Lymphocytic hypophysitis mimicking pituitary macroadenoma

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Summary  Lymphocytic hypophysitis is an uncommon disease with a variable presentation and unclear pathophysiology. We present the case of a 30 year old woman who presented with features typical of a pituitary macroadenoma. She underwent a transphenoidal resection of the mass and histopathological examination revealed lymphocytic hypophysitis. This case illustrates the difficulty in differentiating pituitary macroadenoma and lymphocytic hypophysitis and the variable presentations of lymphocytic hypophysitis. © 2002 Published by Elsevier Science Ltd.

CASE REPORT

A 30 year old Somalian woman presented 1 month postpartum with a 3 month history of deteriorating vision. She had noticed difficulty reading due to blurred vision. She was otherwise asymptomatic. The visual acuity was 6/9 in the right eye and 6/60 in the left eye. She had a dense bitemporal hemianopia. Hormone studies were normal other than borderline thyroid function (Table 1) and the remainder of the neurological examination was unremarkable.

A CT brain scan (Fig. 1) showed a large mass arising from an expanded pituitary fossa with suprasellar extension measuring 2cm in its superoinferior dimension. There was an area of focal low density within the mass and a bony defect in the floor of the pituitary fossa. An MRI (Fig. 1) scan confirmed a mass of pituitary origin with extension into the suprasellar cisterns. It was isointense on T1 and hyperintense on T2 weighted images and had homogeneous contrast enhancement.

A provisional diagnosis of pituitary macroadenoma was made and a transphenoidal resection of the mass was performed. Intraoperatively, the mass was extremely tough and fibrous and adherent to the dura. Frozen section revealed the possibility of lymphocytic hypophysitis and a subtotal excision of the mass within the pituitary fossa and suprasellar cisterns was performed.

Histological examination showed extensive destruction of pituitary acini by a dense infiltrate of T lymphocytes, plasma cells and monocyte-macrophages (Fig. 2). An occasional multinucleate giant cell was identified but no discrete granulomas were seen. The appearances were typical of lymphocytic hypophysitis. No evidence of adenoma was seen.

Postoperatively, the patient made an uneventful recovery. Cortisone acetate was given for three months but she required continuing thyroxine replacement (100 mcg daily). The visual acuity improved to 6/5 bilaterally.

DISCUSSION

Although first described in 1962, lymphocytic hypophysitis remains a difficult clinical entity to characterise. The literature to date has attempted to define clinical indicators to aid in a preoperative diagnosis. Some reports have suggested that conservative management is appropriate in certain circumstances. Our case highlights that the clinical, biochemical and radiological features of lymphocytic hypophysitis, in addition to the intraoperative findings, are variable and inconsistent. This case also reinforces the possible need for surgical intervention when visual failure is present.

To our knowledge there have been 131 reported cases of lymphocytic hypophysitis since 1962. The association with pregnancy and puerperium is significant and has led to the hypothesis that the aetiology is of an autoimmune basis. Lymphocytic hypophysitis is likely to be the most common cause of hypopituitarism in the peripartum patient. Patel et al. presented five postpartum cases that presented with either visual symptoms (especially in late pregnancy) or non-specific symptoms related to hormonal deficiencies in the puerperium. Support for autoimmunity is the association of lymphocytic hypophysitis and thyroiditis. However, whilst antinuclear, antimitochondrial, antimicrosomal, anti-double stranded DNA antibodies have been reported, their detection is often delayed and rarely have antipituitary antibodies been demonstrated on resected specimens using immunofluorescence.

Despite the majority of cases being reported in peripartum women, there have been reports of women developing hypopituitarism and diagnosed with lymphocytic hypophysitis up to ten years after their last pregnancy. In men and perimenopausal women have also been reported. In addition, Honegger et al. comprehensively evaluated clinical features in their series of seven cases of lymphocytic hypophysitis, none of which were associated with pregnancy.

The presenting features of lymphocytic hypophysitis are often indistinguishable from those of a pituitary adenoma. These include symptoms and signs of anterior hypopituitarism and optic chiasmal compression and headache. However, other presentations are also reported, including two cases of men who presented with diabetes insipidus due to lymphocytic

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hypothalamitis\(^7\) and cases presenting with lymphocytic meningitis with subsequent diagnosis of lymphocytic hypophysitis involving the adenohypophysis.\(^6,8\)

The absence of marked hormonal dysfunction in our patient and presence of gross visual failure prompted immediate need for imaging and the preoperative diagnosis of a pituitary macroadenoma. Typically, microadenomas are low density focal lesions on T1 and high intensity on T2, whereas macroadenomas are usually isointense on T1 and hyperintense on T2 weighted images, with marked contrast enhancement. The lesion we report was isointense on T1 and hyperintense on T2 images and had homogeneous contrast enhancement.

Conventional MR findings in inflammatory pituitary disease are far more variable.\(^1,6,9-11\) The shape of the lesions can vary from dumbbell to spherical or elliptical. Most reported cases of lymphocytic hypophysitis appear isointense on T1-weighted images and hyperintense on T2. Contrast enhancement is generally marked but may be homogenous or heterogenous.\(^9\) Triangular enhancement of the pituitary and enhancement of the diaphragma sellae may be pathognomonic but are found in few cases.\(^6,15\) The pituitary stalk may be thickened, normal or not identified.\(^7\) The pituitary fossa may be enlarged or normal with a thin or normal floor thickness. The coronal view of the sellar floor may be planar or depressed (often unilaterally).\(^7\) There may or may not be associated sphenoid sinus mucosal swelling. The size and suprasellar extension are also variable, with no reports highlighting size as a distinguishing feature.

