INTRODUCTION

Lymphocytic infundibuloneurohypophysitis is a rare disorder in which neurohypophyseal function is impaired by an autoimmune process. Although several etiologies for this rare entity have been suggested, its occurrence following transsphenoidal adenectomy has not been reported. A 20-year-old man presented with diabetes insipidus – seven years after successful transsphenoidal microadenomectomy for Cushing’s disease, first diagnosed at the age of 13. Seven years later, he developed fairly rapid onset of polydipsia and polyuria. Magnetic resonance imaging demonstrated swelling of the posterior pituitary gland with thickening of the pituitary stalk. Endocrinological evaluation revealed neurohypophyseal dysfunction without the adenohypophysis being affected. On the basis of these findings, a diagnosis of lymphocytic infundibuloneurohypophysitis was made. The mass lesion of the posterior pituitary resolved after the administration of corticosteroids for two months and no operation was required. Lymphocytic infundibuloneurohypophysitis should be considered in the differential diagnosis of pituitary mass lesions following transsphenoidal surgery, especially when the mass is confined to the posterior pituitary gland with neurohypophyseal function being compromised.

CASE REPORT

Clinical presentation

A 21-year-old man was admitted to our clinic, six months after suddenly developing polydipsia and polyuria. At the age of 13, he had presented with short stature and rapid onset of obesity and was diagnosed with Cushing’s disease for which he underwent a transsphenoidal adenomectomy. His hormonal evaluation at the time showed elevated plasma levels of ACTH and cortisol. No other endocrine abnormality was detected (Table 1). Serum ACTH and cortisol were not suppressed by 2 mg of dexamethasone. However, 8 mg of dexamethasone significantly suppressed both basal levels. An adrenal scintigram showed bilateral adrenal hyperplasia and MR imaging of the brain showed a small intrasellar microadenoma (Fig. 1). A diagnosis of Cushing’s disease was made and he underwent a transsphenoidal microadenomectomy via the sublabial approach. After resection of the tumor, reconstruction of the sella

Delayed lymphocytic infundibuloneurohypophysitis following successful transsphenoidal treatment of Cushing’s disease

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Summary: Lymphocytic infundibuloneurohypophysitis is a rare disorder in which neurohypophyseal function is impaired by an autoimmune process. Although several etiologies for this rare entity have been suggested, its occurrence following transsphenoidal adenectomy has not been reported. A 20-year-old man presented with diabetes insipidus – seven years after successful transsphenoidal microadenomectomy for Cushing’s disease, first diagnosed at the age of 13. Seven years later, he developed fairly rapid onset of polydipsia and polyuria. Magnetic resonance imaging demonstrated swelling of the posterior pituitary gland with thickening of the pituitary stalk. Endocrinological evaluation revealed neurohypophyseal dysfunction without the adenohypophysis being affected. On the basis of these findings, a diagnosis of lymphocytic infundibuloneurohypophysitis was made. The mass lesion of the posterior pituitary resolved after the administration of corticosteroids for two months and no operation was required. Lymphocytic infundibuloneurohypophysitis should be considered in the differential diagnosis of pituitary mass lesions following transsphenoidal surgery, especially when the mass is confined to the posterior pituitary gland with neurohypophyseal function being compromised.

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Keywords: lymphocytic infundibuloneurohypophysitis, Cushing’s disease, diabetes insipidus, corticosteroids

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KEYWORDS: lymphocytic infundibuloneurohypophysitis, Cushing’s disease, diabetes insipidus, corticosteroids

INTRODUCTION

Lymphocytic infundibuloneurohypophysitis is a rare disorder in which neurohypophyseal function is impaired by an autoimmune process. Although several etiologies for this rare entity have been suggested, lymphocytic infundibuloneurohypophysitis following transsphenoidal surgery has not previously been reported. Here, we report a case of lymphocytic infundibuloneurohypophysitis manifesting as diabetes insipidus, seven years after the treatment of Cushing’s disease by transsphenoidal adenomectomy.

