CORRELATION BETWEEN IMAGING TESTS AND ANATOMICOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL CHARACTERISTICS IN A CASE OF SEVERE GIANT CELL TUMOR OF BONE LOCATED AT SPINE

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SUMMARY

Giant Cell Tumor (GCT) is a benign tumor, with a recurrence rate of about 20% - 34% of the cases. It is usually located at long bone epiphysis.
The objective of this study is to report a GCT case in a vertebra, which was early diagnosed as Aneurysmal Bone Cyst (ABC), and to discuss potential differential diagnosis, correlating them to patterns shown on imaging tests.
This patient is a 37 year-old female, with clinical picture of pain in spine and paraparesis that started two months earlier.
An early diagnosis of ACB was delivered. At X-ray, the injury was lithic, with erosion and cortical destruction. Tomography and resonance showed a cystic and hemorrhagic injury, extending to soft parts. Slides review and the analysis of dried surgical matter submitted to HE and immunohistochemical staining with p53 marker allowed for GCT diagnosis.
Many benign lesions present with multi-nucleated giant cells. Imaging tests not always enable a conclusive diagnosis. A definite GCT diagnosis depends on anatomicopathological test, with careful evaluation of the stromal component and positive immunoexpression for p53 protein. Treatment is delivered as surgical resection, with wide margins, followed by instrumentation in cases of tumors located at spine.

Keywords: Giant Cell Tumor/ Surgery; Spine; Immunohistochemistry.

INTRODUCTION

The Giant Cell Tumor (GCT), described by Jaffe et al.[1], in 1940, is considered as a benign tumor, of uncertain biological behavior, with relapse incidence in about 20- 34% of the cases [2]. The malignant variant is rare, occurring only in 10% of the cases and presenting distinct histological characteristics [1].
It occurs more commonly in 30-35 year-old female patients and its usual location is at long bones' epiphysis, especially at the distal third of the femur and radius [3,4].
Spine vertebral affection is rare, being described in 2.9% of GCT cases [5].
X-ray images present a lithic, extensive lesion, without sclerosis, and may be related to pathological fracture [2].
Microscopically, the two major components of the giant cell tumor are stromal cells and multiple-nucleated giant cells. The nature of neoplasic stromal cells is controversial, but it is believed to be mesenchymal, with ultrastructural characteristics resembling fibroblasts [6].
An important correlation exists between surgical staging and GCT diagnosis. The histological grade of GCT does not worth a lot, except for grade-III cases, which constitute sarcomatous lesions with a high degree of malignancy. On the other hand, there are rare cases of metastasis occurring in tumors with microscopically benign appearance (1%- 2% of all cases).

Study conducted at Laboratório Fleury - Department of Pathology

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For being a tumor of uncertain biological behavior, the objective of this study is to report an aggressive-behavior GCT case, located at a vertebra, in a 37 year-old female patient, with discussions about differential diagnoses, emphasizing histological and immunohistochemical characteristics, probing the p53 protein, which helped on providing a definitive diagnosis, in addition to the correlation to imaging tests.

MATERIALS AND METHODS

A female patient, presenting with a painful clinical picture at spine and paraparesis dating two months prior, with no other constitutional symptoms.
Imaging tests were assessed: X-ray, computed tomography, magnetic resonance, and arteriography.
In another service, a first percutaneous tomography-guided biopsy was performed, providing the initial diagnosis of aneurysmal bone cyst. The review of biopsy slides, together with the analysis of dried surgical specimen, submitted to HE staining and immunohistochemical test enabled to provide a giant cell tumor diagnosis.
For the immunohistochemical study, a primary monoclonal antibody, DO-7 clone (DAKO Palts, Copenhagen, Denmark), was used in a dilution of 1/100, ON. Criterion for response positiveness was the verification of brownish nuclear immunomarking in more than 10% of neoplasic cells [7].

