Abstract: Aspergillus infections of the central nervous system are rare and typically involve the brain by contiguous spread from sino-nasal sites. Spinal cord involvement is reported occasionally. Usual associations are immunocompromised states, and post-operative infections are very rare. This is a report of a sixty-six year old post lumbar laminectomy patient presenting with a sub-acute paraparesis followed by fulminant meningoencephalitis which ultimately proved fatal. His MRI showed evidence of chronic paraparesis followed by fulminant meningoencephalitis which ultimately proved fatal. His MRI showed evidence of chronic infection at the surgical site, and features of inflammation within the spinal cord and basal leptomeninges. Hydrocephalus, exudates and haemorrhages were also present. CSF showed neutrophilic pleocytosis with hypoglycorrhachia, and segmented filamentous hyphae were noted on the CSF smear. Cultures grew Aspergillus terreus. CT Thorax showed multiple parenchymal lung nodules with cavitation, consistent with fungal infection. This unique presentation of Aspergillosis highlights the need to consider fungal infections as differentials in paraparetic presentation followed by fulminant meningitis in the setting of prior spine surgery.

Keyword: Aspergillus, cranio-spinal, post-operative

Introduction: Invasive aspergillosis of the central nervous system is a rare and serious disease(1). Brain involvement from sino-nasal sites via contiguous spread is well reported, including in Indian literature (2). However, spinal cord presentations are even less common, and usually result from contiguous spread from the vertebrae. Immunocompromised states and diabetes are known predisposing factors. Infection as a complication of neurosurgical practice is extremely rare (3). In this report, a case of spinal cord involvement following surgery is reported. Case History A sixty-six year old man, who was a diabetic with no major complications, had undergone a lumbar laminectomy surgery previously for claudication pain of the lower limbs. His evaluation had shown lumbar canal stenosis resulting from spondylosis of the lumbar intervertebral discs. Post-operatively he was ambulant without pain or neurological deficits. He then presented after six months with a sub-acute progressive illness over one month, characterised by fever, followed by paraparesis, and then bulbar weakness, followed by progressive obtundation of sensorium. The fever was low grade at onset, then later high grade with chills. On day 8, he noted hesitancy in passing urine, which led to complete urinary retention by day 11.

From day 12, his legs felt progressively heavy, and he could not walk by day 18. From day 20, he was also confused, and developed slurring of speech and confusion. He had also noted a dull constant holocranial headache. On admission (day 24), examination revealed flaccid severe weakness and wasting of both lower limbs. Anal tone was lax. Sensory loss over the inguinal and lower limbs was noted. Plantar and other superficial reflexes were absent (i.e. the abdominal, anal, bulbo-cavernous and cremasteric reflexes). Weakness of the 5th, 7th, 9th, 10th, 11th and 12th cranial nerves bilaterally was noted, with absent jaw jerk and gag reflex. His upper limb motor, sensory and reflexes were normal. He was also disoriented to time and place, but could recount his name and address. His fundus revealed papilledema. Signs of meningeal irritation were present. There was tenderness over the surgical scar site as well. Localisation was suggestive of a myelopathic process involving the lumbosacral spinal cord and nerve roots (conus/ cauda region).

