Austin Journal of Endocrinology and Diabetes

Austin Publishing Group

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Case Report

Infundibulo-hypophysitis: A Case Diagnosed by Magnetic Resonance Images Over Time, with Literature Review

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Received: August 18, 2014; **Accepted:** September 20, 2014; **Published:** September 25, 2014

Abstract

Infundibulo-hypophysitis is a rare type of autoimmune hypophysitis that involves the pituitary stalk and pituitary. It currently has no clear diagnostic criteria, and is often misdiagnosed as pituitary tumor, leading to unnecessary surgery. Here, we present a 50-year-old woman with in fundibulo-hypophysitis who was diagnosed using multiple magnetic resonance images taken over several months at follow-up. We discuss the course of her disease and her treatment, the imaging features of infundibulo-hypophysitis and similar diseases, and review the relevant literature.

Keywords: Pituitary; Auto-immune disease; Diagnosis

Introduction

Infundibulo-hypophysitis (IH) has no clear diagnostic criteria as of yet. As its clinical manifestations are similar to those of pituitary tumor, hypophysitis is often misdiagnosed as pituitary tumor, which can lead to unneeded surgical treatment [1–3]. Imaging helps to diagnose and treat IH, but its details are rarely described in the literature. Here, we describe a case that used magnetic resonance imaging (MRI) over several months to track changes in autoimmune IH and diagnose it at follow-up, and we review the pertinent literature.

Case Presentation

In August 2012, our patient, a 50-year-old woman, began to display polydipsia, polyuria, nausea, vomiting and other symptoms for no apparent reason; her daily water intake was about 4L, with nocturia 5–6 times/d, weight loss of about 10 kg, and blurred vision in her right eye. She had experienced amenorrhea for half a year. She had no previous history of hypothalamus or pituitary surgery. In October 2012, examination at our hospital showed: temperature: 35.6 °C; pulse: 84 /min; blood pressure: 107/81 mmHg; and BMI 23.3kg/m^2, with no binocular visual field defect, some right eye visual loss, systemic rough skin, no thyroid enlargement, no hair change and no abnormalities in heart, lung or abdomen. Her laboratory results showed urine specific gravity: <1.010; blood electrolytes and blood glucose are in Table 1, endocrine related hormones are in Table 2, no abnormal liver and kidney functions; tumor markers CA-199: 30U/mL, CA-125: 17.2IU/mL, AFP: 5.63ng/ml, antinuclear antibodies$^-$, water deprivation-vasopressin$^+$.

The first pituitary MRI results (Figure1A, B) were equivocal. Although we did not exclude pituitary adenoma, after considering the clinical manifestations and auxiliary examination results, our initial differential diagnosis was hypopituitarism or IH. The patient was given experimental corticosteroid immunosuppressive therapy and replacement therapy. For 9 days, the patient complained of polydipsia and polyuria, but her nausea was significantly reduced. Her retested laboratory results were urine specific gravity: 1.012; free T3: 2.86 pmol/l; free T4: 0.61ng/dl; thyroid stimulating hormone: 1.04 uIU/ml; and prolactin (PRL): 1.74 ng/ml (bromocriptine:1.25mg/d × 3d). Her blood electrolytes returned to normal, so she was discharged with continuing replacement therapy outside the hospital.

In January 2013, the patient returned to our hospital with aggravated polydipsia and polyuria, accompanied by nausea in the previous two months and vomiting for 1 week; her body weight had increased by 10 kg, with no headache, no binocular visual field defect and no vision loss, but with systemic hair loss. Physical examination showed: BMI of 28 kg/m^2 (obese), systemic dry skin, eyebrows, hair, armpit hair falling off unlike before, but no thyroid enlargement. Her laboratory results were urine specific gravity: 1.000; blood sodium and chlorine increased (Table 1); and endocrine related hormones decreased from before (Table 2). A new pituitary MRI (Figure 1C, D) showed the HI lesion area reduced and pituitary obviously enlarged. As we considered that pituitary inflammation had decreased pituitary function, we continued her hormone replacement therapy. In 3 days, her PRL was 2.03ng/ml. As the pituitary stalk lesion had apparently increased her PRL, we discontinued her bromocriptine. The patient was discharged after symptoms improved.

