Iranian Journal of NEUROSURGERY
2022, Volume 8

Review Paper

Spinal Giant Cell Tumor in Neurospine Surgery: A Narrative Study

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Citation Mousavi SR, Kalani N, Kazeminezhad A. Spinal Giant Cell Tumor in Neurospine Surgery: A Narrative Study. Iran J Neurosurg. 2022; 8:E-10. http://dx.doi.org/10.32598/irjns.8.10.

http://dx.doi.org/10.32598/irjns.8.10

Article info:
Received: 20 Sep 2021
Accepted: 07 Feb 2022
Available Online: 25 Jun 2022

Keywords:
Giant cell tumor, Spine, Neurospine surgery, Manifestations

ABSTRACT

Background and Aim: Spinal Giant Cell Tumor (GCT) is a primary low-grade malignant aggressive tumor of the spine and is more prevalent in the third and fourth decades of life. Spinal GCT frequently occurs in the sacrum. The most common presentation of spinal GCT is pain. Spinal GCT is seldom observed as an asymptomatic, incidental radiological occurrence. Based on the clinic-radiological findings, differential diagnoses of spinal GCT are Aneurismal Bone Cyst (ABC), plasmacytoma, symptomatic hemangioma, and Tuberculosis (TB). A biopsy is crucial for a definitive diagnosis. Because of the rich vascular supply about 24 hours prior to operation, Digital Subtraction Angiography (DSA) with tumor embolization is recommended. The treatment of choice for these tumors is complete, extralesional surgical resection which is not usually possible. General treatment is resorted as incomplete partial resection following local radiotherapy. The method of choice for reconstruction is cement or metallic cages and because of the high recurrence rate, bone graft is avoided. The local recurrence rate in the spinal column is lower than in other areas.

Methods and Materials/Patients: The spinal GCT incidence, manifestations, diagnosis, and management were concisely reviewed. Using the keywords of GCT, GCT manifestations, GCT complications, GCT management, and GCT incidence, all the relevant articles were retrieved from Google Scholar, Medline, and PubMed, reviewed critically, and analyzed.

Results: Spinal GCT rarely presents as an incidental finding in radiologic studies. Because of the high vascular supply of GCTs, preoperative embolization must be performed. The ideal treatment of spinal GCT is complete surgical tumor excision and when not possible, intralesional resection is an alternative treatment. The prognosis of spinal GCT is not good as other primary spinal tumors because of incomplete excision of the tumor and following high recurrence rate.

Conclusion: Spinal GCTs are complex clinical entities. Operation is obligatory, and postoperative close follow-up is mandatory to stop recurrences early.

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Highlights

• Spinal Giant Cell Tumor (GCT) is a primary low-grade malignant aggressive tumor of the spine and is more prevalent in the third and fourth decades of life with the sacrum as the most common site of involvement.

• Spinal GCT rarely presents as an incidental finding in radiologic studies. Because of the high vascular supply of GCTs, preoperative embolization must be performed. The ideal treatment of spinal GCT is complete surgical tumor excision and when not possible, intralesional resection is an alternative treatment. The prognosis of spinal GCT is not good as other primary spinal tumors.

• Spinal GCTs are complex clinical entities. Operation is obligatory and postoperative close follow-up is mandatory to stop recurrences early.

Plain Language Summary

Spinal GCTs are complex clinical entities. Operation is obligatory and postoperative close follow-up is mandatory to stop recurrences early. They rarely present as an incidental asymptomatic radiologic finding. Imaging studies, especially CT and MRI have a paramount role in the diagnosis of this tumor and in definitive diagnosis, a biopsy from the wall of the tumor is diagnostic. Surgical treatment as extralesional/en bloc resection is an ideal treatment. For effective early diagnosis and prevention of recurrence, close follow-up with a high index of suspicion is important.

1. Introduction

Giant Cell Tumor (GCT) is a complex clinical entity, and since 1818 when it was presented by Cooper and Travers, many new findings in multiple aspects of this tumor have been clarified [1]. GCT is a low-grade malignant aggressive tumor. The most prevalent sites of involvement are the femur, tibia, and radius, the involvement of the spine above the sacrum is rare, and the most common site of spinal involvement is the sacrum [2, 3]. The most common region of involvement in the spine is in the vertebral body but is rarely confined to the vertebral body and may extend to the lamina, spinous process, and paravertebral site. Spinal GCTs destroy the vertebral body and neural arch and create expansile lytic lesions, with pain caused by a stretched periosteum followed by pathological fracture and neurologic symptoms [4, 5]. Because the most common manifestation of spinal GCTs is pain (back pain or low back pain), diagnosis may be delayed. Various treatment strategies, such as complete or incomplete operative resection and adjuvant therapies, such as cement injection, phenol ablation, cryotherapy, and radiotherapy have been described, but the treatment of choice for spinal GCTs is total spondylectomy with appropriate reconstruction for the preservation of spinal integrity [6, 7]. However, because of the proximity of the tumor to important neurovascular structures and vertebral cortex breakage with the tumor, usually complete extralesional resection cannot be done and incomplete partial resection following local radiotherapy is done [8, 9]. Radiation therapy can be given in cases of subtotal resection. For spinal reconstruction, cement or metallic cages are preferred and because of tumor recurrence in grafted bone, the bone graft is avoided. Tumor recurrence is frequently seen after intralesional or incomplete excision. In comparison to other areas, local recurrence in the spine is less, but as an invasive bone tumor, the postoperative recurrence rate of GCT is higher and distant metastasis may occur [10-12]. The main aim of this narrative study was to clarify and discuss these new aspects of GCT.