The development of bulbar deficits and meningeal signs with papilledema suggested a secondary meningitic process with basal skull involvement. Etiological differentials considered were tuberculous, fungal, carcinomatous and lymphomatous infiltrative disorders. Investigation and course in the hospital On day 26, he developed worsening sensorium leading to coma, and required intubation for the same. Pupillary reflexes were present, but he was unresponsive to all other stimuli. He was evaluated with Gadolinium enhanced MRI of the spine and the brain. The MRI spine revealed increased cross-sectional diameter of the lumbosacral cord with long-TR hyper intensity in sub-pial regions. Clumping of the cauda equina nerve roots was also marked. There was evidence of dural thickening and focal inflammatory changes in the vertebrae, apart from the post-operative laminectomy defect. The MRI Brain revealed hydrocephalus of lateral, third and fourth ventricles. There were dense exudates in the basal cisterns and in the ventricles. Diffusion weighted imaging showed restriction in these. Multiple focal infarct were seen sub-ependymally. Gradient-Echo imaging revealed haemorrhages within the ventricles and cisterns. On contrast administration, dense linear leptomeningeal enhancement was noted outlining the roots, spinal cord and brainstem, and ependymal surfaces of 4th ventricle. There was no evidence of involvement in the paranasal sinuses or orbits. Overall features were suggestive of a fulminant infiltrative process involving the spinal cord and meninges.
The chest X ray showed multiple nodules and parenchymal infiltrates bilaterally. CSF studies were subsequently performed, with revealed a marked neutrophilic pleocytosis (over 20,000 cells), with hypoglycorrhachia and elevated proteins. CSF smears analysis revealed multiple septate branching hyphae. On culture, these were characterised as Aspergillus terreus. The patient was started on Antifungal therapy with Voriconazole and deoxycholate Amphotericin. The guarded prognosis was explained to the relatives. Despite therapy, he deteriorated further and succumbed in the 4th week of illness.

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Antifungal therapy with Voriconazole and deoxycholate preparation of Amphotericin. Liposomal amphotericin is also an effective alternative therapy. Other agents to be considered as salvage therapies include lipid formulations, Itraconazole and Caspofungin. (14)

Treatment of aspergillosis is preferentially with Voriconazole, which is proven to be superior to amphotericin. Liposomal amphotericin is frequently reported in patients with solid organ transplants and haematological malignancies. AIDS patients rarely develop aspergillosis though, for reasons unknown. Aspergillosis is with involvement of the sino-respiratory tracts.

Discussion Aspergillus genus is a ubiquitous fungus. The spores germinate to produce a septate hyphal mold, the mycelium. Aerial hyphae reproduce conidia which sporulate to perpetuate the life cycle. Aspergillus fumigatus is the most common pathogen, producing varied clinical manifestations. Specific associations with other species are- A. flavus (sino-nasal), A. nidulans (in patients with chronic granulomatous disease), A. niger (water borne gastro-intestinal tract)(4). A. terreus (from plants, and is amphotericin resistant)(5). Healthy humans rarely develop disease despite frequent inhalation. A spectrum of disease occurs in relation to the host's immune status. Predisposition for infection is seen in prolonged neutropenia, chronic steroid use, prior injury or surgery (6). All natural barriers may be crossed by the fungus, including cartilage and bone. The typical presentation of invasive aspergillosis is with involvement of the sino-respiratory tracts. Fungal sinusitis is usually seen in diabetics, while pulmonary aspergillosis is frequently reported in patients with solid organ transplants and haematological malignancies. AIDS patients rarely develop aspergillosis though, for reasons unknown. Aspergillosis of the central nervous system may involve the brain or spinal cord. Brain lesions include aspergillomas, cerebral abscess, or infarcts secondary to vascular wall invasion or septic emboli. Contiguous spread from the nasal sinuses or orbital apex is the commonest route. Aspergillomas (fungal ball) are firm intra parenchymal lesions, typically in the basal frontal or temporal lobes of the brain. Rarely, spinal cord parenchymal lesions may occur. They exhibit dense inflammation (7,8). Abscesses occur by haematogenous spread, containing a core of liquefactive necrosis, and a surrounding wall of haemorrhagic inflammation. CSF testing for suspected cases is recommended(12). The Galactomannan assay may also be used to monitor response to treatment(13).

This case is a unique presentation of Aspergillosis in view of the clinical presentation and rapidly fulminant course. Dormant infection was probably the result of seeding of the operative site with spores, which led to local infiltration. Rapid dissemination occurred when the CSF compartment was breached. The infection may be linked to development of diabetes, which is known to compromise neutrophil function and predispose to aspergillosis invasion. Important lessons learned are to consider fungal infections as differentials in paraparetic presentation followed by fulminant meningitis in the setting of prior spine surgery, to facilitate early diagnosis and initiation of therapy.

Bibliography