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Case Report

Internal Medicine Section

Iatrogenic Cushing Syndrome to Facial Nerve Palsy: Via Intracranial Tuberculoma-An Interesting Journey

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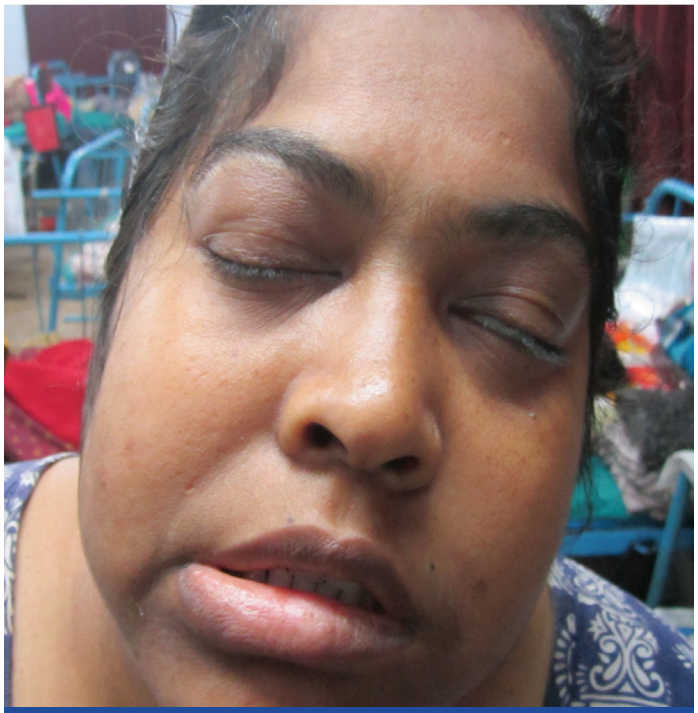
ABSTRACT

Isolated Facial nerve palsy is a less common neurological manifestation of intracranial tuberculoma. Again, tuberculoma can arise following development of Cushing syndrome after prolonged intake of steroids due to origin of immunosuppressed state. Thus exogenous steroid administration leading to iatrogenic Cushing Syndrome which again causing tuberculoma, with facial nerve palsy developing as a manifestation of tuberculoma is not unnatural but definitely a unique scenario. The author reports an interesting case where a patient developed left sided facial palsy following development of intracranial tuberculoma from iatrogenic Cushing syndrome after longterm intake of Dexamethasone as a treatment for low back pain. This situation is rarely reported before.

