

Unusual case of fungal cervical spine osteomyelitis in a patient with amyloidosis causing quadriparesis: A case report

Lee King Peng, MBBS¹, Daniyal Ansari², Serena Diane, MD, MPath³, Ravindran Vashu, MD, FRCS(SN)¹

¹Department of Neurosurgery, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia, ²Faculty of Medicine, St George's University of London, London, UK, ³Department of Histopathology, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia

SUMMARY

We present an unusual case of a 68-year-old lady who was diagnosed to have amyloidosis following chronic anaemia. She was put on systemic corticosteroid therapy for a year. She presented with rapidly progressive quadriparesis. Computed tomography/magnetic resonance imaging showed pathological fracture/dislocation of Cervical C5 vertebrae with cord signal changes, raising suspicion of a metastasis or tuberculous infection. A two-level corpectomy and cervical plating were done as part of a staged procedure. Posterior fixation could not be carried out due to postoperative acute myocardial infarction and exposure to COVID in the ward. Histopathology showed strong positivity of fungal bodies. This case discusses an unsuspecting fungal infection that needs to be investigated in elderly and immunocompromised patients. She subsequently refused further surgery, and instead, long-term rigid cervical collar was applied. She significantly improved from Modified Rankin Scale 5 to 3 in 3 months. Fungal infection should be suspected in similar cases, and ideally, a posterior fixation following 2 level or more corpectomy is a good option. Confounding medical conditions can interfere with surgical planning. Long-term rigid collar is a viable option in selected patients.

INTRODUCTION

Fungal spinal infection is an uncommon condition.¹ We could not identify any reports on patient who were treated for amyloidosis who later developed cervical fungal osteomyelitis. Prolonged systemic steroid therapy is an independent risk factor for fungal infection. When spinal instability ensues, this may result in spinal cord or root compression, resulting in neurological deficit. In general, unless urgent surgical decompression is performed, the prognosis for return of function is questionable. Surgery involves removal of compressing elements and reconstruction of spine by way of spinal instrumentation. The stabilisation allows bone fusion of the involved segments. This process depends on the patient factors as well as spinal construct and may take time. Any immunocompromised state or poor surgical planning may result in delayed or nonunion, and hence, lead to neurological deficits.

Among review of 60 cases of candida vertebral osteomyelitis by Miller (2001), mean age is 50 years old and the

commonest location is lower thoracic or lumbar. Patients typically present with chronic back pain (83%), fever (32%) and neurological deficit (19%) with preceding risk factor of central venous catheterisation, antibiotic usage, immunosuppression or injection drug usage.² There is elevation of ESR in 87% of cases and positive culture in 51%. Management involves surgical debridement and prolonged antifungal therapy, of which commonly used agents include amphotericin B, voriconazole, itraconazole and fluconazole. Prognosis is generally good with cure rate of 85%.³

Williams et al.⁴ reported three cases of fungal spinal osteomyelitis in immunocompromised (post-organ transplant) patients, in which key imaging features include hypointensity of vertebral bodies in T1-weighted sequence, signal changes and enhancement extending into posterior elements, multilevel diseases, preservation of intranuclear cleft in affected discs as well as lack of disc hyperintensity on T2-weighted imaging.

CASE PRESENTATION

We present an interesting case of a 68-year-old lady who initially presented with symptomatic anaemia and was treated for amyloidosis. She was given systemic corticosteroid therapy for 12 months, and her general condition including hematological parameters steadily improved. She was subsequently back to her premorbid state and tapered off corticosteroid treatment.

One year after the systemic corticosteroid treatment, she started developing chronic neck pain and weakness over all four limbs, which progressed over 1 month period. By the time she presented, she was fully alert but bedbound with all limb power of 1-2/5. Modified Rankin Scale as well as Nurick scale was 5. Computed tomography (CT) showed pathological fracture and retropulsion of C5 vertebral body whereas Magnetic resonance imaging revealed the involvement of C4 and C5 vertebral bodies with signal changes, collapse and retropulsion of C5 vertebral body causing spinal cord compression (Figure 1).

