Correspondence

High Levels of Adenosine Deaminase in a Patient with Herpetic Encephalitis and Initial Negative PCR Results

SIR—The finding of high levels of adenosine deaminase (ADA) in CSF samples may be an important diagnostic clue for tuberculous meningitis [1]. We describe a young patient with herpes simplex encephalitis (HSE) and very high levels of ADA in the CSF. In a MEDLINE (PubMed) search of the literature published in the last 15 years, we did not find another case report of high levels of ADA in the CSF of patients with HSE.

A 25-year-old butcher was admitted to our hospital (Hospital Universitario Virgen de las Nieves, Granada, Spain) with a 2-day history of fever, lethargy, headache, behavioral changes, vomiting, and disorientation. No nucal rigidity, seizures, or focal neurological deficit was present. The analysis of CSF samples obtained from a lumbar puncture performed on the patient at the time of admission showed a WBC count of 11 cells/mL (90% lymphocytes), a glucose level of 94 mg/dL, a protein level of 40 mg/dL, and an ADA level of 20 IU/L (as determined with the Ki netic test, Boehringer Mannheim UV, and a Beckman DU-40 spectrophotometer). Treatment with intravenous acyclovir and doxycycline was started. Results of Gram and Ziehl-Neelsen staining, bacterial cultures and cultures on Lowenstein-Jensen medium, and a test for herpes simplex virus (HSV) by PCR of the CSF samples were negative.

After 72 h of treatment, acyclovir was withdrawn from the regimen. The patient's clinical symptoms decreased in severity, but full recuperation was not achieved. Results of a blood culture and a tuberculin skin test performed with 5 units of PPD were negative. Serologic test results were negative for Brucella species, Epstein-Barr virus, cytomegalovirus, *Toxoplasma gondii*, HIV, and *Treponema pallidum*. Findings of an MRI scan of the brain performed on day 7 of hospitalization disclosed right temporal- and frontal-lobe enhancement with mild mass effect. Therapy with intravenous acyclovir, in combination with dexamethasone, was restarted.

On day 8 of hospitalization, a second lumbar puncture was performed and yielded a transparent CSF sample with a WBC count of 80 cells/mL (70% lymphocytes), an RBC count of 10 cells/mL, a glucose level of 47 mg/dL, a protein level of 93 mg/dL, and an ADA level of 22 IU/L. The results of additional Gram and Ziehl-Neelsen staining, bacterial cultures, and cultures on Lowenstein-Jensen medium were again negative, but now the CSF sample was found to be positive for HSV-1 by PCR. Results were also negative for IgM antibody tests for *Borrelia* species and for parotiditis, a Venereal Disease Research Laboratory test, and an agglutination test for *Brucella* species performed on CSF samples. Viral culture of a CSF specimen was negative.

A third lumbar puncture performed at the end of acyclovir therapy (i.e., 14 days after initiation), yielded a normal CSF sample (WBC count, 2 cells/mL; glucose level, 55 mg/dL; protein level, 46 mg/dL). The results of a PCR test for HSV DNA in the CSF sample were negative, and the ADA level was normal (7 IU/L). The patient recovered completely, without neurologic sequelae, and, 6 months after discharge from the hospital, the patient remains free of symptoms.

The determination of ADA levels in CSF samples now forms part of the routine diagnostic work-up for tuberculous meningitis in many countries where tuberculosis is endemic. Evaluation of ADA levels can aid in the early differential diagnosis of tuberculous meningitis [1–3]. It has been reported that ADA levels of >10 IU/L in the CSF of patients with meningitis could be a strong indication of tuberculous meningitis (sensitivity and specificity, 99%) [1], although high levels of ADA have also been found associated with neurobrucellosis and pyogenic meningitis [2], and case reports of meningeal involvement with leukemia or lymphoma [4] and aseptic meningitis [5] have been published.

