Pituitary Tuberculosis


Abstract
Tuberculous involvement of pituitary is extremely rare and is usually not suspected while dealing with pituitary adenomas, even in patients with history of systemic tuberculosis. We report a case of pituitary tuberculoma in a patient who was undergoing treatment for prostatic tuberculosis. Although diagnosis of sellar tuberculomas is difficult on clinical and radiological examinations, pituitary tuberculomas should be considered in the differential diagnosis of suprasellar masses, especially in developing countries as the condition is potentially curable with antituberculous treatment.

INTRODUCTION
Tuberculosis of the central nervous system can occur at any site and in any age group. Tuberculomas in the hypothalamo-pituitary region are rare.1 With the advent of effective chemotherapy supplemented by early diagnosis, immunization and improvement in the standards of living the incidence and severity of all forms of tuberculosis has decreased. Still tuberculosis is responsible for 20% of the intracranial space occupying lesions in India and tuberculomas of the sellar suprasellar region comprise 1% of all intracranial tuberculomas. Given the exceptional site, the clinical diagnosis of tuberculosis as the etiology of the sellar mass is difficult even in patients with history of tuberculosis. Histopathological diagnosis is essential irrespective of the clinical presentation and radiological findings.2,3 We discuss a case of hypophyseal tuberculosis with panhypopituitarism in a patient with tuberculosis of the prostate.

CASE REPORT
This 42 year old non alcoholic male was admitted in our hospital in April 2005 for evaluation of a sellar mass. The patient had an episode of acute pancreatitis in March 2004 which was conservatively managed in a private hospital. He was diagnosed to have prostatic tuberculosis (histologically proven) in May 2004 when investigated for hematuria and was put on antituberculosis therapy. With complaints of polyuria, polydypsia, polyphagia, and decreased libido, patient was detected to have diabetes mellitus in June 2004 and he was started on insulin. The “polys” disappeared but he started developing diffuse headache by November 2004 which was ignored. With progressive worsening of headache, which was occasionally associated with vomiting he began to develop repeated episodes of hypoglycemia in January 2005. Insulin was discontinued. While getting investigated for recurrent hypoglycemia the basal cortisol was found to be low (2.9 mg/dL (normal: 10-20mg/dL)) and he was put on prednisone 5 mg OD from outside. No other pituitary functions were evaluated at that point of time. Polyuria and polydypsia reappeared. After an episode of severe headache, magnetic resonance imaging (MRI) of the brain was taken which showed a sellar mass and he was referred to our hospital. There was no history of visual impairment, convulsions or focal neurological deficits. His mother and brother were diabetics on oral hypoglycemic agents and his wife had tuberculosis of spine which was successfully treated ten years back.

Physical examination including optic fundi was unremarkable. The hormonal profile was as follows: serum cortisol at 8 am: 5.7mg /dL (normal: 10-20mg/dL) on prednisolone, T3: 190 ng/dL (normal: 70-200 ng/dL), T4: 9.5mg/dL (normal: 5.5-13.5mg/dL), TSH: 0.77 mU/ml (0.2-5mU/ml), prolactin 17.3ng/ml (normal: 5-25ng/ml).Calcium, phosphorous and albumin were repeated twice to rule out the possibility of multiple endocrine neoplasia type 1. Serological test for human immunodeficiency virus (HIV) was negative. A repeat MRI of the sellar region revealed a well defined, intense contrast enhancing sellar mass of 3.1x 3.3x 3 cm with suprasellar extension and elevation of the optic chiasm. There was marked thickening of the infundibular stalk (Fig. 1). The lesion was isointense on T1 weighted image (T1WI) and predominantly hypointense on T2 weighted image (T2WI) (Fig. 2). Patient underwent transsphenoidal surgery in April 2005 under glucocorticoid cover with
Fig. 1: (a) Sagittal precontrast T1 weighted image (b) sagittal postcontrast T1 weighted image and (c) coronal postcontrast T1 weighted image shows a mass in the sella with marked thickening of the stalk. The lesion is predominantly solid and displays intense post contrast enhancement. Focal non-enhancing necrotic areas are noted within the lesion.

