Neuroradiology in the Ocular Motility Disorders :
II. Nuclear and Infranuclear Pathway[1]

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The nuclear and infranuclear pathway of eye movement begins from the ocular motor nuclei situated in the brain stem, where the axons originate and form three ocular motor nerves. Although each of the ocular motor nerves follows a distinct route to reach the end organ, the extraocular muscles, they also have common housings in the cavernous sinus and at the orbital apex, where part or all of them are frequently and simultaneously affected by a common disease process. Since the fine details of normal and diseased structures can frequently be seen on radiologic imaging, especially magnetic resonance (MR) imaging, a knowledge of the basic anatomy involved in nuclear and infranuclear eye movement is important. In this description, in addition to the normal nuclear and infranuclear pathway of eye movement, we have noted the radiologic findings of typical diseases involving each segment of the nuclear and infranuclear pathway, particularly as seen on magnetic resonance images. Brief comments on ocular motor pseudopalsy, which mimics ocular motor palsy, are also included.

Index words : Brain, anatomy
Brain, abnormalities
Brain, MR
Nerves, cranial

Normal Nuclear and Infranuclear Pathway

Oculomotor Nerve Pathway

The oculomotor nerve arises from the complex oculomotor nuclei situated ventrolaterally in the periaqueductal gray matter of the midbrain at the level of the superior colliculus. The nuclei consist of groups of large and small multipolar cells which are arranged longitudinally on each side of the midline supplying one of the four extraocular muscles. A single median nucleus controls the levator palpebrae superioris muscle on either side. The interconnecting, paired, wing-shaped Edinger-Westphal subnuclei lie cranial and dorsal to the main nuclei and subserve pupillary function supplied by the parasympathetic fibers for the ciliary ganglion. Axons from the bilateral oculomotor nuclei run ventrally and slightly caudally through the midbrain tegmentum traversing the medial longitudinal fasciculus (MLF), the red nucleus, the substantia nigra, and the medial aspect of the cerebral peduncle, and finally exit the brain stem medial to the cerebral peduncles as oculomotor nerve rootlets which immediately converge to form the oculomotor nerves in the interpeducular cistern (Fig. 1A). At this point, the oculomotor nerve, with its accompanying

parasympathetic fibers, runs forward between the origins of the posterior cerebral and superior cerebellar arteries, lateral and inferior to the posterior communicating artery, and medial to the free edge of the tentorium (Fig. 1B and C) (1, 2). The pupillomotor fibers lie superficially in the nerve just internal to the epineurium, making them vulnerable to compression due to extrinsic pathology such as aneurysm of the posterior communicating artery (3). The nerve pierces the arachnoid and dura mater in the angle between the free and fixed margins of the tentorium to enter the roof of the cavernous sinus and then courses along the superolateral wall, superolateral to the cavernous internal carotid artery. Finally, it enters the orbit via the superior orbital fissure, passing through the annulus of Zinn and divides into a smaller superior branch which supplies the superior rectus and levator palpebrae superioris muscles, and a larger inferior branch which supplies the medial and inferior recti and the inferior oblique muscles (Fig. 1D). The preganglionic parasympathetic fibers originating from the Edinger-Westphal nucleus accompany the inferior branch and reach the ciliary ganglion via a short offset from the branch to the inferior oblique muscle. The ciliary ganglion is a tiny relay station for the parasympathetic fibers and is located between the optic nerve and the lateral rectus muscle in the posterior por-
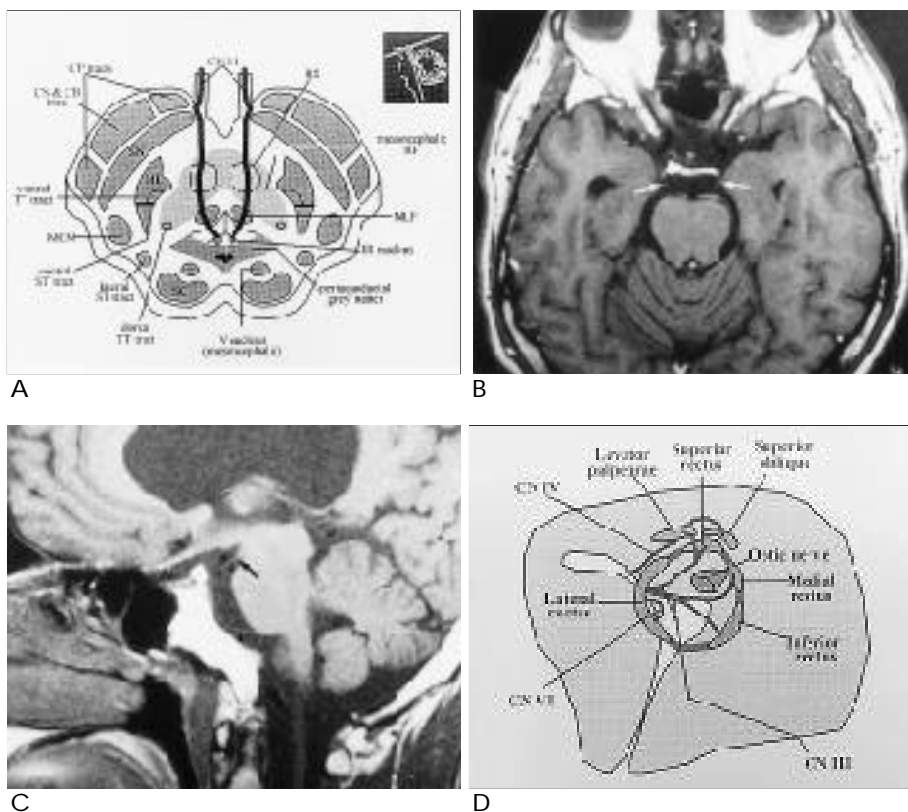

