

Hypopituitarism as unusual sequelae to central nervous system tuberculosis

S. Mageshkumar, Devendra V. Patil, Philo Aarthy J. A., K. Madhavan

Department of Medicine, Stanley Medical College (SMC), Chennai, India

ABSTRACT

Neurological tuberculosis can very rarely involve the hypophysis cerebri. We report a case of an eighteen year old female who presented with five months duration of generalised apathy, secondary amenorrhea and weight gain. She was on irregular treatment for tuberculosis of the central nervous system for the last five months. Neuroimaging revealed sellar and suprasellar tuberculomas and communicating hydrocephalus requiring emergency decompression. Endocrinological investigation showed hypopituitarism manifesting as pituitary hypothyroidism, hypocortisolism, hypogonadotropic hypogonadism, and hyperprolactinemia. Restarting anti-tuberculosis treatment, hormone replacement therapy, and a ventriculo-peritoneal shunt surgery led to remarkable improvement in the general condition of the patient.

Key words: Hyperprolactinemia, hypogonadotropism, hypopituitarism, tuberculomas

INTRODUCTION

Tuberculosis is responsible for 20% of the intracranial space occupying lesions in India.^[1] Central nervous system (CNS) tuberculosis commonly involves meninges, cerebrum, and cerebellum. Rare sites are brainstem, basal ganglia, and thalamus.^[2] Tuberculomas involving hypophysis cerebri account for 1% of all intracranial tuberculomas.^[1] Less than 60 cases of suprasellar tuberculomas have been reported.^[1]

CASE REPORT

An 18-year-old apparently normal unmarried female was admitted with complaints of sub acute onset fever, intermittent headache, neck pain, and altered behaviour for 10 days. She had no significant illness in the past and

had normal menstrual cycles. On examination, she was of thin built and febrile. Her blood pressure was 110/80 mm of Hg and had a regular pulse rate of 102 per min. She had neck stiffness. Kernig's sign was positive. Rest of the systemic examination was otherwise normal. Fundoscopy did not reveal any signs of papilledema. The investigation profile [Table 1] suggested CNS tuberculosis. Contrast-enhanced magnetic resonance imaging (MRI) of the brain showed a right thalamic infarct with multiple ring enhancing lesions in right parietal, occipital and pontine regions along with leptomeningeal enhancement [Figure 1]. There was no other identifiable tuberculous focus. She was started on intravenous dexamethasone and oral antituberculosis treatment (ATT), which included oral isoniazid, rifampicin, pyrazinamide, and ethambutol. Her condition improved. One week later she was discharged. She was asked to continue the ATT and oral prednisolone. But patient was noncompliant and lost follow-up.

She was readmitted five months later with complaints of weight gain, secondary amenorrhea for four months, apathy, excessive somnolence and intermittent headache for two weeks, and binocular diplopia for two days. On examination, she was apathetic, withdrawn, and largely unresponsive to verbal and visual stimuli. Her blood pressure was 110/80

Access this article online

Quick Response Code:



Website:
www.ijem.in

DOI:
10.4103/2230-8210.84881

Corresponding Author: Dr. Philo Aarthy J. A., 2B, Chandrika Apartments, New no.11, Ashoka Avenue, Directors Colony, Kodambakkam, Chennai- 600 024, India. E-mail: aarthy_maria@yahoo.co.in

Table 1: Investigation profile on first and second admission

Investigation	Reference Range	Admission 1 September 2010	Admission 2 February 2011
Blood			
Hemoglobin	12-16 g/dl	11.8 g/dl	11.5 g/dl
Total count	4000- 11000 cells/cu.mm	6800 cells/cu.mm	7,200 cells/cu.mm
Differential count	Polymorphonuclear neutrophils- 50- 70%, lymphocytes- 20- 40%, eosinophils- 0-4%	Polymorphonuclear neutrophils- 66, lymphocytes- 34	Polymorphonuclear neutrophils- 68, lymphocytes- 30, eosinophils- 2
Erythrocyte sedimentation rate	0-20 mm/hr	½ hour- 22 mm/hr, 1 hour-40 mm/hr	½ hour- 24 mm/hr, 1 hour-42 mm/hr
Random blood sugar	75-110 mg/dl	125mg/dl	111 mg/dl
Blood urea	15 -40 mg/dl	18 mg/dl	26 mg/dl
Serum creatinine	0.7-1.2 mg/dl	0.8 mg/dl	0.6 mg/dl
Serum sodium	136-146 meq/l	144 meq/l	128 meq/l
Serum potassium	3.5- 5 meq/l	3.9 meq/l	3.6 meq/l
Serum calcium	8.7-10.2 mg/dl	9.6 mg/dl	9.2 mg/dl
HIV ELISA		Nonreactive	No reactive
Cerebrospinal fluid			
Appearance	Clear	Clear	Clear
Pressure	50-180 mm water	High	High
Sugar	40-70 mg/dl	32 mg/dl	35 mg/dl
Protein	15-50 mg/dl	103 mg/dl	118 mg/dl
Cytology	0-5 mononuclear cells/cu.mm, No atypical cells	8-9 lymphocytes/cu.mm, No atypical cells	9-10 lymphocytes/cu.mm, No atypical cells
Adenosine deaminase	<5 IU/l	8 IU/l	12 IU/l
Gram stain		Negative	Negative
Acid fast bacilli stain		Negative	Negative
Culture and sensitivity		No growth	No growth
TB PCR		Not done	Positive

