

# Giant cell tumor of C2 (axis): A case report and short review of literature

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## ABSTRACT

This is a hospital-based case report of giant cell tumor of C2 vertebra (axis) in skeletally immature patient. It is difficult to diagnose giant cell tumor both clinically and radiologically therefore to differentiate it from other lesions, molecular and genetic studies are warranted. Initial aggressive surgical resection should be adopted if possible. Since giant cell tumor is a radioresistant and no known chemotherapy is available, therefore an alternative medical treatment should also be explored where resection is not possible. Use of denosumab and bisphosphonate may be best alternative in inoperable cases.

**Key words:** Axis, bisphosphonates, en block resection, giant cell tumor, radiotherapy

## INTRODUCTION

Giant cell tumor is a rare, benign, osteolytic neoplasm representing 5% of all primary bone tumors. World Health Organization has classified it as an aggressive and potentially malignant lesion with high rate of recurrence and metastases.<sup>[1]</sup> It occurs in 2<sup>nd</sup>-4<sup>th</sup> decade of life with a slight female preponderance. For some unknown reasons; Indians, Chinese and southeast Asians are more prone for these tumors.<sup>[2]</sup>

This tumor arises at the end of long bones in skeletally mature patients, and 2% occur in the vertebral column above the sacrum. Its incidence is 1.8% in skeletally immature patients. Spine is the fourth leading site of giant cell tumor. Thoracic, cervical, and lumbar regions are affected in the decreasing order of frequency. Incidence in the cervical spine is less than 1.0% of all giant cell tumors.

The management of appendicular giant cell tumors is well-known, but confusion still prevails regarding the optimal treatment of axial tumors. There are many unanswered questions regarding its management and prognosis. It is resistant to chemotherapy as well as radiotherapy. Complete excision is the gold standard of treatment, but it may be associated with potential neurological deficit.<sup>[3,4]</sup>

We present a case report of giant cell tumor of C2 (axis) in an 11-year-old girl along with its radiological and histopathological features. This paper will highlight the diagnostic and therapeutic difficulties in the management of high cervical tumors. To the best of our knowledge, so far only 15 such cases in pediatric's spine have been reported in the world literature.<sup>[5]</sup>

The authors have obtained the permission from hospital academic council for print and electronic publication of this case report.

## CASE REPORT

An 11-year-old female, known case of idiopathic thoracolumbar scoliosis, presented with 1 month history of continuous, severe, and nonradiating neck pain. Pain was aggravated by the neck movements, and relieved by nonsteroidal pain medications. Patient denied any history

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of fever. There was no past medical or family history of any disease. Her examination revealed no neurological deficit.

Laboratory investigations including complete blood count, high sensitivity C-reactive protein, erythrocyte sedimentation rate, serum calcium and parathyroid hormone levels, and renal and liver functions tests were all normal. Tuberculin test was also negative.

Computed tomography scan of the cervical spine revealed expansile, osteolytic bony lesion involving vertebral body, odontoid process, lateral masses, and anterior parts of laminae of C2 [Figure 1].

Magnetic resonance imaging (MRI) showed marrow replacement involving the C2 vertebral body, odontoid and transverse processes. The medullary cavity was enlarged with cortical thinning and expansion. Lesion was hypointense on T1W and isointense on T2W sequences with intense homogeneous enhancement. Magnetic resonance angiography of the neck did not reveal any significant vessel abnormality.

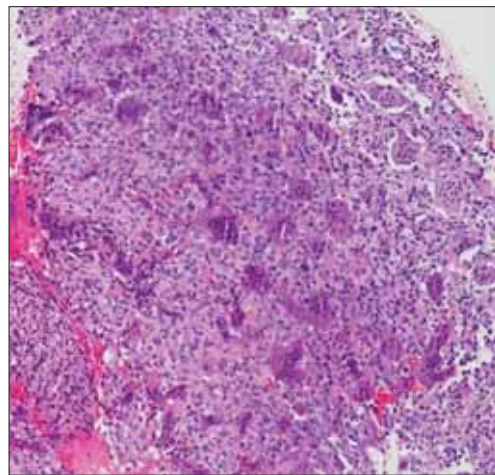
Triple phase whole body nuclear bone scan were performed with Technetium-99m methylene diphosphonate (MDP)-phosphate radiopharmaceuticals. Dynamic blood flow revealed no significant hyperemia or any active lesion in the cervical spine. The blood pool images showed mild increased uptake in the upper cervical region. The late osseous phase showed a warm area of abnormal increased uptake at the second cervical vertebra.

