Aspergillus infections of the lumbar disc spaces

Report of three cases

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In the period of 1 year, three patients were seen at the University of Minnesota Hospitals with lumbar spine syndromes due to Aspergillus. Two patients responded to aggressive surgical debridement and prolonged administration of antifungal agents. A third patient with multiple chronic medical disorders succumbed to bacterial sepsis while undergoing chemotherapy of her mycotic infection.

Case Reports

Case 1

This otherwise healthy 57-year-old man underwent lumbar spinal surgery in May, 1979, at another institution for a disc herniation at the L4–5 level causing leg pain. The procedure was uncomplicated, except that the dura was inadvertently entered. The character of his leg pain changed postoperatively from sharp to dysesthetic. In June, 1979, he underwent reexploration, but the leg pain worsened further. A Penrose drain was left in the epidural space for 24 hours. A single intramuscular injection of corticosteroids was of no benefit. In August, 1979, severe back pain developed and he was referred to the University of Minnesota.

Examination. On admission, the patient was in moderate distress. He was afebrile. There was point tenderness over the middle portion of the lumbar spine. Hemoglobin was 13.9 gm/dl, and the white blood cell (WBC) count was 10,900 cell/cu mm with an unremarkable differential. The erythrocyte sedimentation rates (ESR's) were 56 mm/hr and 72 mm/hr. Apart from a slightly elevated alkaline phosphatase level, the blood chemistry profile was normal. Plain films and lumbar tomograms demonstrated erosion of the end plates of L-3 and L-4, with some demineralization of the subjacent bone. These changes were thought to represent an infectious process in the disc space. Lumbar myelography demonstrated a small extradural mass with irregular contours at the L3–4 level. The cerebrospinal fluid (CSF) protein level was 126 mg/dl.

A Craig needle biopsy of the L3–4 interspace demonstrated chronic inflammatory changes, and special staining demonstrated focally branching fungal hyphae, compatible with Mucor or Aspergillus (Fig. 1). Cultures grew an Aspergillus species most closely resembling the flavus group. On sensitivity testing, minimal inhibitory concentration (MIC) for amphotericin B was 0.31 gm/ml, a value indicating likely sensitivity; 5-fluorocytosine values indicated probable resistance.

Clinical Course. In light of the above findings, intensive conservative therapy was attempted first (Table 1). The patient was placed in a polypropylene body jacket and amphotericin B was initiated in rapidly increasing doses. The total target dose of amphot-
Aspergillus infections of the lumbar disc spaces

### TABLE 1

**Management of Aspergillus disc space infections***

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Organism</th>
<th>Maximum ESR (mm/hr)</th>
<th>Surgical Treatment</th>
<th>Amphotericin B MIC (gm/ml)</th>
<th>Total Dose (mg)</th>
<th>5-Fluorocytosine: MIC (gm/ml)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>A. flavus</em>†</td>
<td>72</td>
<td>biopsy only</td>
<td>0.31</td>
<td>2026</td>
<td>50</td>
<td>relapse</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>biopsy, laminectomy, posterior fusion</td>
<td>—</td>
<td>2000</td>
<td>—</td>
<td>solid fusion, pain-free</td>
</tr>
<tr>
<td>2</td>
<td><em>A. flavus</em></td>
<td>104</td>
<td>biopsy, laminectomy, disc space debridement</td>
<td>0.63</td>
<td>2001</td>
<td>1.5</td>
<td>spontaneous fusion, pain-free</td>
</tr>
<tr>
<td>3</td>
<td><em>A. fumigatus</em></td>
<td>80</td>
<td>biopsy, laminectomy, disc space debridement</td>
<td>0.31</td>
<td>906</td>
<td>0.1</td>
<td>died</td>
</tr>
</tbody>
</table>

* ESR = erythrocyte sedimentation rate; MIC = minimum inhibitory concentration.
† Organism in Case 1 was a species most closely resembling *flavus*.

Amphotericin B was 2000 mg. Over the weeks, the ESR fell to 46 mm/hr and his back pain slowly improved, but the patient never became fully pain-free. Rising creatinine levels necessitated a reduction of the amphotericin B dosage. The patient was discharged on the 34th hospital day and completed amphotericin B therapy to 2026 mg as an outpatient.