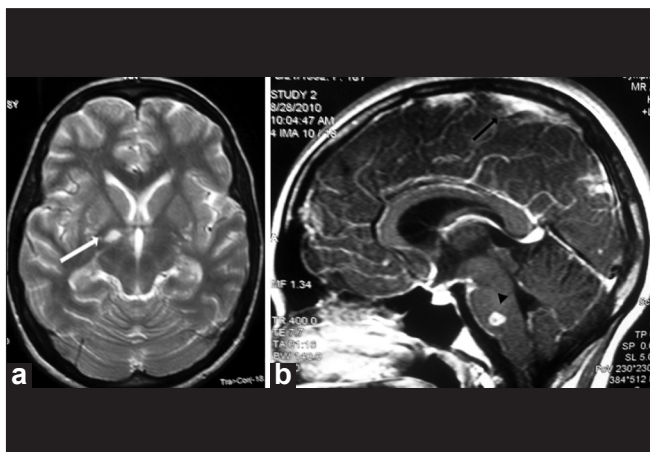


Figure 1: (a) Axial T2-weighted MRI brain demonstrates high signal intensity infarct in right thalamus (white arrow). (b) Sagittal post contrast T1-weighted MRI brain demonstrates ring enhancing lesion (black arrow head) in pons and leptomeningeal enhancement (black arrow)

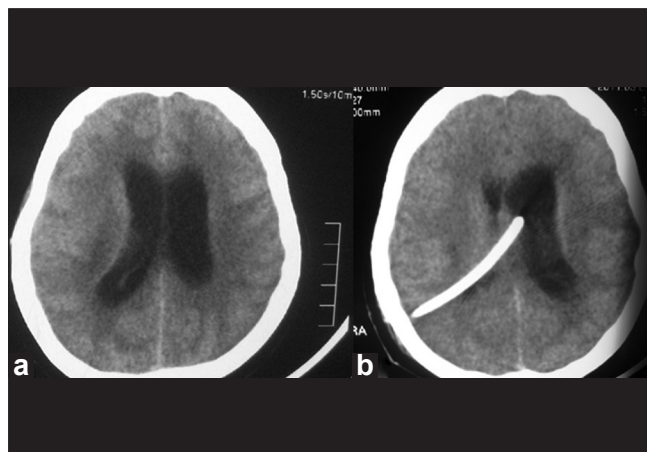


Figure 2: (a) Noncontrast CT brain demonstrates dilated ventricles and cerebral edema. (b) Non contrast CT brain demonstrates *in situ* ventriculoperitoneal shunt tube

mm of Hg and had a regular pulse rate of 88 per min. There was neck stiffness. Kernig's sign was positive. Right lateral rectus palsy was present. Fundoscopy did not demonstrate papilledema. Investigation profile [Table 1] was again consistent with neurological tuberculosis. A computed tomography (CT) scan of the brain showed hydrocephalus with cerebral edema and so an emergency ventriculo-peritoneal shunt was done [Figure 2]. Endocrinological

investigation [Table 2] revealed pituitary hypothyroidism, hypocortisolism, hypogonadotropic hypogonadism, and hyperprolactinemia. Repeat contrast-enhanced MRI of the brain revealed presence of exudates along basal cisterns and meningeal enhancement [Figure 3]. Tuberculomas were seen in sellar and suprasellar region [Figures 3 and 4].