CASE REPORT

Clinical presentation

A 21-year-old man was admitted to our clinic, six months after suddenly developing polydipsia and polyuria. At the age of 13, he had presented with short stature and rapid onset of obesity and was diagnosed with Cushing’s disease for which he underwent a transsphenoidal adenomectomy. His hormonal evaluation at the time showed elevated plasma levels of ACTH and cortisol. No other endocrine abnormality was detected (Table 1). Serum ACTH and cortisol were not suppressed by 2 mg of dexamethasone. However, 8 mg of dexamethasone significantly suppressed both basal levels. An adrenal scintigram showed bilateral adrenal hyperplasia and MR imaging of the brain showed a small intrasellar microadenoma (Fig. 1). A diagnosis of Cushing’s disease was made and he underwent a transsphenoidal microadenomectomy via the sublabial approach. After resection of the tumor, reconstruction of the sella

REFERENCES

turcica floor was performed using autologous fascia, fatty tissue obtained from the thigh and α-cyanoacrylate. No artificial materials were used except for the tissue glue. His post-operative course was uneventful and fulfilled the criteria for remission of Cushing’s disease. Plasma levels of ACTH, cortisol and urinary 17-OHCS after surgery were 5.1 pg/ml, 0.45 μg/dl and 1.1 mg/day, respectively (Table 1). There was no evidence of pituitary adenoma recurrence during the follow-up period.

Seven years after surgery, the patient complained of polydipsia and polyuria. At the outpatient clinic, neurological examination was normal, but his urine volume was measuring 4000–6000 ml/day. Peak plasma and urine osmolalities during water deprivation were 290 and 99 mOsm/kg, respectively. Urinary osmolality increased in response to subcutaneous injection of vasopressin to 321 mOsm/kg. Plasma concentrations of adrenocorticotropic hormones were normal (Table 1). MR imaging demonstrated swelling of the posterior pituitary gland and thickening of the pituitary stalk with homogenous enhancement (Fig. 2). There was loss of the hyperintense signal from the neurohypophysis on T1-weighted images (Fig. 3). These findings had appeared simultaneously with diabetes insipidus. Chest X-ray showed no sign of pulmonary infiltration or bilateral hilar lymphadenitis and fundoscopy showed no retinochoroidal granulomas suggestive of sarcoidosis. The serum angiotensin converting enzyme (ACE) level was 13.4 U/ml (reference value was 7–25 U/ml).

Table 1 Sequential changes of the results of hormonal examination

<table>
<thead>
<tr>
<th></th>
<th>Before transsphenoidal adenomectomy</th>
<th>After transsphenoidal adenomectomy</th>
<th>At the time of DI onset</th>
<th>After steroid administration</th>
<th>Unit and normal value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH</td>
<td>32.6</td>
<td>5.1</td>
<td>35.9</td>
<td>22.3</td>
<td>4.4–48.0 pg/ml</td>
</tr>
<tr>
<td>Cortisol</td>
<td>26.68</td>
<td>&lt;0.45</td>
<td>10.65</td>
<td>4.01</td>
<td>5.40–22.9 μg/dl</td>
</tr>
<tr>
<td>T4</td>
<td>5.5</td>
<td>6.0</td>
<td>–</td>
<td>–</td>
<td>5.50–11.00 μg/dl</td>
</tr>
<tr>
<td>TSH</td>
<td>0.7</td>
<td>3.09</td>
<td>1.366</td>
<td>1.656</td>
<td>0.310–4.690 μg/ml</td>
</tr>
<tr>
<td>GH</td>
<td>3.8</td>
<td>3.02</td>
<td>0.7</td>
<td>0.9</td>
<td>0.1–4.8 ng/ml</td>
</tr>
<tr>
<td>FSH</td>
<td>1.06</td>
<td>10.0</td>
<td>4.38</td>
<td>0.63</td>
<td>1.9–14.9 μIU/ml</td>
</tr>
<tr>
<td>LH</td>
<td>0.5</td>
<td>4.49</td>
<td>2.65</td>
<td>0.63</td>
<td>1.0–10.3 μIU/ml</td>
</tr>
<tr>
<td>T3</td>
<td>0.73</td>
<td>1.31</td>
<td>–</td>
<td>–</td>
<td>0.68–1.70 μg/ml</td>
</tr>
<tr>
<td>PRL</td>
<td>1.0</td>
<td>4.0</td>
<td>8.04</td>
<td>14.36</td>
<td>1.61–18.77 ng/ml</td>
</tr>
<tr>
<td>Free T3</td>
<td>–</td>
<td>–</td>
<td>2.93</td>
<td>2.83</td>
<td>2.5–4.3 ng/ml</td>
</tr>
<tr>
<td>Free T4</td>
<td>–</td>
<td>–</td>
<td>1.1</td>
<td>1.05</td>
<td>0.71–2.85 ng/ml</td>
</tr>
<tr>
<td>17-OHCS (urine)</td>
<td>20.7</td>
<td>1.1</td>
<td>–</td>
<td>–</td>
<td>3.0–5.8 μIU/ml</td>
</tr>
<tr>
<td>17-KS (urine)</td>
<td>7.1</td>
<td>0.3</td>
<td>–</td>
<td>–</td>
<td>3.3–5.8 μIU/ml</td>
</tr>
</tbody>
</table>

