



PITUITARY TUBERCULOSIS-A COMMON DISEASE AT ATYPICAL SITE

Neurosurgery

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ABSTRACT

Tuberculosis of the central nervous system is a consequence of disseminated tuberculosis which usually manifest as meningitis, an abscess or rarely as a tuberculoma. The intracranial tuberculomas especially within the sella, are notorious for simulating as pituitary tumors, affecting pituitary hormonal function and exerting compressive effect on adjacent intracranial structures. Permanent endocrine dysfunction is important sequelae of Tubercular involvement of the sella if discovered late. So it must be investigated early during diagnostic evaluation as the condition is treatable with anti-tubercular therapy (ATT). Although in rare instance surgery may be a favorable option especially for managing extensive intrasellar masses, ATT usually facilitate resolution of such lesion. Long term hormonal replacement therapy may be required for established endocrine dysfunction.

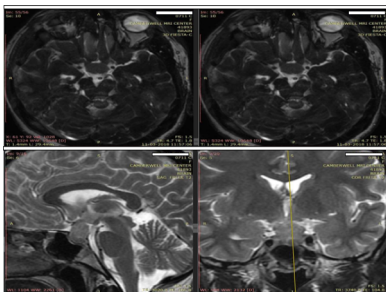
KEYWORDS

Tuberculoma, sella, hormone replacement therapy, Antitubercular therapy etc

INTRODUCTION

Non-functioning sellar masses (NFSM) of the pituitary gland which includes inflammatory and granulomatous lesions have been known to behave like pituitary tumors. Of these sellar tuberculosis (TB) is a rare pathological factor, accounting for 0.15% - 4% of all intracranial lesions though pulmonary TB is common especially in overpopulated country like India. Permanent endocrine dysfunction is important sequelae of Tubercular involvement of the sella if discovered late. So it must be investigated early as the condition is treatable with anti-tubercular therapy (ATT).² We hereby report the presentation of an adult female who displayed visual field defect owing to mass effect on optic chiasma. Initial diagnosis revealed a pituitary macroadenoma which was later proven to be tuberculosis (TB) on histopathological examination. The case here discussed below is aimed at increasing the awareness among clinicians for considering TB as a possible aetiological factor for NFSM. Tuberculosis (TB) is an important cause of morbidity and mortality across the world especially in developing country like India. Intrasellar tuberculomas, however, are extremely rare.

Pituitary adenomas are a diverse group of tumors which arises from the pituitary gland. Historically on basis of size these tumors have been classified into microadenomas (dimension < 1 cm) and macroadenomas (dimension \geq 1 cm). Later this classification has been supplemented by a more comprehensive system based on immunohistochemistry and electron microscopy.³ Depending on their hormonal activity pituitary adenomas can be classified further as functional or nonfunctional. Small, slow-growing and hormonally inactive adenomas are typically identified as incidental findings on imaging or postmortem examinations, on the other hand small, slow growing lesions with high hormonal activity manifest as a clinical syndrome. Adenomas growing fast and nonetheless hormonally inactive may result in symptoms of an intracranial mass specially visual field defect.⁴



CASE HISTORY

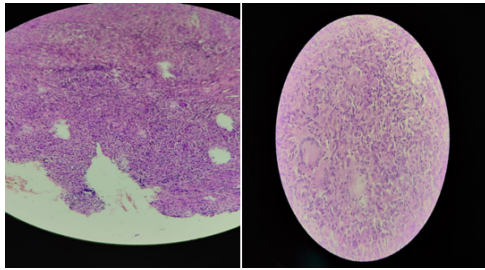
We are discussing an interesting case of a young 36 years old Indian female patient who presented with complaint of intermittent headaches and bitemporal loss of vision (more pronounced in left eye) since last 2 months. The headaches were episodic and associated with photophobia and nausea. Patient took treatment from local doctor but not got relief. Ophthalmoscopic examination of retina and lens reveal no significant abnormality. Patient later consulted neurosurgeon and MRI Sella with contrast done reveals lobulated altered signal intensity lesion is seen arising from sella region with suprasellar extension measuring approx. 14* 17*22 mm (AP*TD *CC), in size showing isointense signal on T1 and hyperintense signals on T2 and flair sequences. It is abutting and splaying the carotid artery bifurcation laterally and causing compression of optic chiasm, however no evidence of compression of third ventricle seen. No extension into bilateral cavernous sinus seen. No evidence of cystic/hemorrhagic changes seen. T1 hyperintense signals are seen in posterior aspect of the lesion - compressed posterior pituitary. On post contrast sequences - there is intense enhancement seen - pituitary macroadenoma.

