Ege Journal of Medicine/ Ege Tıp Dergisi 48(1) : 45-48, 2009

Invasive pulmonary aspergillosis in an immunocompetent infant associated with short term steroid

İmmunkompetan bir infantta kısa süreli steroid tedavisi ile ilişkili invaziv pulmoner aspergilloz

Erdemir A Babayiğit A Olmez D Uzuner N

Karaman Ö Makay B Anal Ö

Dokuz Eylul University, School of Medicine, Department of Pediatrics, Inciralti-İZMİR-TURKEY

Summary

Invasive aspergillosis occurs very rarely in immunocompetent hosts. We report a case of invasive fungal infection in an infant who was treated with short term of inhaled and systemic steroids although there was no detectable immune deficiency. This case was presented in order to demonstrate the potential risk for opportunistic fungal infections in children treated with short term systemic and inhaled corticosteroids.

Key-Words: Invasive aspergillosis, child, short term steroid therapy.

Özet

İnvaziv aspergilloz immunkompetan kişilerde çok nadir görülür. Burada; saptanabilen immün yetmezlik olmamasına rağmen kısa süreli inhale ve sistemik steroid kullanma sonrası invaziv fungal enfeksiyon gelişen bir infantı sunduk. Bu olgu; kısa süreli sistemik ve inhale kortikosteroid tedavisi alan çocuklarda olası fırsatçı fungal enfeksiyon riskini vurgulamak amacı ile sunulmuştur.

Anahtar Kelimeler: *İnvaziv aspergilloz, çocuk, kısa süreli steroid tedavisi.*

Introduction

Invasive aspergillosis is a life-treatening fungal infection that predominantly effects severely immunocompromised patients particularly those with prolonged neutropenia and organ transplantation. Other predisposing factors such as prolonged steroid therapy, malignancy, Human immundeficiency virus (HIV) infection, chronic granulomatous disease and burns have been reported (1-3). Invasive aspergillosis occurs very rarely in immunocompetent patients (4). Here, we describe a previously healthy nine-month-old boy who acquired invasive pulmonary aspergillosis after receiving inhaled and systemic steroid therapy for fourteen and five days respectively. As far as we know, this is the first pediatric immunocompetent patient who developed invasive aspergillosis after short term systemic and inhaled steroid therapy.

Yazışma Adresi: Nevin UZUNER

Dokuz Eylul University, School of Medicine, Department of Pediatrics, Inciralti-İZMİR-TURKEY

Makalenin geliş tarihi: 15.11.2007 Kabul tarihi:26.08.2008

Case Report

A nine-month-old previously healthy boy, referred to our hospital because of fever, cough, dyspnea, wheezing which were persisted despite parenteral antibiotic treatments for five days. Physical examination revealed tachypnea, tachycardia, fever, wheezing, intercostal and subcostal retractions, bilateral crackling rales and rhonchi. His weight was 9 kg (50-75 percentile) and height was 74 cm (90-97 percentile). The oxygen saturation was 80%. Laboratory findings were as follows; hemoglobine: 8,2 g/dl, white blood cell count: 25000/mm^3, platelet: 947000/mm^3 and C reactive protein: 195 mg/L. Chest X-ray detected parenchimal infiltration at right paracardiac region and upper lobe of the right lung. Also a cavitary lesion was seen at the upper lobe of the right lung (Figure 1). High resolution computerized tomography of thorax (HRCT) showed bilateral infiltrations and mosaic pattern. Parenteral cefepime, amikacin and nebulized salbutamol and budesonide treatments were given. Intravenous prednisolone for five days and inhaled budesonide (2x0.5 mg/day) for 14 days were administered because of the persistance of respiratory distress. No microorganism was yielded in the blood culture. Sweat test results were 46 and 40 meq/L. Fecal

fat test was found negative. Acidoresistant bacteria in gastric fluid was negative for the consecutive three days. Tuberculin skin test and family screening for tuberculosis were also negative. Anti HIV test and anti Chlamydia and Mycoplasma antibodies were negative. Adenovirus serology was also negative. He had no fever during the hospitalization and acute phase reactants were decreased to normal limits although the respiratory distress and pulmonary oscultation findings were continued In the HRCT of thorax which is performed 14 days later showed three cavitary lesions (the largest was 11 mm) in the upper lobe of the right lung (Figure 2).

The walls of the cavities were thicker than the bacterial cavity walls resembling aspergillosis and also there was a nodular structure like a fungus ball and invasion along the pulmonary artery which were significant clues for invasive pulmonary aspergillosis. Aspergillus antigen analysed with galactomannan in order to clarify the cause of the cavitary lesion was negative in blood but aspergillus was yielded in the culture of sputum. Intravenous liposomal amphotericin B (3 mg/kg/day) was started because the cavities were developed even with continued antibiotherapy for 14 days. At the sixth week of amphotericin B therapy no cavitary lesions were detected in computerized tomography but there was mosaic pattern and bronchiectasic lesions at retrocardiac areas. Amphotericin B therapy was continued for two weeks after the cavitary lesions disappeared. The patient's immunoglobuline levels and lymphocyte panel which were analysed for evaluating the immun system were given in Table 1. N-formyl-methionyl-leucyl-phenylalanine (fMLP), phorbol myristat acetate (PMA), and Escherichia coli induced oxidative burst activity of the phagocytes were found normal by flow cytometric assay.

