‘Stalkitis’ in a pregnant 32-year-old woman: A rare cause of diabetes insipidus

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SUMMARY

A case of lymphocytic infundibulo-neurohypophyseitis (LINH) or ‘stalkitis’ in a 32-year-old woman who presented with diabetes insipidus (DI) during pregnancy is reported here. The diagnosis was made with MR imaging. The clinical and radiological features of this rare disorder and the differential diagnosis of infundibular mass lesions are discussed. The differentiation from lymphocytic adenohypophyseitis (LAH) is made. No improvement of the DI accompanying LINH is achieved with trans-sphenoidal surgery. Hence, recognition of typical cases with MR imaging and appropriate medical management avoids unnecessary neurosurgery. This is the second reported case of LINH associated with pregnancy and may suggest an association.

Key words: diabetes insipidus; lymphocytic infundibulo-neurohypophyseitis; magnetic resonance imaging; pregnancy; stalkitis.

INTRODUCTION

Lymphocytic infundibulo-neurohypophyseitis (LINH) is a recently recognized condition causing pituitary stalk thickening and idiopathic diabetes insipidus (DI). This condition is very uncommon, being reported in less than 30 cases in the world literature. The first pathological description of LINH was made in 1989 by Kojima et al. who demonstrated at autopsy chronic lymphocytic inflammation limited to the infundibulum, stalk and posterior lobe of the pituitary gland in a man with central DI.1 Subsequently, Imura et al. found nine patients with typical MR appearances of LINH which were confirmed in two cases that were biopsied.2 The term ‘stalkitis’ has been used to describe a case with marked thickening of the pituitary stalk.3 We report a case of LINH presenting with DI during pregnancy which was diagnosed with MR imaging. This is the second reported case of LINH associated with pregnancy and may suggest an association.

CASE REPORT

A 32-year-old woman presented 3 months postpartum with thirst and polyuria which had first developed at 34 weeks gestation. She was breast feeding but had noted a reduction in milk production. She was otherwise well and there was no history of a preceding viral illness. There was also no history of a previous hormonal disturbance and in particular, she had regular periods pre-pregnancy with no difficulty conceiving. Her examination was unremarkable. Blood pressure was normal with no postural hypotension. There was no visual field defect and no optic atrophy.

Initial investigations confirmed DI with a high serum osmolality of 303 mosm/L (range: 280–295) at a time when there was inappropriately low urine osmolality of 56 mosm/L (range: 500–600). Tests of anterior pituitary function showed hypogonadotropic hypogonadism, mild secondary thyroid failure and mild growth hormone deficiency. A serum angiotensin converting enzyme (ACE) was normal.

Magnetic resonance imaging was performed utilizing a 1.5-T Siemens Magnetom Vision system (Siemens, Erlangen, Germany). Images revealed significant widening of the pituitary stalk. Width in the coronal plane at the level of the median eminence was 6 mm. There was abrupt tapering to 1–2 mm at the level of the insertion into the pituitary. The stalk enhanced...
markedly following intravenous dimeglumine gadopentetate (Magnevist Schering AG Berlin, Germany). The anterior pituitary was of normal size and signal intensity. The normal 'bright spot' or high signal intensity of the posterior pituitary on the T1-weighted images was absent (Figs 1–3).

The patient was treated with desmopressin acetate (dDAVP; Minirin, Rhone-Poulenc Rorer, Paris, France) 10 mcg twice daily intranasally with prompt control of her DI. Screening for other autoimmune diseases was negative.

Two months following the diagnosis, the patient remains well on dDAVP. Omitting dDAVP results in polyuria, indicating that DI persists. She has stopped breastfeeding and has minimal lactation. Her prolactin has returned to normal but the patient remains amenorrheic. Thyroid function tests and levels of growth hormone production are essentially unchanged.

DISCUSSION

Lymphocytic infundibulo-neurohypophysis is a rare condition characterized by a chronic inflammatory infiltrate involving the infundibulum, the pituitary stalk and/or the neurohypophysis. The infiltrate consists of T lymphocytes and plasma cells with a scattering of macrophages, eosinophils and neutrophils. Lymphocytic infundibulo-neurohypophysis manifests as DI by causing selective dysfunction of the hypothalamic-neurohypophyseal pathway. Adenohypophyseal function is usually preserved. The natural course of LINH is thought to progress from inflammatory enlargement of the pituitary stalk or posterior pituitary gland to subsequent fibrosis and atrophy. Neuronal loss with gliosis bilaterally in the supra-optic and paraventricular nuclei of the hypothalamus has also been observed. No cases of spontaneous recovery have been reported. Death from the sequelae of DI has been reported in a patient with a lymphoplasmocytic infiltrate in the posterior pituitary gland.

Lymphocytic infundibulo-neurohypophysis is presumed to represent an autoimmune process although the definite pathogenesis remains unknown. Antibodies against magnicellular neurones of the hypothalamus have been detected in some patients. In one study, 33% of patients with idiopathic DI had associated overt autoimmune diseases or endocrine organ specific auto-antibodies. Lymphocytic adenohypophysitis (LAH) is a related disease which may have a similar pathogenesis to LINH; it occurs predominantly in women during pregnancy.
during the postpartum period. Our patient is now the second case of LINH to be reported in the peripartum setting and may suggest a similar association. Such an association would fit with an autoimmune pathogenesis. It has been suggested that LINH and LAH may both be autoimmune in nature but with differing antigens and antibodies mediating each process.