The preoperative diagnosis of pituitary macro adenoma. Per-operatively the lesion was firmly adhered to surrounding structures and hence was partially excised. Post operatively headache improved and urine out put continued to be high but he did not require vasopressin. Histopathological examination of the specimen revealed ill-formed epitheloid granulomas with giant cells and caseous necrosis (Fig. 3). The pituitary parenchyma was infiltrated by inflammatory cells. Ziehl-Neelsen staining did not demonstrate acid fast bacilli and special staining for fungi were negative. A diagnosis of tuberculosis of the pituitary was entertained and pyrazinamide and ethambutol was added for the next three months to the existing anti-tuberculosis treatment comprising of isoniazid and rifampicin which he was taking for prostatic tuberculosis.

Repeat hormonal evaluation done 6 weeks post-operatively was as follows: serum cortisol at 8 am: < 1 mg/dL (normal: 10-20mg/dL) on 5 mg prednisolone, T3: 120 ng/dL (normal: 70-200 ng/dL), T4: 3.2mg/l.

Fig. 2: On the T2 weighted image, the lesion is predominantly hypointense as compared to the adjacent gray matter.

Fig. 3: Histopathology: granulomas with giant cells in the pituitary gland
symptoms in 46%.

revealed that headache is the most common presenting symptom (91%) of the patients, followed by visual disturbance (89%) and fever (90%). The hormonal evaluation data of the patients (58%) who had hormonal evaluation showed anterior pituitary hypofunction. Growth hormone reserve was not assessed in most of the patients. It appears that any axis can be randomly involved without obeying the general order of involvement as noticed in pituitary adenomas. Hyperprolactinemia was seen in 23% of the patients whose endocrine evaluation data was available. Inspite of stalk thickening our patient did not have hyperprolactinemia and such finding has been previously reported. Diabetes insipidus was seen in only 11% of the patients.

Radiologically, pituitary tuberculomas mimic adenomas. As found in our case, pituitary tuberculomas are usually isointense on T1WI MRI images and exhibit intense post contrast enhancement on MRI and CT. According to Patankar et al the T1WI can be hyperintense due to the high protein content. The non enhancing areas seen in the imaging of our patient are likely to correspond with the caseation seen in tuberculomas. Suprasellar involvement was found in 74% of the cases while sellar enlargement was seen in 95% of the cases. Contrast MR imaging characteristically demonstrate thickening of the stalk which is due to chronic inflammatory scarring of the pituitary stalk. The thickening of the stalk is non specific and is described in diverse conditions like neoplasms, sarcoidosis, syphilis, lymphocytic hypophysitis, granulomatous hypophysitis and eosinophilic granuloma. The suprasellar extension can make evaluation of the stalk difficult on neuroimaging. Since CT scan was the imaging modality in many cases actual prevalence of stalk thickening could not be commented. The other MRI findings described with pituitary tuberculosis are peripheral ring enhancement of the mass, enhancement of the adjacent dura and basal enhancing exudates due to meningitis. Isolated stalk thickening, sellar/ suprasellar calcification, apoplexy and erosion of the sellar floor have also been reported in the context of pituitary tuberculomas. The degree of hypopituitarism can be disproportional to the size of sellar lesion. Even with the history of tuberculosis and the typical MRI findings possibility of pituitary tuberculosis was not investigated.

Specific cause of headache in pituitary tuberculosis can be associated meningitic process or infarction caused by inflammatory vasculitis. Fever was almost always present in patients less than 12 years of age while it was much less frequent in adult patients. Females were more frequently affected than males (2:1) and 69% of the patients were females. More than 85% of the affected individuals were less than 45 years. Only 30% of the cases had past or concurrent history of extrasellar tuberculous involvement. About 70% of the cases were reported from India.

