Cranio-vertebral junction tuberculosis

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ABSTRACT

There are variety of diseases which affect the region of craniovertebral junction, including congenital, malignant lesions, traumatic and infective/inflammatory lesions. CVJ tuberculosis is an extremely rare condition, accounting for 0.3 to 1% of all cases of spinal TB. Few case series have been reported in the literature about this rare condition, but there appears to be lack of consensus even on basic issues like whether to undertake surgical intervention or prefer a conservative approach in cases of CVJ TB. These cases can present with a myriad of symptoms and one needs to have a high index of suspicion for early diagnosis. Early diagnosis and treatment is very important for a favorable outcome. In this article, we have tried to review the available literature and also share our experience about this condition so as to have a better understanding of the disease process and have a more rational treatment protocol.

Key words: Cranio-vertebral junction, tuberculosis, spinal tuberculosis, CVJ tuberculosis

INTRODUCTION

Craniovertebral junction (CVJ) is a junction between the cranium and the rostral spinal column and as defined by Wackenheim, CVJ is an area bound superiorly by a line joining the internal occipital protuberance to the spheno-occipital synchondrosis and inferiorly by the lower limit of the body of axis.[1] Variety of the diseases affect this region including congenital, malignant, traumatic and infective/inflammatory lesions.

Among the infective processes, tuberculosis (TB) is an important condition. CVJ tuberculosis is an extremely rare condition, accounting for 0.3 to 1% of all cases of spinal TB.[2-5] However in our previous study on pediatric spine, the incidence of CVJ TB among all spinal TB was nearly 26%.[6] The incidence might increase in future because of the advent of immunodeficiency conditions (AIDS/transplants) and resistant strain of the bacteria. Early diagnosis and treatment are important in preventing long term neurological sequelae.

In this article, we discuss the specific problems associated with CVJ TB and also discuss our experience in the management of CVJ TB. The observations are based on the experience of management of 53 consecutive cases (mean age 27±5.36 years; range 9–63 years) with a male to female ratio of 30:23. These cases were managed during the last 15 years period (1997–2011) at Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India. The data was retrospectively evaluated to see for the nuances of the management (and associated problems) of this small but highly critical area of neuraxis where the brainstem converts to spinal cord.

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INCIDENCE

Tuberculosis remains an important health problem in developing countries. Recent resurgence of TB (especially multi-drug resistant variant) in both developing and developed countries has compounded the already complex problem. Despite TB being a common infection in developing countries and resurging infection in developed countries, spinal TB accounts for only 1% of all TB cases and in 6% in extra-pulmonary TB and 50% of skeletal TB. CVJ TB is still rarer with the reported incidence being 0.3% to 1% of all spinal TB[2-9] and few series (with small number of cases) have been reported about this condition. In pediatric population, the incidence is unknown. But in a series by Kumar *et al.*,[6] CVJ TB accounted for nearly one-fourth of all spinal TB. This Figure might be so high because of referral bias but does indicate a different distribution in children.

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Various risk factors like AIDS, transplant recipients, other immuno-compromised states like malignancy might play a crucial role in the resurgence.

PATHOPHYSIOLOGY AND PATHOGENESIS

CVJ TB usually occurs secondary to TB elsewhere in the body such as pulmonary TB, cervical/mediastinal lymph nodes or other sites. The process by which the infection/disease reaches the CVJ is yet to be understood. It appears that the initial assault of the infection is at the retropharyngeal space and from there the infection progressively involves the ligaments/bone as seen in few cases which initially present with only retropharyngeal abscess and later progresses to AAD.[8] In our experience, we had only two such cases, who initially presented with only dysphagia and later (despite ATT) progressed to AAD.

As the disease progresses, it involves the ligaments (especially the transverse and the alar ligaments) with osteolytic involvement of the odontoid or C1 with resultant subluxation of C1 on C2. With further progression, the anterior and posterior arches of C1, lateral mass of C2 and body of C2 along with occipital condyles are involved, which leads to marked instability of the region.[9]

CLINICAL PRESENTATION

Neck pain and restriction of neck movement are the most common presenting symptoms in cases of CVJ TB. Various studies have reported the incidence of neck pain and restriction of neck movements to be 100%[7-10] or nearly100%.[11,12] In our series, 51 (96%) cases had neck pain and 49 (93%) had restriction of neck movement.

