Case Report

**Lymphocytic Hypophysitis, primary hypothyroidism and type 1 diabetes mellitus. A rare association**

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**ABSTRACT**
We report a 25-year-old female with florid hypothyroidism, subtle hypogonadism, with pituitary mass with suprasellar extension encroaching the optic chiasma and lymphocytic hypophysitis in association of type 1 diabetes mellitus. (Rawal Med J 2010;35:  ).

**Keywords:** Hypophysitis, hypothyroidism, diabetes, hypogonadism.

**INTRODUCTION**
Lymphocytic hypophysitis (LHP) was first described in a post-mortem case in 1962 by Goudi and Pinkerton. It usually affects women during pregnancy, postpartum period, nonpregnant women as well as men. Clinically, LHP presents with hypopituitarism, mass effect and hyperprolactinaemia. Involvement of the infundibulum by lymphocytic infiltrate sometimes gives rise to diabetes insipidus. Radiologically, LHP appears as a pituitary mass. Features that favour LHP are loss of bright spot signal at the posterior pituitary, thickening of the pituitary stalk and enlargement of the pituitary. Histologically, it is characterised by involvement of the pituitary by inflammatory cells, predominantly lymphocytes and variable fibrosis.

We present a case of LHP in a nulliparous woman with complete recovery, associated with primary autoimmune hypothyroidism and type 1 diabetes mellitus.

**CASE PRESENTATION**
A 25-year-old nulliparous lady was referred with six months history of fatigue, cold intolerance, slow speech and thought, constipation and light-headedness in 1995. Few weeks prior to presentation she developed headache and blurring of vision. Her past medical history was unremarkable and her menstrual periods were regular, being on cyclical combined contraceptive pills since 1989. There was no family history of endocrinopathies. Physical examination revealed a typical hypothyroid lady, no goitre, scanty axillary hair, Tanner stage 4 pubic hair and stage 4 breast development. Her visual fields by confrontation and optic discs were normal. She had low free T4 1.5 pmol/L (normal 9-24 pmol/L), low TSH 0.32 mIU/L (normal 0.4-5.0 mIU/L) and modest hyperprolactinaemia 1123 pmol/L (normal <450 pmol/L).

Initial evaluation suggested hypopituitarism and she was started immediately on hydrocortisone 20 mg on the morning and 10 mg on the evening, followed 3 days later by 50 µg of thyroxine daily. Clinic follow up 2 weeks later revealed significant improvement of her symptoms. She had normal serum cortisol 780 nmol/L (normal 138-550 nmol/L), adrenocorticotropic hormone (ACTH ) 14 pmol/L (normal 2-11 pmol/L), follicle-stimulating hormone (FSH ) 3.9 IU/L (normal 5-24 IU/L) and luteinising hormone (LH ) 4.7 IU/L (normal 4.5-24.3 IU/L), despite being on combined contraceptive pills. Pituitary CT scan showed a pituitary macroadenoma that filled the sella and had suprasellar extension, presumably encroaching on the optic chiasm. Formal perimetry revealed normal visual fields. At this point, a decision
was made to proceed with transphenoidal hypophysectomy. Operative course was smooth, however, she developed diabetes insipidus managed by DDAVP spray.

Postoperatively her blood sugars were persistently high. Oral hypoglycaemic agents (Gliclazide) failed to control her blood sugars and she developed ketosis and insulin was instituted. Her islet cell antibodies (ICA) were negative. Neuropathological report revealed normal pituitary tissue with mild lymphocytic infiltrate, mainly T lymphocytes and macrophages suggestive of lymphocytic hypophysitis. She was kept on hydrocortisone, thyroxine, DDAVP nasal spray, Logynon (ethinylestradiol 30µ gand levonorgestrol 50 µg) and insulin. Two months postoperatively, she presented with headache and feeling unwell. Follow up CT scan showed evidence of recent surgery and no abnormality related to pituitary fossa. Contrary to previous results, TSH was high (6.3 mIU/L, 10.4 mIU/L) with normal free T4 despite thyroxine replacement. Antithyroperoxidase antibodies (TPO) were positive at 170.6 IU (normal 0-100 IU), consistent with primary autoimmune hypothyroidism.

A wide antibody screen showed antinuclear, antimitochondrial, antismooth muscle, antiacetylcholine, antiadrenal, antigliadin antibodies to be negative. Dynamic pituitary reserve evaluation one year after surgery showed a blunted Cortisol response to synthetic ACTH, but a normal LH, FSH and TSH responses to Gn RH and TRH. Since January 1997, gradual hydrocortisone weaning was started and was successfully taken off in November 1997. Further pituitary dynamic tests in October 1998 revealed adequate reserves. In April 1999, DDAVP was successfully stopped. In November 1999 she wished to form a family so her contraceptive pills were withdrawn her glycaemic control was optimised and started on folic acid supplements. She delivered a baby in April 2001 by Caesarean section due to macrosomia. A second successful delivery took place in March 2005. She enjoys a good health with no diabetic complications. Her current treatments are insulin and thyroxine.

**DISCUSSION**

Our case showed a long history of endocrine dysfunction manifested by typical hypothyroid features, subtle hypogonadism masked by a prolonged contraceptive pills use and a mild hyperprolactinaemia that suggests a continued partial pituitary function. Despite her presentation with secondary hypothyroidism, resolution of the inflammatory infiltrate postoperatively unmasked primary autoimmune hypothyroidism indicated by progressive rise in TSH, low free T4 as well as positive thyroperoxidase antibodies (TPO). She needed lifelong Thyroxine replacement.

Initial hyperprolactinaemia with subsequent postoperative normoprolactinemia could be explained by involvement of the pituitary stalk by inflammatory infiltrate. Diabetes insipidus is a recognised complication of pituitary surgery. However the gradual decreasing dependency on DDAVP in this case favours involvement of the neurohypophysis by inflammation. The stress of surgery and Hydrocortisone replacement despite initial normocortisolemia triggered diabetes mellitus in this predisposed lady. Primary failure of oral hypoglycaemic agents as well as ketosis favour type 1 diabetes mellitus despite negative islet cell antibodies (ICA).

The pathogenesis of LHP is thought to be autoimmune. Antipituitary antibodies have been detected in some patients. In a quarter of cases it can be associated with other autoimmune disorders. These include autoimmune thyroiditis, diabetes insipidus,
pernicious anemia, adrenalitis and Graves disease.\textsuperscript{10} Since most cases of LHP present as a pituitary neoplasm, they usually undergo surgical resection, which is both diagnostic and therapeutic. Spontaneous recovery of the pituitary function with disappearance of the pituitary infiltrate has been described.\textsuperscript{11} Cases of spontaneous recovery of LHP after steroid treatment have been reported.\textsuperscript{12} Starting this lady on Hydrocortisone preoperatively could have contributed to complete recovery of pituitary reserve. Despite increasing numbers of LHP reported; the triad of LHP, primary hypothyroidism and type 1 diabetes mellitus has not been described before. LHP should be considered in the differential diagnosis of all pituitary masses in childbearing women. Search for other autoimmune disorders should be encouraged.

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