Case Report

Lymphocytic hypophysitis masquerading as transient secondary hyperadrenalism followed by panhypopituitarism

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ABSTRACT

Lymphocytic hypophysitis (LH) is a rare inflammatory disease of the pituitary gland. This condition strikingly shows female preponderance and commonly affects women during pregnancy or in the post-partum period. It's a clinical presentation and radiological features may mimic pituitary adenoma. Though its treatment modality is uncertain steroid remains the 1st option for treatment. Here, we report an unusual case of LHin a 21-year-old female patient where initially, the patient presented with hyperadrenalism and secondary hyperthyroidism followed by pan-hypopituitarism (Addisonian crisis) which is attributed to initial autoimmune destruction of the gland followed by subsequent fibrosis. Thus, it is a rare case report which exquisitely explains this rare presentation and such cases should be investigated thoroughly since there are many differential and response to steroids is remarkable.

Keywords: *Autoimmune, Lymphocytic hypophysitis, Panhypopituitarism.*

Lymphocytic hypophysitis (LH) is a rare inflammatory disease of the pituitary gland. Since the first report in 1962, more than 100 cases have been described [1]. This condition strikingly shows female preponderance and commonly affects women during pregnancy or in the post-partum period [1]. It's a clinical presentation and radiological features may mimic pituitary adenoma. Histologically it is characterized by lymphocytic and plasma cell infiltration of the pituitary gland. Pathogenesis of LH is attributed to autoimmunity because it is associated with other autoimmune diseases and anti-pituitary antibody has been demonstrated in 40% of cases [2]. Though its treatment modality is uncertain, steroid remains the 1stoption for treatment.

Here an unusual case of lymphocytic hypophysitis is described where initially the patient presented with hyperadrenalism and secondary hyperthyroidism which was followed by panhypopituitarism. The present case is rare since most of the cases with lymphocytic hypophysitis present straightway with panhypopituitarism but in our case, the presentation of lymphocytic hypophysitis was with transient hyperfunctioning pituitary gland due to initial autoimmune destruction of the gland leading to a higher blood level of hormones followed by panhypopituitarism. A similar course has been described in autoimmune thyroiditis where there might be initial thyrotoxic features before hypothyroidism occurs.

CASE REPORT

A 21-year-old female patient presented with complaints of headache, asthenia, and blurring of vision for the last 1 month. She gave no history of fever, vomiting, seizure or any other history suggestive of any focal neurological deficits. Menstrual irregularity (amenorrhea) was there for the last three months as the patient was on regular follow-up in the gynecology department but urine pregnancy test was negative.

General physical examination was unremarkable and vitals were stable. There was no evidence of mucocutaneous candidiasis or any hyperpigmentation or albinism suggestive of multiple endocrine involvements. Visual perimetry was suggestive of bitemporal hemianopia.

Complete hemogram, liver functions tests, kidney function tests, serum electrolytes, and chest X-ray were normal. The patient was advised to get contrast-enhanced magnetic resonance imaging (CE-MRI) brain focusing pituitary. Dexamethasone suppression test was positive as the patient had morning 8 am plasma cortisol 87ug/dL and urinary free cortisol was also more than three times high. Plasma adrenocorticotropic hormone (ACTH) was 17pg/mL. The urinary investigations showed higher serum and urinary free cortisol level along with high ACTH and secondary hyperthyroidism denoting hyperfunctioning pituitary gland (Table 1).

The MRI was planned but could not be done as the patient took discharge against medical advice. The patient again presented in the medical emergency after four months. This time she again presented with complaints of altered sensorium for the last 3 days followed by multiple episodes of vomiting. There was no history of convulsions, fever, and headache, weakness of any part of the body and head trauma. The urine output was 3600 mL in 24 hours. Her husband complained that she had her last

Table 1: Blood and urine investigation of the patient at first visit

Hormones	Normal Values	Patient's value
Prolactin	19–25 ng/mL	77 ng/mL
24 hour urinary free cortisol	3.5–45 ug/dL	139ug/dL
8am Serum cortisol	5–25ug/dL	87ug/dL (after overnight dexamethasone suppression)
TSH	0.34–4.25 mIU/mL	5.9 mIU/mL)
Unbound T4	(0.7–1.24 ng/L	2.8 ng/L)

menstruation 7 months ago and the urine pregnancy test was negative. On examination, the patient was hypotensive with central venous pressure of 4cm of water and random blood sugar (RBS) was 56. Her Glasgow coma scale (GCS) was 13. Fundus was normal. Investigations including a complete hemogram, liver function tests (LFTs), renal function tests (RFTs), electrolytes were normal. Non-contrast computed tomography (NCCT) head was normal. Blood culture and urine culture sensitivity were sterile. Urine osmolality was low (230 mosm/L). A possibility of panhypopituitarism was kept though initially, the patient presented with secondary hypercortisolism and secondary hyperthyroidism. Subsequently, the patient's investigation revealed to show panhypopituitarism. In view of past presentation with bitemporal hemianopia, the patient pituitary function tests were repeated. The tests (Table 2) showed signs of panhypopituitarism which are in contrary to the previous investigations (Table 1).