Dynamic MR scans may be performed for the investigation of pituitary disease. Sato et al.\(^10\) concluded from their series of five patients that dynamic imaging could show a delayed contrast enhancement even when the conventional MR seemed to show regression of the inflammatory disease.

The intraoperative features are the most indicative of the diagnosis of lymphocytic hypophysitis. As was found in our

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**Fig. 1** (A) and (B) MRI Coronal images with and without contrast; (C) MRI Sagittal image; (D) CT scan with contrast showing suprasellar extension of tumour.
patient, the mass is typically fibrous and firm and densely adherent to the dura. Normal pituitary is often identified as soft by comparison. Complete transphenoidal excision is variably achieved. Subtotal excision is often due to poor differentiation from normal pituitary or an irregular suprasellar component, or due to dural adherence as in our case. A craniotomy may very occasionally be required to remove the suprasellar portion. Frozen section identified lymphocytic hypophysitis as the likely pathology in our case but an adenoma may not be able to be excluded in some cases.

The gold standard in the diagnosis of lymphocytic hypophysitis is histopathology. Resected glands characteristically show a dense lymphoplasmacytic infiltrate and fibrosis replacing pituitary acini. There is usually an absence of granulomas but variability in the presence of multinucleated giant cells. Examples of all of the above features seen in some specimens give weight to the suggestion that granulomatous hypophysitis is part of the same spectrum with the exclusion of TB and neurosarcoid.

The aim of defining clinical features is to avoid unnecessary surgery. Despite the lack of pathognomonic clinical features, certain clusters of symptoms make the diagnosis more likely. It has been in these patients that the use of steroids has been evaluated as an alternative to surgery. It has also been argued that the natural progression of the disease is of spontaneous resolution without surgery or steroids. Beressi et al. demonstrated the initial success of steroids in a suspected case of lymphocytic hypophysitis, where the complete hypopituitarism was replaced with the gradual recovery of all hormones at nine months. Imaging failed to mirror this improvement, however, and relapse at 14 months led to surgical confirmation of the diagnosis with recommencement of steroids. Meanwhile Gagneja et al. reported a case where histologically proven lymphocytic hypophysitis showed spontaneous resolution on imaging after two years post-diagnosis with incomplete resection and no therapeutic doses of steroids. However microscopic resolution was not evaluated. Both cases had no visual failure and hence a trial of conservative management was justified.

Reports have described trials of steroids with progression of visual defects requiring surgical decompression. Others have shown prompt resolution in mild visual defects in histologically proven lymphocytic hypophysitis (biopsy alone), suggesting that provided the visual symptoms are not gross and progressive, a trial of steroids may be considered. Clearly however, the steroid response is unpredictable, as is the natural progression of the disease. The potential side effects of longterm steroid use must be considered: one case described a patient having bilateral avascular necrosis of the femoral heads after ten months of postoperative steroid use.

CONCLUSION

Despite numerous attempts to create a clinical definition of lymphocytic hypophysitis, the presentation of lymphocytic hypophysitis remains variable. Clinical, biochemical and radiological findings have failed to ensure certainty in the diagnosis, although they can be suggestive. Tissue diagnosis remains essential to exclude pituitary adenoma and avoid inappropriate medical therapy and side effects. The role of biopsy or complete excision is yet to be clarified in cases where visual failure is absent due to variable efficacy of steroids to promote regression. As with our patient, in patients with progressive visual failure, excision is usually necessary.

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REFERENCES

INTRODUCTION

Glioma and meningoia are two common brain tumors, which constitute approximately 58 and 20% of all primary intracranial neoplasms, respectively. The two disease entities have a nearly contrary clinical outcome due to different biological behaviors, in which meningoia, being a fairly benign growth, has the potential, by chance or other etiologies, to associate with numerous other lesions in the brain and elsewhere. However, the simultaneous occurrence of meningoia and gliotic tumors in a patient is extremely rare.

Two primary brain tumors, meningoia, and glioblastoma multiforme, in opposite hemispheres of the same patient

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Summary We report a case with double primary intracranial tumors of different cell types without phacomatosis. The patient was hospitalized due to progressive memory impairment, headaches, dysarthria and right hemiparesis. Initial computed tomographic (CT) examinations revealed a large hyperdense tumor over the right frontal lobe, suggestive of an extra-axial meningioma. Additionally, there was unusual brain edema in the contralateral hemisphere that subsequently proved to originate from an intrinsic tumor. Staged craniotomies were used to treat the patient. Pathological examinations confirmed the two tumors to be a meningioma and a glioblastoma multiforme, respectively. The patient made an uneventful recovery after treatment. Although meningoia and glioma represent two common primary intracranial tumors, the simultaneous development of the two tumors is rare. A randomly occurring event most likely accounted for this linkage in the patient. We suggest that extraordinary brain edema far remote from the primary brain lesion warrants special attention for identifying other potentially undetected lesions. © 2002 Elsevier Science Ltd. All rights reserved.


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