Tuberculosis at the CVJ can present in several ways, for example;[3]

i. Direct compression of the neuraxis by the tubercular abscess/granulation tissue (extradural, rarely intradural/intramedullary)
ii. Bony and ligamental instability leading to a) atlantoaxial subluxation/dislocation; b) upward translocation of the dens causing compression of the medulla or upper spinal cord
iii. Combination of i and ii
iv. Abscesses leading to lower cranial nerve involvement or spinal nerve root compression
v. Dysphagia/airway compromise may occur due to mechanical obstruction
vi. Systemic symptoms.

Based on these mechanisms, other presenting symptoms/signs usually pertain to the occurrence of myelopathy, lower cranial nerves involvement, sensory symptoms or systemic symptoms. Spastic quadriparesis/quadriplegia was present in 60%[10] to 100%[9] of cases depending upon the series with majority of series pining down the incidence to nearly 70%.[7,8,11] In our experience, nearly 77% (41 cases) had spastic quadriparesis/quadriplegia. Sensory involvement was present in 10% to 54% of cases. In our experience, 32 cases (60%) had sensory symptoms/signs. Respiratory distress is a dangerous presentation which is present in a minority of patient with reported incidence being between 11%[9] to 36%.[7] We observed respiratory distress in 11 cases (out of 53) (21%). We graded the cases as follows: Grade 1- only neck pain without neurological deficit ($n=10$); Grade 2- independent with minor disability ($n=14$); Grade 3- partially dependent for activities of daily living ($n=5$); Grade 4- totally dependent for activities of daily living ($n=24$).

Lower cranial nerve involvement could manifest as hoarseness of voice, dysphagia and tongue deviation. The exact incidence of lower cranial nerve involvement is difficult to assess as these symptoms can occur not only because of lower cranial nerve involvement but because of other factors as well. For instance, dysphagia can also be present because retropharyngeal abscess. However, the incidence in literature is between 16%[7] and 53%.[11] This large variation might be because of the above-mentioned factors. Few series have not reported any lower cranial nerve involvement.[8,12] And 18 cases (34%), in our experience, had LCN involvement with hoarseness of voice, nasal regurgitation and dysphagia as the prominent symptoms.

Cerebellar signs/symptoms might be present in a small percentage of cases.[11,13] In our series, 5 cases (9%) had cerebellar signs. TB at other sites is usually not present but must be thoroughly searched for. The incidence of TB at other sites ranges from 8% to 20%. We encountered TB at other sites in 9 cases (17%) out of which 2 had cervical lymphadenopathy and 7 had active pulmonary TB. Among the 7 cases who had pulmonary TB, 2 had evidence (radiological) of abdominal TB. The incidence of systemic symptoms of TB (fever, night sweats and weight loss etc.) has been reported in the range of 40%[10] to 56%.[7] We encountered systemic symptoms in 23 cases (43%).

DIAGNOSIS

Various laboratory tests can be used to point to the diagnosis of CVJ TB. These include specifically total leucocyte count (TLC), differential leucocyte count (DLC), erythrocyte sedimentation rate (ESR) among the

other routinely done hemotological investigations. TLC and DLC appear to be normal in majority of cases. Among the major studies, only Gupta *et al.* (5) have mentioned about hematological investigation. According to them, all cases had a normal hematological investigation (except ESR) indicating that TLC/DLC would not contribute to establishment of diagnosis. However, isolated case reports have reported elevated counts.[13,14]

The more important marker appears to be *ESR*. Various studies have variedly reported the ESR positivity. On analysis of the major series in totality, it appears that the sensitivity of ESR would be nearly 70%.Thus, ESR appears to be an important initial marker for the diagnosis of CVJ TB. This is more important for physicians who examine the patients initially to have a high index of suspicion. As all were cases of CVJ TB, specificity cannot be commented upon. In a study by Rezai *et al.*[15] on spinal TB, out of 15 cases who underwent ESR testing (out of total of 20 cases), 14 had raised ESR. In their study, the mean ESR value was 65 mm in 1st h (however, it is to be noted that none of the cases had CVJ TB- 2 cases had C3 and C2-C3 TB). Similarly all cases of Lal *et al.*[4] had ESR value above 60 mm in 1st h. These studies indicate that value of ESR of more than 60 mm in 1st h is apparently more specific. Whether ESR can be used for follow-up and with what sensitivity needs to be studied.