Endocrine involvement was present in 77% of the patients and it was difficult to detect preferential involvement of any hormonal axis. More than half of the patients (58%) who had hormonal evaluation showed anterior pituitary hypofunction. Growth hormone reserve was not assessed in most of the patients. It appears that any axis can be randomly involved without obeying the general order of involvement as noticed in pituitary adenomas. Hyperprolactinemia was seen in 23% of the patients whose endocrine evaluation data was available. Inspite of stalk thickening our patient did not have hyperprolactinemia and such finding has been previously reported. Diabetes insipidus was seen in only 11% of the patients.

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not considered in the present case because of the rarity of the condition. Several authors have emphasized that diagnosis of tuberculosis should be considered for sellar masses with stalk thickening, particularly in developing countries where tuberculosis remains endemic.

The role of surgery is to establish tissue diagnosis and relieve compressive symptoms. The preferred route for surgery is the transsphenoidal route, as it avoids cerebrospinal fluid contamination and tuberculous meningitis. Peroperatively, tuberculomas of the sella are found to be tough adherent lesions as found in our case. Making complete excision impossible. Even with incomplete excision, post operatively our patient developed fresh hypothyroidism. This raises the question regarding extent of surgery the patients should undergo if there is a preoperative suspicion of tuberculosis. As to long term antituberculous treatment is excellent, as reported by other authors, the surgery should be limited to obtain a histopathological diagnosis and decompression the adjacent structures.

Histopathological examination of our case revealed ill defined caseating granulomas with giant cells which is characteristic of tuberculosis. The presence of caseation differentiates tuberculosis from other causes of granulomatous inflammation of the pituitary like lymphocytic hypophysitis, sarcoidosis and Langherhan’s histiocytosis. Acid fast bacilli were not isolated in our case and most of the authors had reported similar finding. Even though there are reports of pituitary tuberculomas successfully managed without histopathological confirmation many authors emphasized the need of tissue diagnosis before starting patient on specific treatment irrespective of the clinical presentation and radiological findings. Polymerization chain reaction (PCR) technique had been performed successfully in CSF or pathological specimen to detect mycobacterium tuberculosis in special instances.

Antituberculous therapy is mandatory in all cases of pituitary tuberculosis. The chance of tuberculous meningitis is very high in surgically treated intracranial tuberculomas in the absence of anti tuberculosis chemotherapy. There is no consensus regarding the type of antitubercular regimen and duration of the treatment as the experience with tuberculomas of pituitary is limited. We were not able to judge the response to antituberculous therapy in the present case as the patient did not follow up, but in general the response is excellent. As most of the cases have undergone surgery the reduction in the size in repeat imaging cannot be attributed entirely to antituberculous therapy. But there are cases where mass has markedly reduced after partial excision or transsphenoidal biopsy or stereotaxic aspiration. In addition, there are reports of marked resolution of the size of pituitary tuberculoma with antituberculous treatment which was started on the basis of clinical suspicion alone. Reversal of hormonal deficits could not be assessed as most of the reports did not clarify whether the normal hormonal profiles achieved with treatment were maintained after the withdrawal of the hormonal replacements. Our patient was on prednisolone, thyroxine and testosterone replacement and desmopressin nasal spray till the last available follow up. Nevertheless there are reports of normalization of prolactin and improvement of DI on antituberculous treatment without any specific treatment.

In conclusion, although diagnosis of sellar tuberculomas is difficult on clinical and radiological examinations, pituitary tuberculomas should be considered in the differential diagnosis of suprasellar masses, especially in developing countries. It is advisable to have tissue diagnosis before starting any specific treatment. Clinical recognition can limit extend of surgery and avoid the development of new hormonal deficiencies after the surgery as happened in our case. Long term chemotherapy with antituberculous drugs usually results in a good outcome. Since it is not clear whether patients require lifelong replacement of deficient hormones periodic follow up is necessary.

REFERENCES