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Case Series

Pituitary tuberculoma: A verycommon pathology in a very uncommon location

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ABSTRACT

Pituitary Tuberculoma is extremely rare, even in developing countries where tuberculosis is endemic with total reported cases in the literature fewer than a hundred. Misdiagnosis as pituitary adenoma is common and late diagnosis can result in a permanent endocrine dysfunction and/or long-term neurologic sequela. Pituitary Tuberculoma, and mimicking adenomas are very unusual. We report a small case series of a patient with sellar/ suprasellar mass, who presented with severe headache, all these patients didn't have any previous history of tuberculosis and radiological and microbiological evidence of Tuberculosis elsewhere in the body. All these patients underwent endoscopic transsphenoidal resection of the mass and histo pathological examination was suggestive of pituitary Tuberculoma. Antituberculous therapy was started and continued for one year, all three patients had good control of the disease and hormonal profile was normal at the end of one year, though all three patients required a small dose of steroid (Prednisolone 5mg) for the initial three months after surgery.

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1. Introduction

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*. Despite the advance in therapeutic treatment, tuberculosis still remains one of the world's biggest problems. Globally in 2018, an estimated 10.0 million people fell ill with Tuberculosis, equivalent to 132 cases per 100 000 population.¹ Lungs are the most common sites for *M. tuberculosis* infection, presenting as either asymptomatic latent infection or active pulmonary tuberculosis. Extrapulmonary tuberculosis is often difficult to diagnose and necessitated a high index of suspicion. In developing countries, tuberculomas constituted up to 30% of space-occupying intracranial lesions until recently.² However, the incidence dramatically decreased after the advent of antitubercular chemotherapy and now intracranial tuberculoma account for 0.15-4% of

intracranial space-occupying lesion.³

Pituitary tuberculoma is extremely rare, with the first case reported by Coleman et al. in 1940⁴. Up to 2015, only 81 cases of pituitary tuberculoma had been documented in the literature, commonly presenting with gradual onset of headache and visual disturbances with or without systemic symptoms.⁴ We report short case series of pituitary tuberculoma in our institutional experience

2. Case 1

37 years old female came with complaints of headache and projectile vomiting and a history of double vision. No history of fever, cough, weight loss, or anorexia. There was no history of contact with Tuberculosis patients. Physical examination was normal and vitals stable. Cranial nerve examination revealed left-sided sixth nerve palsy. The rest of the physical examination was unremarkable. The endocrine profile revealed Hypothyroidism and

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Cortisol deficiency. Magnetic resonance imaging revealed enlargement of the pituitary gland with sellar and suprasellar extension measuring about 1.9cm x 1.5cm x 2.5cm with thickening of the pituitary stalk thickening of infundibular with engulfing the cavernous segment of right Internal carotid artery (Figure 1). The patient underwent endoscopic transsphenoidal resection of the pituitary lesion. Histological examination revealed a heavily infiltrated pituitary gland by multiple epithelioid cell granulomas with caseous necrosis and few langhans-type multinucleated giant cells. Diagnosis of primary pituitary Tuberculosis was made and four anti-tuberculous medications (isoniazid, rifampicin, ethambutol and pyrazinamide) were commenced (12 months) and was also started on thyroid and steroid replacement therapy. Postoperatively after one month, she had Cerebro spinal fluid rhinorrhea, endoscopic skull base repair was done, she completed a full course of antituberculous therapy, now improved symptomatically and on regular follow up, Post op MRI after one year showed no new lesion (Figure 2).