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C

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Fig. 1. Oculomotor nerve pathway.
A. Diagram of oculomotor nerve nucleus in the midbrain. CB= corticobulbar; CP= corticopontine; CS= corticospinal; MGN= medial geniculate nucleus; ML= medial lemniscus; MLF= medial longitudinal fasciculus; RF= reticular formation; RN= red nucleus; SC= superior colliculus; SN= substantia nigra; ST= spinothalamic; TT= trigeminothalamic.
B, C. Axial (B) and sagittal (C) T1-weighted MR images show oculomotor nerve (white arrows in B and black arrow in C) in the interpeduncular cistern. It lies below posterior cerebral artery and above superior cerebellar artery, nicely demontrated on sagittal image. Note abducens nerve in the prepontine cistern (arrowhead in C).
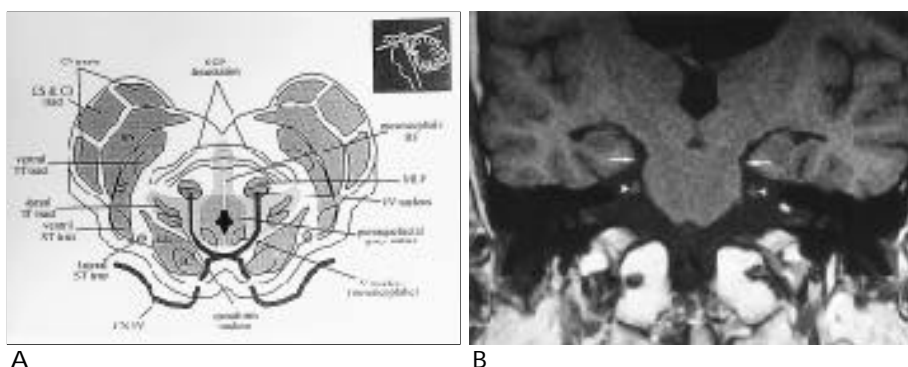D. Diagram of ocular motor nerves in the orbit.

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B

Fig. 2. Trochlear nerve pathway.
A. Diagram of trochlear nerve nucleus in the midbrain.
CB= corticobulbar; CP= corticopontine ; CS= corticospinal; IC= inferior colliculus ; LL= lateral lemniscus; ML= medial lemniscus; MLF= medial longitudinal fasciculus; RF= reticular formation; SCP= superior cerebellar peduncle; SN= substantia nigra; ST= spinothalamic; TT= trigeminothalamic.