Fig. 1 T1-weighted MR imaging with Gd-DTPA before (A) and after (B) transsphenoidal surgery. The intrasellar mass lesion (arrow) was evident with an area of less enhancement (A), which disappeared after surgery (B).

Fig. 2 The sagittal (A) and coronal view (B) of T1-weighted MR imaging seven years after surgery, demonstrating the swelling of the posterior pituitary gland (arrowhead) and thickening of the pituitary stalk (arrow) with homogenous enhancement.

Treatment

A differential diagnosis including pituitary adenoma recurrence of Cushing’s disease, sarcoidosis, granulomatous hypophysitis, and lymphocytic infundibuloneurohypophysitis was made. The typical clinical and radiological findings for lymphocytic infundibuloneurohypophysitis persuaded us to undertake a diagnostic trial of medication (prednisolone administration; 5 mg/day), without surgical intervention. In addition, 2.5 μg of desmopressin acetate (1-deamino-8-D-arginine-vasopressin acetate trihydrate; DDAVP) was administered intranasally twice a day.

Post-treatment course

Follow-up MR imaging showed a marked decrease in the thickening of the neurohypophysis and pituitary stalk two months after treatment, remaining so for another 13 months post-treatment (Fig. 4). Endocrinological examination was normal except for the plasma cortisol level (Table 1). At this time, DDAVP supplementation was decreased (2.5 μg) to once every other day.

DISCUSSION

Lymphocytic adenohypophysitis and lymphocytic infundibuloneurohypophysitis are distinctly different clinical entities caused by different autoimmune processes.1,2 The neurohypophysis is histologically normal in most cases of lymphocytic adenohypophysitis, thus diabetes insipidus is uncommon.3 On the other hand, lymphocytic infundibuloneurohypophysitis presents with central diabetes insipidus,1,4,7 since the inflammation is localized...
to the neurohypophysis. The pathogenesis of lymphocytic infundibuloneurohypophysitis remains unresolved and its occurrence following transsphenoidal surgery has not previously been reported. MR imaging revealed characteristic findings of lymphocytic infundibuloneurohypophysitis, including swelling of the posterior pituitary gland, thickening of the pituitary stalk and loss of hyperintense signal of the neurohypophysis. This was recognized six years after surgery on T1-weighted images. In our case, MR imaging demonstrated swelling of the posterior pituitary gland and thickening of the pituitary stalk. Furthermore, endocrinological examination demonstrated neurohypophyseal dysfunction, while the adenohypophysis was not affected. Based on these findings, a diagnosis of lymphocytic infundibuloneurohypophysitis was made.

The relationship between lymphocytic infundibuloneurohypophysitis and Cushing’s disease in our case is unclear. The possible explanation of this rare association could be as follows. Since hypercortisolism in Cushing’s disease can impair immunological functions, the immunosuppressive state induced by Cushing’s disease could have inhibited the occurrence of lymphocytic infundibuloneurohypophysitis. The subsequent reduction of plasma glucocorticoid following surgery may then have contributed to the occurrence of lymphocytic infundibuloneurohypophysitis. In fact, autoimmune thyroiditis and transient Graves disease have been reported to occur after remission of Cushing’s disease. A latent autoimmune process in the thyroid, suppressed by hypercortisolism, developed into Graves disease after the abrupt reduction of plasma glucocorticoid level induced by surgery. Thus, the same process could have occurred in our case. Besides the autoimmune process mechanism, the surgical procedure may have contributed, at least in part, to the occurrence of inflammation around pituitary gland, especially with the use of artificial materials during surgery. In our case, we used x-cyanoacrylate during reconstruction of the sella turcica floor but do not consider that the infundibuloneurohypophysitis was due to a foreign body reaction.

