Clinical and Experimental Rheumatology 2000; 18: 523-524.

CASE REPORT

Primary aspergillosis of the larynx in a patient with Felty's syndrome

S. Morelli, A. Sgreccia, M.L. Bernardo, C. Della Rocca[1], A. Gallo[2], G. Valesini

Istituto di Clinica Medica I, Istituto di Anatomia Patologica[1], and Istituto di Otorinolaringoiatria[2], Università "La Sapienza", Rome, Italy.

Sergio Morelli, MD; Alessandro Sgreccia, MD; Maria Laura Bernardo, MD; Carlo Della Rocca, MD; Andrea Gallo, MD; Guido Valesini, MD.

Please address correspondence and reprint requests to: Sergio Morelli, MD, Istituto di Clinica Medica I, Università "La Sapienza", Policlinico Umberto I, Viale del Policlinico, 00161 Rome, Italy. E-mail: smorelli@uniroma1.it

Key words: Aspergillosis, Felty's syndrome, rheumatoid arthritis.

ABSTRACT

Herein we report the first case of primary aspergillosis of the larynx in a patient with Felty's syndrome. A 53-year-old man, a florist by profession, with a 12-year history of rheumatoid arthritis and on treatment with steroids, was admitted because of hoarseness, and intermittent fever of 2 weeks' duration. On admission, physical examination and laboratory data showed, among other findings, splenomegalia and neutropenia. At bone marrow examination, normal cellularity with mild dyserythropoiesis was observed. A fiberoptic laryngoscopy showed white plaques on both the true vocal cords. Both culture and microscopic examination of these lesions provided the diagnosis of invasive process by Aspergillus flavus. A computed tomography of the middle ears, paranasal sinuses, and chest was normal. Thus, primary aspergillosis of the larynx and Felty's syndrome was diagnosed, and the patient was successfully treated with granulocyte colony-stimulating factor and systemic antifungal agents.

Felty's syndrome, corticosteroid use, and occupational risk probably rendered our patient susceptible to Aspergillus infection.

Introduction

Aspergillosis is a common infection in immunocompromised patients (1). It can affect any organ but involves most commonly the respiratory tract, since Aspergillus spores are able to enter the respiratory tract with inhaled air (1). Head and neck manifestations of Aspergillosis include nasal, paranasal and otologic diseases. Aspergillosis of the larynx is uncommon and is usually secondary to pulmonary involvement. Primary aspergillosis of the larynx is very rare. In the English literature, it has been described in 12 otherwise healthy patients (2-6) and in 3 compromised patients (7-9). Felty's syndrome consists of chronic reumathoid arthritis, splenomegalia, neutropenia, and recurrent, life-threatening infections. Herein we report the first case of primary aspergillosis of the larynx in a patient with Felty's syndrome.

Case report

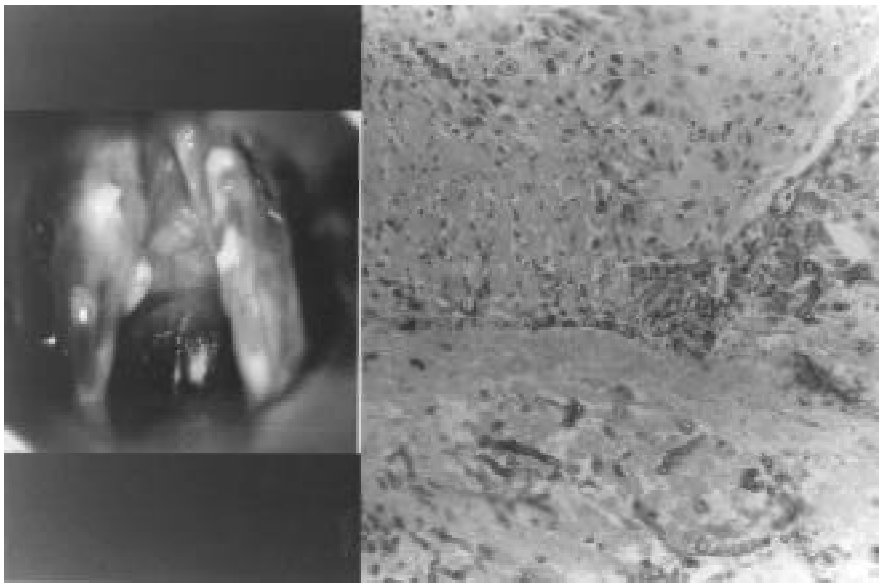
The patient was a 53-year-old man, a florist by profession, with a 12-year history of rheumatoid arthritis. After a brief period of therapy with nonsteroidal antiinflammatory drugs, his treatment was shifted to prednisone (50 mg daily). He was seen in June 1998 because of intermittent fever of 2 weeks' duration. He complained of hoarseness since 10 days. Two months before, he was affected by P*neumocystis carinii* pneumonia successfully treated with cotrimoxazole. On admission, physical examination revealed pallor, brown pigmentation over the tibiae, petechiae in the legs, hepatomegaly, and splenomegaly.

Laboratory data showed hemoglobin 8.3 g/dl, hematocrit 26%, leukocyte count of 700/mm^3 with 33% neutrophils and 62% lymphocytes, serum alkaline phosphatase 121 UI/L, aspartase aminotransferase 70 UI/L, hypoalbuminemia (2.58 g/dl), and hypergammaglobulinemia (1.59 g/dl). Thrombocytopenia (platelets 45,000/mm^3), reduced fibrinogen levels (120 mg/dl), and elevated values for the cross-linked fibrin derivatives (D-dimer > 8 mg/dl) were seen. Plasma electrolytes and urinalysis were normal.