B. Coronal T2-weighted MR image shows bilateral trochlear nerves (arrows) at the tentorial edge. Arrowheads indicate trigeminal nerves.

tion of the orbit. From here the parasympathetic post-ganglionic fibers pass to the globe via the short ciliary nerves to supply the ciliaris and sphincter pupillae muscles (3). Vascular supply to the oculomotor nerve includes the posterior thalamo-perforating arteries that feed the nucleus and midbrain; branches of the basilar, posterior cerebral, and posterior communicating arteries that supply the cisternal segment of the nerve; and branches of the posteiror cerebral artery and meningo-hypophyseal trunk that supply the rest of the nerve (4, 5).

Trochlear Nerve Pathway

The trochlear nerve originates from the trochlear nucleus which is located in the ventral aspect of the periaqueductal gray matter just caudal to the oculomotor nuclei at the level of the inferior colliculus. Axons from the nucleus curve posterolaterally and slightly caudally around the aqueduct to reach the upper part of the superior medullary velum, where they decussate before emerging on the contralateral side of the frenulum veli beneath the inferior colliculus to form the trochlear nerve (Fig. 2A). After exiting the brain stem, the trochlear nerve winds forward around the midbrain within the ambient cistern below the free edge of the tentorium and between the posterior cerebral and superior cerebellar arteries lateral and caudal to the oculomotor nerve (Fig. 2B). It pierces the inferior surface of the tentorium to enter the cavernous sinus below the oculomotor nerve and above the ophthalmic division of the trigeminal nerve (1, 2). On entering the orbit, the nerve passes through the superior orbital fissure superolateral to the annulus of Zinn, and courses medially between the orbital roof and the levator palpebrae superioris muscle to
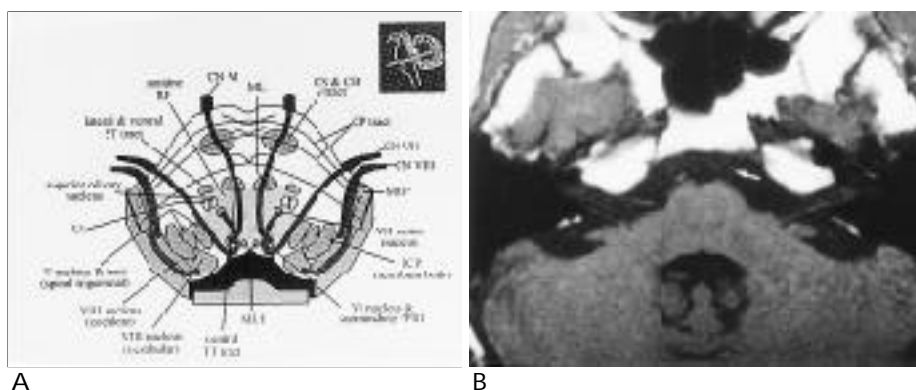
Fig. 3. Abducens nerve pathway.
A. Diagram of abducens nerve nucleus in the rostral pons.
CB= corticobulbar; CP= corticopontine; CS= corticospinal; ICP= inferior cerebellar peduncle; LL= lateral lemniscus; MCP= middle cerebellar peduncle; ML= medial lemniscus; MLF= medial longitudinal fasciculus; PPRF= paramedian pontine reticular formation; RF= reticular formation; ST= spinothalamic; TT= trigeminothalamic.