She was restarted on oral ATT, hydrocortisone, thyroxine,

Table 2: Hormonal profile on second admission

Hormone	Reference range	Test value (Admission 2)
Serum prolactin	4-23 ng/ml	40 ng/ml
Serum follicle stimulating hormone	1-12 mIU/ml	0.1 mIU/ml
Serum leutinising hormone	0.6- 19 mIU/ml	0.2 mIU/ml
Free triiodothyronine	2.4- 4.2 pg/ml	1.9 pg/ml
Free thyroxine	0.8- 1.7 ng/dl	0.5 ng/dl
Thyroid stimulating hormone	0.34- 4.25 mIU/l	0.22 mIU/l
Serum cortisol (8 a.m)	5- 25 mcg/dl	3.9 mcg/dl

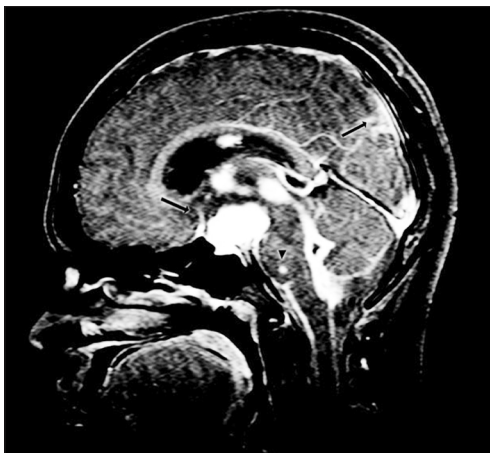


Figure 3: Sagittal post contrast T1-weighted magnetic resonance imaging brain demonstrates smaller pontine tuberculoma (black arrow head) and sellar suprasellar and leptomeningeal enhancement (black arrow)

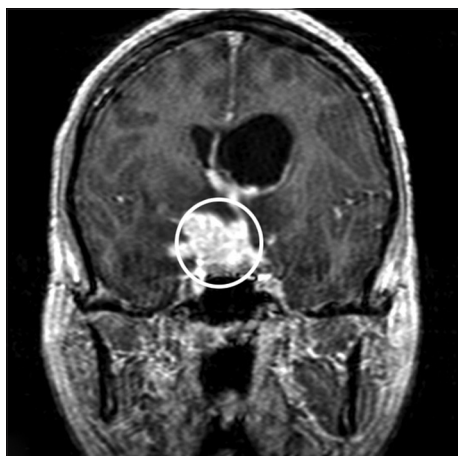


Figure 4: Coronal post contrast T1-weighted magnetic resonance imaging brain demonstrates sellar suprasellar enhancement (white circle)

cyclical estrogen, and progesterone. Her condition dramatically improved up to an extent that she was now capable of carrying out her daily activities independently. She was discharged after rigorous counselling to remain compliant on ATT and hormone replacement therapy.

DISCUSSION

Our case is remarkable because it points to one of the very infrequently seen complication of neurological tuberculosis. Tuberculosis affection of the hypothalamus and hypophysis cerebri is a rare clinical entity. Hypothalamo-pituitary dysfunction due to tuberculosis can be due to the presence of a strategically placed tuberculoma or exudates around the sellar region. Tubercle bacilli are believed to reach the pituitary by hematogenous spread from extra cranial sources or from the infection of skull base.^[2-4]

Tuberculosis meningitis (TBM) has various radiological manifestations. Contrast-enhanced MRI of the brain usually shows leptomeningeal and basal cisternal enhancement, focal infarcts and tuberculomas usually surrounded by hypo attenuating edema (as seen in our case). The incidence of hydrocephalus is as high as 85% in tuberculous meningitis. It is usually of communicating type. The exact pathogenesis of hydrocephalus in tuberculous meningitis is unclear. The hydrocephalus is probably a result of adhesive meningeal reaction, obliteration of archnoid villi themselves or exudation in the subarachnoid space and cisterns of the base of the brain, around optic chiasma, interpeduncular, and prepontine cisterns.

Hypothalamo pituitary dysfunction due to tuberculosis is very rare. Most of the available literature on pituitary tuberculosis is in the form of case reports. Endocrine manifestations were present in 77% of the patients with pituitary tuberculosis.^[1,5] Headache (91%), visual symptoms (46%), anterior pituitary hypo function (58%), hyperprolactinemia (23%), diabetes insipidus (11%) are the usual manifestations seen in a meta analysis of 54 cases of pituitary tuberculosis.^[1,4,5] Our patient had hypogonadotropic hypogonadism and secondary hypothyroidism, which suggests the possibility of hypopituitarism. Even when it was expected to be high in the face of tuberculosis (stress), the 8 a.m. serum fasting cortisol level was low. This suggests the presence of hypocortisolism. There was no visual field restriction, reduced visual acuity, or altered perception of red light. This suggests that there is probably no optic nerve involvement due to tuberculoma or exudation around optic chiasma.