Histopathological examination of biopsy specimen showed a lesion composed of mononuclear cells and giant cells. The giant cells contained a variable number of nuclei, with many cells showing more than 20 nuclei per cell. Nuclei of giant cells showed strong immunopositivity for cyclin D1 (SP4). Some mononuclear cells were also positive. Mitotic figures were not found in giant cells [Figures 2 and 3].

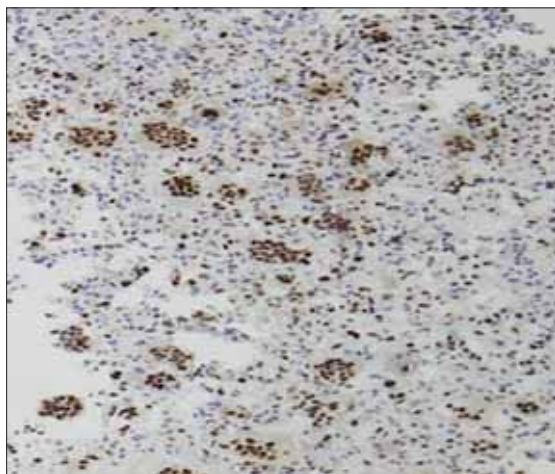
Later, patient was operated at other center where complete resection of tumor was done along with anterior and posterior fixation of cervical spine [Figure 4]. Patient was



**Figure 1:** Computed tomography (CT) scan cervical spine (sagittal view) showing marked destruction of C2 vertebral body



**Figure 2:** Histological appearance of tumor showing multinucleated giant cells and mononuclear cells



**Figure 3:** Nuclei of giant cells showed strong immunopositivity for cyclin D1 (SP4)



**Figure 4:** Barium swallow study showing postoperative cervical spine with anterior and posterior fixation

found neurologically intact and recurrence free, 2 years after surgery.

## DISCUSSION

The histological and radiological findings of our case are consistent with giant cell tumor of bone. The age of the patient may argue against the diagnosis as it is rare in skeletally immature patients. The positive immunostain for cyclin D1 was also supportive of giant cell tumor of bone as overexpression of cyclin D1 and D3 is nearly universal in this neoplasm.<sup>[6]</sup> Additionally, when giant cell tumor arises in the spine, the most commonly involved area is vertebral body. The other lesion that may mimic giant cell tumor of bone is solid variant of aneurysmal bone cyst. Aneurysmal bone cyst is more common in this age group and it frequently involves the spine, most commonly the cervical spine. However, the posterior elements are predominantly affected rather than the vertebral bodies. Aneurysmal bone tumor is characterized by rearrangement of 16q22 and 17p11-13 and giant cell tumor by telomerase associations. Moreover, p63 is also a useful biomarker to differentiate giant cell tumor of bone from other giant cell-rich tumors.<sup>[7]</sup> Genetic studies may be warranted in such cases. Other less likely consideration is brown tumor, but in our case parathyroid hormone and serum calcium levels were normal.

Giant cells are responsible for the aggressive osteolytic activity of the tumor. These cells express RANK (receptor activator of nuclear factor  $\kappa$ B), and stromal cells express RANK ligand (RANKL). RANKL is responsible for osteoclast formation and survival. Denosumab controls bone lysis by inhibition of the RANKL-RANK axis. Its use in a group of 37 patients showed complete elimination of giant cells in all patients. Stromal expression of RANKL decreased after elimination of the giant cells.<sup>[8]</sup>

Bisphosphonates are commonly used to inhibit osteolysis in osteoporosis and in metastatic cancers. Zhang reported three cases, two vertebral and one sacral, with more than 2 years follow-up. These cases were treated with third generation bisphosphonates. Thoracic lesion decreased in size and was replaced with extensive calcification with 6 years recurrence free interval. Lumbar vertebral tumor stopped progressing and new bone formation was noted on follow up CT scan. Sacral tumor decreased in size with concomitant calcification as well.<sup>[9]</sup> Gille *et al.*, reported

giant cell tumor of seventh cervical vertebra which was treated with intravenous bisphosphonates after incomplete excision. Tumor was completely regressed and replaced by new bone without any recurrence up to 3 years follow-up. In view of these reports, bisphosphonates therapy seems to be attractive alternative and/or adjuvant therapy.<sup>[10]</sup>

Our case report clearly shows that management of giant cell tumor of cervical spine is indeed a great challenge. Though surgical approach is still the best treatment for a giant cell tumor of spine but surgical expertise, sophisticated and dedicated spine centers are not available everywhere in the world. Therefore alternative options like therapeutic embolizations, cryosurgery, and trials of denosumab and bisphosphonates should be explored intensively for such type of giant cell tumors.

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