B. Axial T1-weighted MR image shows left abducens nerve in the prepontine cistern at level of Dorello's canal (arrow).
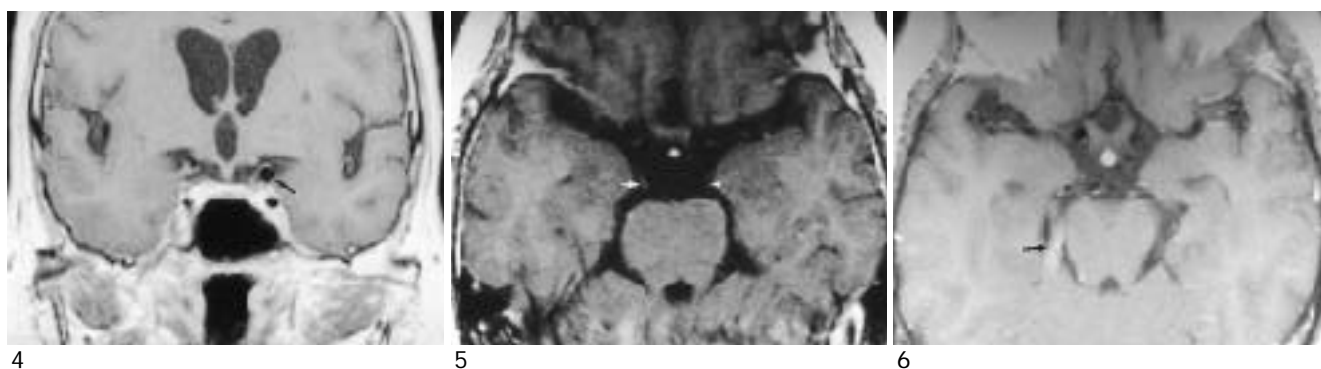

Fig. 4. Isolated pupil-involving oculomotor nerve palsy due to posterior communicating artery aneurysm. Enhanced coronal T1-weighted MR image shows direct contact of left posterior communicating artery aneurysm (arrow) with oculomotor nerve displaced medially in the interpeduncular cistern. Subsequent MR and conventional angiography confirmed it.
Fig. 5. Isolated pupil-involving oculomotor nerve palsy due to meningitis. Enhanced axial T1-weighted MR image shows an enhancement of the right oculomotor nerve (arrow) in 66-year-old woman with meningitis. Note the normal left oculomotor nerve which shows no enhancement (arrowhead).
Fig. 6. Isolated trochlear nerve palsy in a patient with type 2 neurofibromatosis. Enhanced axial
T1-weighted MR image shows a thick tentorial enhancement on the right (arrow). Tentative diagnosis is meningioma.

supply the superior oblique muscle (Fig. 1D). Vascular supply to the trochlear nerve includes the thalamo-perforating arteries that supply the nucleus; the artery of the free margin of the tentorium from the meningohypophyseal trunk; and branches of the inferolateral trunk from the internal carotid artery(4).

Abducens Nerve Pathway

The abducens nerve is derived from the abducens nucleus which lies in the pontine tegmentum, just ventral to the upper part of the fourth ventricle. Homolateral facial nerve axons loop around the abducens nucleus producing a bulge, facial colliculus, in the floor of the fourth ventricle. Axons from the nucleus runs ventrally through the pontine tegmentum and exit the brain stem 1 cm from the midline at the ponto-medullary junction to form the abducens nerve (Fig. 3A). The nerve courses anteriorly between the anterior inferior cerebellar and acoustic arteries, and then ascends in front of the pons before it bends forward to pierce the dura of the clivus passing beneath the petroclinoid ligament and through Dorello' s canal (Figs. 1C and 3B). It continues ventrally between the dura and petrous apex to enter the cavernous sinus (1, 2), where the nerve travels medial to the internal carotid artery and lateral to the ophthalmic division of the trigeminal nerve. It enters the orbit via the superior orbital fissure passing through the annulus of Zinn, lateral to the optic nerve, and innervates the lateral rectus muscle (Fig. 1D). The blood supply to the abducens nerve includes perforators from the basilar artery that supply the nucleus; branches of the ascending pharyngeal artery; and the inferolateral trunk from the internal carotid artery (4).

Nuclear and Infranuclear Pathology Leading to the Ocular Motility Disorders

Patients with lesions located anywhere along the course of the third, fourth, or sixth cranial nerve from the brain stem nuclei to the orbit present with diplopia (double vision). Cranial nerve dysfunction is more commonly localized to an isolated nerve, either unilateral or bilateral, but it may affect two or more nerves or brain stem tracts resulting in complex neuropathy.