We suspected infective or neoplastic pathology causing the compression fracture of C4 and C5 vertebral bodies. Inflammatory marker as well as tumour markers including ESR, CRP, White cell counts, CEA, AFP, CA125, CA19-9 and

This article was accepted: 16 November 2023

Corresponding Author: Lee King Peng

Email: lee_kingpeng@yahoo.com

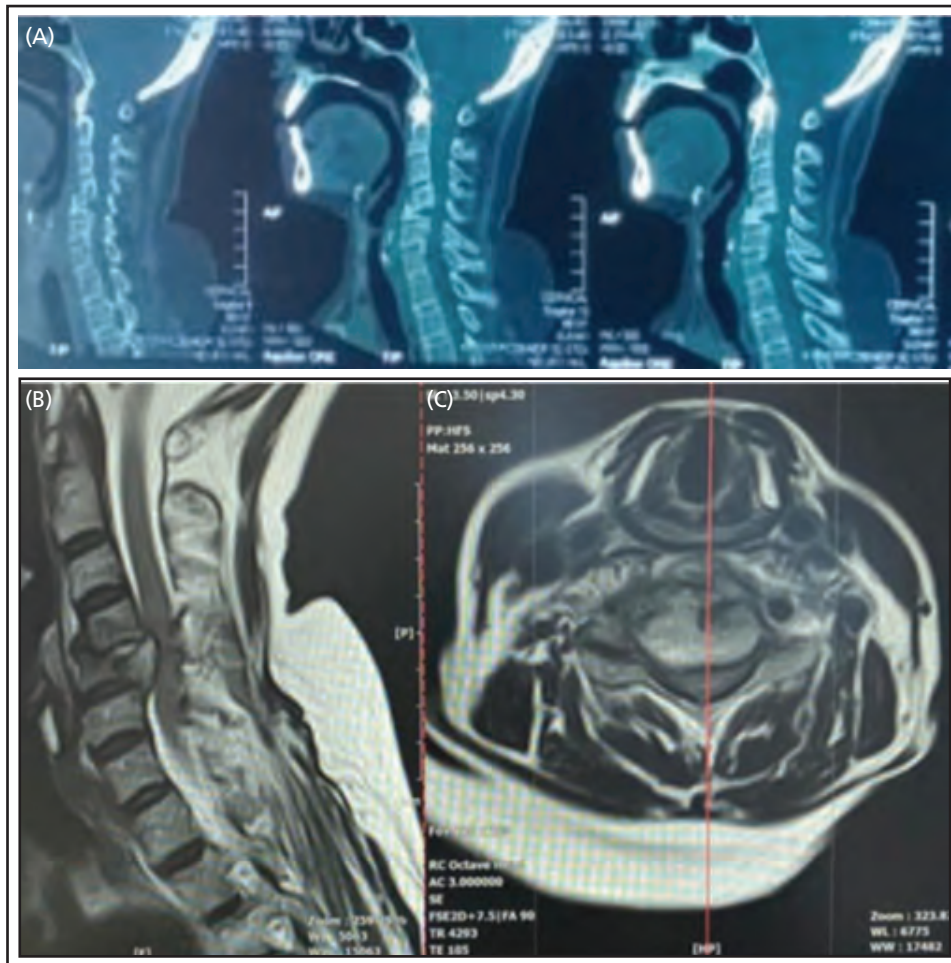


Fig. 1: Preoperative CT cervical (A) and MRI cervical (B, C) showing signal changes and pathological fracture of C5 vertebral body causing spinal cord compression

