Diabetes Insipidus Caused by Lymphocytic Infundibuloneurohypophysitis

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- Pathologic examination at autopsy of a 74-year-old man with central diabetes insipidus revealed that he had a chronic lymphocytic inflammation limited to the infundibulum, stalk, and posterior lobe of the pituitary gland. No meningitis, sarcoidosis, or granulomas were detected, though there was evidence of chronic pancreatitis. In addition, neuronal loss with gliosis was observed bilaterally in the supraoptic and paraventricular nuclei. The unusual localized inflammatory brain lesion was considered to be responsible for the diabetes insipidus.

( Arch Pathol Lab Med 1988;113:1399-1401)

Case descriptions of diabetes insipidus include mainly those in which there are destructive lesions of the hypothalamus and pituitary stalk, such as brain tumors or lesions produced by injury. Rarely, the disease may result from infiltration of the infundibulum by meningitis, tuberculosis, sarcoidosis, histiocytosis X, and lymphoma or leukemia. Diabetes insipidus has occurred as a postpartum complication, and it has also been reported in pregnant women in association with abnormally high levels of circulating vasopressinase. However, 30% of all reported cases of diabetes insipidus are idiopathic, and for these, an autoimmune mechanism has been postulated.

We describe a patient with diabetes insipidus in whom chronic noninfiltrating, amnating inflammation was localized in the infundibulum, stalk, and posterior lobe of the pituitary gland. In addition, bilateral neuronal loss with gliosis was seen in the supraoptic and paraventricular nuclei.

REPORT OF A CASE

A 74-year-old man had been ill for 4 months with polyuria, hypo-osmotic urine, loss of appetite, and elevated serum levels of pancreatic enzymes. At the time of his hospital admission, his serum amylase (590 U/L) and lipase (420 U/L) levels were elevated. In addition, he had elevated immunoglobulin levels: IgG, 23.4 g/L; IgA, 4.7 g/L; and IgM, 3.1 g/L. He also had increased complement levels, with C3 of 0.6 g/L (normal range, 0.8 to 1.4 g/L) and C4 of 0.1 g/L (normal range, 0.1 to 0.2 g/L). The white blood cell count was 2.8 x 10^9/L, with a predominant lymphocyte fraction of 0.74. The erythrocyte count was 3.3 x 10^12/L, and the hematocrit was 0.32.

Additional laboratory studies disclosed the following values: blood urea nitrogen, 5.5 mmol/L; uric acid, 143 mmol/L; potassium, 4.5 mmol/L; and chloride, 106 mmol/L. The urine output was about 3.5 L/d, and the urinary osmotic pressure was 142 mOsm/kg (normal range, 300 to 1000 mOsm/kg). A clinical diagnosis of diabetes insipidus was made. A lesion in the pancreatic body was detected on whole-body computed tomographic scan and endoscopic retrograde cholangiopancreatography. Levels of tumor markers, such as alpha-fetoprotein, carbohydrate antigen 19-9, and carcinoembryonic antigen, were all within the normal range. Surface antibody to hepatitis B virus was positive, but antibodies were negative. While further evaluation of the lesion was being attempted, the serum levels of pancreatic enzymes normalized, but hypernatremia set in, which resulted in disturbances of consciousness and in personality changes. These effects resolved on vasopressin tannate administration. However, the patient died of bronchopneumonia.

PATHOLOGIC FINDINGS

The autopsy findings showed that the patient had bronchopneumonia. The pancreatic lesion was found to be due to chronic pancreatitis.
attitis. There was no sarcoïdosis, tuberculosis, or malignancy.

