** el tumor de células gigantes es una enfermedad que se presenta con mayor frecuencia desde la tercera a la quinta décadas de la vida, sus complicaciones principales son la recidiva, las metástasis pulmonares y la transformación maligna.

Los enfermos con esta última complicación necesitan de procedimientos como la amputación de la extremidad.

**Palabras clave:** tumor de células gigantes; transformación maligna; amputación

## INTRODUCCIÓN

Giant cell tumor (GCT) is an osteolytic lesion that represents 5% of all bone neoplasms. The first description of this disease was made in 1818, but it was not until 1940 that it was differentiated from other bone lesions such as aneurysmal bone cyst (ABC), chondroblastoma and non-ossifying fibroma (NOF) in a more detailed way.<sup>(1)</sup> About 50-55% of GCTs occur around the knee and 10% are located in the distal radius.<sup>(2,3)</sup>

The main clinical manifestations are pain and enlargement, pathological fracture can be detected in 6 to 10% of patients and 10% may present metastases, usually in the lung.<sup>(2,4)</sup>

Imaging examinations such as plain radiography and computed axial tomography show an osteolytic image with classic soap bubble images that may or may not destroy the adjacent cortex. Magnetic resonance imaging helps to define the soft tissue invasion.<sup>(1,5)</sup>

Treatment is usually surgical and consists of resection of the tumor by curettage, en bloc or wide, each with different percentages of recurrence. These procedures are accompanied by others such as the use of hydrogen peroxide, grafting and embolization and drugs such as denozumab; amputation is justified in case of malignancy.<sup>(1,6)</sup>

Malignization of a GCT occurs as a consequence of radiation therapy or from a primary lesion. Malignancy from a giant cell tumor is extremely rare and its incidence is less than 1% of all GCTs. They usually occur in females and a decade after the usual age of presentation of GCT.<sup>(1,7)</sup>

Due to the infrequency of malignant transformation of this tumor, the authors of this work show a patient with a malignant GCT in the right knee.

## PATIENT INFORMATION

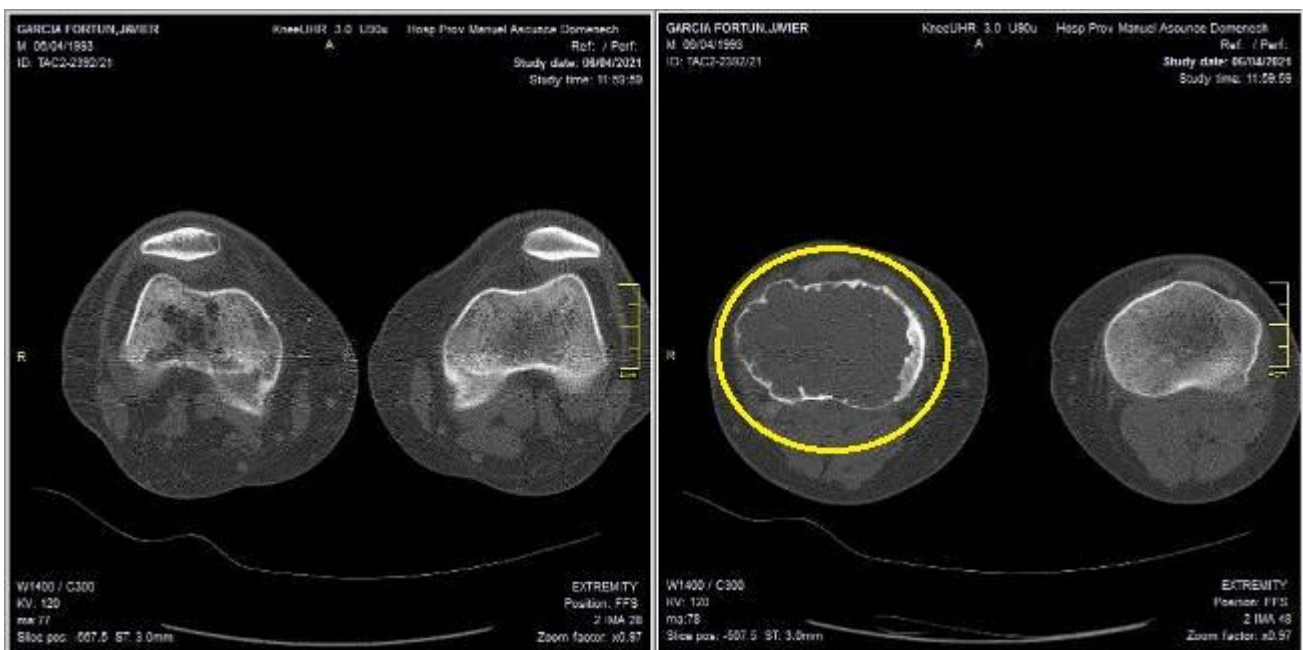
Male patient, 28 years old, white, with no morbid health history, admitted to the Orthopedics and Traumatology outpatient clinic of the "Manuel Ascunce Domenech" University Hospital in the city of Camagüey, in the province of the same name, for presenting a tumor at the level of the right knee accompanied by pain. It appeared two years ago, but it has increased its size rapidly in the last two months.