Despite this progress, low-back pain persisted and the ESR never fell below 30 mm/hr. In January, 1980, the patient was readmitted. Repeat needle biopsy revealed no fungus. Myelography showed that the L3-4 extradural mass had only partially resolved. As a consequence, lumbar laminectomy and posterior interbody fusion were carried out after radical curettage of the disc space. The bone on either side of the disc space was softened and necrotic. A body jacket was reapplied. Because fungal cells were still present in the biopsy specimen, a second 2000-mg course of amphotericin B was administered.

Over the next 10 months, the patient became pain-free, and the neurological deficit in the right leg partially resolved. His ESR decreased to 12 mm/hr. Good osseous union was ultimately achieved, and the patient has now been discharged.

**Case 2**

This healthy 44-year-old man underwent lumbar hemilaminectomy and discectomy at the L5–S1 level in April, 1979, at the University of Minnesota for an uncomplicated herniated disc with free fragments and related left radiculopathy. There was resolution of his initial pain problem, but within 6 weeks he had developed back and contralateral leg pain, necessitating readmission. Repeat plain films were unremarkable. In light of the contralateral radicular picture, the L4–5 and L5–S1 interspaces were explored through a right hemilaminectomy, but the expected disc herniation was not found. No sepsis was noted, and swab cultures of the L5–S1 interspace were subsequently found to be sterile. Leg and back pain were only slightly improved following this operation. Oral dexamethasone was administered for 17 days, but back pain increased in severity, requiring a third hospital admission.

**Examination.** On admission, the patient was markedly distressed by his back pain. The temperature was 38.3°C. There was mild weakness of the right gastrocnemius muscle, and a slightly decreased right Achilles reflex.

The ESR was 104 mm/hr. Hemoglobin, WBC count, and all other laboratory studies were within normal limits. Plain films of the lumbar spine sug-

![Fig. 1. Case 1. Photomicrograph of biopsy material showing profiles of fungal hyphae on a background of degenerated hyaline cartilage. Silver stain, × 400.](image-url)
gested slight demineralization of the L-5 body (Fig. 2 left); tomograms more clearly demonstrated the degree of osseous destruction (Fig. 2 right). A Craig needle biopsy of the L5-S1 disc tissue showed only mild chronic inflammation, but silver-stained sections clearly demonstrated the fungus (Fig. 3). Cultures immediately grew *Aspergillus flavus*. Testing for MIC indicated sensitivity to amphotericin B and 5-fluorocytosine.

**Clinical Course.** The patient was started on a course of both drugs, but severe back pain persisted. One week after biopsy, the patient’s temperature abruptly increased to 39.2°C, and he developed weakness of the right gastrocnemius, tibialis anterior, and extensor hallucis longus muscles, a patchy sensory loss in the right leg, and inability to void. Emergency myelography demonstrated an irregular extradural mass opposite the L-5 body and the L5-S1 interspace.

An emergency laminectomy was performed from L-4 to S-1. Cloudy serous exudate was encountered in the epidural space and in the L5-S1 interspace. Vigorous curettage of the interspace was performed, and cultures of the exudate revealed *Aspergillus flavus*.

Postoperatively, combined amphotericin B and 5-fluorocytosine administration was continued. The patient was placed in a body jacket, and a total dose of 2001 mg of amphotericin B was given. Back pain decreased over several weeks and the neurological deficit resolved. The patient achieved spontaneous fusion over the next year and, when last seen, was pain-free and neurologically intact.

**Case 3**

This 61-year-old woman was admitted to the University of Minnesota Hospitals in October, 1979, for a splenectomy. She suffered from numerous chronic diseases, including diabetes mellitus, nephrotic syndrome, slow disseminated intravascular coagulopathy, and autoimmune thrombocytopenic purpura. She had been treated chronically with vincristine and prednisone for the platelet disorder. Immunoglobulin (Ig) levels for IgE, IgM, IgA, and IgG and serum complement were normal. The carcinoembryonic antigen was elevated to 7.9 ng/ml (normal, 0 to 2.5 ng/ml). The ESR was 14 mm/hr. Fungal serology for histoplasmosis, blastomycosis, and coccidioidomycosis were all negative. Splenectomy was performed without incident and the patient returned home. However, she fell in January, 1980, causing lingering back pain and a gradually developing left L-5 radiculopathy.

