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Article

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Surgical management of giant cell tumor of axis vertebra: review of fourteen cases in literature with a case illustration

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Abstract: Primary spinal giant cell tumor (PSGCT) considered as rare primary neoplasm, with predilection for subarticular location and commonly located at knee joint region, sacrum or distal radius, however, spinal involvent is uncommon and comparatively much rarer in the cervical spine. Further occurrence of giant cell tumor in the Axis vertebra is extremely uncommon and easily misdiagnosed and, thus, treatment is still debated and various treatment modalities and different surgical approaches were utilized during evolution of surgical management. Authors could collect only 14 cases of primary giant cell tumor affecting Axis vertebra in a detailed Pubmed and Medline search, out of which 12 cases were primary and rest two case was recurrent. So authors reviewed in total thirteen cases primary giant cell tumor of Axis managed surgically, including our case. Out of 13 PSGCT, twelve cases were managed with surgical resection and the rest one case was managed with monoclonal antibody using Denosomab monotherapy without any surgical intervention. In the surgical group (n=12), nine cases had two staged surgical procedure, first being posterior fixation followed by anterior approach with resection of tumor while, the rest three had one stage surgical resection including current case. Authors reports a unique case of spinal giant cell tumor developing in a- 38 - year male with history of renal transplant , presented with neck pain and difficulty in walking, neuroimaging revealed a osteolytic mass lesion involving body of axis vertebra with extension into right sided lamina , underwent two stage complete surgical intervention. Authors describes management of such rare locally recurring primary bony pathology affecting axis vertebra as it is not only interesting and challenging and different management modalities, various, surgical approaches and issue of renal osteodystrophy along with pertinent literature is also reviewed briefly.
Key words: Spinal giant cell tumor of axis vertebra, surgical management, two stage treatment, renal osteodystrophy, management

Introduction

The first description of giant cell tumour was put forward by Cooper and Travers in 1918. (1) The "Giant cell tumor" term was coined by Bloodgood in 1919. (2) PSGCT location represent extremely uncommon location, constitute about 5-15 % of all G CT. (3, 4, 5) In PSGCT, vertebral body is more commonly involved compared to the posterior vertebral elements (6, 7). The management of GCT is controversial due to its rarity of occurrence and associated unpredictable behavior. (2-6) In 1940, Jaffe et al. (3) made an attempt to clearly define the definitive patological basis for classifying and differentiating giant cell tumor from similar lesions eg. aneurysmal bone cyst, chondrosarcoma, chondro- myxoma and non-osteogenic fibroma of bone. However, a wide local surgical excision must include adjacent surrounding normal tissue whenever feasible.

Case illustration

A 38 –year male presented with complaints of neck pain for last six months, insidious in onset, which used to get worsened in sitting position and during walking, used to support his head and neck by hand which associated with restriction of neck movement. His significant past medical history included renal transplant in December 2007, at our institute for end stage chronic kidney disease secondary to chronic glomerulo-nephritis associated vasculitis. He was getting regular follow-up with nephrologist and transplant surgery OPD clinic and he was advised to continue medication including, tablet prednisolone 5mg daily, capsule tacrolimus 3.5 mg twice a day, along with antihypertensive medications in addition to injection erythropoietin 100 mcg subcutaneous every three week and iron and folic acid supplementation. In March 2008, had graft dysfunction, graft biopsy was suggestive of antibody mediated rejection with evidence of transplant glomerulopathy. He also suffered cytomegalovirus colitis in 2013.

Routine serum biochemistry revealed blood urea 53 mg/dl and serum creatinine 2.4 mg/dl, while the rest of biochemistry and hemogram were within normal limit. Non-contrast craniovertebral junction computed tomography revealed evidence of osteolytic lesion of axis affecting the second cervical vertebra causing expansion of the body with presence of septation and also extending into right side lamina, cortical breach observed on antero-inferior aspect, causing compromise of the spinal canal with secondary cervical canal stenosis. (Figures 1, 2, 3)

Magnetic resonance imaging of craniovertebral junction, sagittal section image demonstrated presence of heterogeneous signal intensity mass lesion affecting vertebral body of axis, measuring 36 x 30 x 22 mm in size, (Figures 4 and 5 a, b) causing expansion and destructive the vertebral body and also further extending to involving lamina and producing significant mass effect in form of obliteration and indentation of anterior thecal sac and spinal

cord indentation as well as displacement at same level. As he had slightly deranged renal function, planned for two stage surgical excision to avoid further renal function compromise.

