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

To the Editor:

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 (3x10^6 IU/m^2) 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 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 lymphoma; with treatment with drugs such as anti diabetic 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 al reported 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 al 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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Wolfgang Liedtke, MD
(formerly of the Neurology Department
Universitat Tubingen
Tubingen, FRG)
Neurology Department
Universitat Essen
Essen, FRG

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, neurological complications such as ischemic syndrome have been rare. Bernard et al 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 (3x10^6 IU/m^2) 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.
between each cycle. After the third cycle, thoracic and abdominal computed tomographic scans showed a 75% regression of the carcinoma in the lung and complete regression in the liver.

Before rIL-2 treatment, the patient had no neurological or cardiac symptoms. His brain CT scan, as well as his electrocardiogram and echocardiogram, was normal. Anticoagulant therapy was administered following nephrectomy.

One week after the first rIL-2 cycle, a transient paresthesia of the right upper extremity occurred. The only other clinical manifestation of toxicity was fever, which was controlled by paracetamol and indomethacin. Laboratory data were normal except for eosinophilia in peripheral blood.

The rIL-2 was discontinued for 3 weeks, with no further episodes during that time. When rIL-2 was resumed, however, a similar episode occurred again in the right upper extremity. Neurological investigations were otherwise normal. After the third cycle, the neurological symptoms reappeared and were accompanied by a distal motor deficit. Electroencephalogram and brain computed tomographic scan were normal. Three months after the end of treatment, visual disturbances were noted, including decomposition of letters and hallucinations when reading. Examination of the visual field disclosed left homonymous hemianopsia. Brain computed tomographic scan confirmed the presence of a cerebral infarction in the region of the left posterior cerebral artery. Doppler ultrasound revealed no abnormalities and echocardiography was normal. Eight months later all symptoms regressed.

This case, like those reported by Bernard et al, provides strong evidence that rIL-2 treatment, or substances increased by rIL-2 treatment, such as interleukin-1, tumor necrosis factor, or gamma interferon, cause neurovascular toxicity. Many of the adverse effects of rIL-2 treatment have been attributed to vascular leak syndrome, which is commonly associated with rIL-2 treatment.

However, this mechanism can hardly account for our patient's attacks because, like Bernard et al, we did not note hypotension. A possible explanation would be cytokine-induced endothelial activation. However, the age of our patient may have played a part in the genesis of the symptoms.

A. Donnet, MD  
Service de Neurologie  
N. Tubiana, MD  
O. Chinot, MD  
P. Juin, MD  
Service d'Oncologie et de Radiothérapie  
Hôpital de la Timone  
Marseille, France

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A Donnet, N Tubiana, O Chinot and P Juin

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