INTRODUCTION

Lymphocytic hypophysitis is a rare inflammatory lesion of the pituitary gland. It was first reported in 1962 by Goudie and Pinkerton.1 It affects predominantly women in late pregnancy or postpartum period as anterior pituitary hypofunction and/or pituitary mass lesion.2 Diabetes insipidus,3 hyperprolactinemia,2,4 associated growth hormone excess leading to features of acromegaly2,5 have also been reported. Here we report a case of recurrent lymphocytic hypophysitis in a woman who had undergone subtotal adrenalectomy for hypercortisolism 27 years earlier, possibly due to Cushing’s syndrome of autoimmune origin.

CASE REPORT

Mrs. SM, a 50 years lady first visited our hospital in 1969 with the complaints of weight gain, hirsutism, secondary amenorrhoea and infertility. She was diagnosed to be a case of Cushing’s disease based on hormonal investigations. However pituitary imaging was not done then due to nonavailability. Patient underwent subtotal adrenalectomy (left total and right partial). She was put on gradual tapering dose of prednisolone over a month, which she later discontinued. She had 3 successful pregnancies thereafter. Her periods stopped in 1992. She reported to emergency in February, 1996 with an acute episode of headache and vomiting.

Physical examination did not reveal any abnormality except hyperpigmentation of the skin, tongue and knuckles. There were no neurological deficits. Ocular fundi and peripheral visual fields were normal. Her vision was 6/18 (Right eye) and 6/12 (Left eye). Her hormonal profile was: Plasma cortisol-16.8 (7-25 µg/dl), Plasma ACTH > 1000 (0-37 pg/ml). Thyroid profile was within normal range. LH and FSH were in normal range for follicular phase.

A CECT head showed sellar and suprasellar mass. MRI confirmed presence of sellar mass with extension into suprasellar region and sphenoid sinus (Fig. 1a) CT scan for adrenals showed part of medial limb of right adrenal and nonvisualization of left adrenal gland.

With a provisional diagnosis of Nelson’s syndrome, she was subjected to endonasal transsphenoidal microsurgical excision of the pituitary mass. However, the histopathological picture of the biopsy specimen consisted mainly of inflammatory tissue. The inflammatory cells were predominantly lymphocytes with admixture of plasma cells and histiocytes (Fig 1b). Immunohistochemical staining for growth hormone and prolactin showed groups of normal pituitary cells within inflammatory infiltrate (Fig. 1c). This picture was suggestive of lymphocytic hypophysitis.

Patient took prednisolone 5mg daily for few months postoperatively and then tapered it off. She was lost to follow-up thereafter.

In November1998 she again reported in the emergency with sudden onset severe headache, vomiting and diplopia. There was no history of unconsciousness or seizures. On examination, there was ptosis of the left...
The natural course of this condition has been found to be variable. It has resulted in fatal complication in 19% cases in one series. Gradually progressive hypopituitarism as well as partial or total adenohypophysial function recovery have been reported. Recurrence of lymphocytic hypophysitis has been reported in only one case, which occurred 28 months after the first episode. Management of lymphocytic hypophysitis is also a matter of dispute. Corticosteroids have been shown to be beneficial.

The clinical and hormonal profile in the present case was suggestive of Nelson’s syndrome (history of Cushing’s disease and subtotal adrenalectomy, darkening of skin colour subsequent to surgery, high ACTH value with normal cortisol level and presence of a sellar and suprasellar mass). However histopathological examination revealed hypophysitis and no evidence of pituitary tumour. She had symptomatic improvement following transsphenoidal surgery and steroid therapy. The histopathological finding of hypophysitis in the resected mass with improvement after steroid in addition to the history that patient didn’t require steroid supplementation for nearly 3 decades after subtotal adrenalectomy make possibility of Nelson’s syndrome unlikely in this case.

The patient required steroids only for few weeks after the first episode. The second episode after about 30 months of the first episode suggested recurrence of the lesion. This time also her hormonal values showed very high ACTH. She had deficiency of multiple other pituitary hormones. The low free T4 and normal TSH is suggestive of secondary hypothyroidism and normal LH and FSH in the phase of secondary amenorrhoea suggests secondary hypogonadism. Her serum cortisol though normal was possibly inappropriately low, considering that she was under severe stress. Recurrence of symptoms, presence of pituitary mass lesion and regression of the mass following steroid therapy strongly favours the diagnosis of recurrence of lymphocytic hypophysitis.

The association of lymphocytic hypophysitis, which is an autoimmune phenomenon, with other autoimmune endocrine disorders has already been described. Other endocrine manifestations commonly presented with endocrine insufficiency. A few instances of hypersecretion of thyroxine, hypercalcemia due to parathyroid hyperplasia, coexistence with growth hormone producing pituitary adenoma are also reported. However, hypersecretion of adrenocorticotropin hormone in association with lymphocytic hypophysitis has not been described in the literature yet.

Antipituitary antibody has been isolated in patients with lymphocytic hypophysitis. Association of autoantibodies to corticotropin producing cells of the pituitary in patients with Cushing’s disease responding poorly to transsphenoidal microsurgery has been reported. We speculate the presence of stimulatory autoantibody to corticotrophs as the reason of high ACTH in this patient during both the episodes of autoimmune hypophysitis.

In view of the fact that the patient presented with the features of Cushing’s syndrome about 27 years before she presented with lymphocytic hypophysitis, the other possibility is that the patient had hypercortisolism due to adrenocorticotropin hormone producing pituitary adenoma as a part of the autoimmune disease and the other autoimmune condition, lymphocytic hypophysitis developed later. Pituitary or ectopic ACTH source should have manifested during these 3 decades after subtotal adrenalectomy. In patients with Cushing’s disease the
Fig. 1 (a): Coronal T1 weighted Gadolinium enhanced MR images display a large sellar mass with suprasellar, infrasellar and parasellar extensions on the left side. The left internal carotid is inferiorly displaced and the mass spills over lateral to the internal carotid artery.

Fig. 1 (b): Photomicrograph showing chronic inflammatory cell infiltrate comprising chiefly of lymphocytes (H & E x 250).

Fig. 1 (c): Immunohistochemical staining for growth hormone and prolactin showing groups of normal pituitary cells within inflammatory infiltrate.

Fig. 2 (a): Coronal T1 weighted Gadolinium enhanced MR images show extensive recurrence of the sellar-suprasellar mass. Areas of hypointensity within the mass denote necrosis.

Fig. 2 (b): Coronal T1 weighted Gadolinium enhanced MR images show empty sella and complete regression of the sellar-suprasellar mass. The left internal carotid artery is also restored to its normal position.

adrenal tissue left behind and the pituitary lesion normally grows with time when no radiotherapy is given following adrenal surgery. However, this did not happen in this case. CT scan showed residual adrenal tissue of normal size. She was asymptomatic all these years except for increase in the pigmentation. She also had normal pituitary function in these years as she was healthy and had three full term normal deliveries.

To the best of our knowledge, this is the first case of
Cushings’ syndrome and lymphocytic hypophysitis occurring in the same patient. Both the conditions seem may be a part of a rare combination of autoimmune polyglandular endocrinopathy.

REFERENCES


