

CASE REPORT

Large pituitary incidentaloma in a patient with sarcoidosis

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A 60 year old male with a medical history of pulmonary sarcoidosis and chronic low testosterone presented to his allergist for excessive lacrimation. Computed tomography (CT) scan of sinuses ordered for possible blocked nasolacrimal duct revealed an abnormal expansion of the sella turcica. Magnetic resonance imaging suggested a homogeneously enhancing 4 cm soft tissue mass enveloping the internal carotid and abutting the optic nerves. Since the patient indicated no symptoms, it was felt to be consistent with a pituitary incidentaloma. Laboratory investigation showed only minimally elevated prolactin. Visual field testing at the office was normal but computed campimetry was suggestive of few minimally depressed points in the supra-temporal quadrant on the right. Even with high suspicion of neurosarcoidosis, the patient had a surgical indication so he underwent transsphenoidal excision of the mass with no complications. Pathology was consistent with a null-cell pituitary adenoma.

Keywords: *pituitary macroadenoma; MRI; transsphenoidal surgery; incidentaloma; sarcoidosis*

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Ready availability of computed tomography (CT) scan and magnetic resonance imaging (MRI) has led to increased detection of asymptomatic pituitary adenomas, that is, 'incidentalomas', the prevalence of which is estimated at 3.7–20% (1). Pituitary incidentalomas are classified on the basis of size and hormonal activity. Of the non-cystic-appearing incidentalomas, nearly all are pituitary adenomas. As they are not associated with hormonal hyper-secretion, they are often undiagnosed until they grow enough to compress adjacent anatomical structures and thereby cause visual disturbances and/or impaired pituitary function. Most clinically non-functional pituitary adenomas are gonadotropic in origin, as determined by immunocytochemical testing.

Although most pituitary incidentalomas can be safely monitored until early signs appear, the differential diagnosis should consider other entities in patients with pertinent medical history, for example, neurosarcoidosis in this case. Neurosarcoidosis occurs in less than 5% of patients with systemic sarcoidosis. Isolated neurosarcoidosis without systemic involvement is extremely rare (2). Importantly, even with benign pathology, large tumors carry the risk of complications, such as pituitary apoplexy secondary to acute intratumoral hemorrhage, or acute visual loss. We describe the case of a patient with a medical history of sarcoidosis without any systemic involvement that was found to have a pituitary mass.

Case

A 60-year-old male with a medical history of stage I sarcoidosis and chronic hypergonadotropic hypogonadism, with a history of prostate cancer treated with radiotherapy and chemotherapy 10 years prior, self-referred to his allergist for dry eyes with excessive lacrimation. He denied visual disturbances, headache, nausea, vomiting, weakness, weight changes, gynecomastia, sexual dysfunction, sweating, palpitations, heat or cold intolerance, or dry skin. Vitals signs were normal. Fiberoptic nasal endoscopic examination of nasal mucosa, septum, and turbinates was without lesions or masses but did indicate a deviated nasal septum to the right and nasal polyps on the left. There was no thyromegaly. Weber, Rinne, and hearing tests were all normal and the rest of the physical examination was unremarkable. With suspicion for a blocked nasolacrimal duct, a CT scan of the head and sinuses was ordered, which showed an enlarged sella turcica. MRI suggested a homogeneously enhancing 4 cm soft tissue mass centered in the sella turcica, extending into both the left and right cavernous sinuses, encasing 50% of the left cavernous internal carotid artery and displacing the optic chiasm (Fig. 1). Thyroid-stimulating hormone (TSH), free t₄, t₃, GH, IGF-1, and 24-hour urine cortisol levels were normal. The prolactin was minimally elevated (24.4 ng/mL, normal 2.64–13.13 ng/ml). Free testosterone and total testosterone were low (1.7 and

