BRIEF REPORTS

Hepatitis B and Pupil-Sparing Oculomotor Nerve Paresis

Neurological involvement in hepatitis is uncommon but by no means exceptional. A wide spectrum of neurological problems almost exclusively associated with acute hepatitis B virus infection have been described. To our knowledge, we report the first case of acute hepatitis B complicated by external ophthalmoplegia due to isolated third cranial nerve palsy.

A 36-year-old man presented with a 3-week history of generalized body aches, malaise, and tiring easily. He had associated yellow appearance of the eyes and high-colored urine. Within a few days of the onset of jaundice, he had drooping of his right eyelid, double vision, and retro-orbital discomfort. He denied any sensory loss, paresthesias, or weakness of any part of the body. There was no history of fever, headache, or trauma. There was no medical history of diabetes mellitus, hypertension, or symptoms of cerebrovascular, cardiovascular, or peripheral vascular disease; there was no family history of significant vascular disease. He denied any history of alcohol or drug abuse.

At the time of admission, he was afebrile with a pulse rate of 90 (a regular rate, with all peripheral pulses equally palpable). His blood pressure was 100/60 mm Hg. He had icterus but no pallor or lymphadenopathy. His abdomen was soft with an enlarged liver 3 cm below the right costal margin. Neuro-ophthalmological evaluation revealed right-sided ptosis and limitation of superior, inferior, and medial recti right eye movement.

His pupils were 3–4 mm in diameter, equal, and round. They were briskly and equally reactive to light and accommodation. Visual acuity (which was measured by means of Snellen’s chart) was normal at 20/20, and color vision (determined by using pseudoisochromatic plates) was also normal. The swinging torch test was negative. Confrontation method showed the visual fields were normal, and fundus examination was unremarkable. Results of the remaining neurological examination and physical examination were normal.

Laboratory studies disclosed the following values: hemoglobin, 13.1 g/dL; total leukocyte count, 12,2 × 10⁹/L (73% polymorphonuclear leukocytes); erythrocyte sedimentation rate, 8 mm/h; serum bilirubin, 10.75 mg/dL (direct bilirubin, 8.85 mg/dL); serum aspartate aminotransferase, 2366 U/L (normal range, 0–38 U/L); serum alanine aminotransferase, 1490 U/L (0–49 U/L); and alkaline phosphatase, 262 U/L (0–117 U/L). Serum protein levels and renal parameters were within normal limits. ELISA of his serum revealed reactivity to hepatitis B surface antigen and IgM antibodies to hepatitis core antigen. Other viral markers—antibody to hepatitis C virus and IgM antibody to hepatitis A virus—were nonreactive. He also was negative for human immunodeficiency virus. Collagen profile and testing for cryoglobulin were negative. Results of CT of the head were also normal. MRI with gadolinium contrast medium was not done.

The patient’s condition was managed conservatively; as the jaundice cleared, the eyelid droop resolved, and the patient stopped complaining of double vision. Over 2 years of follow-up, the patient did not develop any other neurological symptoms. Hepatitis B surface antigen subsequently cleared, and he developed antibodies to hepatitis B surface antigen.

A vast array of neurological manifestations have been reported to be associated with hepatitis B virus infection. Peripheral nerve involvement and cranial nerve involvement have been described in patients with acute viral hepatitis [1–3]. A syndrome typical of classical Guillain-Barré syndrome has also been described [4]. Other uncommon manifestations that have been previously described include transverse myelitis and myokymia [1, 5].

Given the isolated right-sided transient pupil-sparing third cranial nerve palsy in our patient, the absence of a history of vascular disease and vascular risk factors, and the temporal relationship between jaundice and eye symptoms, we contend that this patient’s third cranial nerve paresis was the result of hepatitis B virus infection.

Pupil-sparing third cranial nerve palsy is believed to be usually ischemic in origin. It is generally transient with virtually complete recovery after a period of weeks to several months. It is usually seen in association with conditions such as diabetes mellitus, hypertension, atherosclerosis, collagen vascular disease, vasculitis, and, less frequently, ophthalmoplegic migraine [6].

The pathophysiological mechanism of neural injury by hepatitis B virus remains speculative. It could be activation of the host’s immunologic response to viral antigen. Deposition of circulating immune complexes of viral antigen and antibody may play an important role in causing ischemic infarction of the third cranial nerve. In addition, it could be due to hypersensitivity angitis.