RESULTS

Imaging tests evaluation is described as below:
At X-ray, lesion was lithic (Figure 1), with bone expansion, erosion and cortical destruction. At tomography and magnetic resonance, the lesion presented cystic and hemorrhagic characteristics, extending to soft parts (Figure 2). After initial diagnosis (in other service) of aneurysmal bone cyst, the patient was treated with embolization, not responding to treatment and with radiotherapy thereafter, yet not observing lesion reduction. Within three to six months after radiotherapy, a fast tumor growth was seen, with a more intense clinical neurological picture. By reviewing the case, we provided the diagnosis of giant cell tumor. The patient was submitted to surgery (Figure 3), with wide neoplasia resection (Figure 4, 5). She presented with an improved clinical picture and is now in a good general condition.

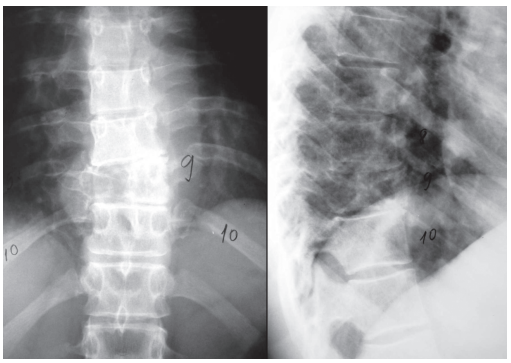

Figure 1 - *X-ray of lithic lesion, with bone expansion, erosion and cortical destruction.*

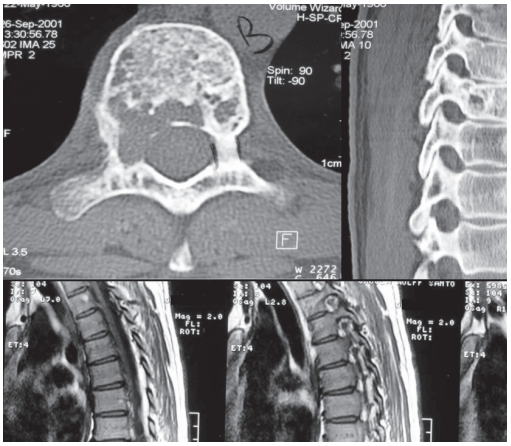

Figure 2 - *Tomography and magnetic resonance showing cystic and hemorrhagic characteristics of the lesion, with soft parts expansion.*

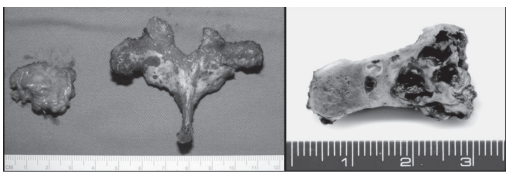

Figure 3 - *Specimen dried by T9 vertebrectomy Posterior way / Anterior way.*

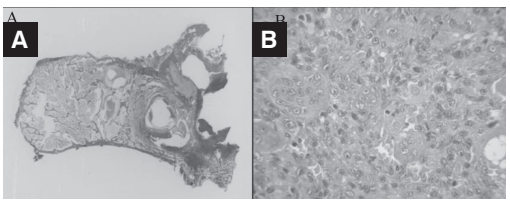

Figure 4 - *(A) Microscopic aspects, HE and (B) GCT with prevalence of single-nucleated stromal cells HE, 400X.*

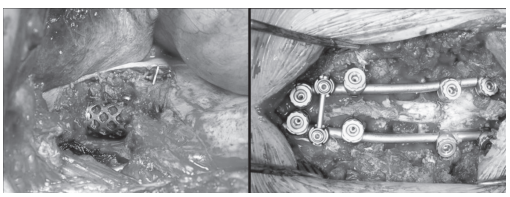

Figure 5 - *Treatment: surgical resection, with instrumentation.*

DISCUSSION

Spinal giant cell tumor usually affects women within 10-30 years old. Multicenter involvement occurs in 1% of patients [8,9]. Sacral and vertebral tumors are difficult to diagnose at early stages, because pain onset usually happens in late stages.
The recommended surgical treatment for GCT at ends is the marginal resection with local adjuvant. However, at spine, this procedure is not always possible, due to the existence of sensitive structures making surgical access difficult, many times being only possible to perform an intralesional excision [10]. Currently, the trend for spine primary tumors is the wide resection of injury, as performed in this case. This procedure reduced a lot the occurrence of local relapse, leading to oncologic cure, with a good functional outcome. There are reports of excellent outcomes with radiotherapy on axial lesions and in non-dryable tumors, where 85% of those tumors did not evolve

after radiotherapy, nor presented malignant transformation in about 10 years of follow-up [11].