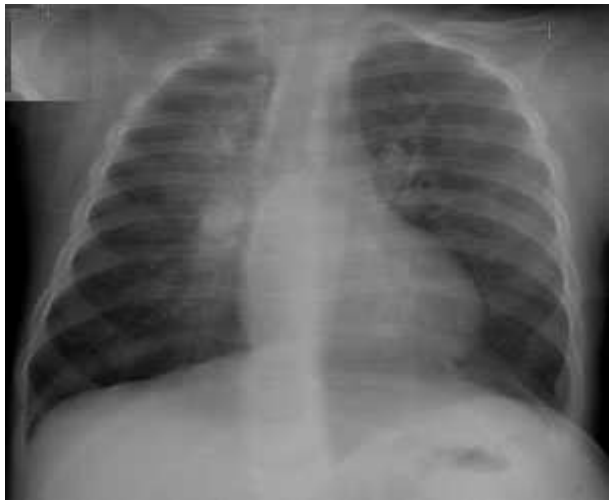

Figure 1. Chest X ray of the patient

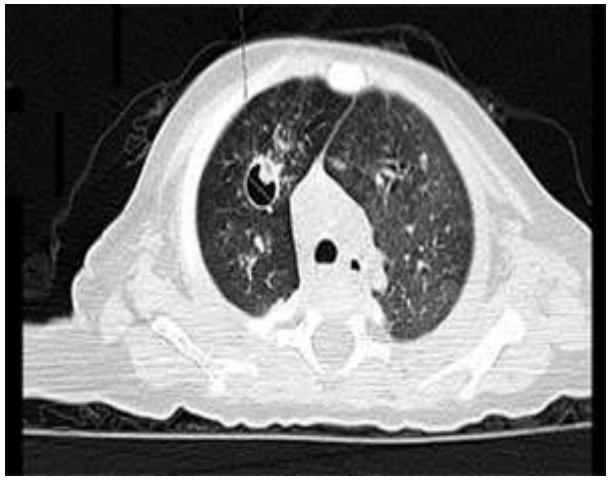

Figure 2. HRCT of the patient

Table 1. Immunologic parameters of the patient

	Patient	Normal
Absolute lymphocyte count (×10^9/L)	6.55	1.7-6.9
IgG (mg/dl)	1200	345 -1236
IgA (mg/dl)	38	14 -159
IgM (mg/dl)	133	43 -207
CD3 (%), absolute counts (×10^9/L)	(56.3%), 3.68	(43 -76%), 0.9-4.5
CD4 (%), absolute counts (×10^9/L)	(24.2%), 1.56	(23 -48%), 0.5-2.4
CD8 (%), absolute counts (×10^9/L)	(32.4%), 2.12	(14 -33%), 0.3-1.6
CD19 (%), absolute counts (×10^9/L)	(21.2%), 1.38	(14 -44%),0.2-2.1
CD4/CD8 ratio	0.75	0.9 - 2.9

Discussion

Aspergillus fumigatus is one of the most prevalent airborne fungal pathogens. Invasive pulmonary aspergillosis is a rapidly extending, life-threatening fungal infection which is generally reported in immuncompromised patients. In our case, the medical history revealed no severe infections and evaluation of the immun system was normal except CD4/CD8 ratio. It was thought that low CD4/CD8 ratio of the patient was probably related with the infection.

Invasive pulmonary aspergillosis was very rarely reported in immunocompetent patients as a cause of low dose and long term inhaled corticosteroid therapy (5,6). Systemic corticosteroids have profound effects on the distribution and function of neutrophils, monocytes, and lymphocytes that predispose to opportunistic fungal infections (7). Corticosteroids elicit peripheral blood monocytopenia. In patients with collagen vascular disease, the incidence of infectious complications increases when the adult equivalent of 20-40 mg of prednisone is administered daily for longer than 4–6 weeks (8,9). While exogenous immune suppression is the greatest risk factor for infection acquisition, polymorphic variation in key immune effector genes likely contributes to disease susceptibility. There is evidence that genetic variation within the plasminogen pathway influences the pathogenesis of this invasive fungal infection (10).

Also two immunocompetent patients with long-term, low-dose inhaled corticosteroid and short-term high-dose systemic corticosteroid therapy were reported with invasive pulmonary aspergillosis (11). In our case, inhaled steroid therapy was started two weeks and systemic steroid five days before the diagnosis of invasive pulmonary aspergillosis. The duration of the steroid therapy in our case was shorter than the cases reported in the literature with invasive aspergillosis.

