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Review Article

Management of spinal giant cell tumors

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Abstract

BACKGROUND CONTEXT: Spinal giant cell tumors (SGCT) remain challenging tumors to treat. Although advancements in surgical techniques and adjuvant therapies have provided new options for treatment, evidence-based algorithms are lacking.

PURPOSE: This study aims to review the peer-reviewed literature that addresses current treatment options and management of SGCT, to produce an evidence-based treatment algorithm.

STUDY DESIGN/SETTING: A systematic review was performed.

METHODS: Articles published between January 1, 1970 and March 31, 2015 were selected from PubMed and EMBASE searches using keywords "giant cell tumor" AND "spine" AND "treatment." Relevant articles were selected by the authors and reviewed.

RESULTS: A total of 515 studies were identified, of which 81 studies were included. Complete surgical resections of SCGT resulted in the lowest recurrence rates. However, morbidity of en bloc resections is high and in some cases, surgery is not possible. Intralesional resection can be coupled with adjuvant therapies, but evidence-based algorithms for use of adjuvants remain elusive. Several recent advancements in adjuvant therapy may hold promise for decreasing SGCT recurrence, specifically stereotactic radiotherapy, selective arterial embolization, and medical therapy using denosumab and interferon.

CONCLUSIONS: Complete surgical resection of SGCT should be the goal when possible, particularly if neurologic impairment is present. Denosumab holds promise as an adjuvant and perhaps stand-alone therapy for SGCT. Spinal giant cell tumors should be approached as a case-by-case problem, as each presents unique challenges. Collaboration of spine surgeons, radiation oncologists, and medical oncologists is the best practice for treating these difficult tumors.

Keywords: Adjuvant therapy; Denosumab; Giant cell tumor; Mobile spine; Sacrum; Spine tumor

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Introduction

Spinal giant cell tumors (SGCTs) are a locally aggressive benign bone tumor that can occur anywhere along the spine. Goals of SGCT treatment are tumor removal, spinal stability, and neural tissue decompression. Choices of treatment are en bloc vertebrectomy and intralesional resection. Because of the proximity of vital structures to the vertebrae, en bloc resection may be too damaging to undertake in some cases. Therefore, intralesional curettage might be the alternative choice in selected cases. Numerous adjuvant therapies can be used with either of these two surgical strategies.

The objective of this article was to review the peer-reviewed literature that addresses current treatment options and management of SGCT to produce an evidence-based treatment algorithm.

Methods

Two independent reviewers (PL, WS) performed a search of the all peer-reviewed relevant literatures in English published between January 1, 1970 and March 31, 2015. Electronic database queries including EMBASE and PubMed were searched using keywords "giant cell tumor" AND "spine" AND "treatment". Additional searches were performed by using reference lists of the retrieved studies that were relevant to SGCT.

Inclusion criteria were studies describing biology, evaluation, and treatment of SGCT. Exclusion criteria were review articles. According to PRISMA flow diagram, both reviewers independently screened abstracts and titles after removing duplicate publications. Then, thorough full-paper readings were performed of the studies that might meet the inclusion criteria to determine final inclusion. Disagreements were solved by discussion for consensus.

Results

There were 752 publications identified through database searching (420 PubMed, 332 EMBASE) and 237 publications were found in both search methods; thus, a total of 515 unique abstracts were screened. Of these abstracts, 142 were selected for full paper review; 81 of these articles were included. Levels of evidence were classified as shown in Table 1.

Epidemiology and presentation

Giant cell tumors (GCTs) are locally aggressive benign bone tumors. Approximately 5% of all primary bone tumors are GCTs. The prevalence of spinal giant cell tumors (SGCTs) is estimated at 2%–15% of all GCTs; incidence is higher in the sacral region and in patients aged 20–40 years [1–6]. Some studies have also reported that SGCTs are more common in female patients [1,2,7,8]. Spinal giant cell tumor patients typically present with pain, and up to 72% of patients also experience neurologic deficits such as radicular pain and motor weakness from nerve root or spinal cord compression [2–4,9–11]. A palpable mass is only rarely appreciated [2].

Although GCTs are generally benign tumors, they can be locally aggressive and can cause considerable osseous destruction and soft tissue extension, often leading to neurologic compromise in the spine. Spinal giant cell tumors have an overall survival rate of 93% [12]. However, GCTs can undergo malignant transformation, hematogenously metastasizing most frequently to the lungs [5,13–15]. However, Tubbs et al. reported that the prevalence of lung metastases in a benign GCT was 3% (13 of 475) [16]. Donthineni et al. reported that 14% of SGCT patients developed lung metastases, suggesting a higher rate of metastasis than the 1%–6% rate reported for extremity GCTs [13,15,17]. A very small fraction of GCTs (2%) undergo sarcomatous change, most often to osteosarcoma. This can occur as a primary malignant GCT or, more commonly, as a secondary malignancy after radiation therapy (RT) of a benign GCT [6].

Radiographic and pathologic diagnosis

The radiographic appearance of spinal GCTs is typically an osteolytic, expansile lesion with significant cortical destruction. Often there is a "soap bubble" pattern and an absence of a sclerotic border. In the spine, GCTs typically involve the vertebral body, and can extend into the posterior elements and paraspinal tissues. Adjacent disks and vertebrae can be involved as well, and pathologic compression fractures are

Table 1
Levels of evidence for primary research question adopted by the North American Spine Society, January 2005

Level	Description
I	High-quality randomized trial or prospective study; testing of previously developed diagnostic criteria on consecutive patients; sensible costs and alternatives; values obtained from many studies with multiway sensitivity analyses; systematic review of Level I randomized controlled trials (RCTs) and Level I studies.
II	Lesser quality RCT; prospective comparative study; retrospective study; untreated controls from an RCT; lesser quality prospective study; development of diagnostic criteria on consecutive patients; sensible costs and alternatives; values obtained from limited studies; with multiway sensitivity analyses; systematic review of Level II studies or Level I studies with inconsistent results.
III	Case control study (therapeutic and prognostic studies); retrospective comparative study; study of non-consecutive patients without consistently applied reference "gold" standard; analyses based on limited alternatives and costs and poor estimates; systematic review of Level III studies.
IV	Case series; case control study (diagnostic studies); poor reference standard; analyses with no sensitivity analyses.
V	Expert opinion