Keywords: Cushing syndrome, Facial nerve palsy, Tuberculoma

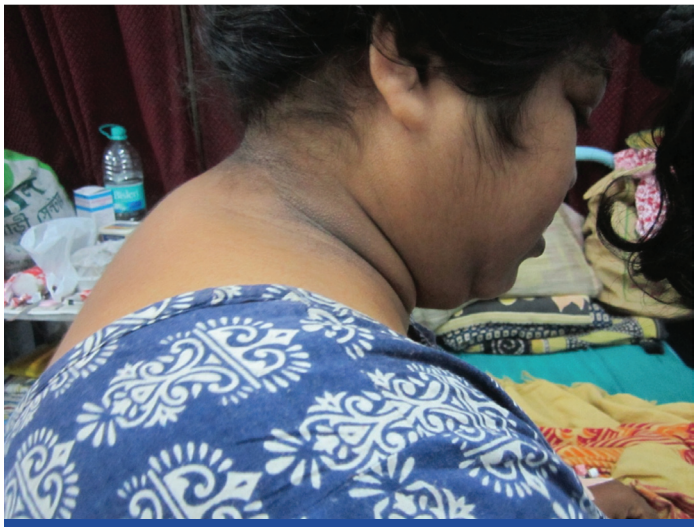
CASE REPORT

A 30-year-old married female presented with insidious onset but rapidly progressive deviation of angle of her mouth to right along with dribbling of saliva from her left angle of mouth for last 20 d. She also complained of a five-month history of puffiness of the face and generalized swelling of the body. She noticed new onset striae over the abdomen during this period. She mentioned complaints of recent onset secondary amenorrhoea, progressively increasing weakness of the proximal muscles. She had a history of in take of tablet dexamethasone 8mg daily for last two years prescribed by her local physician for persistent low back pain. She also gave a history of vague bifrontal headache for last three months. There was no past history of tuberculosis or any family history of tuberculosis. Examination revealed that the patient had moon facies [Table/Fig-1], truncal obesity with acanthosis nigricans [Table/Fig-2],facial puffiness, purples triae over abdomen and thighs, and non-pitting bipedal oedema. Her blood pressure was 150/90 mmHg in sitting position with no postural drop. Neurological examination revealed presence of lower motor neuron type of left sided facial palsy [Table/Fig-1]. Fundoscopy revealed bilateral papilledema with presence of choroid tubercles. Proximal muscle weakness was demonstrated in both upper and lower limbs. Rest neurological examination as well as other systemic examination was within limits was normal. Complete blood counts, renal and liver function tests were within normal limits except mild hypoalbuminemia (2.8g/dl ;N-3.5-5 g/dl). Serum electrolyte levels revealed hypokalemia (K+ -2.8 meq/l;N :3.5-5meq/l). Sputum was negative for Acid Fast Bacilli.HIV serology was negative.As fundus examination showed evidence of papilloedema, therefore, lumber puncture was not done initially in view of the raised intracranial tension. These was no serological evidence of cryptococcosis and nocardiosis. The Mantoux test reading was strongly positive (17×21mm). As a diagnosis of tuberculosis was contemplated, fiberoptic-bronchoscopy was performed which showed no endobronchial lesion, but the bronchial aspirate smear was positive for acid fast bacilli by Ziehl-Neelsen staining and culture showed growth of *Mycobacterium tuberculosis*.Chest X-ray and USG abdomen was normal. DEXA scan suggested severe osteoporosis.8 A.M. Serum cortisol was severely depressed suggesting the presence of Cushing syndrome due to exogenous steroids with endogenous hypocortisolism. Vasculitic profile