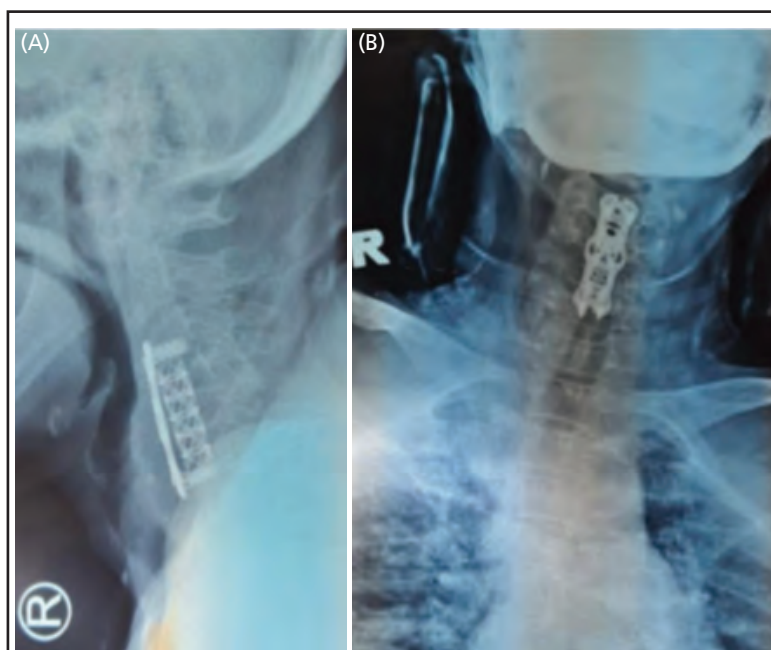


Fig. 2: Showing lateral (A) and anteroposterior (B) view of immediate postoperative cervical X-ray

