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Case Report

Fungal infections of spine: Case series during the COVID times

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ABSTRACT

Fungal infections of the spine are a rare occurrence. We report three cases of Spondylodiscitis due to *Aspergillus fumigatus*, *Candida albicans* and *Scedosporium apiospermum*.

Case 1: 37 year old male, with history of COVID-19 infection one month prior presented with L1-2 Spondylodiscitis. Tissue showed growth of *Aspergillus fumigatus*.

Case 2: 75 year old male was admitted with swelling over low back. Pus aspirated from the swelling and tissue sent from operated site showed growth of *Candida albicans*.

Case 3: 56 year old known diabetic and end stage renal disease on hemodialysis presented with mid back pain since 2 months. Culture showed growth of *Scedosporium apiospermum*.

1. Introduction

Spinal infections due to fungi are rare compared to bacterial infections. Since last few decades, the incidence of fungal infections has been increasing [1]. Fungal infections of the spine range from simple discitis to severe/complicated vertebral osteomyelitis, leading to neurological deficit [1,2]. The major challenge lies in the treatment of fungal infections in the spine.

Attributed to the rarity of fungal spinal infections, literature search reveals limited data with respect to the management of these fungal bugs in spine except a few evidences-based practice referred in smaller case series [1].

2. Case history

Case 1: 37 year old male with COVID-19 infection 1 month prior, came with back pain. There was history of ICU admission, prolonged antibiotic and steroid therapy during his COVID-19 infection. MRI showed L1-2 Spondylodiscitis. L1-2 Posterior Stabilization, Debridement & Fusion with biopsy was done. Biopsy showed growth of *Aspergillus fumigatus*. Histopathological findings were suggestive of acute discitis, but no fungal elements seen. Serum Galactomannan performed was positive. Inj. Voriconazole 200mg Infusion twice daily was given for 5 days and patient was discharged with oral Voriconazole for 3 months. The patient is completely well now and repeat MRI showed resolution.

Case 2: 75 year old male, known case of Spondylodiscitis-L2-3, was admitted with c/o swelling over low back. Patient was a known case of diabetes, Ischaemic heart disease, hypertension and chronic kidney disease. L2-3 instrumented fusion was done 3 months prior. MRI & USG revealed resorption of graft & collection in paravertebral muscles. Pus aspirated under local anaesthesia from the swelling showed growth of *Candida albicans*. Inflammatory markers like CRP and ESR were raised. Blood culture revealed no growth. Beta D glucan test and serum galactomannan test was not done. Patient was operated for Anterior & Posterior Spinal Debridement, Fusion at L2-3 & STIMULAN BEADS application. *Candida albicans* was grown in tissue sent from operated site. It was sensitive to fluconazole, voriconazole, amphotericin B, caspofungin and micafungin by Vitek2 compact system. Injection caspofungin was given for 7 days and patient was discharged with oral fluconazole for 6 months. The patient recovered by 6 months.

Case 3: 56 year old male, known diabetic, hypertensive with end-stage renal disease on hemodialysis presented with mid back pain since 2 months. He had weakness in both the lower limbs and difficulty in walking after two weeks of onset of back symptoms. MRI showed D7-9 Infective spondylodiscitis with epidural collection. Blood investigations showed anemia, lymphocytosis, elevated ESR & CRP. He was operated for D5-11 Segmental Posterior Stabilization, Decompression & Fusion. Histopathological investigations from intra operative samples revealed fungal hyphae suggestive of Phaeohiphomyces. Fungal culture revealed *S. apiospermum* as shown in the Fig. 1. Patient

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Fig. 1. LPCB mount of the slide culture of the fungus showing truncate conidia suggestive of *Scedosporium apiospermum*.

was started on Voriconazole 200mg infusion over 2 hrs twice daily for 5 days. He was discharged with oral Voriconazole 200mg twice daily. Patient died after 1 month, owing to multi-organ failure.

Permission regarding the data mentioned above was obtained from the institutional ethics committee. (IEC KMC MLR 03/2022/94 Dated March 17, 2022). Patient and family consent has been taken.

3. Discussion

The incidence of spondylodiscitis varies from 1 per 100,000/year to 1 per 250,000/year [3]. These infections reported are common in males involving the lumbar spine commonly [1,3,4]. Likewise, all the three cases in this scenario were males, lumbar spine being involved.

The first, was a case of post-COVID L1-2 Spondylodiscitis due to Aspergillosis. The culture findings correlates with the positive results of serum-galactomannan assay, which substantiates the pathogenic role of post-COVID infection of the spine due to *Aspergillus fumigatus*. Recently, post-COVID vertebral osteomyelitis secondary to *Aspergillus* spp. Has been reported from Kashmir in India [5].

Our second case of recurrent Spinal infection (L2-3) due to *Candida albicans* had history of prior surgery for spondylodiscitis with intravenous line insertion. It is unclear whether *Candida* spp. reached the spine via hematogenous spread or was secondary to the initial surgical intervention/intravenous line insertion. Azoles are fungistatic to *Candida* species. Hence, caspofungin being a fungicidal agent is used [2].

