ever, Fernandez et al. [13] recently described a child with recurrent bacteremia despite appropriate repeated antibiotic therapy who was cured only after the removal of the infected catheter. In spite of the typically mild nature of this infection, 3 patients have died, 2 of whom were treated with inappropriate antibiotic regimens [1].

Although infection with *M. mesophilicum* remains rare, it is being reported with increasing frequency. Furthermore, even though most previously reported cases have been nosocomial, the increasing number of chronically immunocompromised patients treated as outpatients is likely to bring patients into contact with the environmental sites where *M. mesophilicum* occurs.

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References


Fulminant Tracheobronchial and Pulmonary Aspergillosis Complicating Imported Plasmodium falciparum Malaria in an Apparently Immunocompetent Woman

We describe an unusual case of fulminant tracheobronchial and pulmonary aspergillosis presenting as acute respiratory distress syndrome. The patient, who was apparently immunocompetent, was admitted with severe *Plasmodium falciparum* malaria but died from aspergillosis.

Imported malaria is an increasing problem in many developed countries. In 1998, 996 cases of imported malaria were recorded in Germany [1]. The case fatality rate associated with imported *Plasmodium falciparum* malaria varies from 0.6% to 3.8% and may be up to 28.5% for severe malaria, even when

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Clinical Infectious Diseases 2000; 30:938-40
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1058-4838/2000/3006-0019$03.00
treated in intensive care unit conditions [2]. Poor outcome is predicted by the occurrence of complications during Plasmodium falciparum malaria, such as coma, hypoglycemia, and respiratory distress. Adult respiratory distress syndrome (ARDS) has always had a fatal outcome [2]. We describe an apparently otherwise healthy woman who died of fulminant tracheobronchial and pulmonary aspergillosis under the aspect of ARDS following P. falciparum malaria.

A 54-year-old woman was admitted to a district hospital because of fever of unknown origin. The patient reported the onset of fever 4 days after returning from a 2-week trip to Kenya. Malaria prophylaxis was not taken. After 2 days of therapy with roxithromycin prescribed by a general practitioner, the patient was admitted to the hospital. On presentation she had a fever (temperature, 40°C), and examination revealed mild hepatosplenomegaly and icterus; her condition was otherwise stable and there were no pulmonary symptoms. No underlying diseases (such as liver cirrhosis or malignancy) were reported, other than hysterectomy for uterine myomatosis several years before. Laboratory evaluation revealed parasitemia with P. falciparum (15% infected erythrocytes and a hematocrit of 46%), a WBC count of 5400 cells/µL, a platelet count of 16,000 cells/µL, a total bilirubin of 7.8 mg/dL (direct bilirubin, 7.1 mg/dL), a prothrombin time of 60%, an aspartate aminotransferase (AST) level of 262 U/L, a lactate dehydrogenase (LDH) level of 1904 U/L, and a creatinine level of 2.9 mg/dL.

Therapy with quinine dihydrochloride plus doxycycline was initiated. Within 24 h, the patient’s condition deteriorated markedly because of altered mental status with severe confusion and delirium, suggestive of cerebral malaria. Midazolam was started for sedation. She became oliguric, her creatinine level increased to 4.7 mg/dL, and she underwent dialysis.

The patient was transferred to our intensive care unit. She presented in a comatose state and was intubated for artificial ventilation. Clindamycin was added as an antimalarial agent. Findings of a chest radiograph were normal, but a CT scan of the brain revealed cerebral edema, which was treated surgically by intraventricular drainage. Exchange transfusion was performed, and continuous hemofiltration was started 12 h later. Parasitemia was undetectable after 48 h, but the patient developed lactic acidosis with progressive deterioration of circulatory and pulmonary function as well as liver failure (bilirubin level, 27.5 mg/dL, AST level, 1550 mg/dL, and LDH level, 7270 mg/dL). Chest radiograph on day 5 showed pulmonary infiltrates (figure 1), and bronchoscopy revealed marked hemorrhage and necrosis in the trachea, and the bronchial tree and trachea were covered with a layer of white mucus. A culture of a bronchoalveolar lavage specimen yielded Aspergillus fumigatus (10^6 cfu/mL) and Enterobacter species. Aspergillus antigen testing from serum was strongly positive (Platelia ELISA; Sanofi Pasteur, Freiburg, Germany; titer for detection of galactomannan antigen was 5.5 (a titer of 1.5 is considered positive). Amphotericin B was started, but on the 6th day after admission to our institution the patient died of ARDS and multorgan failure with shock and lactic acidosis. Autopsy revealed invasive pulmonary aspergillosis, and Aspergillus tracheobronchitis with macroscopically confluent growth of mold in the trachea and bronchi were found.

