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MR of Diabetes Insipidus in a Patient with Erdheim-Chester Disease: Case Report

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Twenty-six cases of Erdheim-Chester disease have been reported since it was first described in 1930 [1, 2]. The typical pathologic feature is an infiltration of foamy, lipid-laden histiocytes and giant cells [3]. Characteristic skeletal radiographic abnormalities are symmetric osteoblastic changes with or without lytic components in the major long bones, especially the diaphysis and metaphysis [4, 5]. Bone-seeking radiopharmaceutical agents and gallium may accumulate in areas of radiographic abnormalities [6, 7]. Extraskeletal involvement with lipid-laden histiocytes has been seen in virtually every major visceral organ [2, 8–11]. CNS involvement is, however, highly unusual, except for retroglobal lesions [9, 11, 12] and infiltration presenting as multiple parasagittal masses [11, 12]. In their review of 19 cases of the disease, Miller et al. [11] found only one instance of central diabetes insipidus and hypopituitarism.

We report a rare case of neurogenic diabetes insipidus associated with Erdheim-Chester disease.

Case Report

A 30-year-old man presented in November 1980 with abrupt onset of polyuria, reaching 15–19 l/day within 3 weeks of onset. Measured osmolalities were 295 mOs/kg (serum) and 117 mOs/kg (urine). After water deprivation he lost 15 lbs, with the serum osmolality increasing to 314 mOs/kg and serum arginine vasopressin (AVP) less than 0.2 μU/ml (expected values for randomly hydrated subjects 0.4–5.3). Urine osmolalities of 161–164 mOs/kg rose to 381 mOs/kg after the administration of aqueous AVP (5 units IM), establishing the diagnosis of central diabetes insipidus. Pitressin in oil, and subsequently intranasally administered desmopressin, were prescribed to control his polyuria.

In December 1980 a skull series and lateral sella radiograph were normal. Serum prolactin was 15.4 ng/ml (normal range = 0–20). In February 1981 a chest radiograph and physical examination were normal. Serum Na and K, and Ca, BUN, blood glucose, T4, and free tyrosine were all within the normal range.
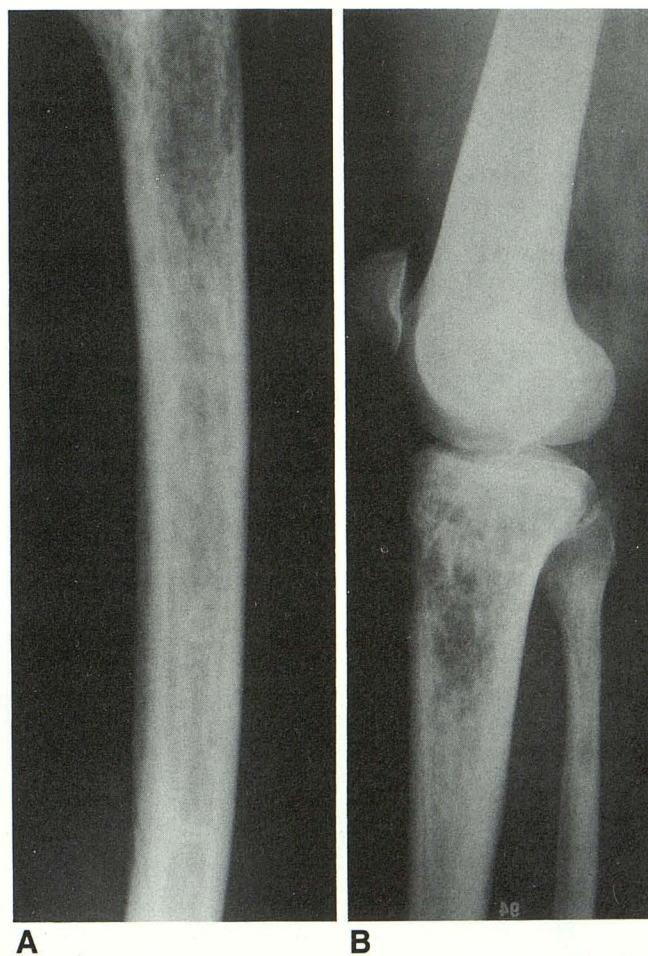

A **B**

Fig. 1.—*A*, Right femur: osteoblastic and osteolytic changes can be noted throughout the femur.

B, Right knee: similar findings noted in right tibia. All long bones showed a similar appearance.