The management of lymphocytic infundibuloneurohypophysitis is still controversial. Surgical intervention should be avoided, as it fails to improve lymphocytic infundibuloneurohypophysitis. In our patient the clinical and radiological findings strongly suggested lymphocytic infundibuloneurohypophysitis, the natural course of which is considered to be self-limiting, we therefore did not undertake surgical intervention. The administration of maintenance dose corticosteroid relieved both the diabetes insipidus and the swelling of the posterior pituitary gland on MR imaging. We thus recommend the use of corticosteroids, although their efficacy on lymphocytic infundibuloneurohypophysitis remains controversial.

In conclusion, we have presented, for the first time, a case of lymphocytic infundibuloneurohypophysitis, manifesting as diabetes insipidus, seven years after treatment of Cushing’s disease by transsphenoidal adenomectomy. Lymphocytic infundibuloneurohypophysitis should be considered in the differential diagnosis of post-transsphenoidal pituitary surgery mass lesions, especially when the mass is confined to the posterior pituitary gland and neurohypophyseal function is compromised. Steroids should be considered as first line treatment when lymphocytic infundibuloneurohypophysitis is the likely diagnosis.
An unusual case of hypertensive encephalopathy

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Summary This case report describes a 59-year-old male who presented with headaches, seizures and hypertension followed by coma. Initial magnetic resonance imaging showed T2 hyperintensities typical of Hypertensive Encephalopathy (HE), the follow up scans showed diffusion-weighted imaging (DWI) hyperintensities which is a rare finding in HE. DWI hyperintensities are typically suggestive of areas of cytotoxic damage, and the presence of these changes makes this case unusual, since the pathogenesis of HE is usually due to vasogenic oedema rather than cytotoxic damage of the brain tissue.

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INTRODUCTION

The radiological findings in Hypertensive Encephalopathy (HE) are variable. Magnetic resonance neuroimaging shows a characteristic posterior leuкоencephalopathy that predominantly affects the white matter of the parieto-occipital regions. These changes are best seen in the T2 weighted images. Studies with DWI imaging show that the leuкоencephalopathy is primarily due to vasogenic rather than cytotoxic oedema. The likely pathogenesis of vasogenic oedema is thought to be hypertensive cerebrovascular endothelial dysfunction, disruption of the blood–brain barrier with increased permeability, cerebral oedema and microhaemorrhage formation. There have been case reports of patients with HE who had hyperintensities in DWI images. It is not clear as to the underlying pathogenesis of these changes, but autoregulatory vasoconstriction leading to hypoperfusion could be a possible mechanism. It is not clear whether HE patients with DWI changes have a poorer prognosis.

CASE REPORT

Our patient was a 59-year-old man admitted to Geelong hospital with a 6-week history of headaches, nausea and vomiting. On the day of admission, he was found confused and brought to emergency department. On presentation, he was disoriented in time and place, GCS score was 14, and he was moving all limbs symmetrically. The blood pressure was raised at 250/90, pulse 80 sinus rhythm, and afebrile. Neurological examination did not reveal any focal deficits, in particular no neck stiffness. Fundoscopy was limited but no abnormalities were detected. Other systems examination was unremarkable.

The background medical history included right sided carotid endarterectomy in 2000 for right hemispheric TIAs and hypertension (160/100) noted six weeks prior to presentation. This was not treated at that time. Medications included Aspirin 150 mg daily. He was a smoker and had an ethanol intake approximately 60 g/day.

Initial investigations on admission showed Hb 163 g/L, platelets $10^9/L, 338 \times 10^9/L$, wcc $338 \times 10^9/L$, ECG revealed sinus rhythm with no left ventricular hypertrophy (LVH), CT brain scan revealed normal attenuation in the upper pons and midbrain suggestive of infarction or central pontine myelinolysis. CSF examination results: WBC 0 per mm$^3$, protein 0.63 g/L and glucose 4.0 mmol/L, HSV PCR, VDRL, cryptococcal and mycobacterial studies were negative.

MRI brain scan performed within 24 h of admission is shown in Fig. 1 which showed extensive signal abnormality throughout the brainstem, subcortical white matter and left temporal lobe. At this time, the DWI images and MR angiogram were normal. The patient was commenced on Aciclovir 700 mg IVI 8 hourly, IV pethidine and IV methyl prednisone 1 g daily for 3 days.

While in intensive care the patient’s blood pressure fluctuated quite markedly (Fig. 2). He was hypertonic in upper and lower