Aspergillus tracheobronchitis has been described predominantly in patients with AIDS and in lung transplant recipients [3, 4]. Reports in immunocompetent patients are rare, and the pathogenesis of this disease in these patients who are not neutropenic or receiving corticosteroids is not well understood [5±7]. To date, the association of Aspergillus tracheobronchitis with tropical diseases, such as malaria, has not been described. In our patient, the clinical presentation suggested the development of ARDS caused by severe malaria rather than pulmonary aspergillosis. The patient had a fulminant course of disease and died within 3 days of the onset of signs on the chest radiograph. It is clear that the fatal outcome is strongly influenced by the presentation of cerebral malaria. The diagnosis could not be made on clinical grounds, but bronchoscopy showed the typical picture of pseudomembranous tracheobronchitis and a tracheobronchial tree covered with a white layer of mucus, as described elsewhere [8].

From this single case, it cannot be concluded that ARDS with severe malaria is caused by tracheobronchial or pulmonary aspergillosis. However, the growing number of reports about Aspergillus tracheobronchitis in apparently immunocompetent patients should prompt further investigation to understand the pathogenesis of the disease.

Figure 1. Chest radiograph on day 5 after admission of a patient with diffuse bilateral pulmonary infiltrates that resemble those associated with acute respiratory distress syndrome.
Fatal Invasive Aspergillosis Complicating Severe Plasmodium falciparum Malaria

We report the first 2 cases of fatal invasive aspergillosis complicating severe malaria. In 2 nonimmune European adults without underlying disease, death was directly ascribable to invasive aspergillosis. We believe that transient malaria-induced immunosuppression allowed massive growth and overwhelming dissemination of preexisting Aspergillus colonization.

We report the first 2 cases of invasive aspergillosis complicating severe Plasmodium falciparum malaria and discuss the pathogenic mechanisms underlying this association. We searched MEDLINE for studies published from 1968 through 1999 that mention “malaria,” “falciparum” or “plasmodium” and “aspergillosis” or “A. fumigatus.”

From 1987 through 1998, 205 patients were admitted to our intensive care unit (ICU) for imported falciparum malaria. The overall mortality rate was 7.3% (15 deaths). In 2 nonimmune European patients, death was directly ascribable to invasive aspergillosis.

Patient 1, a 40-year-old man, was hospitalized in China in 1987 because of fever and jaundice and received a 3-day course of iv corticosteroids for suspected hepatitis. Three days later, because of impaired consciousness (Glasgow coma score [GCS], 12), the decision was made to repatriate the patient. When he arrived in France 2 days later, he was referred to our ICU because of severe malaria with 19% parasitemia, rousable coma (GCS, 11), acute renal failure, and disseminated intravascular coagulation. A chest radiograph showed an alveolar infiltrate in the right upper lobe. The patient’s condition improved slowly with quinine infusion, antibiotics, mechanical ventilation, and hemodialysis. The parasitemia abated within 72 h, and neurologic disorders and pneumonia resolved. On day 12, he rapidly developed unrousable coma (GCS, 5), flaccid tetraplegia, and shock. A cerebral CT scan showed hemorrhagic infarction of the cerebellum and brain. The patient died 4 days later in a deep coma. Autopsy revealed invasive aspergillosis with ulcerated mitral endocarditis and fungal abscesses in the myocardium and lungs (figure 1). The biopsy of a cutaneous lesion yielded Aspergillus fumigatus.

In 1997, patient 2, a 32-year-old man, returned from a trip to Gabon. He had been given oral cefuroxime by his physician for suspected acute sinusitis. Four days later he was hospitalized through the emergency room of our hospital because of fever and jaundice. P. falciparum parasitemia was 48%. A quinine infusion was started and the patient was referred to our ICU. Over the following 24 h his condition worsened rapidly, and he developed unrousable coma (GCS, 5), partial seizures, shock, acidosis, acute renal failure, and acute respiratory distress syndrome. Upon intubation of the patient, macroscopic evidence of esophageal mycosis was noted. Specific tests excluded HIV infection or primary infection. Despite supportive care and parasite clearance within 72 h, his neurologic status failed to improve. On day 3, a bronchoalveolar lavage yielded Aspergillus nidulans and Candida albicans. Intravenous amphotericin B (1 mg/kg/d) was started. On day 5, a tracheal aspirate yielded Pseudomonas aeruginosa, Staphylococcus aureus, and A. fumigatus. Aztreonam and ciprofloxacin therapy was instituted and amphotericin was discontinued, as fungal presence was thought to be a colonization. On day 11, cardiac arrest occurred and resuscitation efforts failed. Autopsy disclosed disseminated aspergillosis with cerebral and pulmonary fungal abscesses.

Fungal infection is thought to be uncommon during severe malaria [1, 2]. In our cases, coincidental occurrence of aspergillosis and malaria is very unlikely because invasive aspergillosis is extremely rare in healthy patients [3]. The absence of a coincident aspergillosis outbreak in our ICU and the short time from admission to aspergillosis onset militate against ICU-