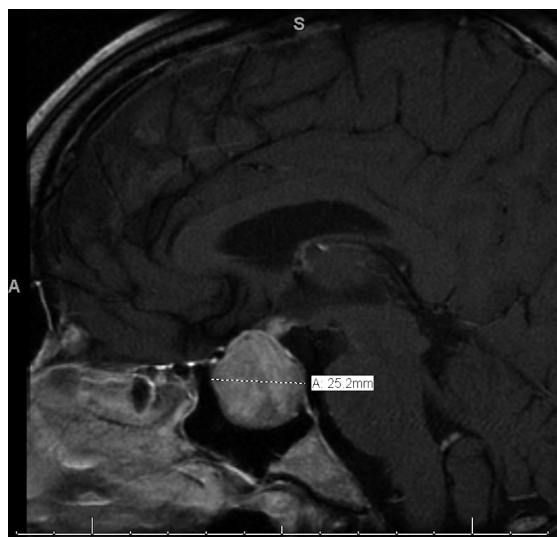


Fig 1. Initial MRI sagittal view showing the pituitary mass (dotted line). Homogeneously enhancing 4 cm soft tissue mass centered in the sella turcica extending into both the left and right cavernous sinus as well as abutting and displacing the optic chiasm.

58 ng/dL, respectively, normal 240–950 ng/dL) with high luteinizing hormone (LH) 20.2 (1.8–12.0 mIU/L) and normal follicular stimulating hormone (FSH) 4.65 (1.5–12.4 mIU/ml) (Table 1).

Ophthalmological evaluation revealed stable visual acuity at 20/25+ in the right eye and 20/20 in the left eye. Non-dilated examination revealed no evidence of ocular involvement from sarcoidosis. There was no afferent pupillary defect or red desaturation. Color vision (Ishihara plates) was normal, brisk, and equal. No optic disc edema or pallor was noted. Confrontation visual field (VF) examination was reported normal at the office; however, VF testing by computer-assisted campimetry was reported as normal in the left eye and with few minimally depressed points in the supra-temporal quadrant of the right eye. The patient underwent combined transseptal transsphenoidal approach with resection of the pituitary neoplasm (Fig. 2). Pathology returned consistent with a null-cell adenoma.

Table 1. Showing pre-op and post-op laboratory values

	ACTH (pg/ml)	Cortisol AM (µg/dl)	TSH (uIU/ml)	Free T4 (ng/dl)	LH (mIU/ml)	FSH (mIU/ml)	Total testosterone (ng/dl)	Free testosterone (ng/dl)	Prolactin (ng/ml)
Reference range	6–50	8.7–22.4	0.4–4.5	0.58–1.64	1.24–8.62	1.27–19.2	240–950	9–30	2–18
Pre-op	38	13.4	4.3	1.6	20.2	4.65	58	1.7	24.4
Post-op	35	15	5.8	0.8	2.1	4.8	58	2.5	6.5

ACTH: adrenocorticotrophic hormone; TSH: thyroid stimulating hormone; LH: luteinizing hormone; FSH: follicular stimulating hormone; Pre-op: pre-operative; Post-op: post-operative.

Discussion

Endocrine incidentalomas are very common diagnoses in primary care. Usually, they are discovered during imaging studies performed for other non-endocrinological reasons and are found in the thyroid, adrenal, and pituitary glands. Pituitary incidentalomas are generally defined as asymptomatic lesions of the pituitary gland and may include pituitary adenomas or other sellar lesions. They are classified based on size and hormonal secretion, that is, microadenomas if they are <10 mm and macroadenomas if they are >10 mm in size.

The prevalence of pituitary incidentalomas has been reported between 3.7 and 20% discovered on neuroimaging (MRI, CT scan) or autopsy (3, 4). However, pituitary lesions >10 mm in diameter have been described only between 0.16 and 0.3% on subjects who underwent CT scan or MRI for unrelated reasons (5, 6). Independent of size, hormonal hypersecretion can occur with any incidentaloma (1 in 1,000 cases), but hyposecretion is usually the result of a macroadenoma (7).

