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deterioration from hyponatremia for a variety of reasons, including being a woman\(^2\) and having a space-occupying lesion, vasogenic cerebral edema,\(^3\) and a hypoxic event.\(^4\) Hyponatremia can lead to cytotoxic cerebral edema, which expands brain tissue and can lead to herniation. No data were provided on either the composition of the intravenous fluid administered on admission or the serum sodium level at the time of the neurologic deterioration. The acute neurologic deterioration may have been precipitated by the administration of hypotonic fluids, which further lowered the serum sodium level. We have previously advocated the administration of isotonic saline as a prophylactic measure to prevent neurologic complications from hospital-acquired hyponatremia.\(^5\)

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DR. HARRIS, EDITOR OF THE CASE RECORDS, REPLIES:

Moritz and Ayus suggest that hospital-acquired hyponatremia played a role in the deterioration in this patient's neurologic condition. Since this is not the diagnostic issue that Dr. Podolsky was asked to address in the Clinico-pathological Conference, physicians involved in the care of the patient provided the following assessment.

Fourteen hours before the seizure, the serum sodium level was 131 mmol per liter, and the glucose level was 212 mg per deciliter. After correction for the elevated glucose level, the effective serum sodium level was 133 mmol per liter.\(^1\) Twelve hours before the seizure, the patient vomited several times, and an infusion of half-normal saline was begun. Immediately after the seizure, the serum sodium level was 127 mmol per liter, and the blood glucose level was 492 mg per deciliter; the corrected sodium level thus remained 133 mmol per liter. After the seizure, boluses and an infusion of normal saline were administered, and the serum sodium level rose to 135 mmol per deciliter. During the remainder of the patient's hospital stay, the serum sodium level remained between 127 and 133 mmol per deciliter, despite infusions of normal saline and correction of blood glucose levels.

The patient's physicians agree that isotonic saline is appropriate fluid replacement for patients with brain edema. However, this patient's serum sodium level does not appear to have been low enough to cause a seizure. Cerebral edema attributable to the large B-cell lymphoma of the brain likely contributed to the seizure. A syndrome of inappropriate antidiuretic hormone secretion may have caused persistent mild hyponatremia.

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1,3-β-D-Glucan in Patients Receiving Intravenous Amoxicillin–Clavulanic Acid

TO THE EDITOR: The fungal component 1,3-β-D-glucan is increasingly used to diagnose opportunistic invasive mycoses in immunocompromised patients.\(^1\)\(^3\) The 1,3-β-D-glucan assay (Fungitell, Associates of Cape Cod) was recently approved by the Food and Drug Administration. We found that the serum samples from two patients with hematologic conditions were positive for 1,3-β-D-glucan during treatment with intravenous amoxicillin–clavulanic acid. Serum samples were negative after treatment was discontinued. Neither patient had evidence of invasive fungal disease. Furthermore, 1,3-β-D-glucan was detected in the amoxicillin–clavulanic acid used to treat these patients.

We then tested 10 serum samples from six patients treated with intravenous amoxicillin–clavu-
Imipenem in Patients with Immediate Hypersensitivity to Penicillins

TO THE EDITOR: It is considered potentially harmful to administer imipenem–cilastatin to patients with IgE-mediated hypersensitivity to penicillins because of a 47.4 percent rate of cross-reactivity (9 of 19 subjects) found in a single study on the basis of positive skin tests involving imipenem reagents.

Between 1997 and 2005, we studied 112 consecutive patients with such hypersensitivity, diagnosed as previously described, in order to assess the cross-reactivity with imipenem–cilastatin and to evaluate the allergic responses to imipenem–cilastatin in patients who had negative skin tests. Our patients had a total of 143 immediate reactions to penicillins. All patients had positive skin tests for at least one of the penicillin reagents.

Ten batches of the amoxicillin–clavulanic acid infusion fluid used during this period (including the five batches used to treat the six patients) were positive for 1,3-β-D-glucan (9414±7774 pg per gram of antibiotic), as opposed to four batches of ceftazidime infusion fluid (10±21 pg per gram of antibiotic, P=0.004). Both drugs were diluted according to standard methods for clinical use, and all diluents (i.e., water and 0.9 percent sodium chloride) were negative for the glucan. A single dose of 1000 mg of amoxicillin plus 200 mg of clavulanic acid contained 2856 to 28,016 pg of 1,3-β-D-glucan, which is 48 to 467 times the cutoff value in 1 ml of serum.

Serum samples from the six patients treated with intravenous amoxicillin–clavulanic acid also had significantly higher levels of galactofuranose antigens (measured with the use of the Platelia Aspergillus enzyme immunoassay, Bio-Rad Laboratories) than the samples from patients treated with ceftazidime (P=0.003) or samples from healthy blood donors (P=0.009). These components are used for the diagnosis of invasive aspergillosis and have previously been reported to be present in piperacillin–tazobactam and amoxicillin–clavulanic acid. In addition, we observed no glucan reactivity in five batches of piperacillin–tazobactam (23±26 pg per gram).

These results are highly suggestive of cross-reactivity of the Fungitell assay with amoxicillin–clavulanic acid. Physicians should be aware of the possibility of false positive 1,3-β-D-glucan results in patients treated with this antibacterial agent. The presence of two different fungal components in the antibiotic provides strong evidence of a fungal origin of the cross-reactive components in the drugs. Given the difficulties encountered in the diagnosis of invasive fungal disease, it would be desirable to eliminate the fungal material from antibiotic agents.

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