In pituitary tuberculosis, contrast-enhanced MRI characteristically demonstrates thickening of the stalk due to chronic inflammatory scarring. The thickening of the stalk is non-specific and is described in diverse conditions like neoplasm, sarcoidosis, syphilis, lymphocytic hypophysitis, granulomatous hypophysitis, and eosinophilic

granuloma.^[1,3-5] The suprasellar extension can make evaluation of the stalk difficult on neuroimaging.^[6] The other MRI findings described are peripheral ring enhancement of the mass, enhancement of the adjacent dura and basal enhancing exudates, sellar or suprasellar calcification, apoplexy, and erosion of the sellar floor.^[1,5] Our patient had T2 weighted non homogenous hyper intensities, which enhanced on contrast in the sellar, suprasellar, and basal cisterns.

Although histopathological confirmation is emphasized by many authors, there are reports of pituitary tuberculosis that have been successfully managed on basis of clinical presentation and radiological findings.^[5] Suprasellar tuberculosis presenting with pituitary-hypothalamic dysfunction can be differentiated from other neoplastic or inflammatory conditions on the basis of serial imaging findings, clinical profile, and response to ATT. When there is no real threat to the life or vision of the patient, then the major indication for a transphenoidal surgery would be for histopathological conformation.^[2] Our patient had characteristic neuroimaging findings (tuberculomas, basal exudates, and leptomenigeal enhancement), hypoglycorrhachia and hyperproteinorrhachia suggestive of CNS tuberculosis during both admissions. The fact that the pontine lesion regressed on ATT further asserts the diagnosis of CNS tuberculosis [Figure 3]. In the background of CNS tuberculosis, noncompliance to treatment, the presence of hypothalamo-pituitary dysfunction, tuberculomas in sellar and suprasellar region almost confirms the diagnosis of pituitary tuberculosis.

Noncompliance to treatment could explain the persistent hyperproteinorrhachia and the development of new tuberculomas. However, there are reports that intracranial

tuberculomas can develop or enlarge during antituberculous therapy and exaggerated host reaction to tuberculous protein is thought to play a role.^[2] This could probably explain the normal pituitary imaging during the first admission in our patient. However, because hormone analysis was not done during the first admission, it is not possible to rule out asymptomatic hypopituitarism.

There is no standardized regimen regarding the drugs, dosages, use of steroids, and duration of treatment for CNS tuberculosis. Treatment is individualized in most of the cases. As the experience with tuberculomas of pituitary is limited, there is no consensus regarding its treatment.^[5] Our patient was treated with a regimen that is usually followed for CNS tuberculosis and hormone replacement therapy.

REFERENCES

1. Sunil K, Menon R, Goel N, Sanghvi D, Bandgar T, Joshi SR, *et al.* Pituitary Tuberculosis. *J Assoc Physicians India* 2007;55:453-6.
2. Jain R, Kumar R. Suprasellar tuberculoma presenting with diabetes insipidus and hypothyroidism-a case report. *Neurol India* 2001;49:314-6.
3. Singh S. Pituitary tuberculoma: Magnetic resonance imaging. *Neurol India* 2003;51:548-50.
4. Ahmad FU, Sarat Chandra P, Sanyal S, Garg A, Mehta VS. Sellar tuberculoma: An unusual infection. *Indian J Tuberc* 2005;52:215-7.
5. Sundar US, Ramteke VV, Vaidya MS, Asole DC, Moulick ND. Suprasellar tuberculoma presenting as panhypopituitarism. *J Assoc Physicians India* 2010;58:706-9.
6. Shukla S, Trivedi A, Singh K, Sharma V. Pituitary tuberculoma. *J Neurosci Rural Pract* 2010;1:30-1.

Cite this article as: Mageshkumar S, Patil DV, Philo Aarthi JA, Madhavan K. Hypopituitarism as unusual sequelae to central nervous system tuberculosis. *Indian J Endocr Metab* 2011;15:259-62.

Source of Support: Nil, **Conflict of Interest:** None declared.