The search for autoantibodies, antibodies to human immunodeficiency virus, and viral hepatitis was negative. A bone marrow aspirate and biopsy showed normal cellularity with mild dyserythropoiesis. A computed tomography of the chest and abdomen was normal except for a mild hepatomegaly, and moderate splenomegaly.

Antibiotic therapy with ceftazidime 2 g t.i.d. and teicoplanin 200 mg b.i.d. was started but the fever persisted. Because of progressive worsening of the hoarseness, he underwent a fiberoptic laryngoscopy, which disclosed the presence of white plaques involving the upper surface of both true vocal cords (Fig. 1a). The supraglottic mucosa appeared normal and the vocal cords were mobile. A large plaque-like whitish lesion was removed from the left vocal cord for histological examination. The biopsy specimen revealed an invasive fungal process with numerous hyphae consistent with Aspergillus (Fig. 1b).

A second direct laryngoscopy was performed to accomplish the removal of all the residual whitish plaques. Tissue cultures from the specimens grew *Aspergil-*



(a) **(b)**

Fig. 1. (a) On fiberoptic laryngoscopy, several plaque-like whitish lesions involving the upper surface of both true vocal cords are shown. **(b)** Specimen of the true vocal cord (hematoxylin and eosin). Below a partially necrotic epithelium, numerous fungal hyphae are seen.

lus flavus. Findings on computed tomography scans of the middle ears and paranasal sinuses were negative. Thus, primary aspergillos of the larynx in a patient with Felty's syndrome was diagnosed and treatment with filgrastim and intravenous amphotericin B (1 mg/kg daily) was started. Under this regimen the coagulation disorder disappeared and the patient became afebrile. Because of a rapid increase in serum creatinine, drug therapy was shifted to amphotericin B colloidal dispersion (Amphocil®). Ten days later, amphotericin B was discontinued and the patient was placed on therapy with oral itraconazole. Two weeks later, the patient was discharged in good conditions. Indirect laryngoscopy, performed respectively 2 and 4 months after discharge, revealed complete recovery of the true vocal cords.

Discussion

Multiple factors probably rendered our patient susceptible to Aspergillus infection. First, Felty's syndrome is associated with an increased frequency of severe infections. The cause of this susceptibility to infection is related either to the defective functioning or to a decreased number of polymorphonuclear leukocytes. In fact, Young and co-workers reported that 70% of their aspergillosis patients had absolute granulocyte counts below 500/mm^3 (1), and some studies have shown that abnormal phagocytosis may cause low resistance even when the absolute cell count is normal (1). Invasive aspergillosis has also been reported in patients with qualitative neutrophil defects and in apparently immunocompetent hosts (10). Secondly, our patient had been on corticosteroid therapy for many years and high-dose steroid therapy has been reported as the only predisposing factor in certain patients, in particular in solid organ recipients (11). On the other hand, our patient also had had pneumocystosis, a well-known disorder in immunocompromised hosts and in subjects who receive cortisteroids for prolonged periods. Finally, the occupational factor must be considered. Aspergillus lives in soil as a saprophyte, drawing nutrients from organic substances such as dead plants, animal scurf or excrement. Since this patient is a florist, he is probably under constant exposure to Aspergillus spores. In fact, 5 of 12 otherwise healthy patients reported in literature may be considered at high occupational risk, since they were either farmers or carpenters (2, 4, 6).

When laryngeal lesions are evaluated in patients with neutropenia, corticosteroid use, and occupational risk, the suspicion of aspergillosis must be raised.

References

1. YOUNG RC, BENNETT JE, VOGEL CL, CARBONE PP, DE VITA VT: Aspergillosis. The spectrum of disease in 98 patients. *Medicine* 1970; 49: 147-73.
2. RAO PB: Aspergillosis of larynx. *J Laryngol Otol* 1969; 83: 377-9.
3. FERLITO A: Primary aspergillosis of the larynx. *J Laryngol Otol* 1974; 88: 1257-63.
4. KHEIER SM, FLINT A, MOSS JA: Primary aspergillosis of the larynx simulating carcinoma. *Hum Pathol* 1983; 14: 184-6.
5. BENSON-MITCHELL R, TOLLEY N, CROFT CB, GALLIMORE A: Aspergillosis of the larynx. *J Laryngol Otol* 1994; 108: 883-5.
6. NONG D, NONG H, LI J, HUANG G, CHEN Z: Aspergillosis of the larynx: a report of 8 cases. *Chin Med J* 1997; 110: 734-6.
7. BOLIVAR R, GOMEZ LG, LUNA M, HOPFER R, BODEY GP: Aspergillus epiglottitis. *Cancer* 1983; 51: 367-70.
8. RICHARDSON BE, MORRISON VA, GAPANY M: Invasive aspergillosis of the larynx: case report and review of the literature. *Otolaryngol Head Neck Surg* 1996; 114: 471-3.
9. KINGDOM TT, LEE KC: Invasive aspergillosis of the larynx in AIDS. *Otolaryngol Head Neck Surg* 1996; 115: 135-7.
10. KLAPHOLZ A, SALOMON N, PERLAMAN DC, TALAVERA W: Aspergillosis in the acquired immunodeficiency syndrome. *Chest* 1991; 100: 1614-8.
11. GUSTAFSON TL, SCHAFFNER W, LAVELY GB, STRATTON CW, JOHNSON HK, HUTCHENSON RH JR: Invasive aspergillosis in renal transplant recipients: Correlation with corticosteroid therapy. *J Infect Dis* 1983; 148: 230-8.