CASE REPORT

Neurosarcoidosis Presenting in the Pituitary Gland with Normal Endocrine Studies

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ABSTRACT—Two cases of neurosarcoidosis in the pituitary gland are presented with a review of past cases from the literature. Previous reported cases have always shown changes in the endocrine axis clinically. These two cases, however, were endocrinologically normal prior to surgery. The evaluation of neurosarcoid in the pituitary, clinically and radiographically, is discussed.

Several pathological entities have been found in the region of the pituitary gland and sella including pituitary adenomas, craniopharyngiomas, Rathke's cleft cysts, arachnoid cysts, gliomas, lymphoma, and sarcoid, among others.^{1,2} While surgical options often are the first line of therapy for these lesions, some entities are best treated medically, at least initially. Such medically treated lesions can include prolactinomas (with high prolactin levels), adrenocorticotrophic hormone (ACTH)- or growth hormone (GH)-secreting tumors in those who are not surgical candidates or have recurrence, lymphoid adenohypophysitis (LA), some radiosensitive germ cell tumors, and sarcoid. Unfortunately, the imaging characteristics of the nonsecreting inflammatory lesions (sarcoid and LA) may overlap substantially with the functioning or nonfunctioning adenomas that are far more common in this location.³ Aside from distinctive endocrinological lab findings (or clinical findings), there may be no noninvasive means to determine the precise diagnosis in these situations. While LA is more common, especially at 1 year postpartum,⁴ sarcoidosis isolated in the pituitary remains rare. Giant cell granulomatous disease, an often similar entity, has been reported in the pituitary since 1862 with and without symptoms but,⁵ in fact, less than 20 cases of pituitary

sarcoid could be found in MEDLINE, and no cases were reported where the endocrine studies were all normal. We present here two cases of pituitary neurosarcoidosis, however, having normal preoperative endocrine studies.

CASE 1

A 33-year-old Indian woman presented with a 3-week history of severe headaches. She denied any visual or other constitutional complaints. Her history prompted a workup that included a magnetic resonance imaging (MRI) scan revealing a 2-cm mass in the sella felt to be consistent with a macroadenoma. Further workup found no endocrinological abnormalities or visual field discrepancies on formal visual field testing. The patient underwent a transphenoidal resection of the mass without incident.

Intraoperatively, a yellowish, firm mass was found after opening the dura. Frozen sections returned a preliminary diagnosis of granulomatous tissue. After further decompression, the wound was closed without pursuing a gross total resection. Final pathology confirmed the diagnosis of granulomatous inflammation of the pituitary without caseating necrosis; special stains for

fungus and acid fast organisms were negative (Fig. 1). She recovered well from surgery and further workup showed a normal serum angiotensin-converting enzyme (ACE) level, a negative chest X ray, and a negative history for uveitis and TB. She has been treated with steroids since the operation with no recurrence at 1 year.

CASE 2

A 23-year-old African-American woman presented with approximately 3 months of headaches and nonspecific vertigo. Her headaches were primarily on the inner angle of the eyes, in the cheeks, and at the top of the head, mostly on the right side. She also felt that her right eye vision was mildly blurry, and she recalled being treated in the past for uveitis in the right eye. A diagnosis of sarcoid was raised at that time, but never documented. Formal visual field testing revealed a small

quadrant defect. An MRI revealed a large sellar lesion thought to be most consistent with a macroadenoma, slightly elevating the optic chiasm. Endocrine studies were normal and she was counseled as to the likely diagnosis of a nonsecreting pituitary tumor. In the operating room, undergoing a transphenoidal approach to the mass, several biopsies of septal mucosal nodules were made and sent for frozen section analysis, returning the diagnosis of granulomatous disease (Fig. 2C). A firm, rubbery mass was encountered in the sella, also giving a frozen (and later final) diagnosis of granulomatous disease. Some cavernous sinus bleeding was encountered while removing pieces of the lesion and a decision to treat the patient with corticosteroids was made and the wound closed. Many giant histiocytes were found, and there was some central, fibrinoid-type necrosis with negative AFB and auramine rhodamine stains. The patient did well with surgery and has since had almost complete resolution of the lesion with steroid treatments.

