

# NEUROLOGICAL BULLETIN

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## **Xanthomatous Hypophysitis: An Unusual Case of a Sellar Mass**

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### The Case

The patient is a 57 year-old man with hypertension, who initially presented to his primary care doctor complaining of impotence and fatigue of two months' duration. Laboratory values taken at the visit showed a decreased testosterone level of 9 ng/dl (reference 180-740), a low free T4 of 0.56 ng/dl (reference 0.7-1.5), and a normal TSH of 1.06 mIU/L. He was referred for an endocrine evaluation and seen one week later. At the endocrinologist's office, the patient denied additional symptoms of headaches and polyuria. Visual fields and cranial nerves II-XII were otherwise grossly intact. Additional laboratory studies showed abnormal values of a low afternoon cortisol of 2 mcg/dl (reference 3-12) that increased to 11 after Cortrosyn, a low LH of 0.8 mIU/ml (reference 2-18), and a low serum testosterone of 3 ng/dl, but normal values for serum potassium, creatinine, prolactin, sodium, and FSH. He was subsequently started on hydrocortisone 10 mg, levothyroxine 0.10 mg, and testosterone 5 mg patches, all once a day, and scheduled for an MRI of the brain.

MRI of the brain showed a 13 mm mass present in the sella extending superiorly into the

suprasellar cistern and impressing the inferior margin of the optic chiasm (Figure 1). The mass appeared homogenous, well-circumscribed, and demonstrated no enhancement on post-contrast imaging. The initial differential diagnosis was atypical pituitary macroadenoma, craniopharyngioma, or Rathke's cleft cyst.

The patient had a formal neuro-ophthalmologic evaluation that demonstrated intact visual fields. He was evaluated by a neurosurgeon who counseled the patient on the options of watchful waiting versus proceeding with transsphenoidal craniectomy. The patient opted to defer surgery and so was scheduled for a follow-up MRI in 6 months time.

On subsequent MRI, the pituitary mass had increased in size from 13 mm to 17 mm and the signal intensity within the lesion had diminished on T-1 sequences, suggesting that there may have been hemorrhage into the mass since the earlier study (Figure 2). There was a ring of enhancement around the periphery of the lesion and a central portion that did not enhance, consistent with a cystic tumor. The optic chiasm was further elevated.

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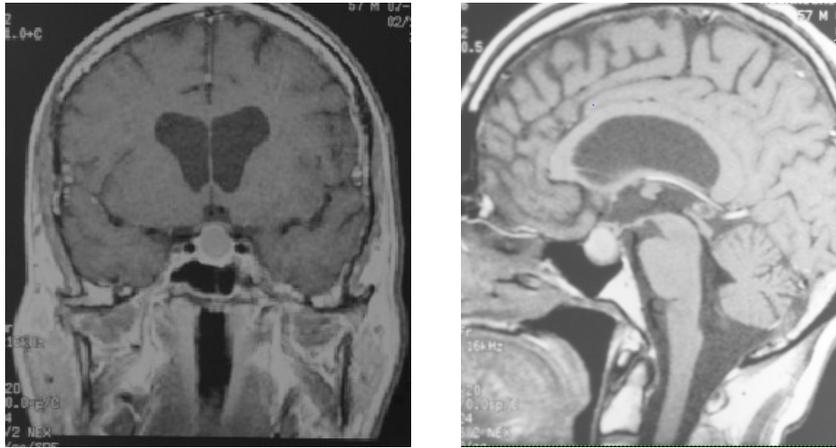


Figure 1: Initial (left) coronal and (right) sagittal T-1 MRI, demonstrating a 13 mm sellar mass.

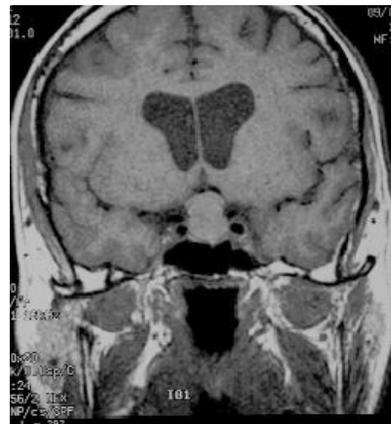


Figure 2: Follow-up T-1 MRI demonstrating growth of the sellar mass from 13 mm to 17 mm.

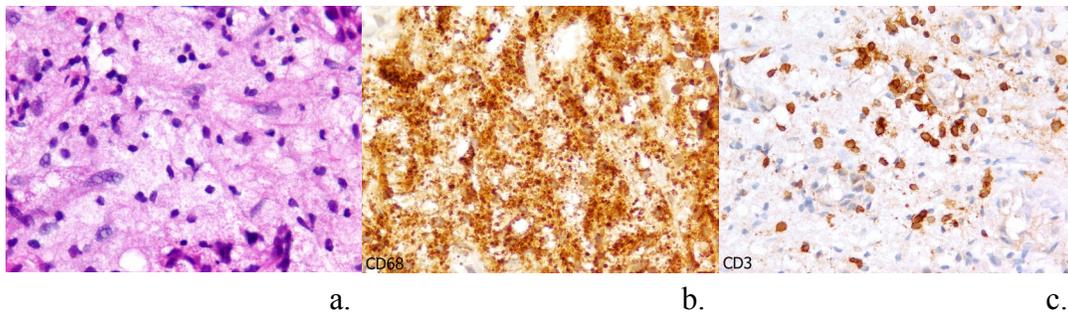


Figure 3: a. Pathology demonstrated the anterior pituitary infiltrated by foamy histiocytes. b. Histiocytes were confirmed by positive CD68 staining. c. Reactive T-lymphocytes were also present, staining for CD3.