The radiological features of LINH include diffuse thickening of the pituitary stalk with a maximum diameter exceeding 3.5 mm at the level of the median eminence of the hypothalamus. The normal smooth tapering of the infundibular stalk is lost and a varying amount of asymmetry may exist. The stalk enhances vigorously after administration of gadolinium. The enhancement may extend into the inferior part of the hypothalamus. When hypothalamic-neurohypophyseal function is absent there is loss of the normal posterior pituitary "bright spot" on T1-weighted images. The hyperintensity of the posterior pituitary on T1-weighted images in normal subjects is related to the phospholipid membrane of the antidiuretic hormone (ADH)-containing neurosecretory granules. The absence of this normal hyperintensity has been shown to closely correlate with a loss of function of the neurohypophysis. However, it should be kept in mind that the normal posterior pituitary bright spot may be absent in ~10% of normal subjects. The anterior pituitary gland in LINH is of normal size and signal intensity.

Stalkitis (LINH) should be distinguished from the more common LAH. Lymphocytic adenohypophysitis is characterized by a chronic inflammatory infiltrate in the anterior pituitary gland, typically causing mass effects and hypopituitarism without DI. It classically mimics a non-functioning pituitary adenoma. Magnetic resonance imaging usually demonstrates a large intrasellar mass, which frequently extends to the suprasellar region. Operative reports of LAH revealed an unusually firm, tough fibrous mass encountered immediately beneath the dura of the sella turcica on trans-sphenoidal surgery with a histologically normal neurohypophysis.

Our patient's clinical presentation with DI and the MRI findings are consistent with LINH. This has been described in one other case presenting in the postpartum period. The extent of compromise of anterior pituitary function in our case is difficult to assess. The patient was able to breastfeed, indicating an adequate prolactin response. The prolactin level initially was elevated but has returned to normal following the cessation of breastfeeding. The patient has hypogonadotropic hypogonadism and amenorrhea but this is characteristic of lactation, and menses may take some time to re-establish after breastfeeding. Patients with LINH have been described with permanent hypogonadotropic hypogonadism and preservation of other anterior pituitary function. Thyroid function tests are consistent with mild secondary thyroid failure. The insulin-like growth factor-1 (IGF-1) level is low, consistent with growth hormone deficiency. Inadequate growth hormone responses to hypoglycaemia have been described in LINH. There is, therefore a mixture of mild anterior pituitary hormone deficiencies. However, the predominant endocrinological lesion is clearly deficiency of desmopressin release from the posterior pituitary, which is consistent with LINH.

Increasingly, LINH is being recognized as a separate clinical entity from LAH, although clearly some overlap does exist. For example, LAH associated with DI has been reported in 14 histologically proven cases. In these patients the anterior pituitary was the principal site of inflammation and there was unequivocal evidence of hypopituitarism. However, thickening of the stalk, resembling that observed in LINH, was frequently noted on MRI. This presumably represents extension of the inflammatory process beyond the adenohypophysis, causing disruption of the hypothalamic-neurohypophyseal axis. The findings in LAH are distinct from those in our patient. Specifically, our patient had a normal-sized anterior pituitary with normal signal intensity and no evidence of intrasellar pathology on MRI. There is, however, some equivocal evidence of anterior pituitary hormonal dysfunction. Interestingly, Nishikawa et al. have recently reported two cases of LINH in which the inflammatory process extends to involve the anterior pituitary. Thus the functional overlap of these two conditions may be explained by local extension of the inflammatory process beyond the original focus. This reasoning may account for the equivocal anterior pituitary dysfunction encountered in our patient.

The differential diagnosis of an isolated infundibular mass lesion in a patient with DI includes sarcoidosis, glioma, lymphoma, germinoma, granular cell tumour, metastasis and histiocytosis. Neurosarcoidosis is relatively rare, affecting only 5% of all sarcoid cases but, if present, it may affect the infundibular stalk alone. However, there were no features to suggest sarcoid in our patient, and a serum ACE level was normal. Primary tumours of the neurohypophysis and infundibular stalk are extremely rare. Glioma, germinoma, and granular cell tumour are reported but are unlikely here because there is no evidence of progressive mass-related symptoms. A single infundibular metastasis would be unusual in a young woman with no evidence of a primary malignancy. Diabetes insipidus and thickening of the central part of the pituitary stalk might be the first presentation of Langerhans cell histiocytosis, and can precede other clinical manifestations by as much as 15 years. However, our patient's age and absence of any other manifestations of histiocytosis are against this diagnosis. The clinical and MRI findings in the present patient are consistent with LINH.

CONCLUSION

We present the second case of 'stalkitis' diagnosed in the peripartum setting. The diagnosis was reached using MRI, thus avoiding the need for a more invasive diagnostic strategy.
REFERENCES


