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Pituitary stalk thickening with diabetes insipidus preceding typical manifestations of Langerhans cell histiocytosis in children

S. Schmitt[1], W. Wichmann[2], E. Martin[1], M. Zachmann[1], E. J. Schoenle[1]

Department of [1]Paediatrics, [2]Neuroradiology, University of Zurich, Steinwiesstrasse 75, CH-8032 Zurich, Switzerland

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Abstract. In up to 25% of cases of children with central diabetes insipidus no organic cause can be documented. We present three boys (age 2.2, 2.3 and 6 years at diagnosis) with acute onset central diabetes insipidus, in whom the only pathological finding using MRI was a thickened central part of the pituitary stalk (> 2.5 mm). Recent reports demonstrate similar MRI findings in adults with Langerhans cell histiocytosis (LCH), sarcoidosis, or tuberculosis, and in children with proven LCH and diabetes insipidus. In those adults with LCH, the pituitary stalk lesion has been histologically verified as a sequela of LCH. In contrast, in two of our three patients pituitary stalk thickening preceded the typical peripheral lesions of LCH by several months, whereas in the third patient there is as yet no evidence of systemic disease. We conclude that thickening of the central part of the pituitary stalk might represent the first manifestations of LCH clinically presenting with diabetes insipidus. MRI investigation of the pituitary stalk in children with unexplained central diabetes insipidus and accurate follow up in patients with thickening of the pituitary stalk in necessary to avoid missing other manifestations of a systemic disease.

Key words: Diabetes insipidus – Pituitary stalk thickening – Langerhans cell histiocytosis – Bone lesions – Histiocytosis-X

Introduction

Central diabetes insipidus (DI) is rare in children. It usually results from neoplasia (pre- or postsurgical), head injuries, infection or intracranial defects such as septo-optic dysplasia [8], or is found in patients with Langerhans cell histiocytosis (LCH) (formerly named histiocytosis X) [5]. Also a familial form with autosomal dominant inheritance is known [10]. In up to 25% of case no organic cause can be documented [14]. Recently, thickening of the central part of the pituitary stalk, detected by MRI, has been demonstrated [15] in adults with DI and LCH, tuberculosis or sarcoidosis and in children with LCH [9].

We present three boys (aged 2.2, 2.3, 6.5 years) with acute onset central DI, in whom MRI revealed similar findings, without any further historical, clinical or laboratory evidence for one of these systemic diseases. In two of them, however, lesions typical of LCH became evident several months later.

Correspondence to: E. J. Schoenle

Abbreviations: DI = Diabetes inspidius; DDAVP = 1-desamino-8-D-arginine vasopression; LCH = Langerhans cell histiocytosis

Case reports

Case 1

This child admitted because of progressive polydipsia and polyuria at the age of 2.2 years. The personal and family history was unremarkable. Fluid intake was about 1.7–2.5 l day. Height, growth velocity, weight and head circumference were normal [12]. DI was diagnosed after a water deprivation test (weight loss > 5%, urine osmolality: 104 mmol/kg, urine specific gravity < 1004, plasma osmolality 285 mmol/kg). Intranasal 1-desamino-8-D-arginine vasopressin (DDAVP) normalized urine and serum values. MRI revealed a symmetrical thickening (3.1 mm) of the central part of the pituitary stalk (Fig. 1a).

Case 2

A 2.3-yar-old boy on admission, had a history of severe perinatal asphyxia but nevertheless normal development for age. Brain MRI had been performed at age 12 and 18 months, showing no anomaly. He was referred for evaluation because of increasing fluid intake during 4 months. Height, growth velocity, weight and head circumference were also normal [12]. Basal fluid intake was about 5.5 l/day. A 1-h trial of water deprivation suggested the diagnosis of DI (urine osmolality 63 mmol/kg, urine specific gravity 1001,