The patient was starting to note some loss of vision, and with the increase in the size of the mass, the patient underwent transsphenoidal resection of his mass. During the operative resection of the mass, thick yellow fluid emerged. Pathology of the mass was consistent with xanthomatous hypophysitis. The specimen demonstrated sheets of foamy histiocytes, confirmed by immunohistochemistry as positive for the macrophage marker CD68, some trapped normal pituitary acini, and scattered reactive T lymphocytes (Figure 3).

After surgery, the patient's vision improved, and he reported only some scant yellow mucous nasal drainage. However, on follow-up evaluation shortly after surgery, the patient complained of having to awaken at least four times nightly to urinate, a difficulty he reported as having started at least one week prior to surgery. Serum osmolality was 305 mOsm/kg (reference 275-295) and urine osmolality 253. A simultaneous antidiuretic hormone level was undetectable and he was begun on 0.05 mg DDAVP by mouth twice daily for his diagnosis of diabetes insipidus (DI). Given that the patient reported that symptoms began prior to surgery, his DI is most likely a result of the hypophysitis rather than a complication of surgery.

Six months after surgery, the patient was feeling well. He remained on the same medical regimen of hydrocortisone 10 mg qAM and 5 mg qPM, levothyroxine 0.1 mg daily, testosterone 5 mg patch daily, and DDAVP 0.05 mg twice daily. Follow-up MRI showed normal appearance to the pituitary stalk, complete resection of the mass and no evidence of recurrence.

## Background

Xanthomatous hypophysitis is an inflammatory disorder of the pituitary gland character-

ized by infiltration of lipid-laden histiocytes, also known as xanthoma cells. While xanthomatous hypophysitis is an extremely uncommon cause of pituitary dysfunction, it is one of the possible causes of a non-hormone secreting mass of the sella turcica. Xanthomatous hypophysitis was first reported in 1998 and only a handful of cases have been described since then in the literature<sup>1</sup>. The cause of xanthomatous hypophysitis remains unknown, with infectious, autoimmune, and localized endothelial dysfunction etiologies each having been postulated<sup>1-3</sup>. The average age at diagnosis is 37, with a 3:1 predominance of females to males<sup>3</sup>.

Xanthomatous hypophysitis commonly presents with headache and decreased libido. Hypogonadism has been present in nearly all reported cases. The visual disturbances and DI found in our patient are uncommon<sup>1</sup>, since most cases of xanthomatous hypophysitis are confined to the anterior pituitary without alteration of the stalk or optic chiasm<sup>1</sup>. However, DI has been described in three previous cases of xanthomatous hypophysitis<sup>1,4,5</sup>. Therefore, xanthomatous hypophysitis should be more routinely included when considering etiologies of DI. The genesis of DI in xanthomatous hypophysitis is poorly understood, but in this particular case might result from either inflammatory infiltration of the pituitary stalk or from compression of the pituitary stalk<sup>4</sup>.

MR imaging is the best modality for evaluation of sellar masses. On T1-weighted images, most cases of xanthomatous hypophysitis appear as a symmetric enlargement of the pituitary gland with round cystic lesions<sup>2</sup>. Reports of xanthomatous hypophysitis have shown a more cystic appearance than other types of hypophysitis. If MRI demonstrates an enlarged pituitary gland, a cystic portion of the mass, and accompanying symptoms of hypogonadism, xanthomatous hypophysitis

should be considered one of the likely causes<sup>6</sup>. Diagnosis cannot be confirmed until the time of surgery with pathological evaluation of the resected pituitary tissue. Pathology demonstrates mixed cell infiltrates of foamy histiocytes and mature lymphocytes and contains cyst-like areas typically confined to the anterior pituitary<sup>2</sup>.

Both medical and surgical treatments have been attempted. Steroids have been found to be largely ineffective in the management of xanthomatous hypophysitis, unlike their utility in lymphocytic hypophysitis<sup>4</sup>. Consequently, surgical resection is recommended in almost all cases both to alleviate symptoms and to confirm the diagnosis. Overall, xanthomatous hypophysitis has a relatively good prognosis: more than 50% of patients recover pituitary function after transphenoidal surgery. In those cases where pituitary function does not improve, it is believed that chronic pituitary inflammation may have led to fibrosis and permanent hypopituitarism<sup>7</sup>.

This case supports that xanthomatous hypophysitis deserves more consistent consideration in the differential diagnosis of sella masses capable of causing both DI and visual impairment.

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