Pituitary macroadenomas presenting as isolated sixth nerve palsy

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Abstract
Pituitary adenoma is the most common cause of sellar masses, after the third decade of life, which may present with various neuro-ophthalmic manifestations. Common visual manifestations of adenoma are visual impairment and third nerve palsy. Here, we are reporting a case of ACTH positive pituitary macroadenoma presenting as isolated sixth nerve palsy without apoplexy in a middle-aged male.

Keywords: Diplopia, pituitary adenoma, sixth nerve palsy.

Introduction
Pituitary adenoma is an eminent pathology comprising a heterogeneous group of tumors with an overall incidence of 20-25% in general population.1 Pituitary adenoma is the most common cause of sellar masses, after the third decade of life, which may present with various neuro-ophthalmic manifestations due to intimate anatomical proximity of pituitary gland with optic chiasma and cranial nerves in the cavernous sinus.2 Visual manifestations of pituitary adenoma range from being asymptomatic to advanced deterioration of visual acuity up to blindness. The classical presentation is bitemporal hemianopia on perimetry secondary to compression of optic chiasma.3 Ocular motility disorders in pituitary adenoma are rare manifestations, only few case reports are available in literature. Lateral extension of tumor into cavernous sinus can cause compression of third cranial nerve, resulting into diplopia and restriction of ocular motility.4 However, isolated sixth nerve palsy is a rare presenting manifestation of pituitary adenoma. These tumors typically grow slowly unless pituitary apoplexy occurs, which is defined as an acute haemorrhagic infarction of the pituitary adenoma resulting into increased intrasellar pressure often resulting in acute onset of headache, nausea, vomiting, ophthalmoplegia and visual loss.5 We report a case of an isolated sixth cranial nerve palsy as the presenting clinical feature of a rapidly expanding ACTH positive silent tumor without any apoplexy.

Case Report
A 44 year old male with no significant past medical history presented to our OPD with a chief complaint of vague headaches and diplopia since 5 days. His ocular examination showed BCVA of 6/6 in both eyes with +3 DS correction with normal anterior segment. Neuro-ophthalmologic exam revealed an isolated, incomplete, right sixth nerve palsy resulting into Right Convergent Squint (RCS) with restriction of right lateral rectus (Figure 1).

Fig.1(a): RLR restriction Fig.1(b): RCS in primary gaze
Humphrey visual field testing with 24-2 testing strategy was normal and dilated fundus examination revealed the absence of papilledema and a normal retinal periphery (Figures 2 & 3). There was no clinical evidence of either myasthenia gravis or thyroid ophthalmopathy.

Fig 2: Right eye fundus Fig.3: Left eye fundus
An MRI of the orbits and brain revealed a large T2W/FLAIR heterogenous hyperintense and T1W hypointense lesion of size 26x27x20 mm with tiny cystic areas, located in pituitary fossa, extending into right cavernous sinus and inferiorly bulging into sphenoid sinus suggestive of pituitary macroadenoma.
The patient was immediately admitted to the neurosurgery department for preoperative studies and scheduled for urgent transphenoidal hypophysectomy. Preoperative and systemic work up was initiated, inclusive of complete blood count, metabolic profile, coagulation studies, sedimentation rate, thyroid function tests, acetylcholine receptor antibodies, (both binding and blocking), angiotensin converting enzyme and pituitary hormones level. All tests were within normal limits aside from an elevated ACE and ACTH. The patient underwent urgent transphenoidal hypophysectomy for this rapidly progressive tumor. Intraoperatively, the tumor was found to have clinical extension into the cavernous sinus. Pathologic examination of the mass demonstrated a pituitary adenoma positive for ACTH immunostain. No frank haemorrhage or necrosis was noted. Post-operatively the patient was placed on intravenous decadron, which was tapered over 10 days. His VIth nerve palsy and horizontal diplopia resolved over the subsequent three months. Now, 6 months after his surgery, he remains free of symptoms with complete ocular motility, 6/6 BCVA and full visual fields.

Discussion
The cavernous sinus contains the carotid artery as well as the oculomotor, trochlear, ophthalmic and maxillary divisions of the trigeminal and abducens nerves. Extraocular palsy generally indicates compression of the cavernous sinus wall or direct extension of the pituitary adenoma into the cavernous sinus. The incidence of ocular palsy occurring with pituitary tumors has been reported to be between 4.6 and 32%. Most commonly oculomotor nerve is affected and rarely abducens nerve get involved. The sixth cranial nerve runs lateral to the internal carotid artery, but medial to the third, fourth, and first and second divisions of the fifth cranial nerves which run superior to inferior within the lateral dural border of the cavernous sinus. It is therefore more often spared because of its more sheltered position within the sinus.

Several published studies had suggested various mechanisms for the pathophysiology of cranial nerve palsies in pituitary adenoma; including either indirect compression on the ocular cranial nerves by compressing the cavernous sinus or direct compression through cavernous sinus invasion. Adenomas that usually invade the cavernous sinus grow through fragile medial sinus wall with mediolateral expansion resulting in lateral displacement of the internal carotid artery, with third nerve compression in the oculomotor trigone. Thus the most commonly involved by the compression is the third nerve. At the oculomotor trigone there is a whole cistern of cerebrospinal fluid which represents a possible route for tumor invasion. Vascular occlusion also has been reported as a mechanism for third nerve palsy, due to compression of its blood supply originating from the internal carotid artery. Other proposed mechanism for ocular palsy was the occurrence of pituitary apoplexy with rapid deterioration of symptoms. Isolated sixth nerve palsy as a presentation of pituitary adenoma is very rare. The sixth nerve passes within isolated fourth nerve palsy very rare except in case of massive compression of the cavernous sinus, involving all the oculomotor nerves.

Conclusion
Pituitary macroadenoma presents as isolated sixth nerve palsy rarely, but we should consider it in cases of acute onset of ophthalmoplegia and diplopia. The most common ocular cranial nerve involved is the isolated third nerve palsy followed by sixth nerve palsy. Early diagnosis and timely tumor excision with cranial nerves decompression has a favourable outcome regarding the improvement of ocular motility.

References
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