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Case Report

A case of hypophysitis in a young male patient

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Introduction

Lymphocytic hypophysitis, which is autoimmune inflammation of pituitary gland, is initially characterised by lymphocytic infiltration and enlargement followed by destruction of pituitary gland. Although most cases occur in females during pregnancy and early post-partum period, it may rarely be seen in males.¹ We describe a young male patient who presented with acute onset pituitary enlargement with left third cranial (oculomotor) nerve palsy, which resolved completely without any residual deficit.

Case report

A 42-year-old male patient presented with history of acute onset bifrontal headache with projectile vomiting of 3 days

duration. There was no history of fever, visual symptoms, altered sensorium or focal neurological deficits. On day 3 of illness, he developed sudden onset binocular diplopia. On examination, he was afebrile and normotensive with no postural fall of blood pressure. He had left-sided third cranial nerve palsy without pupillary involvement. Other cranial nerves were normal. There was no papilledema or any other neurological deficit. Urgent non-contrast computerised tomography scan brain was normal with no intracerebral haemorrhage. Magnetic resonance imaging (MRI) scan of the brain revealed enlarged pituitary gland measuring 12 mm × 19 mm × 10 mm with convex superior border protruding into suprasellar cisterns but not reaching optic chiasma and thickened infundibular stalk, which was in midline (Figs. 1 and 2). Cerebrospinal fluid examination revealed WBC 20/mm³ (lymphocytes), RBC 6/mm³, protein 87 mg/dl and glucose 65 mg/dl (blood glucose 102 mg/dl). Hormonal evaluation revealed basal hypocortisolism (3.2 mcg/dl) with normal ACTH levels (26 pg/ml) suggestive of basal hypocortisolemia or secondary adrenal insufficiency. He showed a normal cortisol response to ACTH stimulation (22 mcg/dl). The rest of the pituitary hormone profile including LH, FSH, prolactin, TSH and free T4 was normal. His urine output was normal and osmolality was 687 mOsm/kg (300–900) suggesting no evidence of diabetes insipidus (DI). Serum electrolytes, glucose levels and renal and liver function tests were normal. Markers of autoimmunity (ANA, dsDNA and anti-TPO antibody) were negative. Serum angiotensin converting enzyme was normal. He was started on oral corticosteroids in anti-inflammatory dose with tablet prednisolone 60 mg daily. Within a week, he had complete resolution of symptoms and left third cranial nerve palsy

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Fig. 1 – Contrast enhanced Magnetic resonance imaging (MRI) scan (Coronal view) of the brain showing enlarged pituitary gland with homogenous enhancement measuring $12 \times 19 \times 10$ mm with convex superior border protruding into suprasellar cisterns with thickened infundibular stalk in midline (Arrow).

Fig. 3 – Follow up post treatment contrast enhanced MRI brain (Coronal view) showing resolution of the pituitary mass.

Fig. 2 – Contrast enhanced Magnetic resonance imaging (MRI) scan (Sagittal view) of the brain showing enlarged pituitary gland with homogenous enhancement.

Fig. 4 – Follow up post treatment contrast enhanced MRI brain (Sagittal view) showing resolution of the pituitary mass.

resolved. Prednisolone was tapered off over the next 8 weeks. His repeat MRI done after 6 months showed complete resolution of the pituitary mass (Figs. 3 and 4) and basal and post ACTH cortisol levels were normal. There was no

residual pituitary hormone deficit. Investigations are tabulated in Table 1. He has been advised regular follow-up for recurrence of hypophysitis and monitoring for pituitary hormone deficiency.

Table 1 – Baseline and post-recovery parameters in the patient with hypophysitis.

