Suprasellar Tuberculoma Presenting as Panhypopituitarism


Abstract
Suprasellar tuberculomas are exceptionally rare. We present the case of a middle aged male who presented with generalised apathy and meningism of two weeks duration. Neuroimaging was suggestive of tuberculomas in suprasellar cistern, while endocrinological investigation showed panhypopituitarism manifesting as pituitary hypothyroidism, hypocortisolism, and hyperprolactinemia. Cerebrospinal fluid examination showed lymphocytic reaction with raised proteins. A diagnosis of suprasellar tuberculoma with panhypopituitarism was made. The patient was started on antituberculous treatment and hormone replacement which led to remarkable improvement in condition of patient and resolution of tuberculous granuloma in follow up imaging.

Introduction
Tuberculomas of central nervous system can occur at any site and in any age group. In developing countries, tuberculomas constituted approximately 30% of space-occupying intracranial lesions before the advent of antitubercular chemotherapy. They still constitute a major health hazard and may account for 0.15-4% of intracranial space occupying lesions. Though they commonly involve cerebrum and cerebellum, they can rarely occur in brain stem, basal ganglia, thalamus. Tuberculomas involving the hypophysis cerebri are extremely rare lesions though not uncommon at post-mortem examinations, and these may occur even in the absence of systemic tuberculosis. Only 54 cases of suprasellar tuberculomas as nonsecreting masses or mimicking secreting adenomas have been reported in the literature. We discuss here a case of a patient with suprasellar tuberculoma presenting with features of panhypopituitarism who responded well to antituberculous treatment and hormone replacement.

Case Report
A 57 year old married male presented to the emergency medical services of a tertiary hospital with history of apathy, unresponsiveness and withdrawn behaviour associated with urinary and fecal incontinence since 10 days. Patient also had headache and projectile vomiting over past 3 days. History of low grade fever, anorexia, weight loss for past one month was given by relatives. He had never had a focal neurological deficit or convulsions. There was a past history of Hansen’s disease four years ago for which he had taken multibacillary multidrug therapy. One year ago he had been operated for orbito-frontal abscess and treated with antibiotics. On examination he was conscious, but appeared apathetic, withdrawn, and largely unresponsive to verbal or visual stimuli. He responded to painful stimuli by withdrawing the limb and grimacing. He was afebrile, with a radial pulse of 68/min and blood pressure of 94/70 mm hg. Pallor, generalised hyperpigmentation and madarosis were seen. The patient was spontaneously moving all four limbs, deep tendon reflexes were uniformly 2+ and plantars were bilaterally extensor. Kernig’s and Brudzinski’s signs were present. Systemic examination was unremarkable.

Investigations showed a raised ESR of 68 mm at end of first hour. HIV ELISA was negative. His magnetic resonance imaging revealed confluent ring enhancing lesions in suprasellar cistern with exudates along basal cistern with meningeal enhancement along planum sphenoidale and anterior hemisphere (Figs. 1, 2). A guarded lumbar puncture was done and cerebrospinal fluid showed 182 cells (all lymphocytes), Protein>200mg/dl, Sugars-60mg/dl, ADA-57 IU/L. Subsequently his endocrinological workup revealed impaired thyroid function test-T3-35.60 ng/dl, T4-3.70 µg/dl, TSH-0.28 µIU/ml. Serum cortisol level at 8 am was low normal- 9.01 µg/dl. Serum prolactin levels were raised (90.4 ng/ml) with normal follicular stimulating and leutinising hormone levels.

On the basis of typical tuberculous neuroimaging lesions with cerebrospinal fluid examination confirming the same, he was treated as cerebral tuberculosis with four drug antituberculous treatment (Isoniazid, Rifampicin, Pyrizinamide, Ethambutol) and oral prednisolone. Oral thyroxine was started for hypothyroidism. On 3 month follow up patient was more alert, oriented, continent for urine and motion and able to feed himself although he was still bed ridden. Repeat magnetic resonance imaging showed marked reduction in size of previous lesions (Fig. 3).

Discussion
Tuberculomas account for 20% of all manifestations of central nervous system tuberculosis in India. This number rises to 47% if only children below 15 years are considered.