A CT scan of the hypothalamic-pituitary region in April 1981 showed slight enlargement of the pituitary stalk, a possible microadenoma, and a partially empty sella. In September 1981 the patient noted decreased libido. Serum testosterone on two separate determinations was 10 and 28 ng/dl (normal = > 250 ng/dl). FSH and LH were within the normal range. Administration of testosterone cypropionate resulted in improved sexual function.

In a repeat insulin tolerance test and TRH test in December 1981 the patient had inadequate levels of growth hormone but normal levels of cortisol, TSH, and prolactin. The patient also failed to respond to L-dopa 500 mg orally in February 1983, with baseline GH less than 1 ng/ml; 30-, 60-, and 90-min specimens were all 1 ng/ml.

In April 1982 the patient sustained a compression fracture of the superior plate of L2 with slight anterior wedging. Otherwise, the lumbosacral spine and bilateral hip radiographs were normal. In September 1983 he fell and sustained a fracture of the radial head. In retrospect there were no changes to suggest Erdheim-Chester disease.

In August 1988, he began to experience aching in his shoulders and arms, with radiographs revealing cortical mottling of both humoral shafts. Alkaline phosphatase, Na, K, Hgb, white blood cells, and ferritin were all within normal limits. In December 1988 he complained of right knee pain over the medial collateral ligament. Radiographs revealed extensive cortical thickening of the right femur and tibia (along with the fibula). Some areas in the medulla appeared sclerotic and others lucent with a ground glass multicystic appearance (Fig. 1). A skeletal survey demonstrated similar involvement of all long bones.

In January 1989 a whole body 99mTc-MDP skeletal scintiphoto survey demonstrated a symmetric, abnormally increased labeling, mainly of the long bones (Fig. 2). In February 1989 the patient underwent a bone biopsy of the right medial tibia, which was read as nondiagnostic. The slides were noted to have collections of foamy histiocytes with fibrosis. The histologic features were again thought to be nondiagnostic, but the radiographic appearance was classical for Erdheim-Chester disease. Lumbar quantitative CT bone densitometry in March 1989 gave a result of 1112.7 mg/cc ± 3.2 (age-gender matched controls = 163.4 ± 28.5).

Over the intervening years, several CT scans were obtained of the hypothalamic-pituitary area. In April 1985 the pituitary stalk width decreased from the previously increased 7 mm down to 4 mm, with no change in the partially empty sella, and possible microadenoma. The most recent CT, in April 1987, was unchanged. An MR study in March 1989 showed a slightly thickened median eminence and upper pituitary stalk, and an absence of high signal intensity on T1-weighted images of the posterior lobe (Figs. 3A and 3B). An area of hypointensity was evident in the anterior portion of the clivus, which might represent abnormal cell infiltration. After IV contrast administration (gadopentetate dimeglumine, 0.1 mmol/kg), the hypothalamus, median eminence, and anterior clivus enhanced; whereas the posterior pituitary showed no change in signal intensity (Figs. 3C and 3D). A follow-up MR study 24 hr later without additional contrast showed no persistence of contrast enhancement.

Discussion

Neurogenic (central) diabetes insipidus represents a hypothalamic defect in AVP biosynthesis. The disorder can occur at any age; it may be familial or due to acquired lesions, with the latter being most common [13, 14]. Acquired causes of central diabetes insipidus are often associated with organic lesions in the hypothalamic-pituitary region, such as granulomatous disease (tuberculosis, sarcoidosis, Langerhans cell histiocytes, Whipple disease) [13], and metastases via either hematogenous spread (breast and lung carcinoma, lymphoma) or CSF seeding (medulloblastoma, ependymoma, germinoma). Pituitary stalks infiltrated by granulomatous disease usually are uniformly thickened, wheras stalk infiltration by tumor generally produces a nodular contour. Both types of pituitary abnormalities can readily be identified with high-resolution CT or MR.