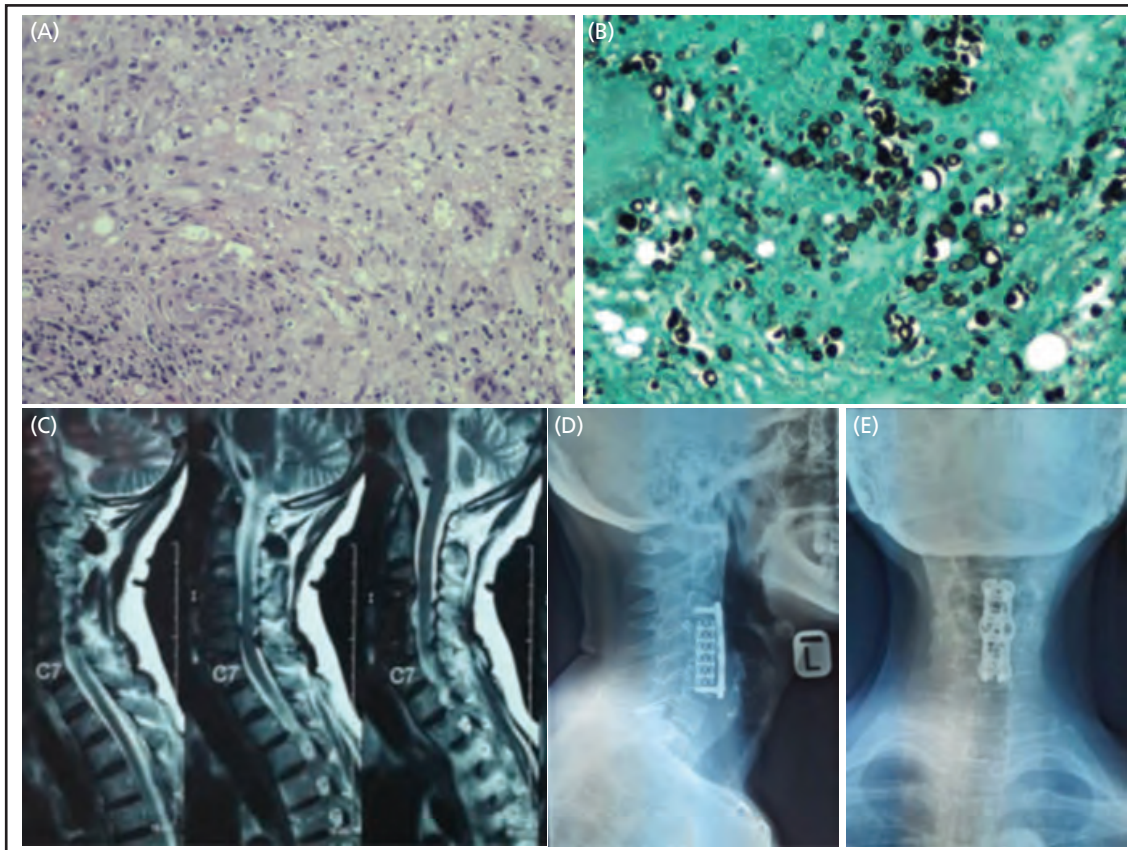


Fig. 3: Histopathological examination of the removed tumour demonstrated bland spindle cells in myxoid stroma with some fibroadipose tissue, smooth muscle, bone (A), and cartilage (B) with overall features suggestive of endobronchial hamartoma. (x40 magnification, haematoxylin and eosin stain)

bHCG were not raised. Workups for tuberculosis were negative. Full septic workups did not reveal any positive growth. Hence, main suspicion was neoplastic process causing the pathological fracture of affected vertebral bodies.

In view of the frank vertebral instability and rapidly progressive neurological deficit, she was planned for a combined anterior and posterior approach for decompression as well as stabilisation with C4-C5 corpectomy and posterior stabilisation in single setting. Intra-operatively the C4 and C5 vertebral bodies were clearly affected with poor bone quality suggestive of involvement of disease. There was greyish lesion, which was moderately vascular, poorly demarcated and unencapsulated noted over the affected vertebral bodies. Intervertebral discs were spared.

C4 and C5 corpectomy, Cage and anterior cervical plate insertion over C3 and C6 vertebral bodies were performed. The quality of C3 and C6 vertebral bodies were also felt to be poor, with less satisfactory screw purchase during anterior cervical plating. Hence, she was planned for a posterior C3 to C6 posterior instrumentation to supplement the anterior fixation. However, after the first stage of surgery, she developed non-ST elevation myocardial infarction on table and was felt to be unstable for the posterior surgery. Hence, it was postponed.

Immediate postoperative X-ray was as shown in Figure 2. Postoperatively, patient improved neurologically to all limb power of 3-4/5 and was able to mobilise with assistance by the end of first week postoperatively. She also developed lower gastrointestinal haemorrhage secondary to antiplatelet treatment from the Non-ST Elevation Myocardial Infarction and was also exposed to COVID in the hospital. In view of the multiple issues, she subsequently was not keen to proceed with the second surgery. As an alternative, she was put on rigid cervical collar, planned for 3-6 months and subsequently discharged with regular physiotherapy and rehabilitation.

1 week postoperatively, histopathological examination revealed chronic inflammatory cells, epithelioid macrophages and fungal spores interspersed in between the inflammatory cells on Haematoxylin and Eosin stain. Grocott-Gomori's (or Gömöri) methenamine silver stain revealed diffuse positivity for fungal infection (Figure 3(A, B)). Ziehl-Neelsen stain was found to be negative for Acid fast bacilli. However, bacterial and fungal cultures including fungal PCR were negative, and it was not possible to determine the fungus species based on histopathology alone.

In view of the histopathological findings, infectious disease consult was sought and she was started on course of antifungal treatment- intravenous amphotericin B for 6 weeks followed by oral fluconazole for 6 months. With

surgery and medical treatment, her neurology continued to improve and she was able to ambulate independently, with a modified Rankin and Nurick scale of 3 by the third month postoperatively. Follow-up MRI revealed adequately decompressed spinal cord (Figure 3C). Dynamic X-rays revealed graft subsidence. Nevertheless, there was evidence of fusion with no subluxation or mobile segment, hence rigid collar was removed by then (Figure (3D, E)). There were no new complications from surgery or medical treatment.

DISCUSSION

We intend to share this case because it is both a rare unsuspecting condition to find the cause of patient condition to be fungal infection. We are also highlighting the management aspect where we were forced to settle for anterior construct only although we had planned an anterior and posterior fixation. This is because in the senior author's experience, two-level corpectomy would need posterior augmentation to produce a firm construct and avoidance of graft subsidence. In this case, we are showing circumstances where patient condition and the autonomy of patient decision dominated over our surgical planning of front-back fixation. Follow up has resulted in mild graft subsidence, which has remained stable both radiologically and clinically. The patient has improved from bedbound quadriparesis to ambulation with a Nurick Grade 3. We also emphasise the importance of requesting for histopathology on top of cultures, which brought to light the diagnosis of this condition.