To our knowledge, no cases directly implicating acute viral hepatitis as the cause of ischemic pupil-sparing third cranial nerve palsy have been reported. We report the first case due to hepatitis B virus.

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Pulmonary Colonization with *Pneumocystis carinii* in Human Immunodeficiency Virus–Negative Patients: Assessing Risk with Blood CD4+ T Cell Counts

Use of PCR analysis has led to detection of low numbers of *Pneumocystis carinii* organisms, which were undetectable by microscopy, in bronchoalveolar lavage (BAL) fluid specimens from immunosuppressed patients who showed no evidence of acute *P. carinii* pneumonia (PCP) [1]. These low levels of parasites were usually considered to reflect pulmonary colonization, but their significance was a subject of controversy. Cases of colonization were described mainly in patients positive for HIV who had blood CD4+ T cell counts of < 400 × 10^6/L [2]. There were little data concerning HIV-negative patients [3]. This study investigates the presence of *P. carinii* DNA in BAL fluid specimens from HIV-negative patients with no evidence of PCP and examines the link between colonization and decreases in blood CD4+ T cell counts in this patient population.

Eighty-two HIV-negative adult patients were admitted to our hospital during 1 year who underwent BAL for disease investigation; all were enrolled in the study. BAL fluid specimens were regularly sent to our laboratory for detection of *P. carinii*. After cytocentrifugation, Giemsa staining, and immunofluorescence (Diagnostics Pasteur, Paris), specimens were examined by microscope. BAL sediment was assayed by Heminested PCR; the specific primers pAZ102-H, pAZ102-E, and pAZ102-L2 were used to amplify the gene encoding the mitochondrial large subunit rRNA [1, 4]. Results of PCR analysis were not used to determine patient management, but patients were followed up to detect the occurrence of PCP. Clinical data and CD4+ and CD8+ T cell counts were obtained retrospectively.

No cases of PCP were diagnosed for 69 patients by both microscopy and PCR analysis. Although microscopic examination was negative, *P. carinii* DNA was detected by PCR analysis in specimens from the 13 remaining patients. Underlying conditions were myeloma (2 patients), sarcoidosis (3), chronic lymphoid leukemia (2), lymphoma (1), renal transplantation (1), corticosteroid-treated asthma (1), hydrocortisone-treated panhypopituitarism (1), diabetes with pulmonary infarction (1), and untreated asthma (1). Except for 1 patient who died of chronic lymphoid leukemia a few days after detection of *P. carinii* DNA, these patients were followed up for 2 to 12 months (median, 6 months). Because they did not develop PCP despite the absence of prophylaxis for PCP, they were considered to be colonized. Thus the frequency of colonization among our study population of HIV-negative patients was estimated at 14%.

CD4+ and CD8+ T cell counts were available for 48 patients; 5 of these were colonized. An increasing risk of colonization was significantly associated with a CD4+ T cell count < 400 × 10^6/L (33.3% vs. 2.8% of patients with higher cell counts; RR, 12; 95% CI, 1.5–97.2; *P* = .01); it was also associated with a CD4+ T cell/CD8+ T cell ratio < 1 (30.7% vs. 2.8% of patients with higher ratio; RR, 10.8; 95% CI, 1.3–87.7; *P* = .015). The highest risk of colonization was in patients with both a CD4+ T cell count < 400 × 10^6/L and a CD4+ T cell/CD8+ T cell ratio < 1 (table 1): 57.1% of patients from this group were colonized, compared with 2.4% of patients from other groups (RR, 23.4; 95% CI, 3.1–180.1; *P* < .001).

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a Four of 7 patients who had CD4+/CD8+ cell ratios < 1 and CD4+ cell counts < 400 × 10^6/L were colonized; underlying diseases were myeloma (1 patient), hydrocortisone-treated panhypopituitarism (1 patient), and sarcoidosis (2 patients).

b Significant difference between 2.4% and 57.1% (RR, 23.4; 95% CI, 3.1–180.1; *P* < .001).

c Only 1 of the 41 remaining patients was colonized; this patient’s underlying disease was untreated sarcoidosis.