Detection of the bacteria by PCR technique can be done. The sensitivity of PCR has been variedly reported in cases of CVJ TB. The positivity ranges from 12.5[9] to 100%.[7] However, in series dealing with spinal TB, the rate of PCR positivity ranges from 41 to 96.2%. In our experience, 37 out of 53 cases (70%) were positive. Taking all the data into consideration, it appears that the net positivity of PCR is nearly 70–75%. The need for PCR thus should be individualized and it might be a useful adjunct for establishing diagnosis especially if it is positive.

Chest X-ray (CXR) is another investigation done in cases suspected of CVJ TB. On analysis of the series which have commented on CXR, total number of CXR which had evidence of pulmonary TB were 31 out of 100 (5 in Behari *et al.* (n=25), 4 in Sinha *et al.* (n=18), 1 in Lal *et al.* (n=6) and 21 in Gupta *et al.* (n=51). It indicates that nearly one-third of all cases of CVJ TB will have X-ray evidence of pulmonary TB (either active or healed). In our series, 22 cases had CXR evidence of pulmonary TB (7 had active disease and 15 had healed lesions).

In an era of MRI and CT, role of cervical spine X-ray is primarily of the initial investigation in a suspected case. Cervical spine X-ray in neutral, flexion and extension view helps in evaluating the mobility of affected spine, atlanto-dental interval, basilar invagination, destruction/erosion of the bones and increase in the prevertebral shadow. Due to destructive nature of the disease, the conventional radiological markers used for the diagnosis of AAD might not be available and in such cases one should use the spinolamellar line. The plain film changes might take as much as 2-6 months for changes to appear as radiographic appearance of erosion will be obvious after 50% of the bone is destroyed.[7] Thus, in all cases, it is advisable to get a computed tomography (CT) and magnetic resonance imaging (MRI). CT would better delineate bony abnormalities like Atlantoaxial dislocation, increased prevertebral shadow, erosion of odontoid/axis body/anterior arch/posterior arch/clivus/occipital condyle/lateral mass, curvature abnormalities.[7,11,12] On the basis of CT CVJ, Lifeso[16] graded CVJ TB into the following grades:

Grade 1- increased prevertebral shadow
Grade 2- AAD and early bony changes
Grade 3- AAD, Gross destruction of bone and pathological fracture

MRI especially with gadolinium contrast enhancement better delineates the soft tissue abnormalities. Prevertebral, paravertebral and epidural collections/granulation tissue are better delineated by MRI. It had been seen that early changes of bone involvement can be picked up on MRI as intensity changes.[12] Spinal cord abnormalities were graded by Krishnan *et al.*[12] into 3 grades as follows:

Grade 1- no displacement of theca and no evidence of compression
Grade 2- displacement of theca but no evidence of compression
Grade 3- compression of the cord with or without degenerative changes such as syrinx or myelomalacia.

In addition to the above-mentioned findings, MRI of active CVJ TB might show altered signal on T1 and high signal intensity on T2 due to replacement of normal fat with inflammatory edematous tissue. In follow-up MRI, increase in the T1 intensity in the previously involved vertebr a suggests recovery. It has been suggested that more than 60% compression of the cord is usually required to cause neurological deficit and more than 75% for causing severe neurological deficit. However, this might not be true always as mild compression might be associated with severe neurological deficit.

MANAGEMENT

Management of CVJ TB is controversial to say the least with various authors advocating varied treatment modalities ranging from pure conservative to surgical interventions. However, in all series, all cases received antitubercular therapy, albeit for varied duration. The

options available are as follows:

i. Antitubercular therapy (ATT) only
ii. Transoral decompression and posterior fusion
iii. Only posterior fusion
iv. Traction.