Patients with Langerhans cell histiocytosis often have other lesions, such as mastoiditis, honeycomb lung, and lytic bone
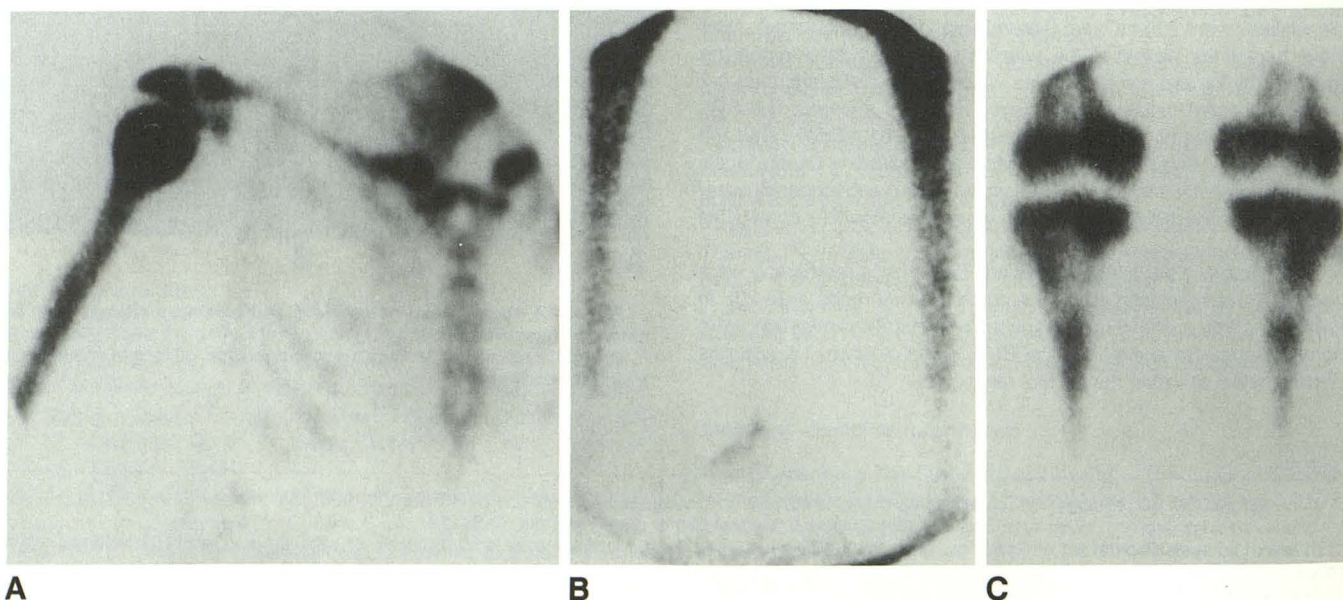

A **B** **C**

Fig. 2.—A–C, 99mTc-MDP whole body bone scan showed increased osteoblastic activity in all long bones such as humerus (A), femur (B), and tibia (C)).

Fig. 3.—A and B, Sagittal (A) and coronal (B) T1-weighted images (600/20) of sella region reveal slightly thickened hypothalamus and upper pituitary stalk (median eminence) (*short arrow*). There is a small area of lower signal intensity in prominent posterior lobe (*long arrow*), simulating a pituitary adenoma. Also, there is an area of lower signal intensity in anterior clivus (*open arrow*). The high signal intensity normally seen in the posterior lobe is not seen.