The diagnosis of invasive pulmonary aspergillosis is based on clinical, radiological and mycological findings. Clinical signs have a low specificity for the disease (12). Although air-crescent and halo signs seen on chest X-ray and CT scans suggest invasive pulmonary aspergillosis, they are neither specific nor sensitive. Bronchoscopy to obtain specimens for cytology or culture may be performed in such patients, but the sensitivity for diagnosis is only about 25 % (13). Galactomannan and nucleic acid detection in serum or in bronchoalveolar lavage (BAL) fluid help to confirm the diagnosis (12). Galactomannan detection using the Platelia Aspergillus test may assist physicians in confirming the diagnosis with a sensitivity and a specificity of 81% and 89% respectively. Physicians still must be aware of the potential for false-positive and false-negative results, thus the test does not replace microbiological and clinical evaluation (13). We couldn't perform bronchoscopy due to persisting respiratory distress of the boy and galactomannan antigen was found negative. Because HRCT showed cavitary lesions and a nodular structure like a fungus ball and invasion along the pulmonary artery despite nonspesific antibiotic therapy and the culture of sputum yielded Aspergillus, we suggested that the diagnosis for this case is invasive pulmonary aspergillosis. Cystic fibrosis was excluded due to normal weight and height percentiles and sweat test results.

The optimal therapeutic management of invasive pulmonary aspergillosis is controversial, ranging from different antifungal drugs to additional lung resection. Amphotericin B has been used for many years as drug of choice for the treatment of invasive pulmonary aspergillosis. The optimal duration of therapy is unknown and dependent on the extent of invasive aspergillosis, the response to therapy, and the patient's underlying diseases or immune status (14). We used liposomal amphoterisin B (3mg/kg/day) for eight weeks for the treatment of invasive aspergillosis.

Our findings add an important evidence that in certain patients, short term inhaled and systemic corticosteroids can exert clinically significant systemic side effects. These patients may be at risk for secondary immunosuppression and opportunistic infection. Practitioners should be aware of these risks when they prescribe these medications especially in asthmatic children.

References

1. Palmer LB, Greenberg HE, Schiff MJ. Corticosteroid treatment as a risk factor for invasive aspergillosis in patients with lung disease. Thorax. 1991;46:15-20.
2. Denning DW. Invasive aspergillosis. Clin Infect Dis. 1998;26:781-803.
3. Cornet M, Fleury L, Maslo C, et al. Invasive Aspergillosis Surveillance Network of the Assistance Publique-Hopitaux de Paris. Epidemiology of invasive aspergillosis in France: a six-year multicentric survey in the Greater Paris area. J Hosp Infect. 2002;51:288-96,
4. Karam GH, Griffin FM Jr. Invasive pulmonary aspergillosis in nonimmunocompromised, nonneutropenic hosts. Rev Infect Dis. 1986;8:357-63.
5. Rello J, Esandi ME, Mariscal D, et al. Invasive pulmonary aspergillosis in patients with chronic obstructive pulmonary disease: report of eight cases and review. Clin Infect Dis 1998;26:1473-5.
6. Ortuno F, Cabello NJ, Salaveria I, et al. Probable invasive pulmonary aspergillosis and inhaled steroids treatment. Enferm Infecc Microbiol Clin 2002;20:131-2.

7. Roilides E, Uhlig K, Venzon D, et al. Prevention of corticosteroid-induced suppression of human polymorphonuclear leukocyte–induced damage of Aspergillus fumigatus hyphae by granulocyte colony-stimulating factor and gamma interferon. Infect Immun 1993;61:4870–7.

8. Staples PJ, Gerding DN, Decker JL, Gordon RS Jr. Incidence of infection in systemic lupus erythematosus. Arthritis Rheum 1974; 17:1–10.

9. Aucott JN. Glucocorticoids and infection. Endocrinol Metab Clin North Am 1994; 23:655–70

10. Zaas AK, Liao G, Chien JW, et al. Plasminogen alleles influence susceptibility to invasive aspergillosis. PLoS Genet. 2008;4:e1000101.

11. Cornet M, Mallat H, Somme D, et al. Fulminant invasive pulmonary aspergillosis in immunocompetent patients: a two-case report. Clin Microbiol Infect 2003;9:1224-1227.

12. Herbrecht R, Natarajan-Ame S, Letscher-Bru V, et al. Invasive pulmonary aspergillosis. Semin Respir Crit Care Med 2004;25:191-202.

13. Wheat L.J. Rapid diagnosis of invasive aspergillosis by antigen detection. Transplant Infectious Disease 2003;5:158-166.

14. Stevens DA, Kan VL, Judson MA. Practice guidelines for diseases caused by Aspergillus. Infectious Diseases Society of America. Clin Infect Dis. 2000;30:696-709.