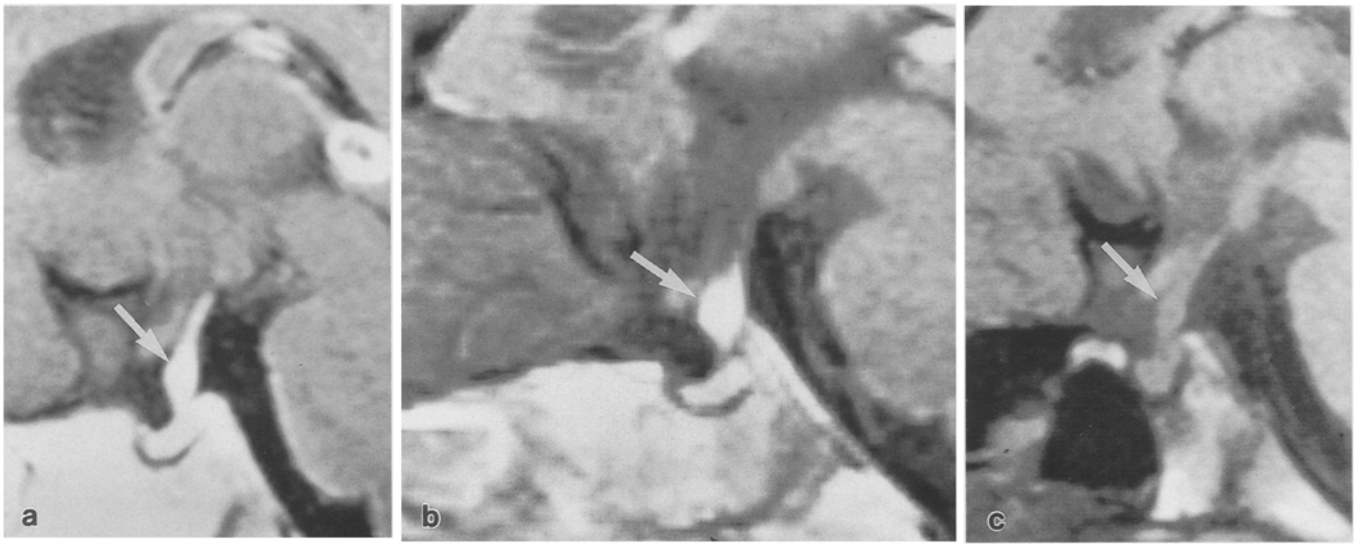

Fig. 1a–c. MRI before (**c**, case 3) and after gadolinium (**a**, case 1; **b**, case 2) in three patients with DI and symmetric thickening (3.0 mm, 3.1 mm and 3.5 mm) of the central part of the pituitary stalk (*see arrows*). Cases 1 and 2 developed typical peripheral lesions of LCH 6 months and 4 months after MRI

plasma osmolality 294 mmol/kg). MRI showed symmetrical thickening (3.5 mm) of the central pituitary stalk (Fig. 1b) as the only pathological finding. On DDAVP medication, the boy was doing well.

Case 3

This patient was referred at age 6 years because of polydipsia and secondary enuresis. His personal and family history are without any relevant events. Height, growth velocity, weight and head circumference were normal [12]. Fluid intake was 5–7 l/day. The diagnosis of DI was made after a water deprivation test (weight loss > 5%, urine osmolality 106–420 mmol/kg, urine specific gravity 1002, plasma osmolality 308 mmol/kg). With intranasal DDAVP all values could be normalized. MRI showed a thickened central part (3.0 mm) of the pituitary stalk (Fig. 1c) and no further cinical or laboratory abnormalities were noted.

Methods

Hormone levels in all three patients were measured using commercial radio-immuno-assays and fluoro-immuno assays.

MRI findings (Fig. 1)

MRI [7] in the three boys revealed symmetrical thickening of the central part of the pituitary stalk (> 2.5 mm) with homogeneous gadolinium contrast enhancement [13]. The high signal enhancement of the posterior lobe, which is seen in healthy subjects on T1-weighted MRI was absent in all, indicating absence of ADH in the posterior pituitary lobe [2, 3, 13].

Clinical, radiological and laboratory follow up

During follow up LCH was diagnosed in two of the three patients 6 months (case 1) and 4 months (case 2) after diagnosis of central DI. Both showed bone lesions – one at the tibia, the other one at the skull – which were surgically removed and classified as histologically typical lesions of LCH according to the Histiocyte Society [4] (tibia biopsy: positive for CD1, CD3 and L26; skull biopsy: positive for S-100 protein and T-cell marker UCHL 1). The third patient did not show any clincial evidence of LCH, tuberculosis or sarcoidosis up to now, whereas MRI of the hypothalamo-pituitary area revealed neither progression nor regression of the pituitary stalk thickening. In all patients, evaluation of the hypothalamo-adenohypophyseal axis did not show any additional hormonal defect besides an elevated serum growth hormone concentration in case 2, which was confirmed several times.

