1 cm below the costal margin, and the liver was felt 2 cm below the costal margin. The right knee joint was mildly swollen. She had multiple dental caries. No other abnormalities were detected.

Laboratory studies revealed a WBC count of 14.9 × 10⁹/L (77% polymorphonuclear cells, 14% lymphocytes, and 7% monocytes), a hemoglobin level of 116 g/L, and an erythrocyte sedimentation rate of 85 mm/h. An echocardiogram revealed severe mitral regurgitation and a vegetation measuring 8 × 10 mm on the posterior leaflet of the mitral valve; the left ventricular function was normal. A chest radiograph showed mild cardiomegaly and congested lung fields. Empirical therapy with intravenous vancomycin and ceftriaxone was started.

Cultures of three separate blood specimens obtained at the time of admission were positive for β-lactamase-producing H. influenzae; the MIC of ceftriaxone for the organism was <0.16 μg/mL. The isolate was identified by means of slide agglutination to serotype f, biotype III. Levels of serum immunoglobulins, immunoglobulin subclasses, and complement were normal. Therapy with vancomycin was discontinued, but therapy with intravenous ceftriaxone (50 mg/kg every 12 hours) was continued. The trough serum bactericidal concentration of ceftriaxone against the isolate was 1:1256.

By the 15th day of hospitalization, the patient was still febrile and her erythrocyte sedimentation rate had increased to 112 mm/h. Several subsequent blood cultures were sterile. An echocardiogram showed an increase in the size of the vegetation and perforation of the posterior cusp of the mitral valve. Because of these findings, the patient underwent surgery. During the procedure, a large vegetation measuring 1.5 × 2.5 cm was found around the perforation in the posterior leaflet of the mitral valve. The vegetation and the perforation were resected, and the posterior leaflet of the mitral valve was repaired.

Two days after surgery was performed, the patient’s fever subsided, and she remained well. She was discharged on the 29th day of hospitalization and completed a 5-week course of intravenous ceftriaxone therapy as an outpatient. At a follow-up visit 6 months later, the patient was asymptomatic. A repeated echocardiogram showed a thickened mitral valve leaflet, mild mitral regurgitation, and normal left ventricular function.

Our patient manifested many of the clinical features of Hib endocarditis: a prolonged febrile course, a large vegetation, progression of the valvular damage despite appropriate antibiotic therapy and microbiological cure, and the need for resection of the vegetation and surgical correction of the valvular insufficiency [4, 5]. Early intervention, before extensive valvular damage had occurred in our patient, allowed for successful repair of the mitral valve and precluded the need for placement of a prosthetic valve. The duration of antibiotic therapy was based on the clinical picture and on reports of successful treatment of Hib endocarditis [4, 5].

The usual source of infection with H. influenzae serotype f is the nasopharynx. In the era before vaccination against Hib was available, the prevalence of nasopharyngeal colonization with H. influenzae serotype f among children was reported to be 0.9% [6]. On the basis of studies that revealed that type b strains release a bactericidal substance that is active against non-b strains, it has been speculated that the rate of nasopharyngeal colonization and subsequent infection with these strains (including type f) may increase as the rate of colonization with type b strains decreases as a result of the increased use of Hib conjugate vaccines [1, 3]. Our case illustrates that the spectrum of invasive diseases due to H. influenzae serotype f is enlarging, and it also demonstrates that this organism can cause endocarditis.

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References

Progressive Multifocal Leukoencephalopathy After Autologous Bone Marrow Transplantation in a Patient with Chronic Myelogenous Leukemia

Before the AIDS epidemic, progressive multifocal leukoencephalopathy (PML) was most frequently associated with chronic lymphocytic leukemia and Hodgkin’s disease as well as systemic lupus erythematosus, sarcoidosis, and organ transplantation [1]. A high incidence of polyomavirus infection of lymphoid-cell preparations has been reported after allogeneic bone marrow transplantation for chronic myelogenous leukemia (CML) and acute monocytic leukemia [2], but this is, to our knowledge, the first case reported after autologous bone marrow transplantation for treatment of CML.

A 31-year-old female developed night sweats and fatigue in December 1985. A complete blood count showed an elevated WBC count (87,000/μL) and an elevated platelet count (1,200,000/μL). Cytogenetic studies showed 100% Philadelphia chromosome. Examination of a bone marrow biopsy specimen showed 1% blastsocytes, and other histologic findings were compatible with those of CML. She received weekly alternating doses of rh-IFN-α (5 × 10⁶

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Stringent in situ hybridization for detection of JC virus was performed with use of avidin/HRP-AEC (stain, hematoxylin-eosin; original magnification, ×500).

Figure 1. Stringent in situ hybridization of brain tissue from a patient who developed progressive multifocal leukoencephalopathy after bone marrow transplantation shows the reaction product (arrows) within nuclei of cells infected with JC virus. DNA in situ hybridization was performed with use of avidin/HRP-AEC (stain, hematoxylin-eosin; original magnification, ×500).

Stringent in situ hybridization for detection of JC virus was performed with use of a commercially available biotinylated DNA probe (Enzo Diagnostics). Several of the enlarged oligodendroglial nuclei showed positive nuclear reactivity, consistent with the presence of JC virus (figure 1). Cytarabine (100 mg/m2) was given iv for 5 days in combination with rh-IFN-α. The patient’s condition remained stable, without definite progression of the leukemia, and she was discharged. The results of follow-up are pending.

JC virus can be identified in lesions by means of immunofluorescent techniques, immunohistochemical techniques, and in situ DNA hybridization with a JC virus biotinylated probe, which confirms the presence of JC virus in oligodendrocytes and astrocytes in brain tissue from patients suspected of having PML [3–5]. We used the latter technique to confirm our patient’s diagnosis. CT and MRI can be useful in localizing the demyelinating lesions; the lack of contrast enhancement on a CT scan is usually helpful in distinguishing these lesions from those of toxoplasmosis [6].

The pathogenesis of PML has remained obscure because the nature of the primary infection, the site of the virus during latency, and the route by which JC virus enters the brain have not yet been determined. Serological studies have indicated that levels of antibody to the virus are maintained throughout life, suggesting that JC virus may cause persistent infection [7]. Our patient was immunocompromised because she underwent autologous transplantation after receiving high-dose conditioning chemotherapy, followed by total body irradiation. She was treated with rh-IFN-α and cytarabine. Several patients have been treated with vidarabine and cytarabine, with varied responses, but there are no controlled data establishing the effectiveness of any therapy [8].

In conclusion, this case indicates that PML may be caused by the JC virus in a patient who is afebrile but has symptoms and signs of CNS involvement while receiving immunosuppressive therapy after autologous transplantation.

References