On physical examination, the tumor was observed on the anterior and lateral aspect of the right knee, with a hard consistency, fixed, larger than eight centimeters, with irregular borders and increased local temperature.

Imaging studies were performed by plain radiography, computerized axial tomography and magnetic resonance imaging. The topogram of both knees showed in the right knee an osteolytic image occupying the entire proximal area without sclerotic borders and very poorly defined (Figure 1). The axial tomographic view showed the osteolytic image below the articular surface (Figure 2). Magnetic resonance imaging showed invasion of the tumor into the surrounding soft tissues (Figure 3).



**Figure 1.** Topogram of both knees: an osteolytic tumor image is observed in the right proximal tibia (yellow circle)



**Figure 2.** Axial view of the computed axial tomography showing an osteolytic image of the right proximal tibia (yellow circle) that occupies almost its entire length



**Figure 3.** MRI image of the right knee showing a tumor of the knee in the right proximal tibia with invasion into the surrounding soft tissues, the image on the left is yellow and the image on the right is red.

Analytical studies showed:

Hematocrit: 0.40%

Glycemia: 6.0 mmol/l

Erythrocyte sedimentation rate: 25 mm/h

Creatinine: 67  $\mu$ mol/l

Alkaline phosphatase: 161

Glutamic oxaloacetic transaminase (GOT): 27

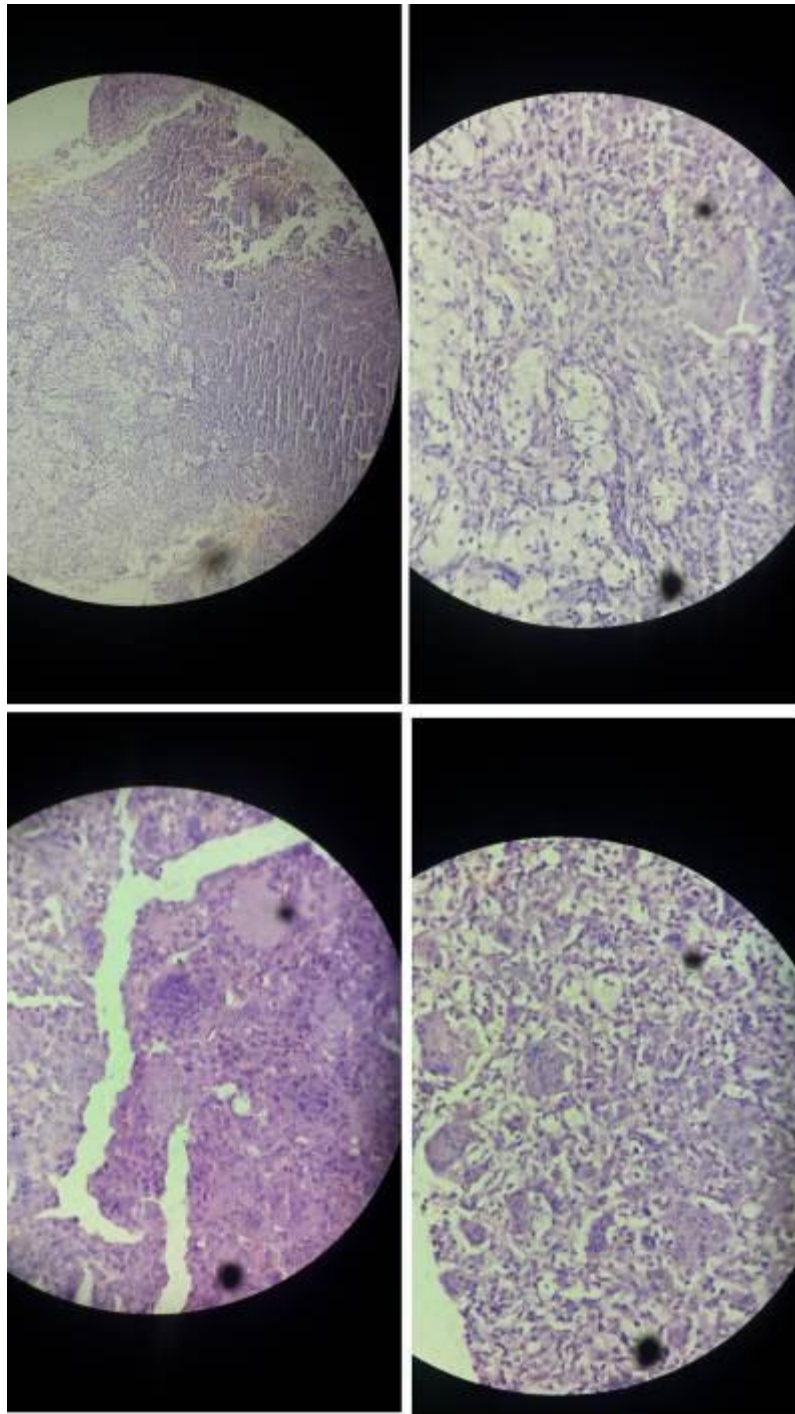
Blood group and factor: Rh O+

Due to all the above elements, it was decided to take the patient to the operating room for an incisional biopsy, which revealed a malignant bone GCT with extension to the soft tissues and intense lymphohistiocytic infiltration.

Taking into account the clinical, imaging and histological elements, the case was discussed in the multidisciplinary team formed by specialists in Orthopedics, Oncology, Radiology and Pathological Anatomy and it was decided, with the consent of the patient and the family, to amputate the limb with a wide margin.

The histological result of the entire tumor specimen after amputation revealed a malignant giant cell tumor of bone with extension to soft tissues and intense lymphohistiocytic infiltration and the presence of abundant multinucleated giant cells of the osteoclast type, uniformly distributed and surrounded by dense accumulations of mononuclear cells. The specimen presented histological grade three, presence of necrosis, high grade mitotic index and presence of lymphovascular invasion (Figure 4).

At the time of diagnosis, the presence of pulmonary metastases was not demonstrated by computed axial tomography, nor was abdominal organ involvement by ultrasound.



**Figure 4.** Tumor histology

## DISCUSSION

Considering the age of the patient, it is within the typical range of this tumor, which is between 20 and 45 years.<sup>(2,8,9)</sup> The female sex is the most affected in relation to the male sex, in a ratio of 1.5 to 1, for this statistical reason the malignant transformations are more frequent in the first one, which does not correlate with the patient presented in this work.<sup>(1,2,10)</sup>

The main localization of GCTs are the bones that make up the knee joint, which is related to the patient presented.<sup>(1,4)</sup>