In various surgical series, prolactinomas and non-secreting tumors each comprise approximately 30–40% of all tumors (8). Non-functioning pituitary adenomas (NFPAs) are a heterogeneous group of tumors that include null-cell adenomas, oncocytomas, gonadotropin-secreting adenomas, adrenocorticotropin, growth hormone, prolactin (PRL), and thyrotropin (TSH) adenomas. Their annual incidence is 4–5 cases per million people with an estimated worldwide prevalence of 50–60 cases per million people (9). Asymptomatic incidentalomas are independently associated with better outcomes (10).

The majority of pituitary adenomas are benign masses that remain clinically silent and are associated with minimal morbidity and mortality. However all the diagnostic possibilities should be considered because hormonal hypersecretion and lesions that can enlarge and impair pituitary hormone production or compress the optic chiasm should be treated and corrected early.

The differential diagnosis of sellar incidentalomas is broad and several types of lesion may be found in the sellar area that may mimic a pituitary adenoma. Such lesions include aneurysm of the internal carotid artery, cranio-pharyngiomas, meningiomas of the tuberculum sellae,



Fig. 2. Post-surgery MRI: Interval resection of previously described pituitary adenoma. Peripherally enhancing soft tissue remains within the pituitary sella with extension to the left cavernous sinus. Findings likely reflect post-operative changes (white arrow).

gliomas of the hypothalamus and optic nerves, dysgerminomas, pars intermedia and Rathke cleft cysts, hamartomas, metastases, sarcoidosis, and eosinophilic granulomas. All of these have different clinical and imaging characteristics that can guide the diagnosis, including patient age, other simultaneous symptoms, previous history, and rate of progression. However, the final diagnosis is only established with tissue pathology.

Once a pituitary incidentaloma is discovered, there are three features that should be addressed: functionality (excess of any pituitary hormone), hypopituitarism, and VF impairment (related to size of the adenoma and mass effect). The most frequent deficit is hypogonadotropic hypogonadism (30%) without hyperprolactinemia (1).

Our patient had a previous history of pulmonary sarcoidosis, so the initial concern was for neurosarcoidosis. However, almost all cases (91%) of neurosarcoidosis are diagnosed with neurologic symptoms or clinical hormonal deficits (11), neither of which were present in our patient. In fact, we found a previous diagnosis of hypogonadism that was not previously addressed, but finally corresponded to a hypergonadotropic hypogonadism without pituitary origin, commonly called andropause. If the deficit was pituitary in origin, it would present with low testosterone and low LH and FSH. Gonadotroph cell adenomas are the most common histological subtype, accounting for approximately 80% of non-functioning pituitary adenomas; however, the secretion of these tumors are usually non-functional subunits of FSH and LH without any function and in rare cases where the FSH

production is functional, it would cause hypergonadism which our patient did not have (12).

Our patient also had inactive pulmonary sarcoidosis at the time of diagnosis and negative ophthalmologic evaluation for sarcoidosis. The MRI findings in our patient was consistent with pituitary adenoma with in-homogeneously expanding pituitary mass with asymmetrical suprasellar extension and contralateral deviation of stalk, that are usually not present in neurosarcoidosis or lymphocytic hypophysitis (Fig. 1) (13).

Our patient presented with bilateral hyper lacrimation as the main symptom. However, the innervation of lacrimal reflex is compound of afferent components of the trigeminal and facial nerve. Only bilateral VII disease as in Bell's palsy will cause bilateral symptoms, while trigeminal disease will cause hypo lacrimation. The afferent VII nerve branch related to the lacrimation track does not have anatomic correlation with pituitary or the cavernous sinus so there was no possible correlation with the presenting symptoms and pituitary finding (14).

Given the size of the tumor and the absence of VF deficits, despite the displacement of the optic chiasm, we concluded that this tumor likely had a slow growth pattern that usually corresponds to non-functioning macroadenoma.

Because the mass was displacing the optic nerves, the decision was made to treat surgically and re-evaluate according to pathological findings. He was found to have a macroadenoma with null-cell pathologic features after immune-histochemical stains. Post-operative MRI showed a 7.6 mm residual mass wrapped around the Internal Carotid Artery, which is being followed with serial MRIs.

