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Invasive epiglottic aspergillosis: A case report and literature review

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ABSTRACT

Invasive aspergillosis is a life-threatening infection in immunocompromised hosts and occurs most frequently in the lungs. Invasive laryngeal aspergillosis is extremely rare. Due to the potential progression of invasive aspergillosis, antifungal therapy must be started immediately in cases involving clinical suspicion of the disease. A 65-year-old male with agranulocytosis complained of sore throat and dysphagia. His epiglottis was covered with caseating granulomatous lesions and the tissue was easily disrupted. A histopathological examination showed an aggressive invasion of *Aspergillus* species and cartilage destruction. Therefore, we made a diagnosis of primary invasive epiglottic aspergillosis. The invasive aspergillosis resolved with antifungal therapy and an increase in neutrophils. It is therefore necessary to include invasive laryngeal aspergillosis in the differential diagnosis when encountering immunocompromised patients presenting with laryngeal granulomatous lesions and laryngitis-like symptoms.

1. Introduction

The number of immunocompromised hosts is increasing with the aging of the population and recent progress in medical technology. Opportunistic infections are primarily observed in immunocompromised hosts, including aspergillosis, an infection caused by *Aspergillus* species. In particular, invasive aspergillosis is important in the clinical setting, as the rate of invasive aspergillosis infection is increasing and may be life-threatening in immunocompromised hosts [1]. Invasive aspergillosis currently constitutes the most common cause of mortality due to infectious pneumonia in patients undergoing allogenic hematopoietic stem cell transplantation [1]. In contrast, although non-invasive aspergillosis is also a cause of morbidity, such complications are seldom life threatening [1]. This report presents a case of invasive epiglottic aspergillosis in a patient with agranulocytosis and also reviews the previous literature on invasive aspergillosis in the larynx.

2. Case report

A 65-year-old male developed paralysis of the legs caused by a spinal arteriovenous malformation and was unable to stand up for 5 years prior to admission. He had a pressure ulcer in the right gluteal region lasting for 2 months that had been treated with antibiotics at a previous hospital; however, the pressure ulcer had not recovered. Accordingly, he was referred to the division of dermatology at our hospital.

On admission, the patient received both antibiotic therapy with meropenem and local therapy. Twenty-one days after admission, he developed a sudden fever with chills. The next day, his blood pressure decreased to 61/36 mmHg, with an absolute neutrophil count (ANC) of 0 cell/μl (Fig. 1). He was therefore diagnosed with agranulocytosis and septic shock caused by *Clostridium perfringens*. Due to the fact that an association with agranulocytosis could not be ruled out, meropenem was therefore discontinued. Agranulocytosis might be triggered by septic shock and thereafter it can transform itself into drug-induced agranulocytosis.

Three days after the onset of agranulocytosis (day 3), the patient reported a sore throat. The sore throat worsened daily, making it difficult for him to eat soft foods. On day 6, he was referred to the division of otolaryngology. A physical examination revealed creamy white plaques on the buccal mucosa and soft palate, and laryngoscopy revealed caseating granulomatous lesions over the epiglottis. *Candida* infection was suspected, and treatment with gargling with amphotericin B was started. A swab of the buccal mucosa showed mycelia consistent with *Candida albicans*. The affected region in the oral cavity disappeared on day 13, although there were no changes in the epiglottic regions. Therefore, the administration of itraconazole oral solution (200 mg once a day) was initiated on day 14. The ANC level recovered to 689 cells/μl on day 15 (Fig. 1) and to greater than 2000 cells/μl on day 19.

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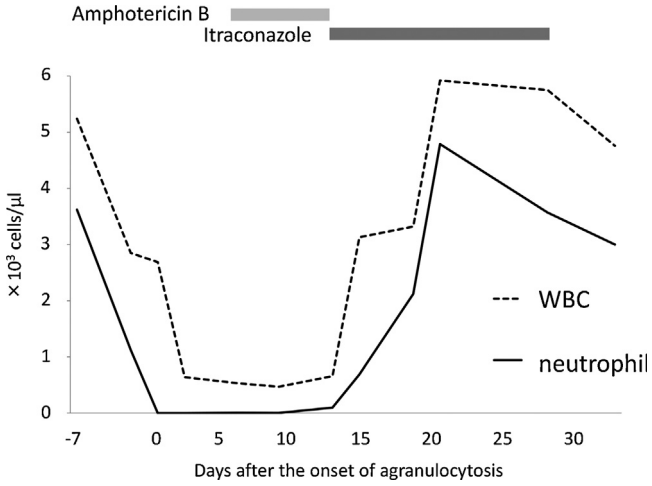

Fig. 1. White blood cell (WBC) count, absolute neutrophil count (ANC) and antifungal agents over the clinical course (days after the onset of agranulocytosis).

On day 22, the caseating lesions over the epiglottis were found to have slightly decreased, although they remained. We attempted suction of the caseating lesion under laryngoscopy; as a result, the epiglottis was easily disrupted (Fig. 2A). A histopathological examination of the disrupted epiglottis showed fungal invasion of the tissue and cartilage destruction (Fig. 3A). The fungal forms were brunching septate hyphae, considered to be *Aspergillus* species (Fig. 3B and C). The titers of β-D-glucan and *Aspergillus* antigens were measured frequently and after the onset of agranulocytosis; however, the findings were negative each time. Chest computed tomography (CT) showed no evidence of pulmonary aspergillosis. Therefore, we diagnosed the patient with primary invasive epiglottic aspergillosis. The results of both a sputum examination and tuberculosis-specific enzyme-linked immunospot (ELISpot) assays were negative.