First stage planned was radical decompression, obtaining specimen for histopathological confirmation and posterior occipitocervical fixation and followed by transoral decompression after first surgery depending on renal functional status in the second stage surgery, as deranged renal function precluded prolonged surgery for combined anterior and posterior approach in a single setting. After anaesthesia clearance, he was taken up for surgery under strict guidance and supervision of nephrologist. He was and taken up for surgery in the prone position. An skin incision from inion to C5 level was given, further dissection was carried out along ligamentum nuchae and Occipital bone, C1 to C4 lamina were exposed. The anterior arch of C1 was removed, laminectomy of C2 and C3 were carried out. The right lamina showed presence of soft, grayish yellow, moderately vascular mass. The c2 body was entered and gross total microsurgical decompression was carried out under, however, the part of the lesion located central part of Axis vertebra was not accessible. After securing hemostasis, posterior occipitocervical fusion was carried out with occipital plate and lateral mass screw fixation of C3 and C4 level. He tolerated surgical procedure well with no fresh neurological worsening or any renal parameters derangement in the post-operative period. X-ray showed implant in proper position. (Figure 6) He underwent second stage transoral decompression after seven months following first surgery. Histopathological examination of specimen showed numerous osteoblastic giant cells, stroma shows oval to spindle cells and features were compatible with giant cell tumor and also received radiotherapy. He is doing well at last follow up after one year following initial surgery.

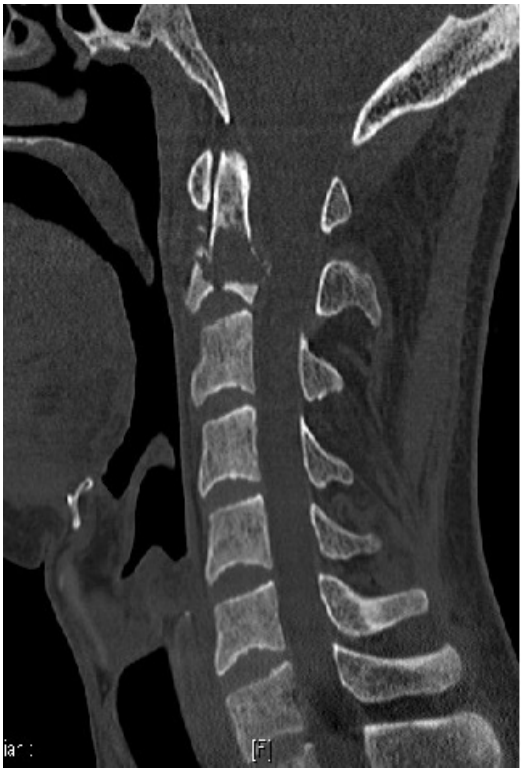

Figure 1 - Computed tomography scan of cranio-vertebral junction, sagittal section image, showing osteolytic lesion of vertebral body and fracture lower endplate of axis vertebra

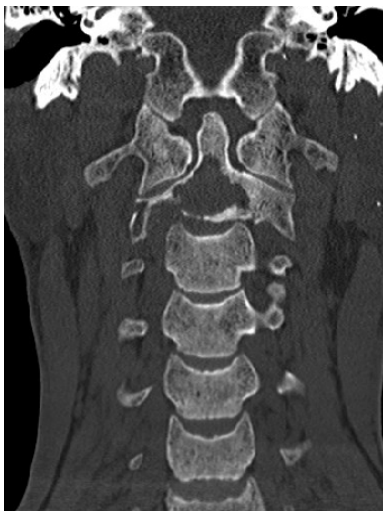

Figure 2 - Coronal section, computed tomographic scan of cranio-vertebral junction image of 38-year male with renal transplant showing osteolytic lesion of vertebral body involving more to right side egg shell like preserved cortex axis vertebra

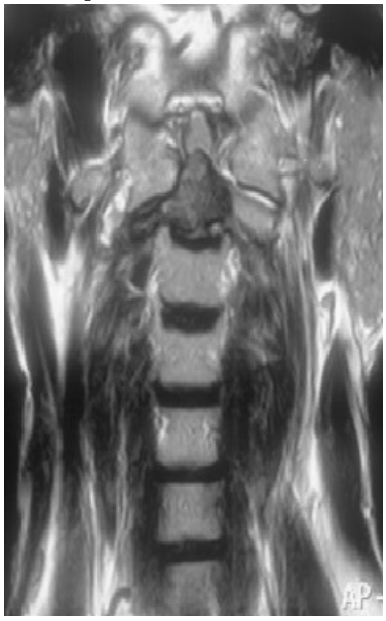

Figure 3 - Magnetic resonance imaging of Craniovertebral junction, Coronal section, T1 weighted image showing osteolytic lesion of vertebral body involving more to right side egg shell like preserved cortex axis vertebra