The treatment of CVJ TB difficult to be standardized and has to be tailored to condition of the patient and the extent of the disease. The main features that dictate the choice of treatment are the neurological status and the grade of the patient, extent of bony destruction, compression of the cord, associated AAD and clinical response to ATT.

The first step in the management of these cases is confirmation of diagnosis. The diagnosis can be confirmed by a histopathological diagnosis as radiological appearance cannot be relied upon completely especially in the absence of retropharyngeal abscess and also because of emergence of multi-drug resistance sensitivity might be of help. The tissue for histopathological diagnosis can be obtained either by CT-guided biopsy or by specimen obtained during a transoral procedure (either decompression or simple aspiration of pus). Even in cases where transoral procedure need not be performed (e.g. case of reversible AAD), tissue might be obtained while doing the posterior fixation.[7,8] However, these procedures are occasionally associated with serious complications. Moreover, the cultures might turn out to be negative and one does not have many ATT drug options. In a selected few cases, it might be prudent to start ATT empirically, especially in cases who have extra-spinal TB and are neurologically stable. In these cases one might wait for 4 to 6 weeks to look for any response. In our experience, 6 cases underwent CT-guided biopsy, 9 cases were started on empirical ATT based on radiological findings (these cases had extra-spinal TB), 10 cases had transoral aspiration of pus (all of which showed granulomas and 3 out of these were AFB positive) and rest underwent transoral decompression and biopsy.

Irrespective of whether surgery is needed or not, ATT is the backbone of the treatment of CVJ TB. All cases should receive ATT with initial four drug regimen (rifampicin 10 to 20 mg/kg/day; isoniazid 5–10 mg/kg/day and ethambutol 15 mg/kg/day in a single daily dose and pyranizamide 20–35 mg/kg/day in two divided doses). The duration of the 4 drug regimen has been variedly reported as 3 months to 18 months.[6,7,11,17] Few authors have also used injectable streptomycin (15 mg/day, maximum 1 g/day) in addition to the 4 drug regimen.[9] The total duration of ATT is usually 18–24 months.[6,11] In case of hepato-toxicity, drug modification in the form of withholding isoniazid/rifampicin needs to be done along with the addition of ofloxacin/streptomycin.[6] The drugs can be restarted if the liver function tests return to normal.

The treatment of CVJ TB is controversial. Tuli[5] proposed prolonged bed rest and cranial traction with the head held in extension. Lal *et al*.[4] proposed one-stage posterior decompression and internal fixation with the use of metal prosthesis with bone grafting followed by immobilization in a hard cervical collar. Others have proposed a two-stage procedure with transoral decompression (TOD) and posterior stabilization with interval between the two with stabilization with halo-vest.[3,16] Behari *et al*.[7] have suggested a one-stage procedure i.e., TOD and posterior fixation/only posterior fixation (PF) for severe grade cases. Cases who had minor or no signs of myelopathy were managed with ATT and hard cervical collar. The use of cervical traction in their series was restricted to cases were it needed to be decided to perform only posterior fusion or TOD and posterior fusion. If reduction occurred on traction, only posterior fusion was done. Gupta *et al*.,[11] in their study were of the opinion that irrespective of the grade of the lesion, initial cervical traction (3 to 10 days) followed by Halo jacket for 3 months along with ATT had a good outcome. However, out of 51 cases this treatment protocol was applied to 16 cases and out of these 16, 11 were of severe grade. In our experience, out of 53 cases 41 cases underwent either TOD + PF or PF. All these cases had severe disease. In the remaining 12 cases, conservative management in the form of ATT and immobilization was done. The follow-up period ranged from 4 months to 6 years (mean 2.7 years). All patients had complete relief in the neck pain on receiving ATT for 3 months. All cases of grade 1[6] maintained their grade and out of 14 cases of grade 2, 8 improved to grade 1 and rest of them remained in grade 2. Out of 5 cases of grade 3, 3 improved to better grade and 2 maintained their grade. Among the 24 grade 4 cases, 21 showed improvement to a better grade. Sinha *et al*. did decompression by transcervical retropharyngeal approach with good outcome, but the number of cases in their study was less to propose this as procedure of choice. Moreover, a randomized study would be needed to decide the choice of surgery, till then it would be preferable to perform TOD. Thus it appears that for cases with either minimal or no signs of myelopathy can be managed by ATT and hard cervical collar. For cases with severe myelopathy, initial conservative management can be tried for 6–8 weeks, provided instability is ruled out. If there is no improvement or deterioration, surgical intervention should be done.

