Idiopathic granulomatous hypophysitis

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A case is described of an elderly woman who presented with headaches, hypopituitarism, and visual disturbances and was found to have idiopathic granulomatous hypophysitis, a rare lesion of the pituitary gland. Preoperative magnetic resonance imaging demonstrated a well-circumscribed lesion, which was isointense on both T1- and T2-weighted imaging and enhanced uniformly with administration of gadolinium contrast enhancement, not unlike a macroadenoma. The present case and 12 other cases from the literature are reviewed.

Key Words * pituitary * idiopathic * granulomatous * hypophysitis

Hypophysitis is a rare inflammatory disorder of the pituitary gland that takes the form of either a lymphocytic[3] or granulomatous process. Granulomatous hypophysitis can be caused by any systemic disease that is capable of forming granulomata, most notably, sarcoidosis, syphilis, and tuberculosis. It can also be related to various other intrasellar lesions such as cysts,[1,6] adenomas,[7] and mucocoeles.[10] Granulomatous hypophysitis, which is identified in the absence of any known underlying or associated pathology, is referred to as idiopathic. There are only 12 cases in the literature of idiopathic granulomatous hypophysitis identified at surgery [2,5,6,8,10,12,13]--as opposed to postmortem diagnoses of this entity--and only three such cases reported with a preoperative magnetic resonance (MR) image. We report a case of idiopathic granulomatous hypophysitis visualized on MR imaging and identified at surgery in an elderly woman. This case is discussed in reference to the other 12 cases reported in the literature.

CASE REPORT

This 72-year-old woman presented with various symptoms occurring over the 12 months prior to admission, which included projectile vomiting, pleural effusion, adrenal insufficiency, and, what appeared to be, viral pericarditis. A pericardial window procedure had been performed, without a definitive diagnosis.

Examination. Because of persistent headaches, computerized tomography (CT) and MR imaging of the head were obtained; they demonstrated a sellar mass with suprasellar extension. Magnetic resonance T1- and T2-weighted images revealed a well-circumscribed, homogeneous sellar lesion with suprasellar

extension measuring 1.8 cm in height. The lesion was isointense to brain parenchyma on all pulse sequences and enhanced fairly uniformly with administration of gadolinium contrast medium. The infundibulum was thickened (Fig. 1).

Fig. 1. Preoperative magnetic resonance T1-weighted gadolinium-enhanced imaging, coronal view (left) and sagittal view (right). The lesion is well circumscribed, homogeneous, and isointense. Note that the infundibulum is thickened.

Endocrinological findings revealed panhypopituitarism. Her thyroxine level was 1.1 $\mu\text{g/dL}$ (normal 4.5-12 $\mu\text{g/dL}$), her thyroid-stimulating hormone level was 0.04 mU/L (normal 0.3-5 mU/L), her follicle-stimulating hormone level was 1.8 mIU/ml (normal 1-26 mIU/ml), her luteinizing hormone level was 0.1 mIU/ml (normal 16-64 mIU/ml), and her prolactin level was 0.5 ng/ml (normal 0-25 ng/ml). The patient received daily doses of prednisone (5 mg) and L-thyroxine (0.1 mg). For several months the patient had also noted progressive visual difficulties. Formal vision testing demonstrated a bitemporal hemianoptic defect, with visual acuity of 20/30 in the right eye and 20/200 in the left eye.

Operation. A transsphenoidal resection of the mass was performed. At surgery, a large, yellow, firm mass was noted. The mass was adherent to the surrounding cavernous sinus and arachnoid. A gross-total removal was achieved except for the very lateral wall.

Pathological Findings and Postoperative Course. Microscopic examination of the lesion demonstrated nonnecrotizing granulomatous adenohypophysitis with dense chronic inflammation, Langhans' and non-Langhans' type multinucleated giant cells, and focal fibrosis (Fig. 2). Immunohistochemical characterization of the chronic inflammation showed predominantly T cells and macrophages, with admixed B cells and plasma cells.

Fig. 2. Photomicrographs, H & E. Left: Low-power photomicrograph displaying multiple granulomata in a background of dense chronic inflammation. Original magnification X 25.

Right: High-power photomicrograph showing multinucleated cells of the Langhans' type within granulomatous inflammation. Original magnification X 100.

Staining for organisms, including Gram, acid-fast, modified Steiner's, and Grocott-Gomori methenamine-silver nitrate, was negative for bacteria, mycobacteria, spirochetes, and fungi, respectively. A skin purified protein derivative test for tuberculosis was negative, as were serum rapid plasma reagin levels for syphilis, and angiotensin-converting enzyme levels for sarcoid. Cultures for bacteria and acid-fast bacillus showed no growth. After surgery, the patient's vision dramatically improved: visual fields and acuity were normal. She was discharged in good condition on a course of glucocorticoid and L-thyroxine replacement therapy.

DISCUSSION

The pathological characteristics of granulomatous hypophysitis were first described in 1911 by Gougerot and Gy[4] and in 1917 by Simmonds.[11] In 1954, Rickards and Harvey[9] reviewed 115 cases of granulomatous hypophysitis from the literature, including 23 idiopathic cases, all of which were diagnosed only at autopsy. Most cases of granulomatous hypophysitis are associated with systemic granulomatous diseases, most notably sarcoidosis, syphilis, and tuberculosis, but which can also include Langhans' cell granulomatosis and various bacterial and fungal processes. Granulomatous hypophysitis can also occur in the setting of other pituitary pathology such as cysts,[1,6] adenomas,[7] and mucocèles,[10] in which cases the inflammatory process may well represent a reaction to the local pituitary lesion.