**Examination.** The patient was an obese, chronically ill woman in moderate distress from her back pain. Plain films of the lumbar spine demonstrated partial destruction of the L-5 vertebral body (Fig. 4). A radionuclide bone scan showed an area of very intense activity over the L5-S1 interspace. A mild mixed motor and sensory L-5 radiculopathy was demonstrated.

The ESR had increased to 80 mm/hr. Lumbar myelography showed “encasement” of the dural sac up to the L-4 level, findings thought to be most consistent with an epidural metastasis. A Craig needle biopsy of the L-5 vertebral body demonstrated only mild chronic inflammation; cultures were sterile. Culture of a second biopsy performed 1 week later promptly grew *Aspergillus fumigatus*, but only silver stains demonstrated the organism. Testing for MIC showed sensitivity for amphotericin B and 5-fluorocytosine.

**Clinical Course.** The patient was started on both
Aspergillus infections of the lumbar disc spaces

Drugs; however, the back pain persisted and she failed to improve neurologically. On the 41st hospital day she underwent lumbar surgical exploration, where brownish-black purulent material was encountered epidurally and in the vertebral interspace. The patient showed little improvement postoperatively. A Hickman catheter was placed for chronic amphotericin B administration; this device became infected with Staphylococcus epidermidis. The patient developed fulminant staphylococcal septicemia, and died. Permission for postmortem examination was denied. She had received 906 mg of amphotericin B prior to her death.

Discussion

Fungal infections, once quite rare, are beginning to occupy a position of increased prominence in the contemporary practice of medicine. Although bacterial processes still constitute the vast majority of postoperative infections with which the neurosurgeon must deal, the occasional mycotic infection commands our attention because of the unusual difficulties in diagnosing and properly treating such a complication.

It is commonly believed that there must be an alteration of the systemic or local tissue immune response in order for a fungal infection to become established. All of our patients had received steroids prior to the onset of their discitis. Two patients had multiple operations shortly before developing an infection, and the effects of local tissue trauma may be important in the pathogenesis of this process. In one patient, a Penrose drain may have served as an avenue of infection, although it is likely that his infection predated this operation. Our last patient (Case 3), although chronically ill, had several studies suggesting at least that humoral immunity was normal. Several authors have suggested that mycotic infection may become well established in the presence of normal humoral immunity, however. This last patient may also have harbored an occult carcinoma, as suggested by the elevated level of carcinoembryonic antigen.

There was moderate difficulty in arriving at a diagnosis of fungal discitis in two of our cases. In Case 2, the disc space was found to be sterile on swab culture. Other authors have commented on the difficulty of obtaining positive fungal cultures from surface swabs, and have emphasized the necessity of culturing tissue fragments. Furthermore, microscopic survey of the tissue failed to show fungal elements when only routine stains were used. Silver staining always demonstrated the organisms. As pointed out by Thibodeau, the ESR is the single laboratory test which accurately reflects activity of the disease.

None of our patients responded well to conservative therapy, and surgery was required in all cases. Although some authors have reported success of mycotic vertebral osteomyelitis with drugs alone, several other groups have emphasized the need for vigorous surgical debridement and sustained antifungal drug.
administration. Radical curettage of the involved bone and disc space resulted in good fusion in the two survivors and would seem to be the procedure of choice. Prolonged antibiotic administration was necessary for eradication of the infection.

Of the 350 known species of the ubiquitous fungus, *Aspergillus*, numerous species are known to be pathogenic for man: *A. flavus* and *A. fumigatus* account for most human disease. The portal of entry of the infection may be the skin, the respiratory or gastrointestinal tracts, or as in our cases, surgical wounds. The association of mycotic infections with the use of certain types of tape and dressing material on surgical wounds has been reported as well. Branched, septate fungal hyphae are common to both *Aspergillus* and *Mucor*, and culture is therefore necessary to differentiate the two genera.

In summary, three cases of *Aspergillus* infection of the disc space are described in detail. Combined surgical and medical treatment seems necessary for cure.

References

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