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,[1,2] 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[3] 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,[4] although it may decrease clinical morbidity.[5] 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.[1-3] 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 patients, 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.

Our results suggest that 100 percent of patients had antibody responses to SARS-CoV during the convalescent phase. The SARS-specific IgG antibody persisted for a long time, but the SARS-specific IgM remained measurable for a much shorter period, suggesting that IgG antibody to SARS-CoV may represent the primary humoral immune response protecting patients against SARS. The profile of antibodies against SARS-CoV was consistent with common findings with regard to acute viral infectious diseases such as hepatitis A.[4] The profile of anti-SARS antibodies may be helpful in the diagnosis and in epidemiologic surveys. The presence of high titers of IgG antibody to SARS-CoV in the patients at the convalescent stage also suggests that a live attenuated or inactivated vaccine for active immunization and a concentrated human SARS-specific IgG antibody for passive immunization could be developed for the treatment of SARS.

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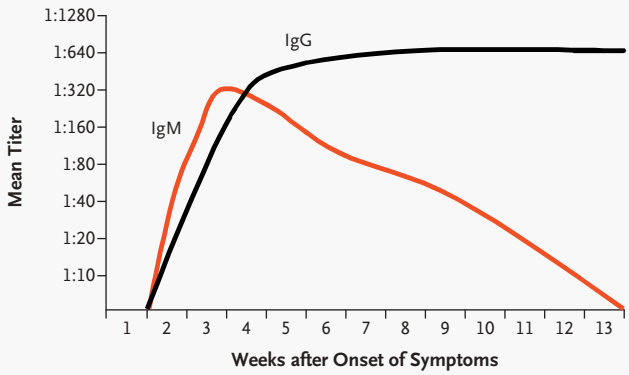

Figure 1. Changing Titers of IgM and IgG Antibodies to the SARS-Associated Coronavirus from the Onset of Illness through the Convalescent Phase.

IgM and IgG were measured at weeks 1, 2, 3, 4, 8, and 12; the mean IgG titer was 1:40 at week 2, 1:256 at week 3, 1:368 at week 4, 1:640 at week 8, and 1:640 at week 12. The mean IgM titer was 1:120 at week 2, 1:320 at week 3, 1:160 at week 4, and 1:40 at week 8. The cutoff value for a positive result was 1:10, and patients with negative results were considered to have a titer of 0 for the calculation of the mean titer.

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