Our third case of D7-9 spondylodiscitis was secondary to *Scedosporium apiospermum*. Review of literature reveals *S. apiospermum* can rarely infect musculoskeletal system and may occur in patients with impaired innate immunity/drug abuse/immunocompromised state [6–8]. The importance of *Scedosporium apiospermum* lies in the fact that it is resistant to amphotericin B (15% susceptible) and 5-flucytosine, unlike *Aspergillus* species [9]. In our case, the final identification of *S. apiospermum* was by fungal culture and phenotypic differentiation of four clinically encountered species of *Scedosporium*: *S. apiospermum*, *S. boydii*, *S. aurantiacum*, and *S. dehoogii* [10,11]. The choice of antifungal therapy (prophylactic/primary treatment) for the treatment of spinal discitis and

osteomyelitis due to fungal etiology, depends on the immune status of the patient [12].

4. Conclusion

Clinicians should be aware that infective spondylodiscitis may rarely be associated with fungal etiology, but can cause higher mortality and morbidity. Early recognition is often delayed. Noninvasive diagnostic tests are unavailable in such cases. Diagnosis may be supplemented by histopathological examination. Fungal culture is confirmatory. Treatment relies on appropriate antifungal therapy. A combination of surgical and medical management was associated with a greater survival rate. Prognosis of the patients actually depends on the etiological fungal agent, the premonitory state and the timing of treatment.

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Conflicts of interest

There are no conflicts of interest.

Credit author statement

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References

- [1] Ganesh D, Gottlieb J, Chan S, Martinez O, Eismont F. Fungal infections of the spine. *Spine* 2015;40(12):E719–28. <https://doi.org/10.1097/BRS.0000000000000903>. PMID: 25816141.
- [2] Johnson MD, Perfect JR. Fungal infections of the bones and joints. *Curr Infect Dis Rep* 2001;3:450–60. PMID: 11559466.
- [3] Chen CH, Chen WL, Yen HC. *Candida albicans* lumbar spondylodiscitis in an intravenous drug user: a case report. *BMC Res Notes* 2013;6(1). <https://doi.org/10.1186/1756-0500-6-529>. PMID: 24325945; PMCID: PMC3878824.
- [4] Dai G, Wang T, Yin C, Sun Y, Xu D, Wang Z, et al. *Aspergillus* spondylitis : case series and literature review. *BMC Musculoskel Disord* 2020;572(21):1–7. <https://doi.org/10.1186/s12891-020-03582-x>.
- [5] Makhdoomi R, Malik N, Charan J, Malik A, Singh S. Spinal aspergillosis: a rare complication of COVID-19 infection. *Egyptian Journal of Neurosurgery* 2022;37(1): 4–6. <https://doi.org/10.1186/s41984-021-00140-y>.
- [6] Larone Davise Honig. *Medically important fungi: a guide to identification*. sixth ed. New York: Elsevier; 1987.
- [7] Cortez KJ, Roilides E, Quiroz-telles F, Meletiadis J, Antachopoulos C, Knudsen T, et al. Infections caused by *scedosporium* spp. *Clin Microbiol Rev* 2008;21(1): 157–97. <https://doi.org/10.1128/CMR.00039-07>.
- [8] Rodriguez-tudela JL, Guarro J, Kantarcioglu AS, Horre R, Estrella MC, Berenguer J, et al. *Scedosporium apiospermum* : changing clinical spectrum of a therapy-refractory opportunist +. *Medical mycology* 2006;295–327. <https://doi.org/10.1080/13693780600752507>. official publication of the International Society for Human and Animal Mycology.
- [9] Usne SHK. *Pseudallescheria boydii* (anamorph *scedosporium apiospermum*) infection in solid organ transplant recipients in a tertiary medical center and review

- of the literature. *Medicine* 2002;81(5):333–48. <https://doi.org/10.1097/00005792-200209000-00001>. PMID: 12352630.
- [10] Gilgado F, Cano J, Gené J, Guarro J. Molecular phylogeny of the *Pseudallescheria boydii* species complex: proposal of two new species. *J Clin Microbiol* 2005;43(10):4930–42. <https://doi.org/10.1128/JCM.43.10.4930-4942.2005>. PMID: 16207945; PMCID: PMC1248451.
- [11] Paaajanen J, Halme M, Palomäki M, Anttila V. Medical Mycology Case Reports Disseminated *Scedosporium apiospermum* central nervous system infection after lung transplantation : a case report with successful recovery. *Medical Mycology Case Reports* 2019;37–40. <https://doi.org/10.1016/j.mmcr.2019.03.003>. PMID: 30956943; PMCID: PMC6431731.
- [12] Papachristou SG, Iosifidis E, Sipsas NV, Maria N, Walsh TJ, Roilides E. Management of osteoarticular fungal infections in the setting of immunodeficiency. *Expert Rev Anti Infect Ther* 2020;18(5):461–74. <https://doi.org/10.1080/14787210.2020.1748499>. PMID: 32213145.