Primary Cutaneous Aspergillosis: Our Experience in 10 Years

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We describe nine patients with primary cutaneous aspergillosis who were diagnosed during the 10-year period between 1987 and 1996. All except one were adults. Seven of those nine cases had an immunocompromised state. Among the immunocompromised patients, six had burn wounds and one was a renal transplant recipient. Aspergillus flavus was isolated from seven patients and A. fumigatus from one, and in one other case the species could not be determined. Three patients who had total burn surface area of more than 70% died. The other patients responded well to extensive surgical debridement with or without institution of oral itraconazole.

Introduction

Primary cutaneous aspergillosis (PCA) is a rare entity. It is most often the result of direct inoculation of Aspergillus species at an intravenous access site or under an arm board or dressing. In other cases the fungus presumably enters through the breaks of skin or open wounds from environmental sites, including the ambient air. In patients with severe burns, Aspergillus occasionally invades through a burn wound.

Most cases of PCA have been reported in immunocompromised patients with AIDS, haematological or lymphoreticular malignancies or in organ transplant patients receiving long-term chemotherapeutic agents. It is curious that most cases of PCA are observed in children; few patients are adults. We report here nine cases of PCA observed during the last decade. All but one of these patients were adults, and only two were immunocompetent hosts.

Patients and Methods

Patients

The patients who were diagnosed for PCA in the mycology laboratory record in the period of 1987–1996 were included in this study. Detailed clinical history and outcome of therapy were noted from clinical records. The clinical data are summarized in Table 1.

Case 1

A 24-year-old man received a related renal transplant in September, 1996. Six weeks after transplant, while he was on cyclosporin, azathioprim and prednisolone, a swelling developed on the left middle finger. The swelling was erythematous fluctuant, capped by few tiny pustules. He gave no history of external injury. Fine needle aspiration from the swelling was performed and dichotomously branched septate hyphae were seen in 10% potassium hydroxide wet mount. On haematoxylin and eosin stain of the aspirated material, plenty of chronic inflammatory cells and multinucleated foreign body giant cells were seen. Culture of the same material grew A. flavus. No bacteria was isolated on culture. Evidence for aspergillosis could not be found at any other site. The patient was treated with local debridement followed by oral itraconazole (100 mg twice daily) for 2 months. The lesion healed after the complete course of medical therapy.

Case 2

A 28-year-old man was referred to our institute from a local hospital, where he was operated twice for ischiorectal abscess. In the first operation extensive debridement was done in the local area and split skin grafting of raw area was performed in the next surgery. He presented to our institute in December 1994, with high fever and vomiting for 1 week and pain in the gluteal region for 2 days. On examination, a 10 cm incised wound with foul-smelling black necrotic material was seen in the gluteal area. From biopsy of the same area, dichotomously branched septeate hyphae were seen on direct microscopy and A. flavus was grown on culture. After extensive debridement and oral itraconazole (100 mg twice daily) for 6 weeks, the lesion healed.

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Table I. Characteristics of the patients with primary cutaneous aspergillosis.

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age(y)/sex</th>
<th>Risk factor and underlying illness</th>
<th>Clinical presentation</th>
<th>Species of fungus isolated</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24/M</td>
<td>Renal transplant</td>
<td>Swelling on left middle finger</td>
<td><em>A. flavus</em></td>
<td>Debridement and itraconazole</td>
<td>Cured</td>
</tr>
<tr>
<td>2</td>
<td>28/M</td>
<td>Post-operative</td>
<td>Necrotizing fasciitis of right gluteal region in skin graft</td>
<td><em>A. flavus</em></td>
<td>Debridement and itraconazole</td>
<td>Cured</td>
</tr>
<tr>
<td>3</td>
<td>35/F</td>
<td>Nil</td>
<td>Necrotic ulcer on left cheek</td>
<td><em>A. flavus</em></td>
<td>Debridement and itraconazole</td>
<td>Cured</td>
</tr>
<tr>
<td>4</td>
<td>36/M</td>
<td>Electric burn (73%)</td>
<td>Eschar formation in burn wound</td>
<td><em>Aspergillus</em> spp.</td>
<td>Debridement</td>
<td>Died</td>
</tr>
<tr>
<td>5</td>
<td>22/F</td>
<td>Thermal burn (80%)</td>
<td>Eschar in burn wound</td>
<td><em>A. fumigatus</em></td>
<td>Debridement</td>
<td>Died</td>
</tr>
<tr>
<td>6</td>
<td>28/M</td>
<td>Thermal burn (97%)</td>
<td>Necrosis and eschar formation in burn wound</td>
<td><em>A. flavus</em></td>
<td>Debridement</td>
<td>Died</td>
</tr>
<tr>
<td>7</td>
<td>11/F</td>
<td>Thermal burn upper limb (25%)</td>
<td>Necrosis and eschar formation in burn wound</td>
<td><em>A. flavus</em></td>
<td>Debridement</td>
<td>Cured</td>
</tr>
<tr>
<td>8</td>
<td>26/F</td>
<td>Electric burn (30%)</td>
<td>Necrosis and eschar formation in burn wound</td>
<td><em>A. flavus</em></td>
<td>Debridement</td>
<td>Cured</td>
</tr>
<tr>
<td>9</td>
<td>22/F</td>
<td>Electric burn</td>
<td>Necrosis and eschar formation in burn wound</td>
<td><em>A. flavus</em></td>
<td>Debridement</td>
<td>Cured</td>
</tr>
</tbody>
</table>

Case 3

A 35-year-old female presented in January, 1994 with eruption on her left cheek. She had been well until 4 months earlier, when a small eruption developed. She manually ruptured the eruption. The lesion progressed to a necrotic ulcer with eschar formation surrounded by erythema. Her leucocyte count had been 10,500/mm³, with absolute neutrophil count of 7,200/mm³. Aspirated pus was examined from the necrotic area. On direct microscopy acute angled branched septate hyphae were seen and *A. flavus* was grown repeatedly on culture. Gram stain of the pus showed many neutrophils and the same type of dichotomously branched septate hyphae. No other organism was visualized on Gram stain or grown on culture of pus. No clinical or radiological evidence of aspergillosis was detected elsewhere in the patient. The patient was immunocompetent. Surgical debridement of the lesion was performed and oral itraconazole (100 mg twice daily) was instituted for 1 month. The lesion was partially healed. The patient did not turn up for further follow-up.

