CLINICAL CONFERENCE

DIABETES INSIPIDUS

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We are presenting the case histories of two children with diabetes insipidus, of particular interest because of the diversity of manifestations, the variance in etiology and the complexity of management. One patient was observed for a period of 3 years, with onset of disease at age 10 years; another was observed for a period of 8 years, with the onset of the primary disease at 2 years and diabetes insipidus 6½ years later.

CASE REPORTS

Case 1

History: This 13-year-old white male was admitted to Sarah Morris Hospital on April 17, 1960, for re-evaluation of diabetes insipidus.

The patient was first seen at another hospital in June, 1957, because of small penis and shortness of stature. Laboratory studies revealed 17-ketosteroids, 2.9 mg/24 hr, and follicle-stimulating hormone in urine, 13.6 units/24 hr. The bone age was 8½ years, and roentgenograms of the skull revealed normal findings. The specific gravity of urine was 1.002; otherwise, findings were negative.

In August, 1958, he was readmitted with complaints of growth failure, polyuria and polydypsia. His weight on the first admission was 71.5 lb (32.4 kg), and on the second, 82.0 lb (37.2 kg), but his height was the same. Water load and pitressin test were diagnostic for diabetes insipidus. An intravenous pyelogram was normal. He developed a short period of hypernatremia, which was corrected with intravenous fluids. The protein-bound iodine value was 6.8 μg; fasting blood sugar, 115 mg/100 ml; and nonprotein nitrogen, 35 mg/100 ml. On October 15, 1958, the specific gravity of urine varied between 1.016 and 1.027 following administration of vasopressin (Pitressin) tannate. Vasopressin was administered in doses of 0.5 to 1.0 cc daily, and the patient responded well.

He did well until the summer of 1959 when he developed almost constant sleepiness. He had been a grade A student, but his work deteriorated. He also became a difficult person to get along with because of uncontrollable emotional outbursts and a definite personality change. His weight had increased considerably but his linear growth remained stationary.

Physical Findings: Physical examination revealed a small obese boy in no acute distress. His height was 130 cm (3rd percentile for 10 years of age) and his weight, 50.2 kg (75th percentile for 13 years of age). The temperature was 98.6°F (37.0°C); pulse, 84/min; respirations, 24/min; and blood pressure, 120/70 mm Hg. No pubic and axillary hair were noted; the penis and testes were smaller than normal. The deep reflexes were slightly hyperactive, with no other abnormal neurologic findings.

Ophthalmologic Findings: Ophthalmologic examination revealed a definite pallor suggestive of optic atrophy of both optic nerves. The disks were flat and the margins slightly ill-defined. The visual fields showed an early binal inferior quadrantanopsia, with a central scotoma in the left eye.

Hospital Course: The patient had a daily temperature of 101 to 103°F (38.3 to 39.4°C), without any signs of infection.
frequently had uncontrollable emotional outbursts. A pneumoencephalogram showed incomplete filling of the third ventricle and no visualization of the anterior recess. After the pneumoencephalogram he became lethargic, slightly dehydrated and walked with a staggering gait. He developed hypernatremia, which was corrected by intravenously given fluids. He was given vasopressin tannate, 0.6 cc. intramuscularly, three times weekly. A diagnosis of hypothalamic tumor was made, but operation was postponed because of the precarious position of the tumor. He was discharged on the twelfth day of hospitalization.

LABORATORY FINDINGS: Roentgenograms of the skull and long bones revealed normal findings. An electrocardiogram showed no significant findings. Other laboratory results were within normal limits.

SUBSEQUENT COURSE: During the following month the patient's symptoms progressed, and his parents took him back to the hospital of his original admission. There an exploratory operation was performed, and he died shortly thereafter. Postoperative diagnosis was probable infiltrating glioma of diencephalon, and a prefixed chiasm.

Case 2

HISTORY: An 8-year-old Negro boy was admitted to Sarah Morris Hospital on December 10, 1958, for the seventh time, complaining of excessive thirst, frequent urination, and bed wetting of 2 to 3 weeks' duration. The family history was not pertinent.

Growth and development had been normal up to the age of 2 years. The first admission was on June 3, 1952, for generalized lymphadenopathy and eczematous eruption involving both arms, and anemia. A lymph node biopsy specimen from the left cervical region lymphoid hyperplasia with giant cells and eosinophilia, "characteristic of allergic reaction." Six months after the first admission a diagnosis of reticulendotheliosis was made on the basis of lymph node and bone marrow biopsy.

The patient complained of pain in the left thigh, and he had generalized lymphadenopathy, exophthalmos, skin lesions, anemia and a low-grade fever. Roentgenographic studies revealed a punched-out lesion in the left femur. Subsequent films revealed multiple punched-out lesions involving skull, spine, extremities and pelvis (Fig. 1). During the following 2 years he was treated with radiation, cortisone and antibiotics, with regression of many of the lesions and progression of others. In 1954 the probable diagnosis of lipid histioctosis of cholesterol type (Hand-Schüller-Christian disease) was considered, but diabetes insipidus was not present.

PHYSICAL FINDINGS: On physical examination at his last admission, on December 10, 1958, he walked with a lordotic gait, and with head held rigid. Marked exophthalmos was present. The skin showed chronic dermatitis with marked scaling and lichenification involving the wrist and hands, and to a lesser degree the popliteal and anti-cubital fossae. The neck showed marked limitation of rotation and extension with absence of normal lordotic curve.

The chest showed increased anteroposterior diameter, with widened intercostal spaces. The lungs were clear and there was a marked lumbar lordosis. The abdomen was protuberant, soft and nontender. The liver was firm and nontender, 1 cm below the costal margin.