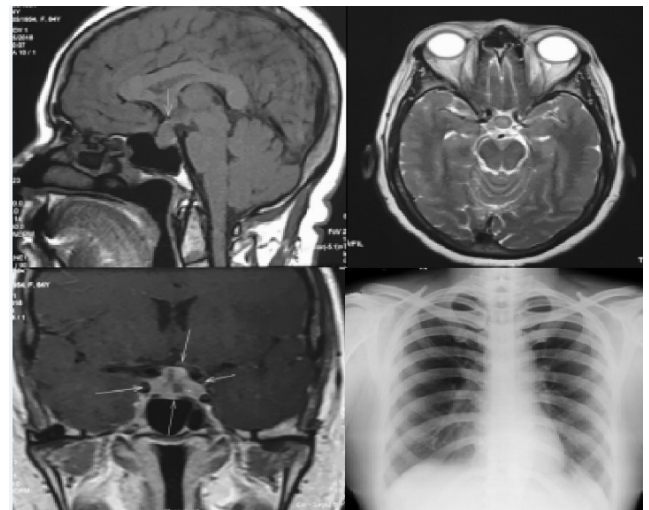


Fig. 3: Pre-operative image of case 2

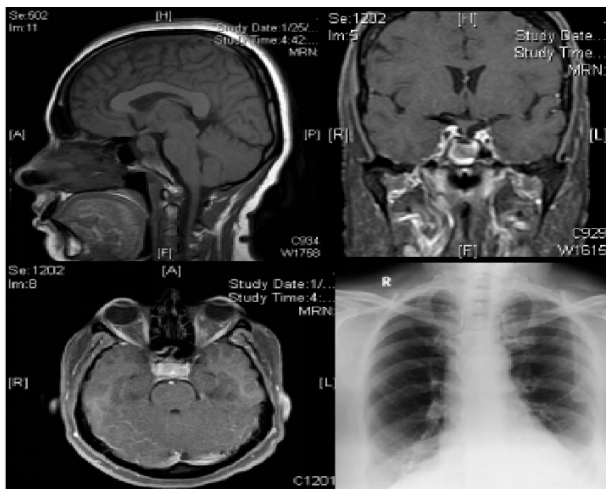


Fig. 1: Pre-operative image of case 1

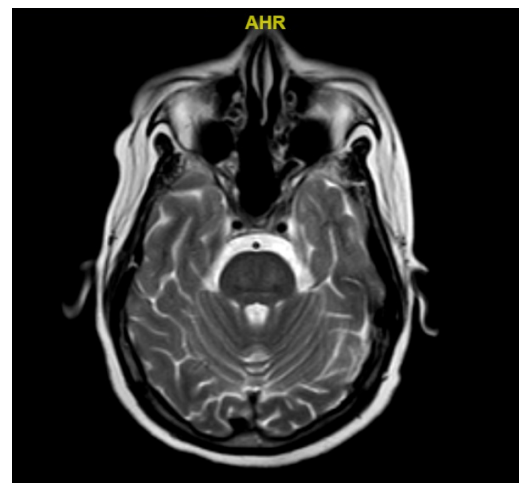


Fig. 4:

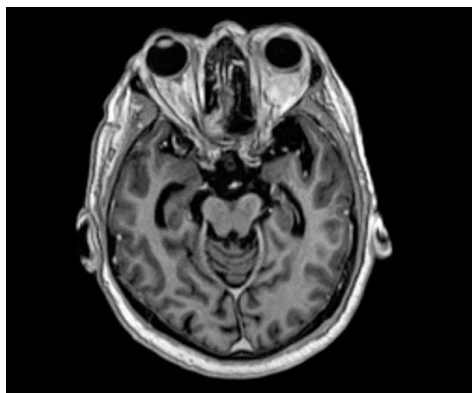


Fig. 2:

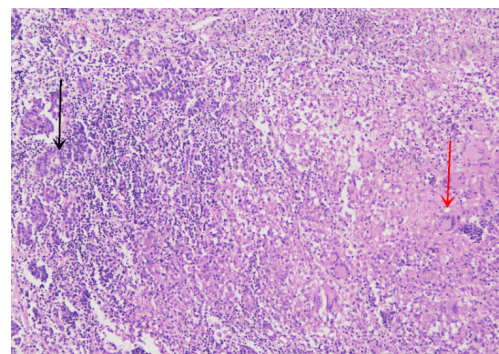


Fig. 5: HPE of case 3, Black arrow normal pituitary, Red- Giant cells

3. Case 2

A 63-Year-old female presented with complaints of headache for 1 month. Headache was mainly located in the bifrontal region with the gradual diminution of left eye vision for two months. On examination, the patient was conscious, oriented, and afebrile, vitals were normal. Ophthalmological examination revealed bitemporal hemianopia with visual acuity 6/6. Cranial nerves were normal with no motor or sensory deficits. Biochemical, endocrinological, and haematological profile was normal. Chest roentgenogram showed a normal study. The pituitary hormonal profile was normal. Magnetic resonance imaging of the Brain showed an enlargement of the pituitary gland seen with heterogeneously enhancing necrotic lesion and subtle indentation of optic chiasma of size 2.3 x 1.41 x 1.40 cm (Figure 3). The patient underwent endoscopic transsphenoidal resection of the pituitary lesion. Intraoperatively consistency of the lesion was soft so sent for a frozen biopsy. It revealed - ill-formed granulomas - suggestive of tuberculosis, so partial resection was done. Histopathological examination revealed few epithelioid cell granulomas and few Langhans type multinucleated giant cells noted with Focal caseating necrosis seen. The postoperative period was uneventful. Diagnosis of primary pituitary Tuberculosis was made and four anti-tuberculous medications (isoniazid, rifampicin, ethambutol and pyrazinamide) were commenced (12 months). Post-op MRI after one year showed no new lesion (Figure 4). She completed a full course of anti-tuberculous therapy and is now on regular follow-up.

4. Case 3

49 years old female admitted with complaints of Headache for 1 week. General physical examination and neurological examination were normal. The Endocrinological profile revealed Cortisol deficiency. Magnetic resonance imaging of the brain showed Evidence of contrast-enhancing sella / mass with suprasellar extension measuring about 1.8cm x 1.5cm x 1cm in the pituitary fossa, Infundibular stalk deviated posteriorly, and the lesion was abutting both Internal Carotid artery with no evidence of engulfment. The patient underwent endoscopic transsphenoidal resection of the pituitary lesion. Intraoperatively consistency of the lesion was soft so sent for a Frozen biopsy, which revealed - ill-formed granulomas - suggestive of tuberculosis, so partial resection was done. Histopathological examination (in Eosin and hematoxyline stain) revealed Granulomas composed of epithelioid histiocytes, rimmed by lymphocytes with central caseous necrosis and Langhan type of giant cells are seen (Figure 5). Diagnosis of primary pituitary Tuberculosis was made and four anti-tuberculous medications (isoniazid, rifampicin, ethambutol and pyrazinamide) were commenced (12 months) and

started on steroid replacement, now she completed the full course of antituberculous therapy and symptomatically improved and was on regular follow up.

5. Discussion

Pituitary adenomas are the most common lesions of the sellar region, but it is important to consider unusual non-adenohypophyseal lesions in the differential diagnosis of a sellar mass, including inflammatory and infectious processes.⁵

The variety of clinical and radiological presentations of pituitary tuberculomas and the low reported rate make accurate preoperative diagnosis almost impossible.⁶

Our cases did not present any evidence for systemic or primary active tuberculosis.

