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Hematogenously Acquired *Aspergillus* Vertebral Osteomyelitis in Seemingly Immunocompetent Drug Addicts

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A BROAD VARIETY of microorganisms can cause vertebral osteomyelitis in subjects who use illicit drugs intravenously.[1] *Aspergillus* species are ubiquitous in nature and have been found in as many as 25% of heroin samples,[2] yet they have been implicated in only one previously reported case of spinal infection, perhaps because they generally cause invasive disease only in persons who have defects in their phagocytic cells. We now report the occurrence of *Aspergillus* vertebral osteomyelitis in two drug abusers whose polymorphonuclear leukocytes (PMNs) were studied and found to be normal both in number and in function. Both patients recovered uneventfully after combined medical and surgical therapy.

Reports of Cases

Case 1

The patient, a previously healthy 34-year-old black male house painter, was admitted to hospital for low back pain of two months' duration. He had used heroin intravenously for ten years but said he was not an alcoholic, did not have diabetes mellitus or a history of hepatitis, was not homosexual and had not had trauma or a back operation. The physical examination showed no abnormalities except for localized mid-lumbar back pain. Complete blood counts, blood chemistry levels and results of liver function tests were normal. Roentgenograms showed narrowing of the L1-2 interspace with minimal destruction of bone. On histologic examination of specimens obtained at open biopsy and a laminectomy, there was invasion of bone by fungi, which proved to be *Aspergillus fumigatus* by culture. Antibodies to the human immunodeficiency virus (HIV) were not detected. Delayed-type hypersensitivity skin testing showed reactivity to *Candida* and *Trichophyton* antigens. Lymphocytes proliferated normally in response to phytohemagglutinin, concanavalin A and pokeweed mitogen. The patient's PMNs showed a normal capacity both to ingest and to kill a reference bacterial strain.[3] He recovered after receiving 2,000 mg of amphotericin B during a 60-day treatment period.

ABBREVIATIONS USED IN TEXT
HIV = human immunodeficiency virus
PMN = polymorphonuclear leukocyte

Case 2

An otherwise healthy 30-year-old black man was admitted to evaluate thoracic back pain of three months' duration. He had a ten-year history of intravenous heroin abuse but no other predisposing conditions. On physical examination there was focal tenderness over the sixth thoracic vertebra. Complete blood counts, blood chemistry levels and results of liver function tests were normal. A roentgenogram of the chest disclosed no parenchymal or pleural disease. The T6-7 interspace was narrowed and the contiguous vertebral bodies were extensively eroded. Material obtained by a Craig needle biopsy grew *Aspergillus terreus*. The patient received 2,000 mg of amphotericin B during the next two months. Because of intermittent fevers and a progressive kyphotic deformity, he underwent laminectomy with rib graft arthrodesis. Histologic examination showed persistence of fungal elements, but cultures were negative. Six months later the patient was in good health with only occasional mild back pain. At that time, an enzyme-linked immunosorbent assay for antibodies to HIV was negative; lymphocyte proliferative responses to phytohemagglutinin, concanavalin A, pokeweed mitogen, *Candida*, diphtheria toxoid and tetanus toxoid were all normal, and his PMNs phagocytosed and killed the reference bacterial strain normally.

Discussion

In adults, invasive *Aspergillus* infection is generally thought to occur in a clinical setting that is characterized by severe compromise of phagocytic function.[4,5] This clinical association, supported by various laboratory observations, has implicated mononuclear and polymorphonuclear phagocytic function as being critical to host defenses against this organism. Mononuclear phagocytes serve to kill the fungus in its conidial stage, while PMNs provide the major defense against mycelia; invasive infection generally occurs only when both lines of phagocytic cells are damaged.[6] Humoral and cell-mediated immunity seems to play little, if any, role in resistance. Thus, patients with hypogammaglobulinemia[4] or