In July, 2013, the patient returned with dizziness, nausea, vomiting and declining physical fitness; her daily water intake (about 2–3L/d) and urination frequency had decreased. Her urine specific gravity was then 1.020 and blood sodium and potassium levels were normal. She had increased blood HCO_3^-, which was thought to be caused by digestive juice loss rom vomiting (Table 1). Her endocrine related hormone levels suggested central hypopituitarism (Table 2). As a pituitary MRI plain scan (Figure1E, F) showed no pituitary stalk thickening and the pituitary volume was significantly reduced,

Table1: Blood electrolytes and glucose.

index/tim (normal range)	2012.10	2013.1	2013.7
Na (136-144mmol/l)	154.40	152.50	143.40
Cl (96-108mmol/l)	107.90	110.50	106.00
K (3.5-5.5mmol/l)	3.34	4.10	4.27
Ca (2.04-2.71mmol/l)	2.63	2.37	2.83
Mg (0.7-1.1mmol/l)	1.18	0.88	0.82
HCO_3^-(20.5-28.5mmol/l)	24.70	35.20	34.30
GLU (3.8-6.1mmol/l)	6.57	5.14	4.81

Na natrium; Cl Chlorine; K Potassium; Ca calcium; Mg magnesium; HCO_3^- bicarbonate radical; GLU glucose

Citation: Hou N, Wang C, Liu X, Sun X. Infundibulo-hypophysitis: A Case Diagnosed by Magnetic Resonance Images Over Time, with Literature Review. Austin J Endocrinol Diabetes. 2014;1(5): 1025.

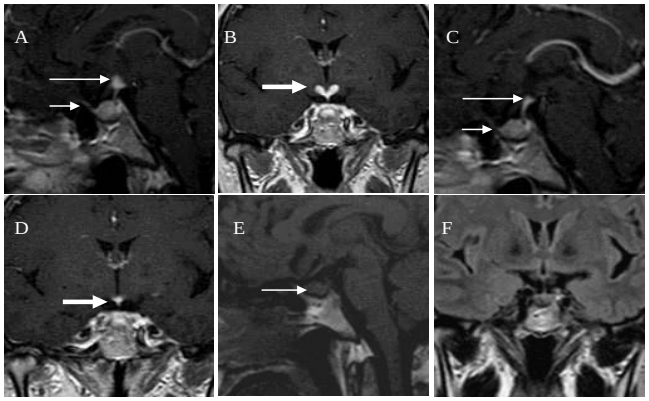

Figure 1: MRI images over time of 50-year-old female patient with infundibulo-hypophysitis.
August 2012: (A) Sagittal enhanced scan shows hypothalamus and infundibulum enlarged significantly (long arrow), with no significant pituitary stalk shift; the pituitary is swollen and the meninx is thickened and significantly enlarged, presenting the "dural tail sign" (short arrow); and (B) Coronal enhanced scan shows infundibulum is enlarged homogeneously, as "bean sprout" sign (thick arrow).
October 2012: (C) Sagittal enhanced scan shows infundibulum strengthening foci reduces more significantly than that in figure (A). The pituitary stalk has thickened and is significantly enlarged, especially on the top (long arrow), and the pituitary is still swollen (short arrow); and (D) Coronal enhanced scan shows upper pituitary stalk is thickened and enlarged (wide arrow). July 2013: (E) Sagittal scan; development of hypothalamus nipple is obscured, pituitary stalk is narrower and pituitary volume is reduced significantly (thin arrow); superior border of pituitary is rough; and (F) Coronal scan shows pituitary stalk is narrower compared with (B) and (D), and the upper pituitary stalk is greatly reduced.

autoimmune IH was diagnosed. Then the patient was discharged with continuing replacement therapy outside the hospital

Discussion

Lymphocytic hypophysitis is the major cause of IH, which is a type of autoimmune disease. Pituitary biopsy is the gold standard for diagnosis of autoimmune hypophysitis, but as this is not easy to carry out in clinical work, autoimmune hypophysitis is often misdiagnosed. The ability to make a correct diagnosis and avoid surgery with the aid of MRI, clinical manifestations and endocrine hormone determination is therefore practical.

The patient presented with central diabetes insipid us as her first symptom. Her initial examination showed high PRL (>200 ng/ml). A pituitary MRI showed the hypothalamus and infundibulum were enlarged significantly, pituitary stalk had no obvious shift, and the pituitary was swollen, which implied inflammation, although pituitary tumor was not ruled out. Hormone tests suggested central hypogonadism and central hypothyroidism. We attributed the high PRL to inflammation of the pituitary stalk or hypophyseal portal system, which interfered with dopamine secretion in the hypothalamus and infundibular nodule, or because the inflammation directly damaged PRL secretary cells, thus releasing PRL into the circulation [4]. So a PRL tumor was not considered for the time being.