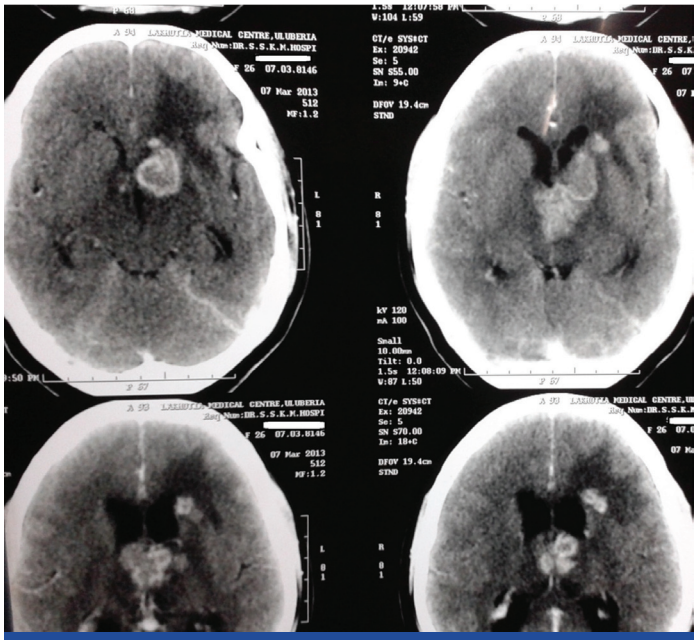


[Table/Fig-1]: Showing left sided complete facial palsy

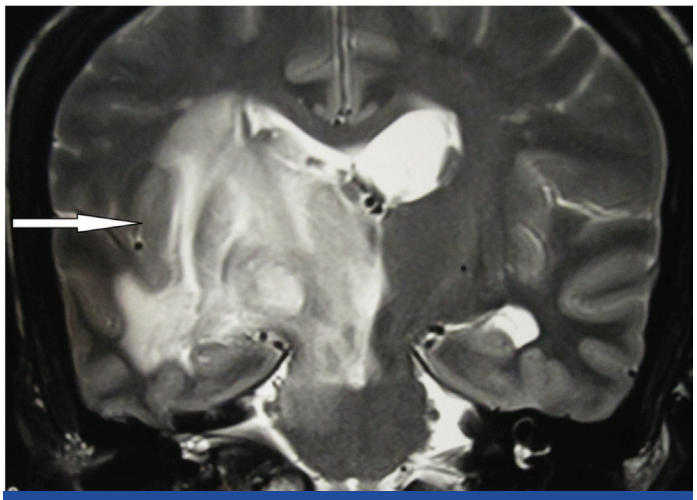
including ANA, Rheumatoid Factor, C3, C4 were within normal limits. Serum ACE was normal. CSF study done after 5 days after institution of mannitol (to decrease cerebral edema) revealed normal protein (35mg/dl;N 20-40mg/dl) and a cell count of 3/cmm(N 0-5/cmm) with normal Adenosine deaminase activity (9 U/L; N:<10). PCR did not show growth of *Mycobacterium tuberculosis*. Contrast Enhanced CT brain showed presence of multiple ring enhancing lesions in parietal lobe,occipital lobe and brainstem suggestive of tuberculoma [Table/Fig-3]. Axial and coronal non-contrast T2-weighted images and T2 FLAIR images showed hypo-intense lesions with oedema around the lesions [Table/Fig-4]. Contrast-enhanced axial and coronal T1 weighted images showed peripheral ring-like enhancement of the lesion [Table/Fig-5]. Leptomeningeal enhancement was however, not seen. MR spectroscopy demonstrated a decrease in NAA/Cr and increase in Cho/Cr which



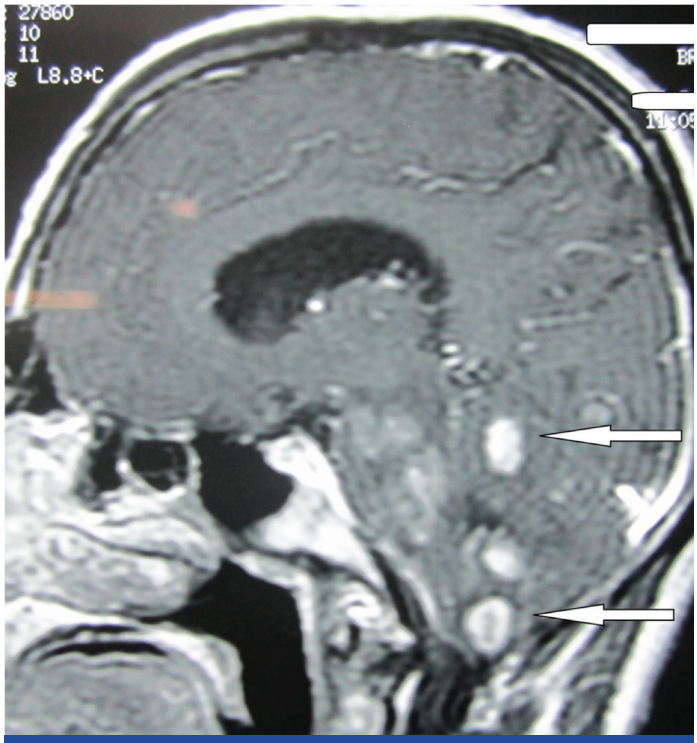
[Table/Fig-2]: Showing truncal obesity with acanthosis nigricans



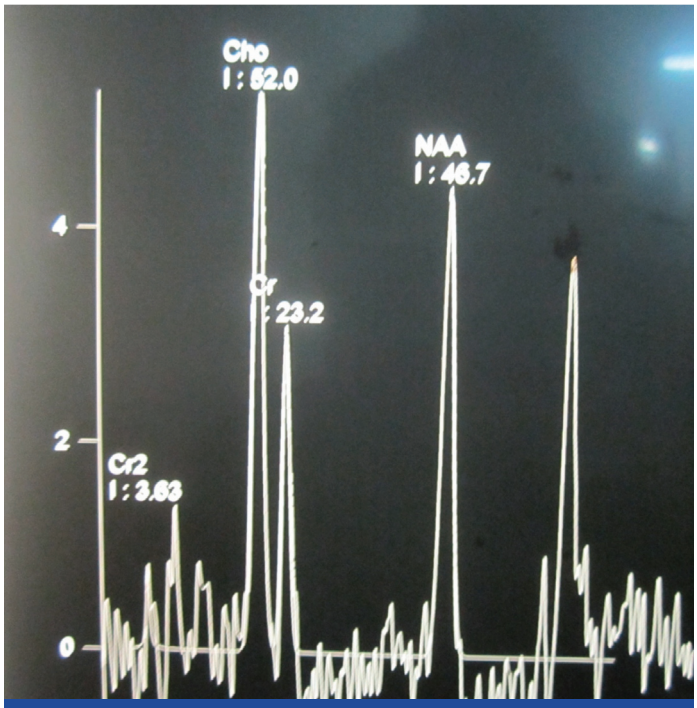
[Table/Fig-3]: Showing multiple tuberculomas with hydrocephalus in CECT brain