2. Methods and Materials/Patients

This study was a narrative study on the GCT of the spine. To provide up-to-date information on GCT of the spine, we concisely reviewed the spinal GCT incidence, manifestations, diagnosis, and management. Using the keywords of GCT, GCT manifestations, GCT complications, GCT management, and GCT incidence, all the relevant articles were retrieved from Google Scholar, Medline, and PubMed, reviewed, and critically analyzed.

3. Results

Based on the narrative study, the following results about incidence, manifestations, treatment, differential diagnosis, and outcome of this tumor were obtained.

4. Discussion

Incidence

About 6.5% of all GCTs occur in the spine with half occurring in the sacrum and about 7-10% of primary tumors of the spine are GCTs. The most common age for the occurrence of spinal GCTs is the third or fourth decades. The incidence of GCTs in females was twice as high as in males [13, 14].

Clinical manifestations

The onset of spinal GCT presentations is insidious and progression is slow over several months. The most prevalent presentation of spinal GCTs is pain. The expansile lesion with or without vertebral collapse and spinal instability causes pain. Following pain, with the encroachment of the tumor to the spinal canal, a neurological deficit occurs. Spinal GCT as an asymptomatic, incidental radiological finding is not common. Common clinical manifestations are as follows [15-24]:

Pain: This is the most common manifestation because of vertebral destruction and periosteal stretching. In patients with sacral involvement, there is localized low-back pain that may radiate to one or both lower limbs.

Neurological deficit: This occurs because of canal encroachment and cord compression. Neurological symptoms are commonly subtle but bowel or bladder incontinence, leg weakness, or sexual dysfunction can occur.

Structural deformity of the spine: Spinal GCT creates an expansile osteolytic lesion with the following mild vertebral collapse to a complete vertebra plane with blurring or loss of cortex and resultant structural deformity. Occasionally, a tumor can weaken a vertebra to such an extent that the vertebra breaks after relatively minor trauma. This is called a pathologic fracture.

Metastatic manifestations: About 10% of GCTs are malignant and metastatic involvement occurs in about 1%-6% of these tumors. The most common site of metastasis is the lung. Solitary metastases to regional lymph nodes, the mediastinum, and the pelvis have been reported nonspecific abdominal pain, early satiety, and change in bowel/bladder habits.

Imaging studies

X-ray: In spinal GCT radiology, there is an expansile osteolytic lesion with the vertebral body in association with blurring or loss of cortex and associated soft-tissue mass. Because of the destructive effect of this tumor, the vertebral pedicle is deformed or completely disappeared [25].

Computed Tomography (CT) scan: The tumor has a soft-tissue density with no evidence of mineralized matrix. CT scan shows the tumor to be totally hypodense (areas of hemorrhage or necrosis) and hyperdense areas with a sclerotic rim at the periphery of the tumor. In the lytic areas of the cortex with an associated soft tissue mass, the cortex may be thinned, penetrated, or disappeared. The CT finding of GCT that is helpful in the diagnosis of this tumor is paradoxical appearance as the sclerotic border at one side of the tumor and expansile remodeling and breakthrough of the cortex at the opposite side because when the lesion is eccentrically distributed, the sclerotic rim appears at the opposite side of eccentric extension and remodeling at the same side of the eccentric extension. A radiographic "soap bubble" appearance, especially at the border of the tumor opposite the eccentric side is created because of some bony septa arising from the border of the tumor extending inside the lesion. This appearance is demonstrated in the axial image [26-31].

Magnetic Resonance Imaging (MRI): Spine GCT has heterogeneous signal intensity on all MR sequences. The following MRI findings can be observed that are helpful in differential diagnosis [32-35]:

• Low-to-intermediate signal intensity of solid parts of tumor are observed in T2-Weighted (T2W) MRI. Because of the high signal intensity on T2W MRI in most other spinal neoplasms, such as metastases, lymphoma, and chordoma, this will be useful in the differential diagnosis of this tumor.

• Hemosiderin deposition in GCT shows low signal intensity on all sequence images with the nodular, zonal, whorled, or diffuse pattern. Because of the sensitivity of gradient-recalled echo images to hemosiderin, the areas of low signal intensity are exaggerated on T2W images.

• Because of the multiloculated lesion with thickened trabeculae, fibrous septa, or hemosiderin deposit, there are curvilinear low-signal areas on both T1W and T2W images on MRI of spinal GCT.

