Inadequate Antidiuretic Hormone Secretion After Sagittal Sinus Thrombosis Caused by Protein S Deficiency

To the Editor:

A 64-year-old woman presented to our department one day after the onset of an alternating hemiparesis, more severe in the legs. Two episodes of motor leg seizures had occurred. She had no headache. At the age of 20 years, she had had recurrent deep leg vein thrombosis, as had her father, sister, and, subsequently, her daughter. The patient was disoriented and slightly aphasic and apractic. Physical examination revealed right gaze palsy, homonymous hemianopia, and hemiparesis, more severe in the leg. Neither papilledema nor neck rigidity was present. She developed epilepsy partialis continua of the right leg.

A contrast-enhanced computed tomographic scan revealed a 1.5 × 1 cm² bleed in the left parieto-occipital region. Angiography demonstrated thrombosis of the superior sagittal sinus, and deficiency of protein S with a free protein S level of 12% (total protein S being 68%) was found by the use of an ELISA kit (Boehringer, Mannheim, FRG). Repeated chest x-ray and abdominal ultrasound showed no abnormalities. We excluded pathological conditions known to cause cerebral sinus thrombosis, including deficiency of protein C, antithrombin III, and neoplastic diseases.

Anticoagulation with heparin was initiated immediately and replaced by vitamin K antagonists after 4 weeks. The area of the hemorrhage increased to 6 × 6 cm² on day 2 and became space occupying. The patient developed a central breathing disturbance resembling Biot’s breathing. Dexamethasone treatment resolved the breathing disturbance, although the coma and hemiplegia were unchanged. Recovery was slow, but steady. The patient received anticonvulsive treatment with phenytoin.

After 3 weeks, the patient developed hyponatremia of 123 mmol/l. She had a fluid balance of over 1,500 ml, a serum osmolality of 273 mosmol/l, a urine osmolality in a 24-hour urine collection of 573 mosmol/l, and a urine specific gravity of 1,030 g/l. Creatinine clearance rate was 80 ml/min; blood urea nitrogen level was 51 mg/dl; and creatinine level was 1.0 mg/dl. Serum potassium and calcium levels were normal. Fluid intake was restricted to 100 ml/24 hr, with recovery of hyponatremia and fluid balance within 4 days.

With residual hemianopia, mild aphasia, dysgraphia, dyslexia, dyscalculia, and ideational apraxia, she was transferred to rehabilitation. On reexamination 4 months later, she was physically well and showed slight improvement of her deficits.

To assess a genetic disorder, a pedigree was established (Figure 1). The younger of two grandchildren had a low free protein S level of 4%; the older boy was borderline at 34%. The daughter and sister were not examined because they were receiving coumarin. Afflicted family members of the first through the third generations suffered deep venous thrombosis from early adulthood to the age of 60 years, showing the different phenotypic expression of the same genetic disorder.

Inadequate antidiuretic hormone secretion may be associated with malignant disorders such as bronchogenic, pancreatic, duodenal, breast, or other carcinomas, leukemia, and lymphomas; with treatment with drugs such as antidiabetic medication, antineoplastics, tricyclic antidepressants, and general anesthetics; with lung disease such as tuberculosis, pneumonia, abscess, chronic nonspecific respiratory syndrome; and with central nervous system disorders such as head injury, infections, and subarachnoid hemorrhage. A thorough search revealed none of these in our patient.

Bousser et al² deemed 10 of 38 patients to have idiopathic intracranial sinus thrombosis, but did not determine their proteins C and S levels. No patient in this largest published series developed a syndrome of inadequate antidiuretic hormone secretion as a complication of sinus thrombosis. Cros et al³ contributed the first well-described case of sinus thrombosis caused by hereditary protein S deficiency.

We report the association of protein S deficiency with sagittal sinus thrombosis and inappropriate antidiuretic hormone secretion to inspire others to a search for the mechanism of a presently obscure condition.

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References


Neurological Ischemic Attack and Interleukin-2 Therapy

To the Editor:

While neuropsychiatric changes have often been observed in association with recombinant interleukin-2 (rIL-2) treatment,¹ neurological complications such as ischemic syndrome have been rare. Bernard et al² reported two cases of ischemic syndrome. In this report, we describe a case of ischemic syndrome in a patient treated by continuous rIL-2 infusion for metastatic renal carcinoma.

A 70-year-old man with renal carcinoma metastatic to lung and liver underwent nephrectomy in April 1989, followed by three cycles of rIL-2. Each cycle consisted of a bolus of Vinblastine (0.1 mg/kg) followed 15 days later by two sequential 6-day periods of continuous infusion of rIL-2 (3 × 10⁶ IU/m²) per day (gift from Eurocetus). The patient was allowed 24 hours of rest between the two infusion periods on day 22 of the cycle. This protocol was used without neurological complications in 14 other patients. Because a partial response was obtained after the first cycle, two additional cycles at the same dose were conducted, with a 1-week rest
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