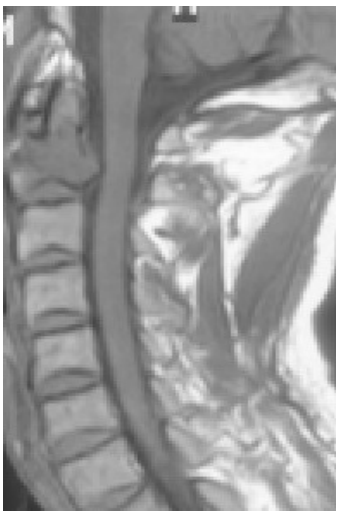

Figure 4 - T1 weighted image isointense lesion involving vertebral body of axis
Magnetic resonance imaging of Craniovertebral junction, sagittal section image showing mass causing compression of cervical cord

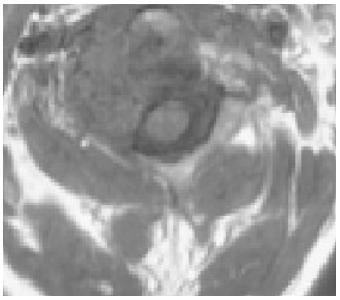

Figure 5a - axial section T1 weighted image

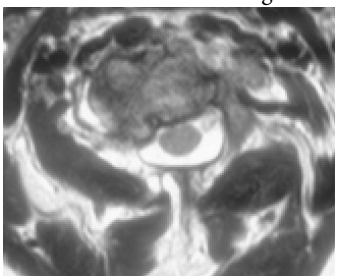

Figure 5b - axial T2 weighted image
Axial section Magnetic resonance imaging of Craniovertebral junction

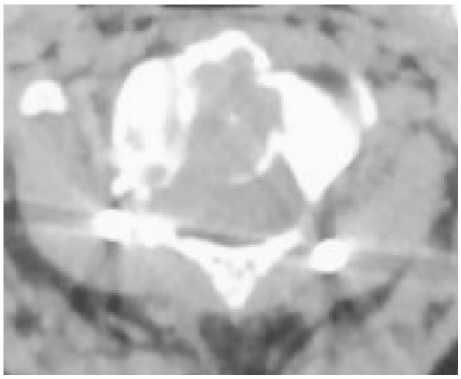

Figure 6a - axial section image

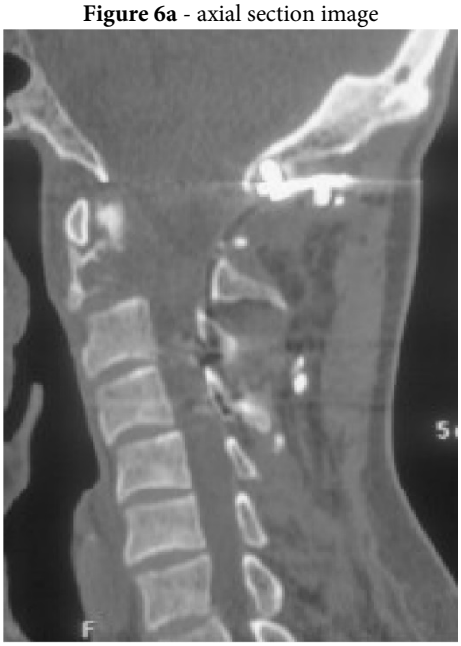

Figure 6b - sagittal section Craniovertebral junction CT scan

Post-operative computed tomography scan, showing evidence of laminectomy with metallic artifact of implant in situ

Discussion

Giant cell tumour is commonly distributed in subarticular location with predilection for knee joint region, sacrum, distal radius and proximal radius, and those located in appendicular regions, usually remain centered in the epiphysis plate and extend eccentrically beyond epiphyseal boundary. (3, 4) However, vertebral column involvement is very rare 9 and overall the cervical region localization accounts for less than 1% of overall occurrence of giant cell tumors. (4)

Due to unpredictable behavior, in general only a third of total cases ultimately remain truly benign, while the rest two-third cases may progresses ultimately to either become locally invasive or may show metastasis to distant focus. In 1982, Fabiani et al (10) did a detailed review could collect a total of 66 cases PSPCT including their own two cases, which were located in the spinal column and 30 % occurred in cervical spine region, another 45 % in thoracic and 25% in lumbar region respectively.