Discussion

DI most often occurs as a sequela of acute or systemic disease [1, 5, 6, 8, 10]. With advanced imaging techniques [7, 13], we found a thickening (> 2.5 mm) of the central part of the pituitary stalk in three boys initially diagnosed as idiopathic DI. Tien et al. [15] recently made the same observation in adults with LCH (verified by stalk biopsy) and in adults with tuberculosis or sarcoidosis. Maghnie et al. [9] described similar lesions in five children with DI and already diagnosed LCH of bone, skin and liver.

In contrast to the recent reports our patients presented with DI and pituitary stalk thickening as the primary symptom. Within 6 months after the onset of DI, typical peripheral bone lesions of LCH developed in two of the three patients. This suggests, that the thickening of the pituitary stalk might – in analogy to the patients of Tien et al [15] – represent a local manifestation of LCH responsible for the DI. We suspect that the same is true for our third patient, in whom no evidence of LCH, tuberculosis or sarcoidosis so far has been found. DI may precede manifestations of LCH for as long as 15 years [11].

We conclude that in children with central DI, special attention should be paid to the appearance of the pituitary stalk using MRI with gadolinium administration which is the most sensitive examination for the various

manifestations of LCH in the central nervous system [7, 13]. According to recent reports our results suggest that pituitary stalk thickening might represent the first infiltrative lesion of LCH. In children biopsy of the thickened pituitary stalk for histological verification of the aetiology is not justified. Pituitary stalk thickening due to tuberculosis or sarcoidosis has not been shown to occur in children, but should also be considered. Therefore careful clinical follow up is required to avoid missing further clinical signs of systemic disease. In addition the question arises whether or not the reported pituitary stalk thickening in children with DI should be classified and treated as cerebral manifestation of LCH according to international LCH study protocols. This might influence the current staging and therapeutic intervention in patients with LCH.

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References

1. Buchfelder M, Fahlbusch R, Walther M, et al (1989) Endocrine disturbances in suprasellar germinomas. Acta Endocrinol (Copenh) 120:337–342
2. Cacciari E, Zucchini S, Carla G, et al (1990) Endocrine function and morphological findings in patients with disorders of the hypothalamo-pituitary area: a study with magnetic resonance. Arch Dis Child 65:1199–1202
3. Chiumello G, Di Natale B, Pellini C, et al (1989) Magnetic resonance imaging in diabetes insipidus (letter). Lancet I (8643): 901
4. Chu T, D'Angio GJ, Favara B, et al (1987) Histiocytosis syndromes in children. Lancet I:208–209
5. Dunger DB, Broadbent V, Yeoman E, et al (1989) The frequency and natural history of Diabetes insipidus in children with Langerhans cell Histiocytosis. N Engl J Med 321:1157–1162
6. Gnehm HE, Bernasconi S, Zachmann M (1979) Posttraumatic anterior pituitary insufficiency in childhood. Helv Paediatr Acta 34:529–532
7. Graif M, Pennock JM (1986) MR Imaging of Histiocytosis X in the central nervous system. Am J Neuro Radiol 7:21–23
8. Greger N, Kirkland RT, Clayton GW, et al (1986) Central diabetes insipidus. Am J Dis Child 140:551–554
9. Maghnie M, Villa A, Arico M, et al (1992) Correlation between magnetic resonance imaging of posterior pituitary and neurohypophyseal function in children with diabetes insipidus. J Clin Endocrinol Metab 74:795–800
10. Miyamoto S, Sasaki N, Tanabe Y (1991) Magnetic resonance imaging in familial central diabetes insipidus. Neuroradiology 33:272–273
11. Pomarède R, Czernichow P, Rappaport R, et al (1980) Le diabète insipide pitressonsensible de l'enfant. Arch Fr Pediatr 37: 37–44
12. Prader A, Largo RH, Molinari L, et al (1989) Physical growth of Swiss children from birth to 20 years of age. First Zurich longitudinal study of growth and develoment. Helv Paediatr Acta [Suppl] 52:1–125
13. Rosenfield NS, Abrahams J, Komp D (1990) Brain MR in patients with Langerhans cell histiocytosis: findings and enhancement with Gd-DTPA Pediatr Radiol 20:433–436
14. Tien R, Kucharczyk J, Kucharczyk W (1991) MR imaging of the brain in patients with diabetes insipidus. Am J Radiol 157: 123–132
15. Tien RD, Newton HT, McDermott MW, et al (1990) Thickening pituitary stalk on MR images in patients with diabetes insipidus and Langerhans cell histiocytosis. Am J Neuro Radiol 11:703–708