HOSPITAL COURSE: The patient continued to have polydypsia, with a high fluid intake and output. The specific gravity was constantly low. During a test period there was no increase in the specific gravity after use of hypertonic saline solution or nicotine (Fig. 2). There was definite decrease in output and increase of specific gravity following intravenous use of vasopressin (procedure by S. Zaltzman, Department of Pediatric Research), establishing the diagnosis of diabetes insipidus. Therapy was started with triamcinolone, 40 mg daily for 20 days, followed by gradual reduction and with-
drawal after 55 days. The patient was also given vasopressin tannate in oil, 7 days after initiation of steroid therapy. The urine output decreased with use of vasopressin, and normal output and specific gravity resulted when the dosage was maintained at 1 cc every other day. The dosage of vasopressin was subsequently decreased to 0.8 cc. every other day. The patient was discharged after the tenth week of hospitalization with normal urinary output and specific gravity. The osteolytic lesions in the extremities were almost completely resolved, and skull lesions showed marked resolution (Fig. 1).

Two years later he was doing remarkably well in spite of exophthalmus, diabetes insipidus, ankylosis of his neck, protuberant abdomen, lordosis and shortness of stature. The diabetes insipidus was controlled, and the child attended public school. However, a skeletal survey on October 13, 1960, showed new lesions of the skull; the remainder of the skeleton appeared unchanged (Fig. 3).

**COMMENT**

One of the two children had diabetes insipidus with progressive hypothalamic involvement, apparently due to an infiltrating glioma in the region of the floor of the third ventricle; the other developed the classic symptoms of lipid histiocytosis of cholesterol type (Hand-Schüller-Christian syndrome) as a sequel to severe generalized, lipid reticuloendotheliosis. The prognosis...
for the second patient for many months was discouraging because of the progressive and extensive destruction of bone. However, with courses of x-ray therapy, antibiotics and steroids, gradual resolution resulted. However, a later skeletal survey revealed new lesions in the skull. The diabetes insipidus remained under control. As noted, he was stunted in growth, probably a result of two factors: 1) primary disease with bone destruction and 2) extensive skeletal radiation, and possibly deficiency of growth hormones resulting from anterior pituitary involvement.

We shall comment briefly on etiologic and clinical diagnostic possibilities in general with regard to diabetes insipidus and shall demonstrate the role of the hypothalamus in relation to the clinical manifestations.

Wilkin's classified diabetes insipidus clinically into three groups: 1) organic diabetes insipidus; evidence of an organic lesion in the region of the posterior pituitary or hypothalamus; responsive to vasopressin; 2) idiopathic diabetes insipidus; no evidence of disease or injury; responsive to vasopressin; and 3) nephrogenic diabetes insipidus; a disturbance of water excretion; nonresponsive to vasopressin.

Our two cases are in Group 1. On the other hand, the etiologic distribution in 124 patients with true diabetes insipidus reported by Blotner was 56 (45%) of the idiopathic type and 36 (29%) of the type secondary to primary brain tumor. For the remaining 32 (26%) there was fairly good distribution among a number of conditions.

Of further interest is Bauer's report of 60 cases of hypothalamic disease; necropsy revealed neoplasm in 51, inflammatory lesions in 7 and degenerative lesions in 2. Sexual abnormalities occurred in more than
60%, diabetes insipidus in more than 33%, psychic disturbances in more than 33%, somnolence in 30%, obesity in 25% and thermodysregulation in 21%. Our first patient presented all of these symptoms and signs.

Although diabetes insipidus was the second most frequent sign of hypothalamic disease in Bauer’s series, it was not an early one. In only 2 of 21 patients with diabetes insipidus was it the first evidence of hypothalamic dysfunction. This was true in both of our cases. In our first, hypogenitalism, obesity and slow growth preceded diabetes insipidus by at least 2 years; in the second, reticuloendotheliosis existed 6 years before symptoms of diabetes insipidus.

The hypothalamus is situated in the floor and lateral walls of the third ventricle and is limited anteriorly by the lamina terminalis and posteriorly includes the mammillary bodies. Since most pathologic conditions of the hypothalamus usually involve one-third to two-thirds of this 4-gm organ, and since this small area contains approximately 15 to 20 paired nuclear centers, it is not surprising that disease in this area is manifested by complex symptomatology.

According to Hawes et al. and Wilkins, five clinical syndromes and the principle nuclear involvement in the hypothalamus have been described: 1) hyperthermia due to destructive lesions of the posterior nuclei; 2) hypersonmia due to lesions of the posterior nuclei and mammillary bodies; 3) the adiposogenital syndrome that occurs with lesions in the tuber cinereum and lateral nuclear masses; 4) diabetes insipidus often accompanied by hyperthermia due to lesions in the supranoptic nuclei; and 5) autonomic epilepsy due to sympathetic or parasympathetic disturbances from various portions of the hypothalamus.

Experimentally it has been shown that lesions involving other areas of the hypothalamus may cause rage phenomena, polyphagia, obesity, anorexia and cachexia, sexual disturbances, either hypogonadism or precocious sexual development, hyperglycemia, hypoglycemia and disturbance of electrolyte balance.

Thus a combination of symptoms and signs may occur when there are extensive or rapidly expanding lesions, stimulating and/or destroying various hypothalamic nuclei.

Blotner recently demonstrated primary degeneration of the supraopticohypothalamic system at necropsy in three cases of true idiopathic diabetes insipidus.

REFERENCES

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