There are 12 cases reported in the literature of patients with granulomatous hypophysitis diagnosed antemortem for which no etiology could be identified. Ours is a thirteenth case (Table 1).

TABLE 1
SUMMARY OF CHARACTERISTICS AND FINDINGS IN 13 PATIENTS WITH GRANULOMATOUS HYPOPHYSITIS*

Authors & Year	Age (yrs), Sex	Signs & Symptoms	Endocrine Status	Radiological Findings	Operative Findings	Follow-Up
Del Pozo, et al., 1980	28, F	HA,E	hypopit	CT: enhancing intrasellar mass	firm mass	good hypopit
Taylor & Duff, 1980	50, M	HA, CNIII palsy	NA	CT: normal	diffuse edema (biopsy)	good (h), CNIII somewhat improved
Hassoun, et al., 1985	65, F	E	hypopit	CT: rarefaction of dorsum sella with normal sella volume	firm mass	good (h)
Scanarini, et al., 1989	19, F	E	high pro, DI, mild hypopit	CT: hypointense mass with ring enhancement	creamy, gray-yellow fluid	good
Scanarini, et al., 1989	57, M	HA,E, CNIII palsy	hypopit	CT: isodense mass that enhanced & extended to cavernous & sphenoid sinuses	firm, capsulated mass	good (h), CNIII somewhat improved
Scanarini, et al., 1989	58, M	E	hypopit	CT: isodense mass that enhanced	fibrous, capsulated mass	good (h)
Siqueira, et al., 1989	37, M	HA,E	hypopit	CT: intrasellar/suprasellar mass with patchy enhancement	necrotic material within thick capsule	good (h)
Higuchi, et al., 1993	46, F	V,E	hypopit, high pro	CT: intrasellar/suprasellar enhancing mass, thick infundibulum	hard, calcified mass	good (h), vision improved
Higuchi, et al., 1993	55, F	E	DI	T1 MR: intrasellar/suprasellar mass, isointense, with homogeneous enhancement & thickened infundibulum	abnormal fibrous tissue	good (h)
Higuchi, et al., 1993	55, M	V,E	hypopit	T1 MR: intrasellar/suprasellar mass, isointense, with homogeneous enhancement & thickened infundibulum	avascular, gray-red fibrous tissue (biopsy)	good (h), vision improved
Pamir, et al., 1993	41, F	E	high pro	CT: intrasellar/suprasellar mass poorly enhancing with few irregular hyperintensities. T1 MR: isointense homogeneous mass. T2 MR: heterogeneous mass with irregular hyperintensities	firm, capsulated mass	good
Pamir, et al., 1993	36, F	E	high pro	CT: intrasellar/suprasellar mass, isodense, with poor enhancement	fibrous, firm capsulated mass	good
Brisman, et al., 1996 (present case)	72, F	HA,V,E	hypopit	T1 MR: intrasellar/suprasellar mass, isointense & homogeneous, with homogeneous enhancement & thickened infundibulum T2 MR: isointense, & homogeneous	firm, yellow mass	good (h), vision improved

* CNIII = cranial nerve III; DI = diabetes insipidus; E = endocrine disturbance; (h) = hormone replacement therapy; HA = headache; high pro = elevated prolactin level (> 20 ng/dl); hypopit = hypopituitary; V = visual disturbance.

Unlike lymphocytic hypophysitis, which usually occurs in young women,[3] idiopathic granulomatous hypophysitis is more evenly distributed among men and women (five men, eight women) and occurs at an average age of 47.6 years (range 19-72 years). Twelve of the 13 reported patients presented with endocrine symptoms, three presented with visual disturbances, and two presented with apoplexy (sudden

headache and third nerve palsy). Unlike patients with granulomatous hypophysitis secondary to sarcoidosis, patients with idiopathic granulomatous hypophysitis present less commonly with diabetes insipidus (two of 13 cases). Nine of the 13 patients presented with hypopituitarism, and four had moderately elevated prolactin levels (20-150 ng/ml). Panhypopituitarism in association with a rather modestly enlarged pituitary lesion (mostly confined to the sella turcica) may suggest the diagnosis of idiopathic granulomatous hypophysitis. Another suggestive feature is a thickened infundibulum, which was noted in four of the 13 cases.

Radiographically, idiopathic granulomatous hypophysitis shows some degree of enhancement on both CT and MR imaging and is most commonly mistaken for a pituitary adenoma. On T1-weighted MR imaging the lesion appears homogeneously isointense to brain parenchyma and enhances homogeneously. At surgery, the lesion appears as a firm mass, and postoperatively, patients uniformly do well. Surgical debulking tends to improve visual disturbances but not the hypopituitarism.

The patient described in the present case is older, at 72 years of age, than any of the patients previously reported. The pleural effusion and pericarditis are of interest, although no connection could be found between systemic inflammatory abnormalities and the patient's granulomatous pituitary disorder.

CONCLUSIONS

In summary, idiopathic granulomatous hypophysitis is a rare disorder of the pituitary gland that carries a good prognosis. Treatment consists of hormone replacement therapy when hypopituitarism is present, biopsy if the presence of a systemic disorder is suspected and cannot be otherwise diagnosed, and debulking if the lesion is large and the optic chiasm is compromised.

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