• There are some focal cystic regions with low intensity in T1W images and high intensity in T2W images without enhancement.

• Bleeding areas with high intensity on T1W and T2W images and fluid-fluid levels may be visible.

The above findings are not specific and are common in Aneurismal Bone Cyst (ABC). Occasionally there is a fibrous capsule around the margin of the tumor as a thin sclerotic border with a band of low-signal intensity around the margin of the tumor. Because of the rich vascular supply of these tumors, there is a marked enhancement in contrast-enhanced CT and MRI. If there is the enhancement of solid components on T1W MRI with contrast, this is in favor of GCT with an ABC (secondary ABC) rather than pure ABC (primary ABC) [32-35].

Differential diagnoses

ABC: The most prevalent lesion associated with secondary ABC is GCT and must be differentiated from primary ABC. ABC of the spine usually involves the posterior parts of the spine, the age range is below 20 years, and on MRI, has a purely cystic appearance If there is the enhancement of solid components on T1W MRI with contrast, this is in favor of GCT with an ABC (secondary ABC) rather than pure ABC (primary ABC) [26, 36, 37].

Plasmacytoma: Plasmacytomas are tumors in cases with an age range of above 40 years. Cystic change is not usual, and there are bony septa on CT scans and curvilinear low-signal intensity on MRI causes an appearance of sulci of the brain (minibrain appearance) [30].

Symptomatic hemangiomas: These tumors show irregular vertical trabeculae but marked pathological compression of vertebral bodies is infrequent in hemangioma. For symptomatic hemangiomas, there are the following helpful diagnostic findings: marked hyperintensity on T2W images and an undamaged cortex in the vicinity to a paraspinal or epidural mass [31].

Treatment

Complete surgical excision is the treatment of choice in spinal GCT. Radiotherapy as a therapeutic option in unrespectable cases of GCT is not satisfactory for vertebral lesions because of possible spinal cord myelitis and malignant transformation of the tumor. Chemotherapy is another therapeutic option. Because of overexpression of the Receptor Activator of NF-KB Ligand (RANKL)and its receptor in GCTs, denosumab may be an effective alternative therapy. However, this is not a suitable therapeutic option for the treatment of GCT due to its toxic effects and normally benign nature of GCT. Therefore, there is no standard chemotherapy protocol for GCTs [38-44].

As mentioned above, the ideal treatment for spinal GCT is complete extralesional/en bloc resection, which is usually not possible for two reasons: adjacent important neurovascular structures and vertebral cortex breakage. Therefore, the usual treatment option is marginal or intralesional resection, with complete intralesional curettage and excision followed by local radiotherapy. For increasing the yield of the diagnostic features in the histology/frozen section, it is better to take the sample from the tumor wall rather than the tumor substance. With modern radiotherapy techniques, there is no chance for malignant transformation of GCT, especially by keeping the total radiation dose under 50Gy. Preoperative embolization about 24 hours before the operation, because of the rich vascular supply of the tumor, decreases blood loss and creates a dry surgical field for meticulous resection of tumor and hemostasis. Because of the risk of infarction of the cord, if there is a common feeder between the cord and the tumor in DSA, embolization cannot be carried out. After complete surgical tumor removal, reconstruction surgery must be done by cement or metallic cages with avoidance of bone graft because of the high recurrence rate of tumor in the grafted bone. Postoperative radiotherapy also decreases graft fusion rate.

Prognosis

The prognosis of spinal GCT is better than non-spine types. Local recurrences and metastasis are less observed in spinal GCTs than GCTs in other locations. In spinal GCTs, recurrence rates are higher in the following conditions: operation is done in the first center after arrival without referral to a tertiary center, involvement of vertebral body and posterior elements by GCTs in contrast to GCTs limited to the vertebral body, and tumoral involvement of spinal canal and paraspinal musculature. For diagnosis of recurrences in the GCTs, the physician must have a high index of suspicion. If there is any suspicion of recurrence, a biopsy must be done to prove this, unless it is very obvious on the CT/MRI. For monitoring the postoperative status of a tumor, a CT scan over a one-year period, and for minimizing postoperative recurrence rates, postoperative irradiation are recommended [9-12, 15, 36, 45-48].

5. Conclusion

Spinal GCTs are complex clinical disorders. They rarely present as incidental asymptomatic radiologic findings.

Imaging studies, especially CT and MRI have a paramount role in the diagnosis of this tumor and for definitive diagnosis, a biopsy from the wall of the tumor is diagnostic. Surgical treatment as extralesional/en bloc resection is the ideal treatment. For effective early diagnosis and prevention of recurrence, close follow-up with a high index of suspicion is important. Adjuvant treatments, including radiotherapy and chemotherapy, need more conclusive detailed studies.

Ethical Considerations

Compliance with ethical guidelines

No human or animal subjects participated in this study. There were no ethical considerations to be considered in this research.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

Acknowledgments

We would like to thank the Clinical Research Development Unit of Peymanieh Educational and Research and Therapeutic Center of Jahrom University of Medical Sciences for providing facilities for this work.

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