Letters to the Editor

Invasive aspergillosis in juvenile systemic lupus erythematosus. A clinico-pathologic case

Sirs,

Infection is the most important cause of morbidity and mortality in children and adolescents with systemic lupus erythematosus (SLE) (1-3). Although most infections are bacterial (1, 2), the opportunistic organisms constitute almost 50% of the total, mainly *Candida albicans* and *Pneu - mocystis carinii*. Aspergillosis is seldomly described in juvenile SLE (4, 5). We report a patient with juvenile SLE complicated by invasive aspergillosis.

An 11-year-old girl who lived on a farm was diagnosed as having juvenile SLE based on the association of intermitent fever, malaise, general lymphadenopathy, hepatosplenomegaly, alopecia, malar rash, photosensitivity, bullous lesions resembling bullous pemphigoid, pericarditis, hemolytic anemia, leukopenia, hypocomplementemia, positive antinuclear and anti-DNA antibodies. Treatment with prednisone 2 mg/kg/d in April 2001 led to clinical improvement. Forty-five days later the patient presented pneumonia treated with antibiotics at home. Despite the correct treatment of pneumonia and SLE,the patient returned to the hospital with acute respiratory and heart failure (pericarditis and myocarditis). Laboratory tests indicated leukopenia, neutrophenia with < 500 cells/mm and proteinuria of 1.32 g/24h. Intravenous pulse therapy with methylprednisolone for 3 days and ceftriaxone were administered. However, the patient presented daily fever with negative blood and urine cultures, especially aspergillus culture.

As a consequence, empiric treatment was introduced with broad spectrum antibiotics (vancomycin and cefepime), which were subsequently changed to vancomycin, meropenem and fluconazole without any improvement. New pulse therapy with methylprednisolone was administered and intravenous gammaglobulin 2 g/kg without bringing disease activity and infection under control. In July, she gradually developed progressive renal, cardiac and respiratory failure, together with persistent pancytopenia, and including neutrophenia during the entire hospitalization. Initially, the chest radiographs showed a lobar infiltrate in the left lung field, and subsequently presented patchy infiltrates in both lung fields and pleural effusion in right side. Fluconazole was changed to amphotericin B with no improvement in respiratory failure and the radiograph pattern. Despite immediate treatment, 12 days after the introduction of amphotericin B the patient died. Postmortem examination showed bilateral invasive lung aspergillosis with fungus balls surrounded by an acute inflammatory reaction (Fig. 1), severe gastrointestinal bleeding, extradural, supra-renal hemorrhage and focal proliferative glomerulonephritis (World Health Organization Class III).

Invasive aspergillosis (IA) can involve every organ and system, but the respiratory tract is almost always affected (5). Most patients present dyspnea, cough and sometimes hemoptysis, and chest radiograph generally shows patchy lung infiltrates. This clinical picture in SLE patients is nonspecific, suggesting either lupus activity or infection (4, 6, 7). More than 90% of patients with invasive pulmonary aspergillosis had previously received corticosteroids, immunosuppressive therapy, severe granulocytopenia or broad spectrum antibiotics (4-9). Aspergillosis presents a diagnostic and therapeutic challenge, and as a result most patients are diagnosed postmortem (5). Mortality of IA depends on the degree and duration of granulocytopenia, the organs affected and the delay in therapy. Reported overall mortality is over 80% (6, 9). Amphotericin B, alone or in combination with 5-fluorocytosine or rifampin, is the major therapeutic regimen for IA, but the optimal duration of therapy is still unknown (6, 10). Infusions of granulocytes or granulocyte-macrophage colony-stimulating factor may be beneficial in certain patients, although our patient has received granulocyte colony-stimulating without any improvement (4). One reason for delayed diagnosis and treatment of aspergillosis is the multisystem disease caused by the organism, which may mimic SLE. We conclude that the diagnosis of IA is often delayed or missed, in part because of limited awareness of this condition. Early diagnosis and treatment may help improve the prognosis of this severe infection.

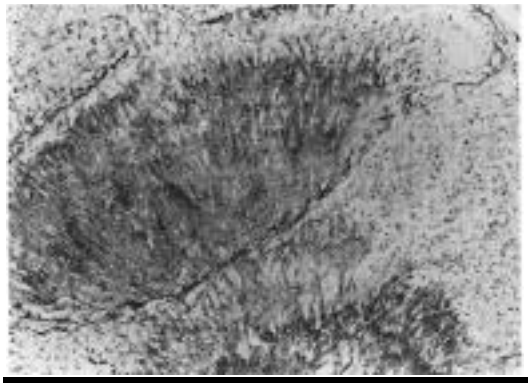

Fig. 1. Grocott stain showing septate hyphae branching at acute angles compatible with *Aspergillus sp* in lungs (100x).

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