Figure 1. (A) T1-weighted pregadolinium coronal view of the sellar lesion, which ultimately was diagnosed as sarcoid in this patient. (B) T1-weighted postgadolinium coronal view of the same lesion. Note the nature of the diffuse, but somewhat heterogeneous, quality of enhancement, making the lesion difficult to distinguish from more typical pituitary adenomas. (C) Histologic study of this lesion showed noncaseating pituitary granuloma (hematoxylin-eosin, 400 $\times$) typical of sarcoid.

Figure 2. (A) T1-weighted pregadolinium sagittal view of the sellar lesion. (B) T1-weighted postgadolinium axial view of the same lesion. Again, note the quality of variation in contrast enhancement, making it indistinguishable from an adenoma. (C) Noncaseating microgranuloma from a biopsied septal mucosal nodule (hematoxylin-eosin, 400 $\times$) encountered on the surgical approach. (D) Again, histologic examination showed noncaseating pituitary granuloma (hematoxylin-eosin, 200 $\times$), consistent with sarcoid.

DISCUSSION

Although a rare entity, pituitary sarcoid has been previously reported as typically having profound changes within the endocrinologic axes.⁶⁻⁸ Such changes have included obesity,⁹ psychosis,¹⁰ diabetes insipidus,¹¹ amenorrhea,¹² hypoglycemia,¹² and significant pituitary insufficiencies (in various combinations).^{6,13,14} Here, however, we have two cases that involved large pituitary lesions, but no abnormal endocrine findings. These two cases are taken from an overall series of approximately 150 resected pituitary lesions operated on during the past 6 years by the same surgeon (M.J.K.). In fact, other than the small visual field deficit in one patient (related to the pressure of the lesion on the chiasm), neither case had anything much more specific in the history than headaches. Case no. 2 did have a prior history of uveitis, adding the diagnosis of sarcoid to the differential. With no prior cases in the literature of pituitary sarcoid having normal endocrine findings, however, such a diagnosis still seemed to be an unlikely possibility.

Neurosarcoid, where sarcoid is found in the central nervous system, accounts for approximately 5% of all cases of sarcoidosis.^{13,15} Of these, Stern et al¹⁵ have reported that 48% initially presented with the neurological symptoms. Ultimately, 97% of the patients in their study were found to have other systemic manifestations of the disease. Typically, sarcoid presents in other organs such as the eyes, skin, lymph nodes, bones, muscles, lungs, and parotid gland. When it is found in the nervous system it seems to affect cranial nerves (the VIIth, in particular), promote a basal arachnoiditis or meningoencephalitis, or organize in posterior fossa nodules.^{13,15,16} While histologically distinct (containing noncaseating granulomas with lymphocytic infiltrates¹⁷), radiological diagnoses of this entity remain often indistinguishable from macroadenomas where they can be relatively unenhancing or enhancing, symmetrically midline and inhomogeneous.^{3,18}

Sarcoid has also been reported in the pituitary associated with a Rathke's cleft cyst,¹⁹ and a sarcoid lesion with its own cyst,²⁰ making the finding of pituitary sarcoid, even in the presence of a cyst on imaging, still possible. Hallgren et al²¹ reported an interesting set of cerebrospinal fluid (CSF) studies that might differentiate various inflammatory central nervous system reactions from neurologically "healthy" patients. These included levels of lactoferrin, lysozyme, and β -2 microglobulin (β -2 μ). In patients with sarcoid, they found significantly increased lysozyme and β -2 μ levels but normal lactoferrin. In pituitary adenomas, their study found a pattern similar to this in half of the patients, though the lysozyme levels were still not as elevated as they were in the sarcoid patients. ACE levels in

sarcoid are elevated in serum in 83% of patients with active pulmonary disease, but CSF levels are normal. However, approximately 50% of patients with neurosarcoid have elevated ACE levels in the CSF.²²

Our findings intraoperatively (as described above), combined with frozen section analysis and at least the passing thought of sarcoid in one's differential might avoid a more dangerous and needless dissection because these lesions respond favorably to steroid treatments.^{15,23,24}

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