The brain, which weighed 1300 g, appeared normal on the exterior, except for a thickened pituitary stalk. Microscopically, severe chronic inflammatory cell infiltration was noted in the infundibulum (Fig 1), stalk, and posterior lobe of the pituitary gland, but its anterior lobe was intact. The inflammatory cells consisted mainly of small lymphocytes with predominant T-cell markers and a few B-cell markers, and they included a few plasma cells with k and l light chains, indicating polyclonality. No S100-positive histiocytes were observed. No inflammatory changes were evident in other parts of the brain or in the meninges. Loss of neurons, with an astrocytic reaction, was observed bilaterally in the paraventricular and supraoptic nuclei (Fig 2, top left and bottom left). The remaining neurons were stained immunohistochemically with vasopressin, but they were markedly decreased in number, compared with those in an age-matched control subject (Fig 2, top right and bottom right). Vasopressin immunoreactive fibers of the infundibulum and posterior lobe were also diminished in number. Other parts of the brain, including the subthalamus, thalamus, cerebral cortex, and white matter, were well preserved. There was no evidence of disorders affecting the hypothalamo-pituitary system, such as sarcoïdosis, histiocytosis X, tuberculosis, or neoplastic processes.

**COMMENT**

The patient described herein was diagnosed as having chronic lymphocytic infundibuloneurohypophysitis, with bilateral neuronal loss of supraoptic and paraventricular nuclei. The brain lesions were considered to be responsible for the patient's diabetes insipidus; however, exclusive inflammatory involvement of the hypothalamo-pituitary system seen in this patient is a rare cause of diabetes insipidus. Similar inflammatory lesions causing diabetes insipidus were described by Nagashima et al., but in that patient, the inflammatory changes were present throughout the nervous system, with demyelination as a prominent feature. In our patient, the inflammation was limited to the infundibulum, stalk, and posterior lobe of the hypophysis, which are not subject to the blood-brain barrier. As to the degeneration of supraoptic and paraventricular nuclei that occurred in our patient, Treip has pointed out that these nuclei could degenerate as a retrograde axonal change following develop-
Diffuse Fatal Pulmonary Microembolism of Retroperitoneal Extravascular Origin

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- A 34-year-old woman who had type I diabetes mellitus for 22 years and chronic renal failure for 2 years underwent a combined kidney and pancreas transplantation. Her uremia and insulin-depending disappeared thereafter. However, she suddenly developed acute respiratory distress and died 22 days after the surgery. Diffuse pulmonary microemboli composed of necrotic tissue debris, fat cells, and muscle fragments were found. The source of the emboli was apparently a localized liquefying hematoma with necrotic muscle and fat in the left retroperitoneal space. Although such an occurrence seems to be extremely rare, the present case demonstrates that a liquefying hematoma with necrotic tissue in a confined space may indeed give rise to fatal pulmonary microembolism. (Arch Pathol Lab Med. 1989;113:1401-1403)

Other than the usual intravascular thrombus formed by coagulated blood, the source of an embolus can be extravascular. Almost any type of tissue may be aspirated into blood vessels and give rise to emboli. Emboli of fat, air, bone marrow, amniotic fluid, trophoblasts, decidual tissue, brain, liver, bile, and adipose tissue have been reported. Even foreign substances such as cotton fibers, Dacron and Teflon of cardiac valve prostheses, starch, talc, parasites, intravascular catheters, bullets, and metallic mercury can give rise to emboli. Described here is a patient who underwent a combined kidney and pancreas transplantation. She suddenly developed diffuse pulmonary microembolism and died 22 days after the surgery. The microemboli were composed of necrotic tissue debris, similar to the tissue found in a retroperitoneal organizing and liquefying hematoma. The mechanism for developing pulmonary microembolism from such a confined retroperitoneal hematoma is discussed.

REPORT OF A CASE

A 34-year-old woman who had insulin-dependent diabetes mellitus for 22 years and chronic renal failure, not yet requiring dialysis, for 2 years was elected to receive a combined kidney and pancreas transplant. The donor pancreas had an aortic cuff, portal vein, and duodenum attached to it. The pancreas was placed intraperitoneally with the aortic cuff anastomosing to the right common iliac artery, the portal vein to the inferior vena cava right above the entrance.