Another important lesson of the case we describe is that the initial PCR test results were negative for HSV, an example of a finding that has been reported recently [6]. HSV DNA could not be detected early in the clinical course of HSE, probably because a very low number of copies of HSV DNA were present in the initial CSF sample [6].

We have described herein a patient with HSE whose case had 2 particular aspects with notable clinical implications. First, the finding of elevated levels of ADA in CSF samples may be strong evidence for the presence of tuberculous meningitis, but, as in the case described above, this finding should be carefully evaluated in the context of the rest of the clinical data present. Second, for patients with important clinical and neuroimaging findings that raise suspicion of HSE, a negative PCR result for HSV-1 early in the course of infection does not rule out the presence of HSE, and a second lumbar puncture and another PCR test for HSV should be performed.

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Risk Factors for Nursing Home–Acquired Pneumonia

We have read with interest the article by Mylotte [1]. The purpose of our letter is to report a study about risk factors for nursing home pneumonia [2]. We conducted a retrospective study at the North Chicago VA Hospital between 1 January 1997 and 1 July 2000. This study was based on chart reviews and did not require patient consent. The study was approved by the internal review board of the North Chicago VA Hospital. All patients from a single long-term care facility who were admitted to the acute care setting with a diagnosis of pneumonia were included in the study. Patients were matched by age and sex with other patients from the same facility who had been admitted to the acute care setting with diagnoses other than pneumonia.

Baseline demographic and clinical data for patients with pneumonia and patients without pneumonia was collected by electronic chart review. Cases of pneumonia were identified using standardized definitions. Statistical significance of differences in demographic characteristics was determined by using χ^2 analysis and Student's t test. Univariate analyses for risk factors of first episodes of pneumonia were performed using commercially available software.

Table 1. Selected characteristics of male patients, with and without pneumonia, admitted to the acute care facility.

Characteristic	Patients with pneumonia (n = 96)	Patients without pneumonia (n = 106)
Age, years	74.5 ± 13.2	74.6 ± 11.3
Mortality at 3 months, % of patients	17.7	17.0
DNR order, % of patients	36.5	30.2
Body mass index	25.4 ± 4.1	25.7 ± 6.9
Hematocrit, %	38.0 ± 7.0	37.4 ± 6.3
Creatinine, mg/dL	1.4 ± 0.9	1.6 ± 1.4
Albumin, g/dL	3.8 ± 0.6	3.1 ± 0.7

NOTE. Data are mean ±SD, unless otherwise noted. DNR, do not resuscitate; BMI, body mass index.

Ninety-six patients with pneumonia and 106 patients with a diagnosis other than pneumonia were included in this retrospective study. Several demographic characteristics, biometric measures, and laboratory findings did not differ significantly between the 2 groups (table 1).

When patient data were examined using univariate analysis, patients with pneumonia were found to be more likely to have dysphagia, have a history of chronic obstructive pulmonary disease, or have congestive heart failure; use major tranquilizers, use steroids, or use a gastric or nasogastric tube; or to be bedridden.

Vomiting; poor dentition; a history of alcohol or tobacco abuse; a history of diabetes mellitus, dementia, stroke, congestive heart failure, seizures, or cancer; and previous use of antacids or steroids did not appear to be potential risk factors (table 2). Use of pneumococcal and flu vaccinations was very similar in both groups, and the possible protective effect of these vaccinations could not be determined.

The use of major tranquilizers and steroids have not been reported previously as risk factors for nursing home–acquired pneumonia. They are biologically plausible mechanisms for development of this disease. Unfortunately, we did not differentiate between the presence of nasogastric or gastrostomy tubes and included both as a single category. Therefore, we cannot conclude that a gastrostomy tube increases the risk of nursing home–acquired pneumonia.

We believe that use of major tranquilizers, use of steroids, and presence of a gastrostomy tube should be taken into account in further multivariate analyses of risk factors for nursing home–acquired pneumonia.

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