In this case, our provisional diagnosis was malignancy or tuberculosis. The fungal positivity was unexpected. Nevertheless, it was not possible to determine the fungus species based on histopathology alone. There was also a question of possible contamination, however with the diffuse positivity Grocott-Gomori's stain, the possibility was ruled out. Challenges of conventional culture tests in diagnosing fungal infections include the low sensitivity, long turnaround time, laborious process and failure of many cryptic fungal species to be isolated and grown on common fungal culture media.⁵ Despite advances in molecular-based diagnostic methods, it has limitations if the volume of fungal DNA is low in relation to proportion of human DNA, test amplification control and suboptimal analytical sensitivity of PCR, which can be strain dependent.⁶ In our case, another factor was the bone biopsy sample was sent for PCR analysis 1 week postoperatively, which could lead to sample degradation and hence false negativity.

We also believe her chronic steroid usage to treat her symptomatic anaemia secondary to amyloidosis could have predisposed her to cervical fungal osteomyelitis.

This patient presented with progressive neurological deficit, which required surgical decompression and stabilisation. Ideally, this would need a two-level corpectomy and posterior

fixation. Although the C4 vertebral body is seemingly normal on the CT scan, it appeared to show hypointensity on T1WI MRI and intraoperatively, appeared to be diseased with the presence of greyish lesion. Prolonged steroids, age and poor nutrition could be contributing factors to the poor bone quality of C3 and C6 vertebrae. Posterior C3–C6 instrumentation was initially planned in the same setting to augment the anterior construct. However, the second stage surgery was abandoned due to intraoperative hemodynamic instability and non-STEMI. Our main concern at that point was possible graft subsidence and instability on follow-up. However, she continued to improve neurologically with the rigid cervical collar and follow-up imaging revealed evidence of fusion with adequate decompression. Hence, after long discussion with family and patient, we decided to treat her conservatively.

From our literature review, there are so far no cases of patients treated for amyloidosis who later presented with fungal vertebral osteomyelitis requiring decompression and stabilisation. Hence, the rarity of this condition adds to the value of reporting this case.

CONCLUSION

Fungal culture should indeed be added to the array of investigations in elderly, immunocompromised and those with systemic corticosteroid therapy. Ideally, posterior fixation is needed in cases of two or more levels of corpectomy. When medical condition prohibits, prolonged cervical collar is a viable alternative with regular surveillance to ensure bone fusion.

ACKNOWLEDGEMENT

The authors would like to acknowledge Mr. Azmi bin Alias, the Head of Department of Neurosurgery, Hospital Kuala Lumpur .

REFERENCES

1. Khazim RM, Debnath UK, Fares Y. *Candida albicans* osteomyelitis of the spine: progressive clinical and radiological features and surgical management in three cases. *Eur Spine J* 2006; 15(9): 1404-10.
2. Zussman, BM, Penn DL, Harrop JS. Surgical management of fungal vertebral osteomyelitis. *JHN J* 2010; 6: 5-9.
3. Miller DJ, Mejicano GC. Vertebral osteomyelitis due to *Candida* species: case report and literature review. *Clin Infect Dis* 2001; 33(4): 523-30.
4. Williams RL, Fukui MB, Meltzer CC, Swarnkar A, Johnson DW, Welch W. Fungal spinal osteomyelitis in the immunocompromised patient: MR findings in three cases. *AJNR Am J Neuroradiol* 1999; 20 (3): 381-5.
5. Fang W, Wu J, Cheng M, Zhu X, Du M, Chen C, Liao W, Zhi K, Pan W. Diagnosis of invasive fungal infections: challenges and recent developments. *J Biomed Sci.* 2023; 30(1): 42.
6. Khot PD, Fredricks DN. PCR-based diagnosis of human fungal infections. *Expert Rev Anti Infect Ther.* 2009; 7(10): 1201-21.