Along with this luteinizing hormone (LH), follicle stimulating hormone (FSH) levels were low. The patient was started on steroids and subsequently, the patient improved drastically. The urine volume and osmolality improved after nasal desmopressin. Contrast-enhanced magnetic resonance imaging (CE-MRI) Brain (Fig. 1 and 2) was suggestive of symmetric enlargement of the pituitary gland and homogeneous post-contrast-enhancement with stalk thickening highly suggestive of Lymphocytic Hypophysitis. Other possibilities were ruled out as a serum angiotensin-converting enzyme (ACE),

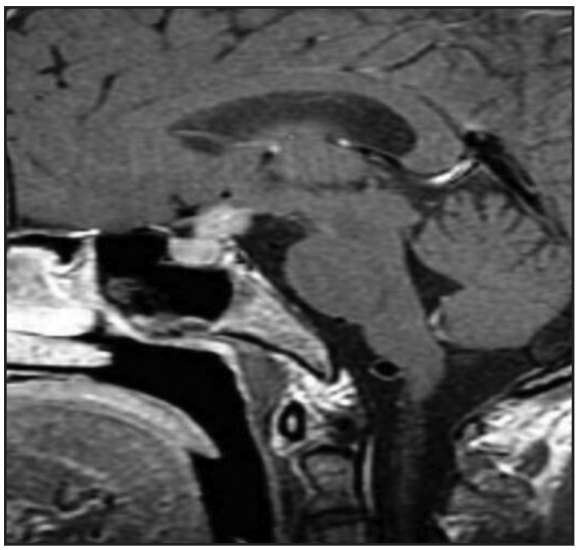

Figure 1: Enlarged pituitary gland

Table 2: Blood and urine investigation of the patient at the second visit (after 4 months)

Hormones	Normal Values	Patient's value
fT4	0.7–1.24 ng/L	2.1 ng/L
8am Serum cortisol	5–25ug/dL	1.2ug/dL
Cortisol 8pm	0–10 ug/dL	0.5 ug/dL
Cortisol (after 250 ug IM cosyntropin)	<500 nmol/L	300 nmol/L
TSH	0.34–4.25 mIU/mL	1.7 mIU/mL)
ACTH	6–76 pg/mL	2pg/mL
Insulin like growth factor (IGF-1)	116–258 ug/dL	53ug/dL
Arginine vasopressin (AVP)	>1 pg/mL	0.7pg/mL

Mantoux, Venereal disease research laboratory (VDRL) and anti-nuclear antibody (ANA), anti-TPO(thyroid peroxidase) antibodies were negative. Contrast-enhanced computed tomography (CECT) chest and abdomen pelvic organ was normal. A possibility of the autoimmune polyglandular syndrome was also ruled out in view of clinical features and investigations. Cerebrospinal fluid (CSF)showed a moderate increase in protein(82mg/dL) with a total cell count of 50cells/ uL, lymphocytes being 80% and rest polymorphonuclear leucocytes. Adenosine deaminase (ADA) was 6. Serological investigations for hepatitis B, C, Cytomegalovirus (CMV), Ebstein Barr virus (EBV), toxoplasma and HIV were negative. CSF mycobacterial culture was negative. The patient and attendant denied transsphenoidal pituitary biopsy. The patient condition got improved, was discharged on steroids and nasal desmopressin and followed up in the out-patient department.

DISCUSSION

Lymphocytic hypophysitis is a rare inflammatory disease of the pituitary gland. Besides lymphocytic hypophysitis, granulomatous and xanthomatous hypophysitis and inflammatory pseudotumor of the pituitary are the other histopathological conditions that complete the spectrum of primary hypophysitis [1,2,3,4]. The presence of diabetes insipidus at presentation almost completely rules out the diagnosis of pituitary adenoma and raises suspicion of infiltrative or inflammatory diseases. MRI signs, like the triangular shape of the upper pituitary [5,6,7] and adeno-pituitary impairment, mainly involving corticotrophic and thyrotrophic functions are suggestive of lymphocytic hypophysitis [8]. Slight lymphocytic/ monocytic pleocytosis in the CSF without clinical meningitis has been documented in some cases of lymphocytic hypophysitis [9] which was present in our case too. Other possibilities with high ADA in the background of CSF lymphocytosis were ruled out. Lymphocytic hypophysitis is a chronic inflammatory process that responds to corticosteroid treatment. However, both lack of response to steroids and a recurrence of symptoms during steroid treatment have been reported [2].