The common sites of intracranial tuberculomas in adults are cerebral hemisphere, basal ganglia and cerebellum. Children are said to develop infratentorial tuberculomas more often than adults. Rare sites like pituitary, brainstem, cerebellopontine angle and cavernous sinus have been reported. Tuberculomas of the hypothalamic-pituitary axis are rare. In a metaanalysis of 54 reported cases of pituitary tuberculosis worldwide, 70% of the cases were from India. More than 85% of the affected individuals in these reported cases were less than 45 years of age with 69%...
of the patients being females. Headache was the most common presenting symptom (91%), followed by visual symptoms in 46% of patients. Fever was present in all patients less than 12 years of age while it was much less frequent in adult patients. Only 30% of the cases had past or concurrent history of extrasellar tuberculous involvement. Endocrine manifestations were present in 77% of the patients. Anterior pituitary hypofunction was seen in 58% cases. Hyperprolactinemia was seen in 23% and Diabetes insipidus was seen in 11% of the patients. In the present case there was a past history of subacute orbito-frontal abscess which had been drained and treated with antibiotics. No tissue diagnosis was available. It is possible that the abscess was tuberculous in origin, secondary to pyomeningeal inflammation. The concomitant basal meningitis could have been the focus from where the seeding into hypophyses could have occurred. Concurrent meningitis with tuberculomas is rare. In a large series of a study of CNS tuberculomas, associated meningeal inflammation has been noted in only 0.5% patients by Ramamurthy, 3% patients by Arseni C, and 7% patients by Rao and Dinkar. It is unclear why some patients develop the relatively more benign tuberculoma while others develop meningitis in CNS tuberculosis. Immunological responses mounted by the individual patient may be the determining factor.

Radiologically, pituitary tuberculomas are usually isointense to hyperintense on CT scan. On T1W MRI images they are hypo to isointense but can be hyperintense too due to the high protein content on T2-weighted images, it can appear as a hyperintense lesion or a hyperintense center surrounded by a hypointense rim. Non enhancing areas correspond with the caseation seen in tuberculomas. Contrast MR imaging characteristically demonstrates thickening of the stalk due to chronic inflammatory scarring of the pituitary stalk. The thickening of the stalk is non specific and is described in diverse conditions like eosinophilic granuloma, granulomatous and lymphocytic hypophysitis, sarcoidosis, syphilis and neoplasms. 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. In tuberculosis endemic countries, the diagnosis of tuberculosis should be considered for sellar masses with stalk thickening. If systemic signs differentiating the afore mentioned differential diagnoses are not elicitable, the issue may need to be resolved by a tissue diagnosis. Our patient presented with clinical evidence of gross hypothyroidism and signs of Addisons disease. The marked apathy could have been due to hypothyroidism or previous frontal lobe involvement. Laboratory investigations revealed central hypothyroidism. The low normal 8 am serum cortisol was considered significant as one would expect a rise in cortisol in face of stress. The inflammatory signs of tuberculosis could have been suppressed due to overriding gross hypothyroidism. Such a situation may also be obtained in military tuberculosis where signs and symptoms of addisonism may mask any inflammatory sign due to tuberculosis. Our patient was treated with thyroid hormone and mineralocorticoids- glucocorticoid replacement and antituberculous medication. Due to the hypothyroid and
addisonian state, patient was not subjected to the stress of biopsy. The patient's general apathy and cognition improved remarkably in the ward to the point of being able to take care of self and feed himself. At 3 month follow up the MRI showed resolution of original lesions.

Though histopathological confirmation is emphasized by many authors, there are reports of pituitary tuberculomas having been successfully managed on basis of clinical presentation and radiological findings. Stereotactic biopsy as an alternative to craniotomy with a diagnostic yield up to 85% is another option. Medical management is the mainstay, and role of surgery is only to establish tissue diagnosis and relieve compressive symptoms. Response to antituberculous therapy has been reported to be excellent, with marked resolution of the size of pituitary tuberculoma. The exact role of antituberculous therapy in reversing the hormonal deficits could not be assessed. We have not been able to withdraw hormonal support and watch the clinical response, to determine this. Nevertheless there are reports of normalization of prolactin and improvement of diabetes insipidus on antituberculous treatment without any specific hormone replacement. Particular mention should be made of possible worsening of headache and visual symptoms in the early phase due to enhanced inflammatory edema. Here the role of steroids in management appears twofold, contributing to reducing the inflammatory edema in early treatment phase and maintaining the glucocorticoid axis. There is no consensus regarding the type of antitubercular regimen and duration of the treatment as the experience treating them is limited. Routinely the use of Isoniazid, Rifampicin, Pyrizinamide, Ethambutol for initial two months followed by first two for prolonged period is advised. Overall mortality has been reported to be 10%.

In conclusion, although diagnosis of pituitary tuberculomas is difficult on clinical and radiological examinations, it should be considered in the differential diagnosis of suprasellar masses, especially in developing countries. Clinical recognition can limit unwarranted surgery and progression of endocrinopathy.

References