[Table/Fig-4]: Showing mass lesion with significant surrounding edema in coronal t2 weighted imaging of brain. Compression of frontal horn of lateral ventricle due to edema can be seen



[Table/Fig-5]: Showing multiple ring enhancing lesions in sagittal section of contrast enhanced MRI brain



[Table/Fig-6]: Showing choline:creatinine ratio >1, decreased naa:choline in mr spectroscopy

was more than 1.0 [Table/Fig-6]. Antituberculous treatment (ATT) was initiated with 4 drug therapy (Isoniazid, Rifampicin, Ethambutol, Pyrazinamide) according to standard protocol. Simultaneously patient was put on tapering courses of oral steroids(Prednisolone 30 mg/day initially) to deal with the CNS TB and endogenous cortisol deficiency simultaneously. Oral Acetazolamide (250 mg TDS) was also instituted to decrease cerebral oedema and oral pyridoxine (50 mg/day) to counter Isoniazid toxicity. The headache gradually diminished and facial palsy resolved partly after 17 d. Neurosurgical treatment(including ventriculo-peritoneal shunt) was ruled out due to good response to ATT and acetazolamide as well as patient's choice. Patient was discharged in stable condition after 25 d with advice to follow-up in OPD.

DISCUSSION

The aetiology of LMN type facial paralysis includes diverse conditions such as traumatic, infectious, inflammatory, neoplastic, paraneoplastic, vascular and idiopathic. Standard workup for LMN type facial palsy includes an imaging study and CSF study including

culture of infectious organisms like HSV, *Borreliaburgdorferi, Mycobacterium tuberculosis*; vasculitic profile including ANA, Rheumatoid factor, etc. Areas in the skull and brain that are most likely to reveal probable aetiology and therefore become especially important to carefully visualize during imaging are the skull base, meninges, and cerebello-pontine angle. These regions are best examined by contrast enhanced MRI [1].

Cushing syndrome can result from administration of potent corticosteroids in different forms like oral as in this case, intravenous or even topical if used for prolonged periods [2]. Cushing syndrome either endogenous or exogenous can lead to flare up of latent infections including tuberculosis. Reactivation of tuberculosis becomes especially relevant in India. This may manifest in any form –pulmonary or extra- pulmonary including central nervous system involvement. It can be noted that tuberculomas can develop independent of meningeal involvement. Furthermore, tuberculomas with or without hydrocephalus can be the sole CNS presenting feature in reactivated tuberculosis [3].

Brain tuberculomas are intracranial space occupying lesions.They clinically manifest with features of raised intracranial tension as headache, seizures, impairment of consciousness and signs of focal neurological involvement. Conversely, 25 to 85% of patients are asymptomatic [4]. This focal deficit includes LMN facial palsy. The relevant pathophysiology includes direct involvement of pons i.e space between “direct” and “involvement” and pressure on facial nucleus or rarely by causing hydrocephalus. The index patient demonstrated both hydrocephalus as well as tuberculoma in pons and so either of them or both might have contributed to the facial palsy. The cerebrospinal fluid examination usually reveals lymphocytic or monocytic pleocytosis i.e space between “monocytic” and “pleocytosis” and no space between “pleo” and “cytosis” with often low glucose level and high protein content. However, CSF study may be absolutely normal as in the index case [5].