CONCLUSION

CVJ TB is a rare condition and has a varied clinical presentation. One needs to have a high index of

suspicion if one encounters a case with neck pain, neck restriction and raised ESR. CT CVJ and MRI with gadolinium contrast enhancement are the investigation of choice for both establishing a diagnosis and planning the management. For cases with no/minmal signs or symptoms of myelopathy, a conservative approach with ATT and hard cervical collar is usually sufficient. For severe cases, initial conservative management for a period of 6–8 weeks can be tried especially if there is no instability. If no improvement/deterioration, then surgical intervention needs to be done. Depending upon reducibility, decision on doing TOD can be made. Posterior fixation is needed in all cases where surgical intervention is needed.

REFERENCES

1. Wackenheim A. Radiologic diagnosis of congenital forms, intermittent forms and progressive forms of stenosis of the spinal canal at the level of the atlas. Acta Radiol Diagn 1969;9:759-68.
2. Desai SS. Early diagnosis of spinal tuberculosis by MRI. J Bone Joint Surg Br 1994;76:863-9.
3. Edwards RJ, David KM, Crockard HA. Management of tuberculomas of the cranio-vertebral junction. Br J Neurosurg 2000;14:19-22.
4. Lal AP, Rajshekhar V, Chandy MJ. Management strategies in tuberculous atlanto-axial dislocation. Br J Neurosurg 1992,6:529-35.
5. Tuli SM. Results of treatment of spinal tuberculosis by "midde path" regime. J Bone Joint Surg Br 1975;57:13-23.
6. Kumar R, Srivastava AK, Tiwari RK. Surgical Management of Pott's disease of the spine in paediatric patients: A single surgeon's experience of 8 years in a tertiary care center. J Paed Neurosci 2011;6:101-8.
7. Behari S, Nayak SR, Bhargava V, Banerji D, Chhabra DK, Jain VK. Craniocervical tuberculosis: Protocol of surgical management. Neurosurgery 2003;52:72-81.
8. Shukla D, Mongia S, Devi BI, Chandramouli BA, Das BS. Management of cranio-vertebral junction tuberculosis. Surg Neurol 2005;63:101-6.
9. Sinha A, Singh AK, Gupta V, Singh D, Takayasu M, Yoshida J. Surgical Management and outcome of tuberculous atlanto-axial dislocation: A 15 years experience. Neurosurgery 2003;52:331-9.
10. Kotil K, Dalbayrak S, Alan S. Craniovertebral junction Pott's disease. Br J Neurosurg 2004,18:49-55.
11. Gupta SK, Mohindra S, Sharma BS, Gupta R, Chhabra R, Mukherjee KK, *et al*. Tuberculosis of the craniovertebral junction: Is surgery necessary? Neurosurgery 2006;58:1144-50.
12. Krishnan A, Patkar D, Patankar T, Shah J, Prasad S, Bunting T, *et al*. Craniovertebral junction tuberculosis: A review of 29 cases. J Comp Assist Tomogr 2001;25:171-6.
13. Kanaan IU, Ellis M, Safi T, Al Kawi MZ, Coates R. Craniocervical Junction Tuberculosis: A rare but dangerous disease. Surg Neurol 1999;51:21-6.
14. Lee DK, Cho KT, Im SH, Hong SK. Craniovertebral junction tuberculosis with Atlantoaxial dislocation: A case report with review of literature. J Korean Neurosurg 2007;42:406-9.
15. Rezai AR, Lee M, Cooper PR, Errico TJ, Koslow M. Modern Management of spinal tuberculosis. Neurosurgery 1995;36:87-98.
16. Lifeso R. Atlanto-axial tuberculosis in adults. J Bone Joint Surg Br 1987;69:183-7.
17. Kalra SK, Kumar R, Mahapatra AK. Tubercular atlantoaxial dislocation in children: An institutional experience. J Neurosurg 2007;107(2 suppl):111-8.

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