Giant cell tumor usually occurs in third or fourth decades of life, with a mean age of 27 years and show slight female preponderances. Spinal GCT frequently presents with pain over the spinal column, progressive paraparesis or quadriparesis, however sphincter disturbance is less common. Authors in a detailed literature search of PSGCT involving Axis vertebra, could find only 12 primary case of PSGCT in the literature (4, 6, 9, 16, 17, 18, 22) (Table 1) and additional another two had recurrent GCT 8. (23)

Radiograph may show selective involvement of vertebral body with soap-bubble appearance associated with rarefaction and expansion of the vertebral body are important characteristic feature and may be helpful aid in preoperative diagnosis of the vertebral mass lesion and accordingly surgical intervention can be planned.

TABLE 1

Review of primary giant cell tumor occurring in the Axis vertebra

s.no.	Author/ reference	No. of cases	Year	Age/ Sex	Site of lesion	stages of Surgical resection	Surgical approach
1.	Honma et al.[9]	2	1989	-	Axis	single	Trans lingual and mandible splitting approach with fusion of spine from the atlas to the third cervical vertebra
				-	Axis	Single	
2.	Shirzadi et al. [6]	1	2011	15-year/ male	Odontoid process	Single stage surgery	Initial Surgery
3	Cebula et al.[4]	1	2012	-	Body and lateral masses of axis vertebra - C2 giant cell tumor colonized by aneurysmal bone cyst	Two stage	Preoperative embolization with two staged surgical intervention
4.	Hiromasa et al [16]	1	2012	23-year/ Female	- Body and vertebral arch of axis vertebra - cranial part of C3 vertebra on posterior	Two stage	First - Posterior fusion with surgical resection and Second - Anterior approach spinal tumor extirpation and anterior fusion
5	Chen et al. 18	5	2015	27-year/ Male	Axis vertebra	Two staged	First ¯ Posterior occipito-cervical fixation with Second- intralesional curettage
				36-year/ Female	Axis vertebra	Two staged,	First- Posterior fixation Second stage - intra-lesional curettage
				24-year /Female	Axis vertebra	Two stage	First - posterior occipito-cervical fixation Second - intra-lesional curettage
				45-year /Female	Axis vertebra	Two stage	First - Posterior occipito-cervical fixation Second stage - Partial resection
				23- Year /Male	Axis vertebra	Two stage	First ¯ Posterior occipito-cervical fixation with 2nd stage partial resection
6	Mattei et al. [17]	1	2014	22 -year/ Female	Vertebral body and odontoid process	Non-surgical	Monotherapy with Denosumab monoclonal antibody designed to inhibit the receptor activator of nuclear factor kappa-B ligand led to long-term remission
7	Bakhsh et al.[22]		2015	11–year/ Male	Body and odontoid process	Two staged surgery	First - posterior decompression and posterior fixation, followed by anterior decompression and fixation
	Current case	1	2017	38–year/ Male	Body of axis and right lamina	staged	First - posterior decompression and posterior fixation, Second stage – transoral decompression

Computed tomography clearly delineates the extent of lesion, bony outline and spinal stability, involvement of foramen transeversarium and vertebral artery encasement. The CT angiography may better delineate the course of vertebral artery and delineates its relation to lesion. MRI spine is considered as investigation of choice and typically shows hypointense mass lesion on T1 W image, and without significant alteration on T2 W image, also clearly delineates thecal sac and any spinal cord distortion as well as any associated co-existing intradural pathology or myelomalacia or cord signal alteration due to pressure effect. (4, 11)

Histologically, the giant cell tumour is characterized by well vascularized lesion, uniformally composed of spindle or oval shaped undifferentiated stromal cellswith evenly dispersed numerous large multinucleated giant cells. (2, 3, 5) Stromal cells and evenly dispersed numerous giant cell resemble each other in regard to nuclei. However, the giant cell is also found in osteogenic sarcoma, chrondroblastoma, osteoblastoma, fibrous dysplasia, brown tumor and aneurysmal giant cell tumors. But distribution of giant cell may be either focally distributed or very few in number and giant cell size may be small and having few nuclei in these tumors.