Hormone therapy is an effective treatment for autoimmune IH. Glucocorticoid pulse treatment is preferred abroad [5], but the therapeutic dose, duration and curative effect are controversial [6]. Our short-term application of immunosuppressive therapy with glucocorticoid did not prevent progression of the patient's disease;

Table 2: Endocrine hormones.

index/time (normal range)	2012.10	2013.1	2013.7
FT_3 (3.1-6.8 pmol/l)	3.19	2.83↓	3.15↓
FT_4 (0.93-1.7 ng/dl)	0.61↓	0.93↓	0.65↓
sTSH (0.27-4.2 uIU/ml)	5.22↑	1.04↓	0.62↓
FSH (25.8-134.8 IU/L)	6.70↓	2.45↓	4.96↓
LH (7.7-58.5 IU/L)	<0.10↓	<0.10↓	0.10↓
E_2 (<10-39.5 pg/ml)	<5.00	<5.00	5.00
PRL (3.38-24.02 ng/ml)	360.40↑	185.00↑	40.6↑
COR (442±276 nmol/l)	645.48	66.79↓	13.52↓
ACTH (7.2-63.3 pg/ml)	27.19	5.20↓	1.35↓

FT_3 free triiodothyronine; FT_4 free thyroxine; sTSH Sensitive Thyroid Stimulating Hormone; FSH Follicle-Stimulating Hormone; LH Luteinizing Hormone;E_2 estradiol; PRL prolactin; COR cortisol; ACTH Adrenocorticotropic Hormone

after 3 months (January 2013), the patient presented with exacerbated symptoms; her prednisone dose was reduced to 15mg/d. An MRI showed the area of infundibulum was enlarged and its foci reduced, pituitary stalk was thickened and enlarged, pituitary enlarged, and pituitary hormone levels further reduced; we continued to use hormone replacement therapy. Nine months after the initial diagnosis (July 2013), the patient's MRI showed that her pituitary had narrowed; hormone tests suggested panhypopituitarism. Eventually, autoimmune IH was diagnosed.

The patient's pituitary MRIs over time showed the evolution of her IH, from the "bean sprout" enlargement, to the disappearance of the lesion and narrowing of the pituitary. The present study suggests that hypophysitis MRI manifestations include symmetrical and diffuse enlargement of the pituitary; sellar bottom's bone destruction is less, the sellar bottom is flat; when the lesion spreads to suprasellar region to invade the infundibulum and hypothalamus, the pituitary stalk thickens and the dura is also involved, leading to the "dural tail sign." This is an important imaging sign to distinguish pituitary tumor and hypophysitis [7, 8]. Over time, the ultimate outcome of lymphocytic hypophysitis may include an empty sella turcica [9], which some scholars [10–12] believe may be the ultimate outcome of lymphocytic hypophysitis. However, a diagnosis of hypophysitis should rule out pituitary adenoma, craniopharyngioma, and germinoma [13].

An MRI of pituitary micro adenoma often shows as an asymmetrically enlarged pituitary, apparently filled by a defect, with a shifted pituitary stalk. The enlarged microadenoma may appear less dense than normal glands, which can cause gland asymmetry or pituitary stalk separation [14]. A pituitary tumor generally does not show a "dural tail" sign [4].

Craniopharyngioma is often seen in the suprasellar region, and presents with normal structure of pituitary and pituitary stalk; the pituitary's compression deformation can be seen in intrasellar craniopharyngioma; calcification of the cystic tumor wall is the characteristic manifestation of the disease [13,15], and helps to identify it.

Germinoma is more common in children, and presents as hypopituitarism and diabetes insipid us. It may appear with a thickened pituitary stalk and absence of the high signal of neurohypophysis—easily misdiagnosed as hypophysitis [16,17,18]. It is sensitive to radiation, and can be given experimental treatment if doubted. Presence of cerebrospinal fluid, alpha fetoprotein and serous human chorionic gonadotropin levels facilitates its diagnosis [13].

Therefore, to patients suspected of having hypophysitis, we should combine clinical manifestations and examinations of hormone and imaging to make comprehensive assessment of patients' condition. Symptomatic treatment and regular follow-up imaging observation are helpful to diagnose and treat this disease.

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Austin J Endocrinol Diabetes - Volume 1 Issue 5 - 2014
ISSN : 2381-9200 | www.austinpublishinggroup.com

Citation: Hou N, Wang C, Liu X, Sun X. Infundibulo-hypophysitis: A Case Diagnosed by Magnetic Resonance Images Over Time, with Literature Review. Austin J Endocrinol Diabetes. 2014;1(5): 1025.