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# *Aspergillus* osteomyelitis: Epidemiology, clinical manifestations, management, and outcome

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## KEYWORDS

*Aspergillus*;  
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**Summary** *Background:* The epidemiology, pathogenesis, diagnosis, and management of *Aspergillus* osteomyelitis are not well understood.

*Methods:* Protocol-defined cases of *Aspergillus* osteomyelitis published in the English literature were reviewed for comorbidities, microbiology, mechanisms of infection, clinical

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manifestations, radiological findings, inflammatory biomarkers, antifungal therapy, and outcome.

**Results:** Among 180 evaluable patients, 127 (71%) were males. Possible predisposing medical conditions in 103 (57%) included pharmacological immunosuppression, primary immunodeficiency, and neutropenia. Seventy-three others (41%) had prior open fracture, trauma or surgery. Eighty (44%) followed a hematogenous mechanism, 58 (32%) contiguous infections, and 42 (23%) direct inoculation. *Aspergillus* osteomyelitis was the first manifestation of aspergillosis in 77%. Pain and tenderness were present in 80%. The most frequently infected sites were vertebrae (46%), cranium (23%), ribs (16%), and long bones (13%). Patients with vertebral *Aspergillus* osteomyelitis had more previous orthopedic surgery (19% vs 0%;  $P = 0.02$ ), while those with cranial osteomyelitis had more diabetes mellitus (32% vs 8%;  $P = 0.002$ ) and prior head/neck surgery (12% vs 0%;  $P = 0.02$ ). Radiologic findings included osteolysis, soft-tissue extension, and uptake on T2-weighted images. Vertebral body *Aspergillus* osteomyelitis was complicated by spinal-cord compression in 47% and neurological deficits in 41%. Forty-four patients (24%) received only antifungal therapy, while 121 (67%) were managed with surgery and antifungal therapy. Overall mortality was 25%. Median duration of therapy was 90 days (range, 10–772 days). There were fewer relapses in patients managed with surgery plus antifungal therapy in comparison to those managed with antifungal therapy alone (8% vs 30%;  $P = 0.006$ ).

**Conclusions:** *Aspergillus* osteomyelitis is a debilitating infection affecting both immunocompromised and immunocompetent patients. The most common sites are vertebrae, ribs, and cranium. Based upon this comprehensive review, management of *Aspergillus* osteomyelitis optimally includes antifungal therapy and selective surgery to avoid relapse and to achieve a complete response.

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## Introduction

*Aspergillus* osteomyelitis is a debilitating and severe form of invasive aspergillosis.<sup>1–4</sup> Patients suffering from *Aspergillus* osteomyelitis may suffer protracted pain, immobilization and loss of function. As the population of immunocompromised patients continues to expand, *Aspergillus* osteomyelitis will likely increase in direct relation. There have been various case series, which review a selected aspect of *Aspergillus* osteomyelitis, a specific host population, a single institutional experience, or multi-center case registry.<sup>1–165</sup> While these reports have contributed to our knowledge of *Aspergillus* osteomyelitis, there is no contemporary comprehensive review of literature by which to understand the epidemiology, clinical manifestations, diagnosis, management, and outcome of *Aspergillus* osteomyelitis using a large and highly detailed case analysis. We therefore conducted an extensive literature review of *Aspergillus* osteomyelitis using high stringency detailed case criteria to provide such a resource for the diagnosis and treatment of this serious infection.

## Methods

### Study design

This is a comprehensive review of reported cases of *Aspergillus* osteomyelitis as published in the English literature. We initiated our search by reviewing all English references as published in PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>) using the key words: *Aspergillus*, aspergillosis, osteomyelitis, arthritis, and bone. We then carefully included only well-described references for single case reports or case series that provided sufficient data. After this

initial series of reports was reviewed, individual references listed in each publication were again reviewed for ascertainment of additional case reports.

### Criteria for inclusion and exclusion of cases of *Aspergillus* osteomyelitis

Cases selected in the initial screen were then included in the final analysis if the following data were available: documentation of *Aspergillus* osteomyelitis, anatomical location of infection, underlying condition, therapeutic intervention, and outcome. Cases not including this essential information, or if after being reviewed, did not contain sufficient data by which to draw definitive conclusions, were excluded. Among other parameters sought, but not obligatory for inclusion of a case in the analysis, were comorbidities, clinical manifestations, radiological features, and inflammatory markers. Cases of aspergillosis complicating arthroplasty and prosthetic joints were considered to be septic arthritis and excluded unless there was clear documentation of osteomyelitis. Cases consisting only of *Aspergillus* sinusitis were excluded due to lack of consistent criteria used in defining concomitant osteomyelitis.

### Definitions

The following definitions were used throughout the study.  
Mechanisms of bone infection.

**Direct inoculation:** Seeding of bone tissue by trauma or surgical manipulation.

**Hematogenous:** Seeding of bone tissue by bloodborne route.

**Contiguous:** Seeding of bone tissue from an adjacent focus of *Aspergillus* infection.

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