Tuberculomas are either round or lobulated, solitary or multiple. They can be located supratentorially or infratentorially. CT and MRI are the main imaging modalities used in the localization and characterization of brain tuberculomas [6]. Depending on stage of evolution, tuberculomas appear on brain CT scan as normal(in early cerebritis stage), hypodense (established granulomatous stage)isodenseor hyperdense lesions (central caseating stage). They range in size 1-10cm in diameter and show a peripheral ring enhancement and often surrounding oedema following contrast medium administration [7]. Although the sensitivity of CT in diagnosing intracranial tuberculoma is 100% and its specificity is 86%, the positive predictive value has been reported to be as low as 33% even in a high-incidence population in India [8].

Magnetic resonance imaging is slightly superior to CT in demonstrating the extent of lesions, especially in brainstem tuberculoma [9]. Non-caseating granulomas are usually hypo-intense on T1 weighted images, and hyper-intense on T2 weighted images. Caseating granulomatous lesions with a solid centre appear relatively hypo- or iso-intense on T1 weighted images, and iso- or hypo-intense on T2-weighted imaging. With gadolinium administration, T1 weighted images often show ring-enhancing lesion [10]. MR spectroscopy may be helpful in differentiating tuberculomas from other intracranial mass lesions. Tuberculomas have a high peak of lipids, more choline, and less N-acetylaspartate and creatine at MR spectroscopy. MR spectroscopy is characterized by a prominent decrease in NAA/Cr and slight decrease in NAA/Cho [11]. The choline/creatine ratio is usually greater than 1 in tuberculomas as in our case.

The usual differential diagnosis of tuberculoma includes glioma, lymphoma, metastasis, neuro-cysticercosis and pyogenic abscess, all of which appear remarkably similar in CT and MRI. As the diagnosis of brain tuberculoma based on imaging alone is presumptive only, presence of supportive findings such as history of fever, high ESR, positive tuberculin test and positive response to anti tuberculous treatment gain significant importance [12]. Although surgical excision including CT-guided stereotactic biopsy is the gold standard and help to establish the histological diagnosis and rule out the close mimickers in radiologic imaging, yet it is not usually required in characteristic clinical scenario with other supportive investigations. Its use in this era of MRI,MRS and PCR is reduced to only controversial situations.However, when diagnosis is still uncertain after extensive investigations, histology is mandatory to differentiate tuberculoma from other infectious or neoplastic disease. Tissue culture is also of particular value in multidrug-resistant cases [13].

Extracerebral involvement must be systematically investigated, but remembering that isolated tuberculosis of the central nervous system represents 40 to 70% of cases. A past history or evidence of active tuberculosis elsewhere in the body can usually be found in the rest of the cases. Pulmonary tuberculosis is the main associated extracranial involvement. But only 30% of patients with brain tuberculoma have a positive chest radiograph suggestive of pulmonary tuberculosis [4]. The absence of features of tuberculosis on chest X-rays as in the index patient, therefore should not rule out the possible existence of brain tuberculomas in suspected cases.

Standard Anti-tuberculous Treatment (ATT) is the treatment of choice for brain tuberculomas. A four-drug therapy(comprising Isoniazid, rifampicin, pyrazinamide, and ethambutol or streptomycin) is continued for two months followed by two-drug therapy (Isoniazid, rifampicin). Classically, total duration of treatment is 18-24 mnth, or until the disappearance of intracerebral lesions or their resolution into a calcification [14]. Evidence of a new intracranial tuberculoma, or of expanding existing lesions, which are an immune-mediated, paradoxical response to antituberculous therapy, does not necessitate a change to the antituberculous regimen [15]. With the use of steroids to control the brain oedema and its resultant mass effect and increased intracranial pressure, and barring the infrequent requirement of refractory ventriculo-peritoneal shunt for hydrocephalus, almost all tuberculomas of the brain, irrespective of their size, can be cured by medical treatment.With appropriate and timely treatment, mortality is only 10% [14].

CONCLUSION

Thus in an appropriate clinical scenario like a background of Cushing syndrome, a tubercular origin of facial palsy should not be missed as it is curable and urgent evaluation warranted. The diagnosis of tuberculosis with CNS involvement in this case was first suspected because of the stigmata of Cushing syndrome and complaint of headache and demonstration of Mantoux positivity and confirmed by characteristic lesions in CECT , MRI and MRS of brain and good response to ATT.

CONSENT

Informed consent was taken from the patient regarding the publication of this case report.

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