C and D, Postcontrast sagittal (C) and coronal (D) T1-weighted images (600/20) of sella show mildly prominent enhancement at median eminence (*long arrow*). The posterior lobe low-signal area is not intensely enhanced (*short arrow*) and the low-signal area in clivus enhanced with contrast (*curved arrow*).
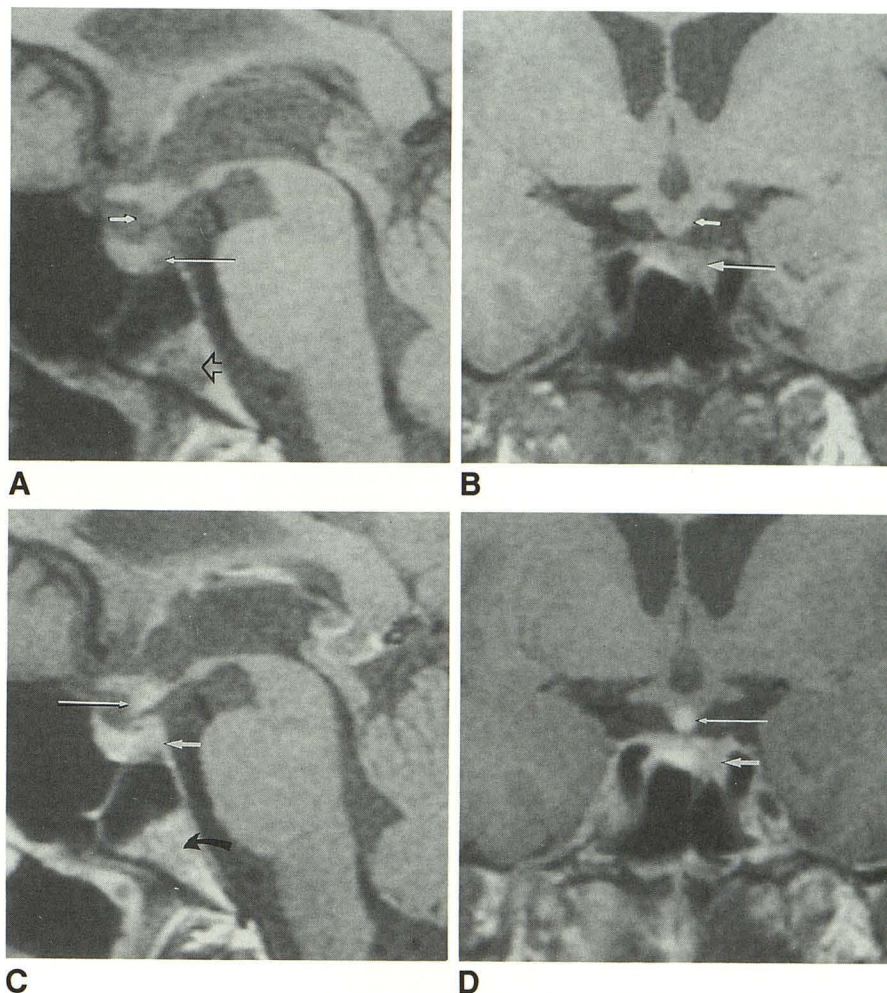
lesions; while those with tuberculosis or sarcoidosis usually have abnormal chest radiographs. Usually, patients with hematogenous metastatic disease are older, and the diabetes insipidus is transient. Patients with hypothalamic region CSF metastases from a pineal germ cell tumor frequently have Parinaud syndrome resulting from a primary tumor involving the tectum. Rarely, metabolic dysfunction (hypokalemia, hypercalcemia) or even disseminated intravascular coagulation can induce clinical symptoms of central diabetes insipidus [15].

We previously reported a case of Erdheim-Chester disease with CNS infiltration presenting multiple parasagittal masses, with persistent enhancement with gadopentetate dimeglumine noted on T1-weighted images 6 days after contrast administration [12]. While the precise mechanism of the contrast enhancement is unknown, it seems possible that the intact gadolinium complex was phagocytosed by histiocytes.

In the present case, there was abnormal enlargement of the median eminence and pituitary stalk, but only slight contrast enhancement of the median eminence. The differential diagnosis for a patient with diabetes insipidus and enlargement of the hypothalamus would include Langerhans cell histiocytosis [16], germ cell tumor [17], hypothalamic glioma,

craniopharyngioma [18, 19], tuberculosis or sarcoidosis [20], and distant metastases [21]. In this case, however, the radiographically distinctive symmetric osteoblastic findings in peripheral long bones suggested the diagnosis of Erdheim-Chester disease. The occurrence of diabetes insipidus and bone symptoms in the same patient suggests Erdheim-Chester disease with involvement of the hypothalamus, but in the absence of biopsy results this remains unproved. The enhancing lesion at the anterior clivus might represent another infiltrative lesion. There is at least one reported case [11] of central diabetes insipidus and other pituitary deficiencies presenting several years before the onset of symptoms leading to the diagnosis of Erdheim-Chester disease.

The origin of the hyperintense signal of the posterior pituitary on T1-weighted images is currently a matter of considerable debate [22–26]. Although the absence of high signal intensity in the posterior lobe is not diagnostic of central diabetes insipidus, we have never observed a hyperintense posterior pituitary in any diabetes insipidus patient, including a recent series of 30 cases (Tien, unpublished data). Hyperintensity of the posterior lobe has also been observed in 63–100% of healthy subjects in different studies [23, 25, 27]. Patients with central diabetes insipidus and Langerhans cell

histiocytosis have a combination of thickened pituitary stalk and absence of high signal intensity of the posterior pituitary [16, 24]. In a previously reported case of Erdheim-Chester disease [12] the patient had a normal-appearing posterior pituitary with a hyperintense signal on T1-weighted images, but this patient did not have diabetes insipidus.

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