A recent study indicated that post-operative residual tumor was detected in 8.9% of patients with asymptomatic incidentalomas, as compared with 31.2% of patients with symptomatic incidentalomas and multivariate analysis confirmed that having an asymptomatic incidentaloma was independently associated with a better outcome (10). However, this study did not differentiate between asymptomatic incidentalomas in macro or microadenomas and we believe that, even without symptoms, the size of the tumor would change the final prognosis.

The 5-year recurrence-free survival in patients with incidentaloma has been reported as 86.8% (8); however, early diagnosis and comorbidities assessment remains the key to avoid not only mortality but also morbidity, as visual impairment and hypopituitarism are usually irreversible in patients with slow tumor enlargement.

References

1. Shirodkar M, Jabbour SA. Endocrine incidentalomas. *Int J Clin Pract* 2008; 62: 1423–31. doi: 10.1111/j.1742-1241.2008.01831.x.
2. Pawate S, Moses H, Sriram S. Presentations and outcomes of neurosarcoidosis: a study of 54 cases. *QJM* 2009; 102: 449–60. doi: 10.1093/qjmed/hcp042.

3. Molitch ME, Russell EJ. The pituitary 'incidentaloma'. *Ann Intern Med* 1990; 112: 925–31.
4. Chidiac RM, Aron DC. Incidentalomas. A disease of modern technology. *Endocrinol Metab Clin North Am* 1997; 26: 233–53.
5. Yue NC, Longstreth WT, Jr, Elster AD, Jungreis CA, O'Leary DH, Poirier VC. Clinically serious abnormalities found incidentally at MR imaging of the brain: data from the cardiovascular health study. *Radiology* 1997; 202: 41–6. doi: 10.1148/radiology.202.1.8988190.
6. Vernooij MW, Ikram MA, Tanghe HL, Vincent AJ, Hofman A, Krestin GP, et al. Incidental findings on brain MRI in the general population. *N Engl J Med* 2007; 357: 1821–8. doi: 10.1056/NEJMoa070972.
7. Chanson P, Daujat F, Young J, Bellucci A, Kujas M, Doyon D, et al. Normal pituitary hypertrophy as a frequent cause of pituitary incidentaloma: a follow-up study. *J Clin Endocrinol Metab* 2001; 86: 3009–15. doi: 10.1210/jcem.86.7.7649.
8. Katznelson L, Alexander JM, Klibanski A. Clinical review 45: clinically nonfunctioning pituitary adenomas. *J Clin Endocrinol Metab* 1993; 76: 1089–94. doi: 10.1210/jcem.76.5.8496297.
9. Losa M, Mortini P, Barzaghi R, Ribotto P, Terreni MR, Marzoli SB, et al. Early results of surgery in patients with nonfunctioning pituitary adenoma and analysis of the risk of tumor recurrence. *J Neurosurg* 2008; 108: 525–32. doi: 10.3171/JNS/2008/108/3/0525.
10. Losa M, Donofrio CA, Barzaghi R, Mortini P. Presentation and surgical results of incidentally discovered nonfunctioning pituitary adenomas: evidence for a better outcome independently of other patients' characteristics. *Eur J Endocrinol* 2013; 169: 735–42. doi: 10.1530/EJE-13-0515.
11. Langrand C, Bihan H, Raverot G, Varron L, Androdias G, Borson-Chazot F, et al. Hypothalamo-pituitary sarcoidosis: a multicenter study of 24 patients. *QJM* 2012; 105: 981–95. doi: 10.1093/qjmed/hcs121.
12. Snyder PJ. Gonadotroph cell adenomas of the pituitary. *Endocr Rev* 1985; 6: 552–63.
13. Bellastella A, Bizzarro A, Coronella C, Bellastella G, Sinisi AA, De Bellis A. Lymphocytic hypophysitis: a rare or underestimated disease? *Eur J Endocrinol* 2003; 149: 363–76.
14. Neuro-Ophthalmology Virtual Education Library (NOVEL) (2005). Walsh & Hoyt: disorders of lacrimation. University of Utah – Spencer S. Eccles Health Sciences Library. Available from: <http://novel.utah.edu/AAO-NANOS> [cited March 2014].