Cases 4–9

Six patients with burn wound infection due to *Aspergillus* species were diagnosed during the period from 1987 to 1996. The details of these patients are mentioned in Table I. All these patients had third degree burn wound injury. In addition, the mean absolute neutrophil count of these patients was 10,580 ± 336 and the diagnosis of fungal invasion of burn wound was made on 6.3 ± 2.6 post burn weeks. Three patients who had TBSA more than 30% developed acute renal failure terminally.

Biopsy samples were collected from eschar in burn wound of each patient. On histology, dichotomously branched septate hyphae were seen on direct microscopy and *Aspergilli* were grown on culture.

Discussion

Cutaneous aspergillosis may be primary or secondary. Secondary cutaneous aspergillosis occurs as a result of haematogenous dissemination or by extension to skin from contiguous anatomic structure and presents as eruptive maculo-papules; whereas the rare type, PCA, begins as an erythematous fluctuant nodule and pustules or a plaque which undergoes rapid ulceration with central black eschar. In our nine cases of PCA, the diagnosis was made on the basis of: typical skin lesion; presence of dichotomously branched septate hyphae on direct microscopy and growth of *Aspergillus* species on culture of biopsy or pus from lesions; absence of other organisms in a stain and culture of sample; absence of clinical, radiological and microbiological evidence of aspergillosis elsewhere.

In our case 2 and cases 4–9 the diagnosis was confirmed by demonstration of dichotomously branched septate hyphae in tissue on histology and growth of *Aspergilli* on culture. In cases 1 and 3 no biopsy sample was collected. Acute angled branched septate hyphae along with inflammatory cells was seen on direct microscopy of aspirated material of the lesions and *A. flavus* was
grown on culture. No bacteria was seen or grown from the same aspirated material and the lesions healed after debridement and itraconazole therapy. Therefore, the most likely diagnosis of both the cases (cases 1 and 3) is PCA. However, the cause of small eruption at the beginning in case 3 is not clearly understood. The patient might have had PCA, or A. flavus may have entered as secondary invader while the eruption was manually ruptured.

PCA is a rare disease and occurs mainly in immunocompromised patients. To date, only six cases of PCA have been reported in immunocompetent hosts. Two patients in this series had no underlying disease. In our second patient, the infection occurred in grafted skin. In an earlier report, aspergillosis occurred in grafted skin of a diabetic patient. Our patient had no underlying illness to predispose PCA other than two excisions of ischiorectal abscesses and split skin graft in perineum.

Although burn wounds are often colonized by mycelial fungus and yeast, true fungal invasion of the burn wound is rare. In an earlier study, we observed burn wound colonization either due to Candida or Aspergillus species in 52% patients with third degree burn injury. During the present study, six patients were diagnosed to have burn wound infection due to Aspergillus by demonstration of fungi on histology and growth on culture. Invasion of burn wound by fungi occurred after prolonged hospital stay in these patients, as it was detected only at mean 6.3 ± 2.6 post burn weeks. Infection of burn wound due to mycelial fungi is rare in comparison to yeasts. In a study over a 15-year period, the incidence of burn wound infection due to mycelial fungi was 4.8%, and Aspergillus species accounted for 2.4% infections.

Most cases of PCA have been reported in children, though adults predominate numerically in cases of aspergillosis at other sites. However, except for one female child of 11 years, all our cases of PCA were adults and the majority of them were females.

The majority of PCA cases were caused by A. flavus, although cases have been caused by A. fumigatus, A. niger, A. terreus and A. ustus. Among our nine patients, A. flavus was the responsible agent in seven cases, A. fumigatus in one patient. In another case, the species of Aspergillus could not be determined.

Cutaneous aspergillosis may respond better to treatment than other forms of aspergillosis because the abnormality is recognized early, the lesion is localized and the treatment is instituted quickly. The lesions in immunocompetent hosts are easily cured with debridement only or with the addition of antifungal therapy. Even in most of the compromised patients, neutropenia resolved soon after institution of antifungal therapy. To avoid higher toxicity of amphotericin B, itraconazole (100 mg twice daily) was prescribed for these localized lesions in addition to debridement in our first three cases. All these patients responded well, including the renal transplant recipient.

Therapy for burn wound aspergillosis is unsatisfactory and mortality varies from 30% to 78%. In a study of 172 patients with severe burns, Candida wound infection was detected in 20.7% patients. Those patients subsequently developed disseminated candidiasis and 90.6% patients died. But the experience regarding disseminated infection from burn wound aspergillosis is limited. Three of our six patients died who had total burn surface area (TBSA) of more than 70%. The patients succumbed before institution of antifungal therapy, as the diagnosis of fungal wound infection was made very late. It is not clear whether the death in these patients was due to disseminated aspergillosis or to unrelated causes. The three patients who had TBSA less than 30% responded to debridement of infected wound only. However, institution of amphotericin B rather than itraconazole may be required after local debridement in patients with TBSA more than 30% to prevent the development of invasive aspergillosis.

In conclusion, PCA, though rare, is being increasingly recognized in recent years and it correlates with the increased frequency of fungal infections in tertiary care hospitals.

References

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