Other studies show malignant transformation in 6% of GCT patients, with 69% of those cases having previously received radiotherapy [12]. Adjuvant treatments include cryotherapy, phenol and cement [10,13,14].

Many benign lesions, including COA present multiple-nucleated giant cells at microscopy, such as the chondroblastoma, osteoblastoma and brownish tumor of hyperparathyroidism [3], with all those lesions being commonly seen at spine, as opposite to GCT. Imaging tests not always enable a conclusive diagnosis, since those lesions may present an early aggressive pattern, with erosion and cortical destruction. A definitive diagnosis depends on anatomicopathological test (Figure 6), with careful examination of the stromal cell component. The presence of fusiform cells, with evident eosinophilic nucleolus, in addition to frequent mitosis, favors the diagnosis of giant cell tumor.

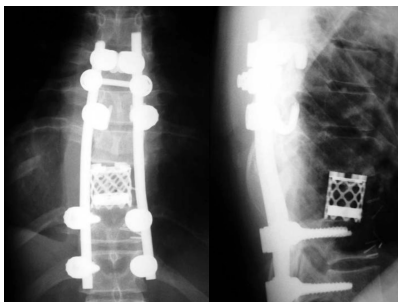

Figure 6 - *Evolution: patient with good general status, ambulating (6 months postoperatively).*

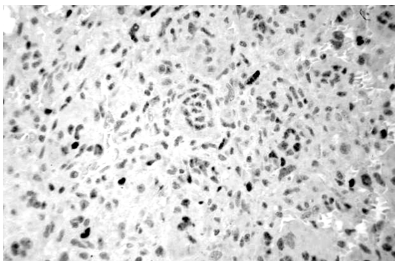

Figure 7 - *Positive immunoexpression for p53 in stromal cells and in multiple-nucleated giant cells.*

A positive immunoexpression for p53 protein (Figure 7) seen on stromal cells, on anatomicopathological test matter, has aided the final GCT diagnosis, since the major differential diagnosis in these cases would be with COA, and p53 protein would probably not be positive in pseudoneoplasic lesions, which would also rule out the brownish tumor.

Today, it is known that the presence of neoplasia consists of the accumulation of multiple genetic events phases. Mutations of the p53 tumoral suppressor gene are among the most common abnormalities of human cancer. The p53 gene is a nuclear phosphoprotein of 53kd located at the short arm of chromosome 17. It is associated to cellular cycle control, DNA repair, cell differentiation, and apoptosis [15]. This gene's byproduct is a cellular protein expressed in low levels on non-transformed cells and acts as a negative regulator of cell division. In transformed and neoplasic cells, the levels of p53 protein are usually high, which provides a selective advantage for the development of a neoplasic phenotype. That protein now has a long half-life and may be detected by an immunohistochemical method, an cells nuclei, which helps on identifying neoplasic-nature lesions. Reports of its immunoexpression already exist in GCT [5,7], which could help on differentiating GCT from pseudoneoplasic lesions also showing numerous multiple-nucleated giant cells.

Surgical treatment of patients with spinal tumors, today, is the wide resection of the neoplasia by two-way or posterior-way followed by instrumentation. This procedure enables less relapse occurrences and a good functional outcome. Spinal cord compression signs need surgical decompression with laminectomy.

CONCLUSION

The giant cell tumor is a lesion of difficult histological and radiological diagnosis, comprehending several differential diagnoses. Current treatment for tumors located at spine is surgical resection, with wide margins, which constitutes the significant factor in preventing a potential relapse and the occurrence of metastasis.

An immunohistochemical study probing for p53 may be used as an ancillary method for a definitive GCT diagnosis associated to histological aspects.

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