In the differential diagnosis of GCT, from the imaging point of view, other lesions should be taken into account, such as OAK, chondrosarcoma, chordoma and telangiectatic osteosarcoma.<sup>(2,9,11)</sup>

When taking into account the histological features there are tumors with similar features that should be ruled out such as giant cell granuloma, QOA, brown tumor of hyperparathyroidism, malignant fibrous histiocytoma, chondroblastoma and FNO. In the case of this patient, the main disease to rule out due to age and imaging characteristics is OAGC, which is usually located in the metaphyseal area and then extends to the epiphysis, an element that differentiates it from GCT, which is of epiphyseal type from the beginning. The histology of GCT has solid components in the tumor, and in OAC these elements are present when secondary changes occur.<sup>(1,9)</sup>

The three most reported complications in patients with GCT are recurrence, which varies from 15 to 50%, the presence of pulmonary metastases, in 5%, and malignant transformation, which is the rarest.<sup>(7,12)</sup>

From the histological point of view, malignant transformation of GCT can be of the fibrosarcoma, undifferentiated pleomorphic sarcoma and osteosarcoma type, as in the patient presented in this work.<sup>(1,9)</sup>

GCT malignization is of two types: primary, when it occurs at the starting point of a benign tumor at the time of diagnosis, and secondary, when it appears after treatment at the site of primary origin (it occurs more frequently after radiotherapy). In this case presented we are dealing with a primary type, in which the patient took two years to seek specialized medical care.<sup>(11,12)</sup>

At present there are advanced genetic (H3F3A gene) and molecular studies that help in the early diagnosis of malignancy in patients with GCT, the p53 mutation is associated with recurrence and malignant transformation. Immuno-histochemically, GCTs are positive for CD68, CD45 and CD33.<sup>(1,3)</sup>

Although the most commonly used surgical treatment modality is resection, either through a wide or radical margin, amputation is justified in patients with aggressive GCT or with histologically proven malignant transformation as in the patient presented in this work.<sup>(1,2,12)</sup>

GCT is a disease that occurs more frequently from the third to the fifth decades of life; its main complications are recurrence, pulmonary metastases and malignant transformation. In general, patients with the latter complication require procedures such as limb amputation.

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## CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

## CONTRIBUTION OF THE AUTHORS

AÁL: Conceptualization, data curation, formal analysis, research, methodology, project management, software, supervision, validation, visualization, writing the original draft, writing (review and editing).

YCGL: Conceptualization, research, project management, validation, writing the original draft, writing (review and edit).

MFD: data curation, methodology, software, visualization.

JCG: formal analysis, methodology, supervision, writing the original draft, writing (review and editing).