S. no.	Parameter	Baseline (at diagnosis)	Post-recovery (at 6 months)
1	Sodium (mmol/l)	138	140
2	Potassium (mmol/l)	4.2	3.8
3	Urine osmolality (Osm/kg)	687	784
4	ACTH (pg/ml)	26	–
5	Cortisol (basal), mcg/dl	3.2	10.5
6	Cortisol (post-ACTH), mcg/dl	22	33
7	LH (IU/l)	3.4	5.7
8	FSH (IU/l)	4.2	4.5
9	Prolactin (ng/dl)	10	12
10	Testosterone (ng/dl)	281	320
11	TSH (mIU/l)	1.68	3.2
12	Free T4 (ng/dl)	1.2	1.4

Discussion

This young male patient presented with acute onset headache with third cranial nerve palsy and, on evaluation, was found to have diffuse enlargement of pituitary with thickened stalk in the midline, which resolved completely with oral corticosteroid in anti-inflammatory doses. There was transient basal hypocortisolemia with normal ACTH levels, which resolved following recovery from hypophysitis. Response to ACTH was preserved, which is possible in a recent onset of secondary adrenal insufficiency (ACTH deficiency). Underlying autoimmune aetiology and sarcoidosis was excluded by appropriate screening tests.

Hypophysitis is a rare condition characterised by inflammation of the pituitary gland, which may involve the anterior, posterior pituitary or the whole gland with a prevalence on autopsy studies of 0.24–0.88%.¹ Although classically described in post-partum women, it has rarely been noted in men too.^{1,2} Mode of presentation is with sudden severe headache with diffuse pituitary enlargement, which in severe cases may present with visual deficits due to mass effect.^{2,3} In severe cases, it needs to be differentiated from subarachnoid haemorrhage, pituitary apoplexy and vasculitic disorders. Pituitary hormone deficiency of varying degree may be seen although ACTH deficiency is invariably noted and is one of the first hormones to be involved.⁴ Very rarely, isolated ACTH or TSH deficiencies have been reported like in our patient who had isolated ACTH deficiency without involvement of other hormones.¹ Neurohypophysial involvement resulting in DI is also seen uncommonly.⁵

Diagnosis is suspected in relevant clinical setting with a symmetrically enlarged pituitary mass lesion (thickened stalk remaining in midline), which enhances homogeneously with contrast. Dynamic-contrast MRI can help differentiate it from a pituitary adenoma, which is a frequent differential diagnosis. It responds well clinically and radiologically to corticosteroid therapy in anti-inflammatory doses. It may present with recurrences and as a sequelae with empty sella and variable pituitary hormone deficiency. Hypophysitis variably causes partial or complete deficit of the anterior pituitary hormones, mainly ACTH followed by TSH, gonadotropins, and PRL because of direct damage due to autoimmunity on the pituitary acinar cells. They produce the classic signs and symptoms of hypoadrenalism, hypothyroidism and

hypogonadism. The deficiency of prolactin manifests itself in the post-partum period as lactation failure. Histopathological diagnosis is confirmatory but is seldom available unless surgical decompression has been performed in cases with severe mass effect not responding to steroids or those cases where surgery has been done inadvertently suspecting a pituitary tumour. Antibody testing for diagnosis of hypophysitis is not available for diagnosis other than in research settings.

Autoimmune hypophysitis should be kept in mind with a high index of suspicion in patients presenting with unexplained symmetrical pituitary enlargement and pituitary hormone deficiencies. Pituitary apoplexy usually occurs in glands with pre-existing adenoma and presents dramatically with sudden onset headache, hypotension and visual deficits. Hypophysitis presents relatively gradually over a few days; in these cases, surgery should be withheld unless medical management fails and they should be followed up for pituitary hormone deficiencies initially and thereafter.

The exact aetiology of hypophysitis is not known but autoimmunity is considered the likely mechanism. These patients are found to have anti-pituitary antibodies and other autoimmune conditions such as Hashimoto's thyroiditis and Graves' diseases, type 1 DM, Addison's disease, hypoparathyroidism, chronic atrophic gastritis and pernicious anaemia.¹ Our patient did not show any clinical or biochemical evidence of other autoimmune conditions and tests for the commonly available autoantibodies were negative.

Treatment of hypophysitis includes measures to reduce the size of pituitary gland and replacement of deficient hormones. For reducing the pituitary size, drugs, surgery and radiotherapy have been tried. Current literature favours the use of corticosteroids before resorting to surgery. Glucocorticoids serve the dual function as anti-inflammatory agents as well as replacement of deficient adrenal function. Periodic follow-up for recurrence of hypophysitis should be done. These patients may develop pituitary hormone deficiency as sequelae of hypophysitis in the long run and hence annual follow-up for pituitary function must be performed.

Conflicts of interest

The authors have none to declare.

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