MRI Sella with showing lobulated altered signal intensity lesion arising from sella region with suprasellar extension showing isointense to hyperintense signal on T2 MRI splaying the carotid artery bifurcation laterally and causing compression of optic chiasm.

On examination, her body weight was 76 Kg, height was 155 cm, blood pressure (BP) was 122/80 mmHg. Systemic examination was otherwise unremarkable. Laboratory examination revealed fasting blood glucose (FBG) = 72 mg/dL (normal, 70 - 100 mg/dL); blood urea 30mg/dl, serum creatinine 0.9mg/dl serum sodium 136 mg/dl and serum potassium 4.5 mg/dl. TLC 7800/cumm Neutrophil 68% eosinophils 03 %, lymphocytes 27% and monocytes 02 %, platelets count was 273000/lakhs. Prothrombin time was 12 sec, bleeding time was 2.30 minutes and clotting time was 4.40 minutes. Thyroid stimulating hormone (TSH) 1.43 mIU/L (normal, 0.34 - 5.6 mIU/L); thyroxine (T4) 5.10 μ g/dL (normal, 4.5 - 10.90 ng/dL); and 8 am serum cortisol 7.92 μ g/dL (normal 6.7 - 22.6 μ g, serum follicle stimulating hormone (FSH) 6.97 mIU/mL (normal, 1.27 - 19.26 mIU/mL); serum luteinizing hormone (LH) 0.54 mIU/mL (normal, 1.24 - 8.62 mIU/mL); serum prolactin (PRL) 13.22 ng/mL (2.8 - 29.2 ng/mL). CXR, ECG found to be normal, HIV and HBS report are negative CSF fluid reveal no significant abnormality except mild elevated protein level and report for CSF culture for AFB was insignificant.

After surgery (endoscopic excision of tumor by trans-sphenoidal approach) patient's vision improved. The surgical pathology report

reveals granulomatous hypophysitis consistent with tubercular pathology



Granulomatous hypophysitis consistent with tubercular pathology

Diagnosis of primary pituitary TB was made and four anti-tuberculous medications (isoniazid, rifampicin, ethambutol and pyrazinamide) were commenced and ATT was started according to weight of the patient and patient showed marked improvement in her symptoms.

DISCUSSION

In absence of other organ involvement only involvement of pituitary gland is extremely uncommon and only less than a hundred cases have been reported in various studies. Highest percentage (70%) of pituitary TB cases reported in various studies were from the Indian subcontinent for which the high prevalence of TB in Indian subcontinent might be an explanation.⁵ Srisukh et al in their study of pituitary tuberculomas, found that young people were the most commonly affected by the disease and majority of affected cases were females. The most common presenting symptoms are headache and visual disturbances and there is absence of constitutional symptoms of TB like fever is characteristic. About 24% of cases Hypofunction of the anterior pituitary gland and hyperprolactinemia were seen.⁶