In our case, the patient was evaluated in her initial presentation, that time it revealed hyperfunctioning pituitary gland and later she presented with panhypopituitarism with secondary amenorrhea. In

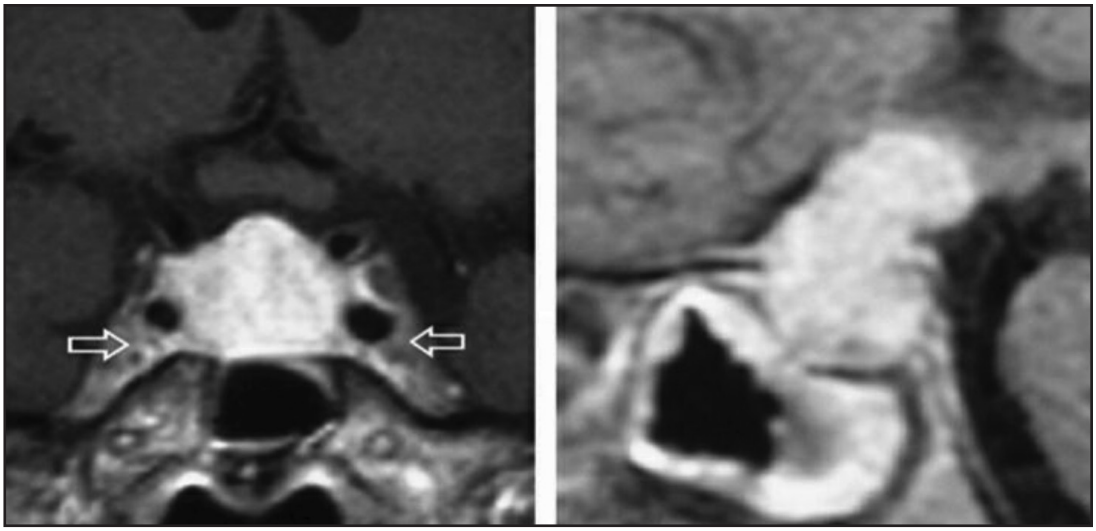

Figure 2: Homogeneous enlargement of pituitary and stalk thickening

our patient transient hyperadrenalism was very interesting finding which can be explained by lymphocytic destruction leading to an outpouring of hormones in the blood before panhypopituitarism sets in. Similar findings are found in Hashimoto thyroiditis where there is transient hyperthyroidism followed by hypothyroidism. Other very close differential diagnoses (like pituitary adenoma, infiltration, Sheehan syndrome) were also ruled out as they are very unlikely to cause initial hyperfunctioning of the pituitary gland. To confirm the diagnosis we had to rule out other possibilities which came out negative. MRI Brain was also suggestive of LH. LH displays MR imaging features that closely reflect the underlying histopathology. Lymphocytic and granulomatous hypophysitis are characterized by lymphoplasmacytic infiltration, destruction of endocrine cells, interstitial widening and fibrosis, hypervascularity, and multinucleated giant cells (the latter prominent in the granulomatous and rare in the lymphocytic form). In keeping with these pathologic changes, the MR imaging features typical of LH are a symmetric enlargement of the pituitary gland, a homogeneous appearance both on pre-and post-gadolinium images, and an intense gadolinium enhancement. In contrast, pituitary adenomas are typically asymmetric as they sprout toward the suprasellar cistern and cavernous sinus shows heterogeneous enhancement, likely a reflection of inner cystic or necrotic areas [10] and had a lower gadolinium uptake than the normal adenohypophysis, consistent with the notion that adenomas have lower vascular attenuations than the normal pituitary tissue [11]. A strong enhancement is to be expected only in the presence of secondary inflammatory changes, which are rare (approximately 1%) in nonfunctioning adenomas [12].

CONCLUSION

Lymphocytic hypophysitis is a disorder of females which needs exhaustive workup and a long follow-up. Any female with hormonal dysfunction should be investigated and followed up to diagnose LH. The patient may present transiently with hyperfunctioning pituitary gland followed by panhypopituitarism.

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