The mechanism by which Tuberculous bacilli spread to the pituitary gland without apparent involvement of other body organs still remains unclear. Hematogenous spread and extension of tuberculous infection from the paranasal sinuses have been suggested in previous reports.⁷ About 70% of pituitary Tuberculosis cases reported in the literature were from the Indian subcontinent which can be attributed to the high prevalence of Tuberculosis in this part of the world.⁷ In a very recent comprehensive review of 81 previously published cases of pituitary tuberculomas, Srisukh et al.⁸ found that young people were the most commonly affected by the disease and almost 73% of affected cases were females, but in our short case series, all are females. Headache and visual disturbances were the most common presenting symptoms and the absence of constitutional symptoms of Tuberculosis, such as fever, was characteristic. A study by Sharma, et al.³ reported that history or existing tuberculous infection elsewhere in the body was present only in 30% of patients. In cases reviewed of sellar tuberculoma, the history of tuberculosis was present in 28.5% (10/35). So tuberculosis in the sellar area cannot be excluded from the list of differential diagnoses even if there is no evidence of systemic tuberculosis. Magnetic resonance imaging is considered as the best radiological modality to diagnose pituitary lesions; however, differentiation between pituitary tuberculoma and adenoma on the basis of Magnetic resonance imaging findings can be very difficult. Previous reports have suggested that thickening of the pituitary stalk can be useful to differentiate pituitary tuberculoma from adenoma.⁹ Because of its rarity, sellar tuberculoma is seldom considered in the differential diagnosis and is often mistaken for pituitary macroadenoma, which is the most common tumour in this region. Although rare, the presence of infundibular thickening and enhancement of the adjacent dura should suggest the presence of a granulomatous lesion like tuberculoma.¹⁰ In our case series, only one case showed thickening of the pituitary stalk. However, this sign is non-specific and can be seen in a variety of other

inflammatory and neoplastic lesions of the pituitary gland such as sarcoidosis, syphilis, lymphomas, and Wegner's granulomatosis.

The transsphenoidal approach is the preferred one for dealing with sellar tuberculoma because it provides a histological diagnosis, allows a local cure and avoids contamination in the cerebrospinal fluid (CSF).¹¹ Surgical intervention is to decompress adjacent structures and also confirm the diagnosis of tuberculoma. The most important therapy for sellar tuberculomas is the antitubercular drug regimen and it is started on the basis of the histopathological report. A typical finding on histologic examination of pituitary tuberculoma is the demonstration of caseating granuloma. Ziehl-Neelsen stain for Tuberculous bacilli is usually negative.^{12,13}

The appropriate management of pituitary Tuberculoma is starting of antituberculous regimen (for a prolonged time 9-12 months) and hormonal replacement therapy if there is a deficiency. Surgical intervention is usually reserved for diagnostic or decompressive purposes.¹⁴ In some cases, an initial trans-sphenoidal biopsy was performed and later craniotomy was done and the tumour was excised.¹⁵

In our short case series, a final diagnosis of primary pituitary tuberculosis was made based on typical histological findings. There was no evidence of other systemic or pulmonary Tuberculosis after extensive radiologic and microbiological investigations.¹⁶ Hormonal profile was done pre-operatively just prior to surgery to look for any steroid or thyroid hormone replacement if needed, one patient had a normal endocrinological profile, while the other two had Cortisol deficiency and one had thyroid hormone deficiency in addition to Cortisol deficiency, pre operatively we replaced thyroid and Cortisol hormones prior to surgery in these two patients and post-operatively after two weeks we used to repeat hormonal profile for dose adjustment and then after every one month. As per the literature,¹⁷ suprasellar extension is a risk factor for post-operative Cerebrospinal fluid leak after endoscopic transsphenoidal surgery, in our series two patients had a suprasellar extension of mass (cases 1 & 3) and one patient had postoperative Cerebrospinal fluid leak (case 1).

6. Conclusion

Though diagnosis of sellar tuberculomas is difficult on clinical and radiological examinations, pituitary tuberculomas should be considered in the differential diagnosis of Sellar/suprasellar masses, especially in developing countries even if there is no previous history or contact with Tuberculosis or evidence of tuberculous infection elsewhere in the body.

As is advisable to have tissue diagnosis before starting Antituberculous drugs, surgery remains one of the mainstays of treatment not only for obtaining a histopathological sample for diagnosis

but also for decompression of surrounding structures. Clinical recognition, pre operative and intra-operative suspicion (Frozen section Biopsy) can limit the extent of surgery and avoid the development of new hormonal deficiencies after the surgery since the condition is curable without disturbing the pituitary function. Long-term antituberculous drug therapy (one year) usually results in a good outcome. Since it is not clear whether patients require lifelong replacement of deficient hormones periodic follow-up is warranted.

7. Conflict of Interest

None.

8. Source of Funding

None.

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