TB of the pituitary which is nonetheless rare in frequency is a cause of secondary granulomatous hypophysitis which is reported by some studies in developing countries.⁷ It predominantly manifests as a tuberculoma (tumour-like masses of tuberculous granulation tissue ranging from 2 to 12 mm in diameter that forms in the parenchyma of the brain associated with widening of the pituitary stalk (TB hypophysitis). It can undergo caseation resulting in a pituitary abscess, or haemorrhagic infarction leading to pituitary apoplexy.⁸ Earlier studies have reported intrasellar tuberculomas arising from direct extension of infection from paranasal sinuses, especially in females.⁹ Owing to their compressive effects, varying degrees of anterior pituitary dysfunction can develop later with or without central diabetes insipidus. Hypopituitarism with hyperprolactinaemia occurs, that causes galactorrhoea and amenorrhoea in females and decreased libido in males. Imaging studies show involvement of paranasal sinuses and pituitary fossa, along with thickening and nodularity of the pituitary stalk along with it involvement of clivus may occur. On MRI, TB pituitary abscesses appear isointense to hypointense on T1-weighted images and hyperintense on T2-weighted images. Due to high protein content they may appear hyperintense occasionally on T1-weighted images. These signal characteristics are nonspecific and overlap those of pituitary adenomas and other granulomatous lesions. TB abscesses may show peripheral contrast enhancement and adjacent meningeal enhancement on contrast-enhanced MRI. There may be suprasellar extension or impingement upon the optic chiasm.¹⁰⁻¹¹ Histopathologically, they are classically characterized by a central area of caseation necrosis surrounded by epithelioid cells, lymphocytes, plasma cells and Langhans's giant cells. Differential diagnosis includes sarcoidosis, syphilis and other granulomatous inflammations. Acid-fast bacilli (AFB) are usually not demonstrable.¹²

There is no indication of surgery except for obtaining biopsies for confirming diagnosis because these lesions resolve with appropriate ATT;¹³ nevertheless our patient in review required surgery due to established visual field defect and radiological evidence of mass extension. For avoiding cerebrospinal fluid contamination Transphenoidal route is the safest approach. During surgery findings of a thickened hypophyseal stalk, greyish firm nonsuckable mass with caseation along with thickened dura, serve as important signs of a tuberculoma.¹⁴⁻¹⁵ ATT is mandatory and cases that present with signs and symptoms of hypopituitarism require hormone replacement therapy.¹⁶

Intrasellar tuberculomas pretend as pituitary adenomas and hence it should be considered in the differential diagnosis of suprasellar masses. By restricting the extent of surgery we can prevent the anticipated occurrence of hormonal deficiencies which can follow surgery.² The clinicians may misdiagnose pituitary tuberculoma as pituitary adenoma and the main diagnostic modality is histopathological examination of the pituitary lesion. For diagnosing pituitary lesions MRI is considered the best radiological modality but differentiation between pituitary tuberculoma and adenoma on the basis of MRI findings can be very difficult. Some findings have suggested that thickening of pituitary stalk can be useful to differentiate pituitary tuberculoma from an adenoma.¹⁷ But this sign again is non-specific and may be seen in a variety of other inflammatory and neoplastic lesions of the pituitary gland such as syphilis, sarcoidosis, lymphomas, and Wegner's granulomatosis. Some scholars advocate the pattern of enhancement may be a useful tool in differentiating tuberculomas with other pituitary lesions.¹⁸ However clinicians should be sceptic to avoid unnecessary invasive procedures in such an important and vital part of the body. On histologic examination of pituitary tuberculoma the typical finding is caseating granuloma. Ziehl-Neelsen staining for TB bacilli is usually negative.¹⁹ The prognosis of pituitary TB depends on the timing of diagnosis and initiation of proper anti-tuberculous medications so we should emphasize on early diagnosis and early use of ATT which can result in full restoration of endocrine and neurologic functions. Whereas late diagnosis and treatment may result in permanent endocrine dysfunction. There is lack of literature regarding the optimal duration of anti-tuberculous medications so a longer duration (9–12 months) which is used for central nervous system TB, may be a reasonable and pragmatic approach. The indications for surgical intervention should be limited for diagnostic or decompressive purposes. If pituitary functions are compromised Hormone replacement therapy may be needed.^{6,20} In our patient diagnosis of primary pituitary Tuberculosis was made based on typical histopathological findings and moreover the ethnic origin of the patient (Indian subcontinent) support our diagnosis where TB is very prevalent.

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