Itraconazole therapy was applied for 2 weeks. Consequently, the patient's sore throat completely recovered, and the caseating granulomatous lesions disappeared (Fig. 2B). The invasive epiglottic aspergillosis was thus considered to have been successfully cured. Furthermore, his other diseases were also successfully treated and he was subsequently discharged from the hospital on day 63.

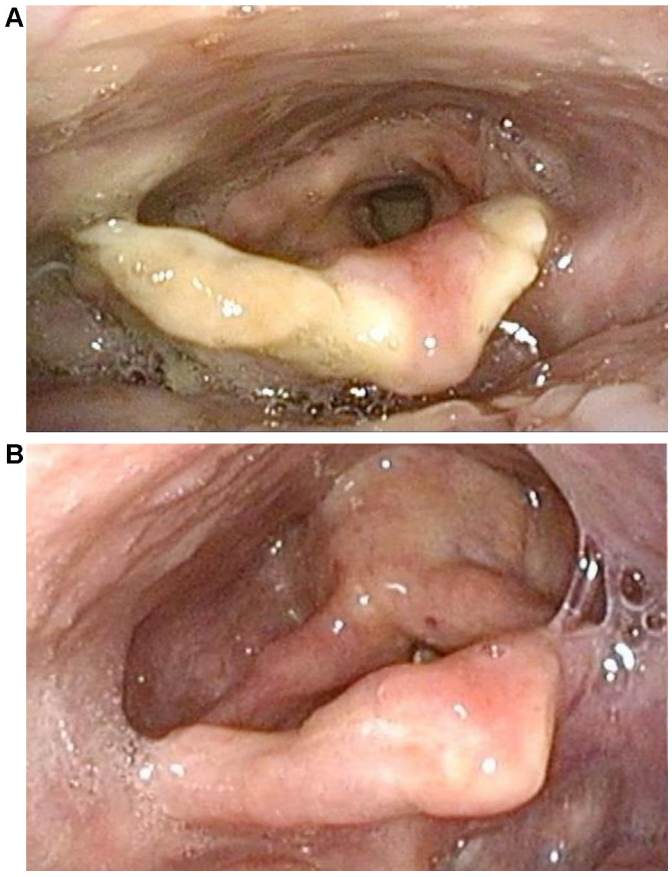

Fig. 2. (A) Before the biopsy, laryngoscopy revealed caseating lesions over the epiglottis and disrupted tissue on the right side. (B) Fiberoptic laryngoscopy performed prior to hospital discharge showed the disappearance of the caseating lesions and the defect involving the right side of the epiglottis.

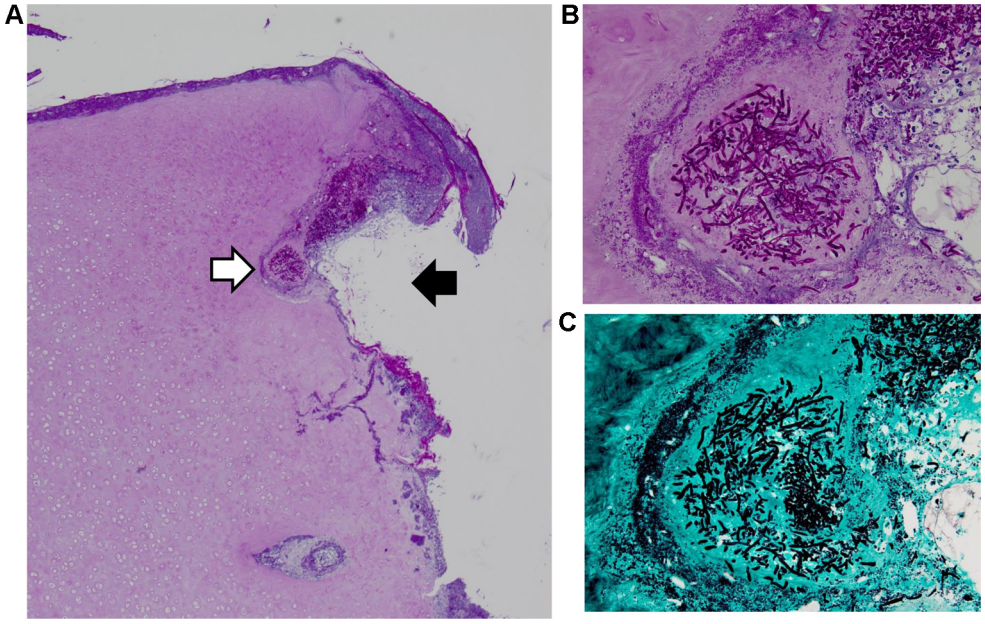

Fig. 3. Histopathological examinations of the disrupted epiglottis demonstrated aggressive invasive aspergillosis. (A) The epiglottic cartilage is destroyed and forms a dimple within the surface (black arrow). A fungus ball invades the cartilage at the bottom of the dimple (white arrow) (hematoxylin and eosin stain, low-power field). Hematoxylin and eosin stain (B) and Gomori's methenamine silver stain (C) show septate with dichotomously branched fungal hyphae (high-power field).

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