

meet criteria for active CLL.<sup>1</sup> Treatment has, of course, varied over the years, from chlorambucil to fludarabine-based combination regimens. Interestingly, in our series, only 3 of the 18 patients with Binet stage A disease and low ZAP-70 expression required treatment, whereas 20 of the 26 patients with high ZAP-70 expression were treated. The main clinical variables, including age, did not differ between the two groups. Thus, with ZAP-70 analysis we were able to identify a group of patients with a bad prognosis, irrespective of the clinical stage. Finally, the relation among ZAP-70 expression, clinical variables, and survival should be assessed in larger series of patients.

The source of the monoclonal anti-ZAP-70 antibody used for flow cytometry was Upstate Biotechnology.

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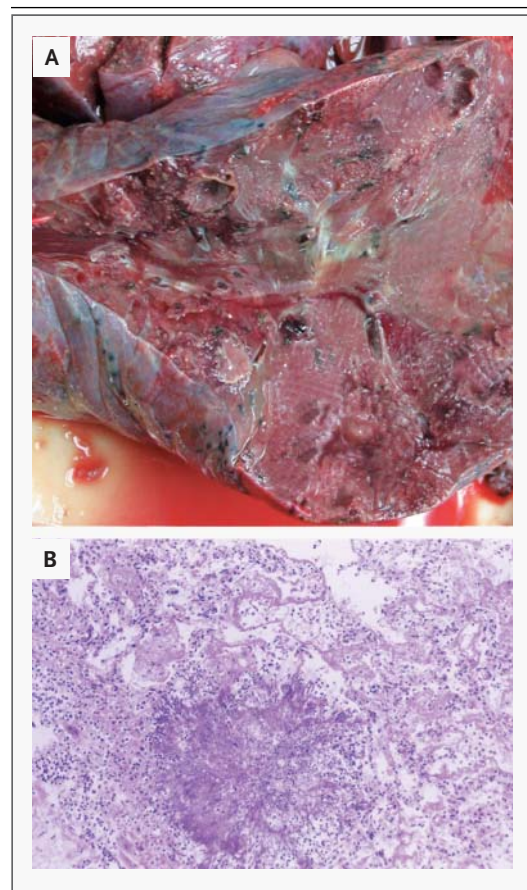
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## Fatal Aspergillosis in a Patient with SARS Who Was Treated with Corticosteroids

**TO THE EDITOR:** We report the case of a patient with severe acute respiratory syndrome (SARS) who died of aspergillosis after prolonged treatment with corticosteroids. The patient was a 39-year-old male physician based at the intensive-care unit of a small hospital in Guangzhou, China; he had no concurrent medical illness. Many patients with SARS were admitted to the hospital where he worked during the eight weeks before April 4, 2003, when he presented with a sore throat and a low-grade fever (37.3°C). Five days later, he had a high fever (38.5°C) and a low leukocyte count ( $3.4 \times 10^9$  per liter; 63.6 percent neutrophils and 26.2 percent lymphocytes), and he was admitted to the hospital with suspected SARS.

The patient was treated with twice-daily methylprednisolone (80 mg in the morning and 40 mg in the evening) for two days; the dose was decreased to 20 mg twice daily as the fever subsided, on April 12. The fever recurred on April 14, and chest radiography showed an infiltrate in the left lower lobe; the leukocyte count was  $13.5 \times 10^9$  per liter (94.0 percent neutrophils and 6.0 percent lymphocytes). Methylprednisolone was given again (20 mg in the morning and 80 mg in the evening), and the patient

was transferred to a larger hospital on April 15. Intravenous methylprednisolone therapy (80 mg twice daily) was then administered. The patient's



**Figure 1. Specimens of the Lung.**

Panel A shows the cut surface of a lung. The pathological specimen in Panel B shows extensive hyaline membranes, desquamated epithelial cells, and exuded monocytes in alveoli (hematoxylin and eosin,  $\times 100$ ). *Aspergillus* mycelia were observed on microscopical examination of the abscess and were isolated by culture as well.

clinical condition improved; he had no fever and could walk without dyspnea. The infiltrate in the left lung diminished in density, and the dose of methylprednisolone was reduced to 40 mg twice daily on April 19.

On April 29, the patient was again dyspneic, and radiographs showed a left basilar infiltrate. Bone marrow aspiration revealed suppression of all three cell lineages. On May 4, the patient was transferred to a university teaching hospital. Methylprednisolone (240 mg twice daily) was given, but the next day the oxygen saturation fell to 60 percent, and endotracheal intubation was performed to allow mechanical ventilation. The patient showed signs that were consistent with the presence of tentorial herniation; his pupils were fixed and dilated. Computed tomographic examination of the cranium showed diffuse cerebral edema with localized hemorrhage. Enzyme-linked immunosorbent assay and indirect immunofluorescence established the presence of specific antibodies against a SARS-associated virus in the serum. The fungal culture of sputum obtained on April 14 was negative; the bacterial cultures of sputum obtained on May 2 and May 4 were negative as well. Despite massive supportive care, the patient died on May 7.

Autopsy showed SARS-associated pathologic changes,<sup>1,2</sup> including consolidation, hemorrhage, and edema of the lungs; proliferation and desquamation of alveolar epithelial cells; exudation of monocytes, lymphocytes, and plasma cells in alveoli; and formation of hyaline membranes. In addition, there were multiple lung abscesses containing aspergillus (Fig. 1). There was also cerebral edema,

diffuse cerebral hemorrhage, aspergillus meningitis, and multiple brain abscesses containing aspergillus. Multiple abscesses containing aspergillus were also found in the heart, liver, kidney, spleen, stomach, pancreas, and adrenal glands.

In this patient, it is likely that SARS infection induced mild immunosuppression<sup>3</sup> and that immune function was further suppressed by high-dose corticosteroid treatment. At this time, it has not been established whether corticosteroid treatment has an effect on SARS-associated mortality,<sup>4</sup> although it may decrease clinical morbidity.<sup>5</sup> We speculate that use of corticosteroids over the course of many weeks led to the serious secondary aspergillus infection that contributed to the death of this patient. We urge caution and restraint in the use of corticosteroids in the treatment of SARS.

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## Profile of Specific Antibodies to the SARS-Associated Coronavirus

**TO THE EDITOR:** A novel coronavirus called the severe acute respiratory syndrome (SARS)-associated coronavirus (CoV) has been identified as the causal agent of SARS.<sup>1-3</sup> To understand the humoral immunity to this virus, we studied the profile of IgM and IgG antibody responses to SARS-CoV. IgM and IgG antibodies were analyzed by an indirect enzyme-linked immunosorbent assay in 20 patients with SARS from week 1 of their illness to week 12 and in 103 healthy contacts.

All 20 patients tested negative for IgM and IgG at week 1 after the onset of symptoms. Of these pa-

tients, 16 tested positive for IgM and 17 tested positive for IgG at week 2 (Fig. 1). All 20 patients were IgG-positive after week 3 and continued to have high levels of IgG up to three months after the onset of symptoms. The IgG titers were low at the beginning of week 2 (mean, 1:40, with the cutoff for a positive result being 1:10), increased to an average of 1:256 at week 3, and peaked at 1:640 at week 12. The IgM titers peaked during the acute or early convalescent phase and then declined with IgM disappearing by the end of week 12. All 103 healthy contacts tested negative for IgM and IgG.