CASE REPORT

ARTICULAR ASPERGILLOSIS: TWO CASE REPORTS AND REVIEW OF THE LITERATURE

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SUMMARY

We report two cases of septic arthritis of the knee caused by Aspergillus: one by Aspergillus terreus in a cirrhotic patient and the other by Aspergillus fumigatus after vascular graft infection. The recovery of these organisms in synovial fluid should be considered as pathogenic, particularly in immunocompromised hosts. The pathogenic mechanism is discussed and the literature is reviewed.

KEY WORDS: Septic arthritis, Aspergillus terreus, Aspergillus fumigatus, Cirrhosis, Vascular graft.

Aspergilli are ubiquitous in the environment, notably in potted plants, dust or food condiments. More than 300 species of Aspergillus have been identified, but only a few are considered as pathogenic for human beings, notably A. fumigatus, A. flavus, A. niger and A. terreus. Aspergillosis generally occurs in immunocompromised hosts, especially neutropenics (leukaemia) or after organ transplantation. Musculoskeletal involvement is uncommon; vertebrae and ribs are the preferential sites, the joint is still less frequently affected.

To our knowledge, only five cases of Aspergillus septic arthritis have been reported [1–5]. We describe two new cases of septic arthritis caused by Aspergillus and review in the literature; interestingly, one case is the first due to A. terreus.

CASE 1

A 51-yr-old man with a 9 yr history of ethanolic cirrhosis was admitted to our department because of a 3 month history of synovitis in the right knee, and fluctuating fever for 60 days (38°C). This patient also had a history of several bacterial catheter infections over the past months with secondary septicemia. No immunocompromised state or previous fungal infection were reported. Physical examination confirmed a 38.1°C temperature and a swollen right knee (Fig. 1). The patient was given an oral suspension of itraconazole (200 mg twice a day). Because of poor response during the first 3 weeks, arthroscopic debridement with a motorized shaver and synovial biopsy were performed. Histopathological findings consisted of mycotic filaments amongst the synoviocytes using periodic acid–Schiiff stain (Fig. 2). Three months later, he was doing well and blood analysis was unremarkable.

CASE 2

A 69-yr-old man was admitted because of pain and tightness in the right calf and foot. Six months prior to admission, he had undergone an expanded polytetrafluoroethylene (PTFE) iliofemoral bypass for dissection of the right external iliac artery. The postoperative course was uneventful. On physical examination, the patient had no fever. A pulsating mass was palpable in the right iliac quadrant and painful erythematous nodules were noted along the right calf and sole of the right foot. Blood chemistry was unremarkable except for ESR (75 mm/h). Three sets of blood cultures remained sterile. Angiography revealed a false mycotic aneurysm of the right common iliac artery which was surgically removed 2 days later and a femorofemoral bypass graft with the saphenous vein was performed. During the following month, the patient did well, but suddenly experienced pain in the right knee with swelling and limited range of motion. New blood cultures remained sterile. Arthrocentesis yielded serous fluid with 7300 WBC/mm³. Culture was positive for A. fumigatus. Intravenous amphotericin-B was administered (60 mg i.v. every 48 h) over a 6 week period. Oral itraconazole (600 mg daily) was subsequently given for 9 months and an arthroscopic debridement was performed. The follow-up was maintained for at least 3 yr; the patient is doing well without evidence of recurrence.

DISCUSSION

Aspergillar bone and joint infection is rare. Bone involvement is common during aspergillar sinusitis...
Aspergillar osteomyelitis occurs at any age and the localization is mostly vertebrae and ribs [7, 8].

Aspergillus arthritis is very rare; only five cases have been reported in the literature [1–5]. The clinical pictures are summarized in Table I.

Of our two cases, one illustrates an unusual aspergillar infection with \textit{A. terreus}. This fungus is widespread in the environment; when recovered clinically, it is generally considered as a saprophyte, but \textit{A. terreus} is an accepted aetiological agent of onychomycosis [9], and sporadic reports have described serious deep infections such as s.c. abscess [10], bursitis [11], endocarditis [9], pneumonia [12], osteomyelitis [13–16], meningitis or disseminated aspergillosis [17]. As with other \textit{Aspergillus} species, infection by \textit{A. terreus} appears when an underlying debilitating disease or immunosuppressed state is present [9, 18]. Rippon \textit{et al.} [19] have shown that the virulence of strains of \textit{A. terreus} found in humans was higher than that of strains found in soil. In the present case, it is unlikely that \textit{A. terreus} was a contaminant or secondary invader as it was isolated in pure culture from synovial fluid and synovium. Typical hyphae were identified in the synovium.