The natural history of PSGCT without treatment consist of enormous growth of tumor size, causing pressure effect on adjoining neurovascular structure leading to pathological fracture, malignant transformation and even distant metastasis. Management of GCT is surgical excision, however, wide surgical excision is not possible in cases of vertebral column lesion because of proximity to critical relation to spinal cords and vertebral artery in a single stage. (3, 5, 7) As single stage surgery involving anterior and posterior approaches produces significant alarming morbidity. (6, 9) The staged surgical approaches are devised and also used to ensure maximum resection of mass lesion with reduction in the morbidity. (4, 16, 17) All cases of PSGCT involving axis vertebra in literature were subjected for surgical resection (4, 6, 9, 16, 17) except one reported by Mattei et al. al (18) without surgical intervention and he was managed with monoclonal antibody using Denosomab monotherapy. In the surgical group of PSGCT, eight cases underwent staged surgical procedure, first stage being posterior fixation followed by anterior approach in the second stage (4, 16, 17) current case was also managed in staged procedure. However, two cases, reported by Homnma et al. (9) underwent anterior bases approach utilizing translingual and mandible splitting route with fusion of spine extending from atlas to third cervical vertebra and one caes also reported by Shizardi et al. managed with single stage decompression surgery. (6)

Cases with Giant cell tumor often show recurrence and there is wide range of variation depending upon the nature, route of surgical approaches, fixation, expertise of surgical team and extent of surgical decompression. About 20-40 % recurrence rate is observed after simple curettage, however recurrence rate significantly decreases with more radical surgical procedure utilization followed by adjuvant therapy. In staged tumor resection

surgery, may provide better chances of radical decompression with appropriate fixation and further minimizing morbidity. (9)

If tumour recurs, further repeat biopsy of mass lesion is advisable to exclude recent malignant transformation, (8) followed by surgical resection and replacement of bone defects with suitable bone grafting and appropriate bony fixation which may prevent further recurrence. At recurrence, if the histopathological grading of tumour is higher, the lesion usually tends to invade vertebral body as well as posterior elements as compared to those confined to vertebral body alone (20 % versus less than 6 %). (13) Periodic regular follow-up with detailed neurological examination with neuro imaging is recommended for five-years. (8)

PSGCT is are generally considered histologically benign; however, can also exhibits locally aggressive behavior with a relatively high local rate recurrence of up to 60%, if treated with curettage but it also carries the potential for distant metastasis, commonest to the lung, noted in upto 4% of cases. (19)

Bone and mineral disorder may occur frequently in renal transplant recipient and usually carry a high risk of bone fracture and associated morbidity. (20) A spectrum of a bone diseases are observed following the renal transplantation which may include osteoporosis. The pathophysiology of such bone disorders after transplantation results due to complex interplay of factors ie pre-existing renal osteodystrophy, immunosuppression and alterations in the parathyroid hormone-vitamin D-fibroblast growth factor 23 axis and altered mineral metabolism. (20)

Alterations in the metabolism of calcium, phosphorus and magnesium minerals and parathyroid hormone, alkaline phosphatase, vitamin D and can have significant impact. Calcineurin inhibitors are linked to development of fresh osteoporosis, steroid therapy may cause additional osteoporosis and varying degrees of occurrence of the osteonecrosis. Immunosuppressant may impair osteoblast proliferation and differentiation Differentpharmacologic management are suggested withdrawal of steroid therapy, and supplementation of bisphosphonates, vitamin D derivatives, and denosumab are proposed. (21)

PSGCT is locally invasive with variable is relatively a low radiosensitive tumor, so radiotherapy is usually reserved for surgically inaccessible or inoperable cases. However, radiation therapy also carries a risk of occurrence of high grade sarcoma in surrounding tissues. (13) Chemotherapy trial with Adriamycin has been tried for skull-base GCT. Recently Mattei et al. al (18), reported a 22 year female managed primarily with monoclonal antibody using Denosomab without surgery.

As surgical fixation in cases, with renal transplantation is double edges sword, as surgical resection without fixation may severely limit the extent of surgical resection and carry a chances of large residual. However, spinal fixation also carry risk of implant failure due to associated osteoporosis, continued therapy with steroid, immunosuppression medication. Author advocates a balanced

intervrention and tailored made therapy should be utilized for treatment in cases with PSGCT of Axis with renal transplantation and more frequent follow-up with neuroimaging to look for stability of implant and early detection of the tumor recurrence is highly important.

Conclusion

Early diagnosis and surgical management with spinal stabilization can help in preserving good neurological status, staged surgical procedure represents definitely a viable option for management of primary giant cell tumor affecting Axis vertebra. While dealing with osteolytic pathology of Axis vertebra, possibility of giant cell should also be considered despite rare occurrence as surgery can provide definitive surgical management along with adjuvant therapy and recently monoclonal antibody therapy is also showing promise for locally invasive and locally recurring primary lesion and neurosurgeons and radiologist must be aware of this pathology.

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