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TABLE 1.—*Previously Reported Cases of Hematogenously Acquired* Aspergillus *Vertebral Osteomyelitis in Adults*

Case	Author	Age, yr	Sex	Aspergillus Species	Underlying Disease or Causes of Immunosuppression	Treatment	Outcome
1	Grossman, 1975[10]	44	♂	*fumigatus*	Renal transplant; long-term use of prednisone, azathioprine	Amphotericin B	Died of myocardial infarction
2	Ingwer et al, 1978[11]	49	♂	*fumigatus*	Renal transplant; long-term use of methylprednisolone, azathioprine	Debridement, amphotericin B	Died of gastrointestinal hemorrhage
3	Tack et al, 1982[12]	61	♀	*fumigatus*	Idiopathic thrombocytopenic purpura; long-term use of prednisone	Debridement, amphotericin B	Died of staphylococcal sepsis
4	Byrd et al, 1982[13]	52	♀	Unknown	Renal transplant; long-term use of prednisone, azathioprine	Debridement, amphotericin B	Died of *Pseudomonas* sepsis
5	Seligsohn et al, 1977[14]	42	♀	*terreus*	Alcoholism, cirrhosis, intravenous drug abuse	Amphotericin B	Recovered
6	Roselle and Baird, 1979[15]	54	♂	*flavipes*	Cerebral edema; dexamethasone use in recent past	Debridement, amphotericin B	Recovered
7	McKee et al, 1984[16]	22	♂	*fumigatus*	Glucose 6-phosphate-dehydrogenase deficiency	Debridement, amphotericin B	Recovered
8	This report	34	♂	*fumigatus*	Intravenous drug abuse	Debridement, amphotericin B	Recovered
9	This report	30	♂	*terreus*	Intravenous drug abuse	Debridement, amphotericin B	Recovered

the acquired immunodeficiency syndrome[7] are not at increased risk for the development of these infections.

Review of the seven previously reported cases of hematogenously acquired *Aspergillus* vertebral osteomyelitis (Table 1) indicates that while four patients had clear evidence for suppression of PMN function (cases 1 to 4), three others had only potential or mild abnormalities in this regard (cases 5 to 7). There was no evidence of impaired function of either phagocytic cell line in the cases reported herein. Normal PMN phagocytosis and killing of a reference bacterial strain showed that the complex biochemical processes that modulate ingestion and oxygen radical formation were intact. Although the microbicidal activity of macrophages was not directly studied, these cells supported normal lymphocyte proliferative responses indicating that they were able to recognize, ingest, process and present antigen appropriately. Assays of phagocytosis and killing of *Aspergillus* were not done. Although an apparently specific defect in phagocytic killing of *Aspergillus* has been reported by Italian investigators,[8,9] this has been manifest early in life with recurrent *Aspergillus* infections and a poor response to therapy.

The elevations of immunoglobulin M and circulating immune complexes and the false-positive VDRL and rheumatoid factor tests that are commonly found in addicts suggest that some degree of immunologic abnormality results from parenteral heroin abuse.[17] Defective phagocytic function, however, has not, to our knowledge, been previously shown. Thus, the occurrence of *Aspergillus* vertebral osteomyelitis in our patients, neither of whom had recognizable immunologic defects, indicates that this infection may occur as a result of transient suppression of phagocytic function or in the absence of detectable immunologic dysfunction.

It is of special interest to note that patients who lack obvious evidence for immune suppression usually do recover when treated with standard medical and surgical therapy (Table 1, cases 5 through 9). A recent report has suggested that pulmonary infections in nonimmunocompromised patients[18] may be cured by the prompt institution of treatment with amphotericin B.[18] The uniformly poor outcome in disseminated *Aspergillus* infections thus seems to be confined to patients who have more profound and persistent defects in immune function; these persons are expected to respond poorly to treatment and to die of the infection or of complications of their underlying illnesses. It is to this group of patients that new approaches to treatment should be directed.

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