Case 2 reveals an invasive aspergillar infection after vascular graft infection, possibly due to direct contamination during surgery. Interestingly, the appearance of the arthritis 1 month later would suggest haematogenous spread.

Immunosuppression was present in five of the seven reported cases, due to renal transplantation, diabetes mellitus, haematological malignancy or cirrhosis, and in two patients after surgical procedure. In some cases, prolonged granulocytopenia (neutropenia) and/or antibiotherapy have also been associated with invasive aspergillosis [18]. Virulence factors of aspergilli, such as soluble factors which reduce complement C3b binding to fungal cells, were not found [20].

In our first case, a defect in cellular immunity

\begin{figure}
\centering
\includegraphics[width=\textwidth]{image1.png}
\caption{T2 SPIR MRI of the right knee showed synovitis (arrows) and fluid with oedema (*) of the lateral femoral condyle (case 1).}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{image2.png}
\caption{Microscopic aspect of synovium of the right knee (case 1). Within synoviocytes (S), mycotic filaments (arrows) were identified. Periodic acid–Schiff stain, original magnification ×1000.}
\end{figure}
<table>
<thead>
<tr>
<th>Ref.</th>
<th>Age/sex</th>
<th>Underlying disease</th>
<th>Joint</th>
<th>Invasive aspergillosis</th>
<th>SF</th>
<th>Bone</th>
<th>Synov.</th>
<th>Synovial fluid (CC/mm³)</th>
<th>Aspergillus species</th>
<th>Portal of entry</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29/M</td>
<td>ORTX</td>
<td>Knee</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>17200 61% N</td>
<td>fumigatus</td>
<td>Local steroid</td>
<td>AmphoB</td>
</tr>
<tr>
<td>2</td>
<td>66/M</td>
<td>Diabetes mellitus</td>
<td>Knee</td>
<td>NR</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>NR</td>
<td>fumigatus</td>
<td>Haematogenous</td>
<td>ItraK</td>
</tr>
<tr>
<td>3</td>
<td>64/M</td>
<td>TLHR</td>
<td>Knee</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>NR</td>
<td>niger</td>
<td>Surgery</td>
<td>AmphoB</td>
</tr>
<tr>
<td>4</td>
<td>30/M</td>
<td>ORTX</td>
<td>Wrist</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>NR</td>
<td>fumigatus</td>
<td>Direct inoculation</td>
<td>Debridement</td>
</tr>
<tr>
<td>5</td>
<td>1/M</td>
<td>Aplastic anaemia</td>
<td>Knee</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>NR</td>
<td>fumigatus, flavus terreus</td>
<td>Skin</td>
<td>AmphoB</td>
</tr>
<tr>
<td>Case 1</td>
<td>51/M</td>
<td>Cirrhosis</td>
<td>Knee</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>128000 92% N</td>
<td>fumigatus</td>
<td>Haematogenous?</td>
<td>ItraK, Debridement</td>
</tr>
<tr>
<td>Case 2</td>
<td>69/M</td>
<td>Vascular surgery</td>
<td>Knee</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>7300 84% N</td>
<td>fumigatus</td>
<td>Surgery</td>
<td>AmphoB, ItraK, Debridement</td>
</tr>
</tbody>
</table>

NR, not reported; ORTX, orthotopic renal transplantation; TLHR, total left hip replacement; SF, synovial fluid; Synov., synovium; CC, cell count; ItraK, itraconazole; AmphoB, amphotericin B; Rifam, rifampicin.
due to cirrhosis as described by Paronetto [21], in combination with prolonged antibiotic use, probably played a major role in the occurrence of Aspergillus infection, but no phagocyte function or myeloperoxidase deficiency were evaluated. Moreover, no sign of Aspergillus pulmonary infection was found. Kammer [22] found only three positive blood cultures in 39 patients with Aspergillus endocarditis. So it was perhaps unsurprising that blood cultures were sterile in our case. On the other hand, the entry of infection was at first not known and direct inoculation seems unlikely.

In case 2, inoculation with airborne fungal spores most likely occurred during surgery. Operating room ventilation systems have been reported to harbour such organisms [18]. After intra-operative inoculation, a prosthetic graft may serve as a nidus for fungal colonization and predispose to locally invasive infection or haematogenous spread.

To conclude, septic arthritis caused by Aspergillus species is rare. The recovery of these organisms in synovial fluid should not be casually dismissed as representing colonization, particularly in immunocompromised hosts.

REFERENCES