Isolated oculomotor, trochlear and abducens nerve palsy

Many reports have shown that abducens nerve palsy is the most common isolated ocular nerve palsy, followed by palsy of the oculomotor and trochlear nerves (2, 6, 7). The long intracranial course contributes to this susceptibility of the abducens nerve to injury by a variety of abnormalities. Oculomotor nerve palsy can be categorized as complete or incomplete and external (pupil-sparing) or internal (pupil-involving). Total complete third nerve palsy is manifested as exotropia, ptosis, or mydriasis. The most common cause of a pupil-sparing palsy is microinfarction due to diabetes or hypertension, in which radiologic examination usually reveals no abnormality (5, 8). The most common cause of a pupil-involving third nerve palsy is aneurysm, which most frequently involves the posterior communicating artery (Fig. 4). Because pupillary involvement may oc-
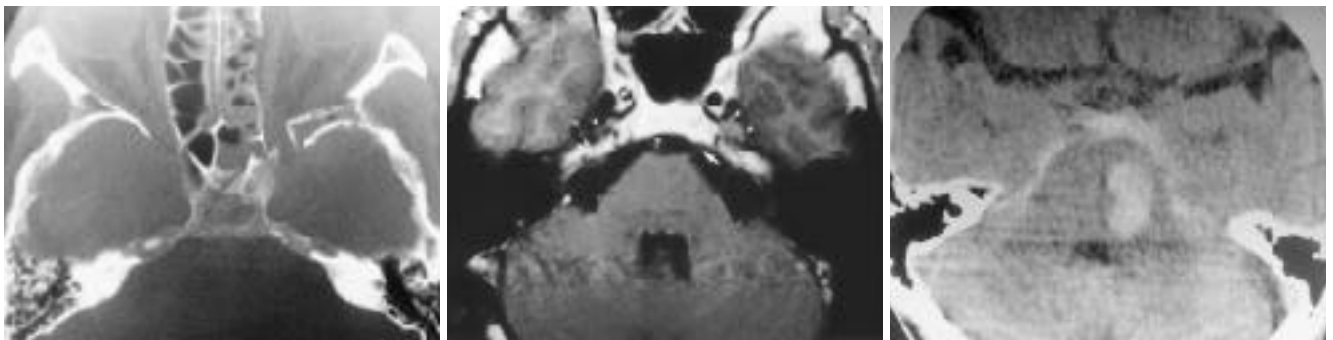

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Fig. 7. Abducens nerve palsy due to head trauma. Axial CT shows multiple fractures in the left sphenoid bone extending to the right side of clivus. The patient had right abducens nerve palsy as well as left blindness due to optic nerve injury.
Fig. 8. Abducens nerve palsy due to leptomeningeal metastasis from lung cancer. Enhanced axial
T1-weighted MR image shows a nodular thickening of the left abducens nerve (arrow). Also noted are multiple enhanced nodules within trigeminal cistern in both sides, representing metastases along root bundles of trigeminal ganglion (arrowheads).
Fig. 9. Raymond syndrome. Axial CT scan shows a large left pontine hemorrhage. Clinically, the patient had left abducens nerve palsy and right hemiplegia that resulted from simultaneous involvement of abducens nerve fasciculi and corticospinl tract.

cur later in the clinical course, it is important to note that a normal pupillary response does not entirely exclude an aneurysm (2). Likewise, pupillary involvement is not infrequent in ischemic disease. Head trauma and neoplasm are also important causes of third nerve palsy. Other less common causes of this condition include complications of intracranial surgery, multiple sclerosis, viral neuritis, sinusitis, meningitis (Fig. 5), and connective tissue disease (1, 2, 4, 5-7).

Patients with isolated trochlear nerve palsy present with vertical diplopia which worsens on downward gaze. Trauma is the most common cause of isolated trochealr nerve palsy followed by vascular insults. Other less common causes include neoplasm, aneurysm, viral neuritis, meningitis (Fig. 6), hydrocephalus, and postsurgical complication (1, 2, 4, 6, 7, 9).

Isolated abducens nerve palsy results in esotropia and abduction failure. The intranuclear interneuron where synapses occur beween the ipsilateral paramedian pon-

tine reticular formation (PPRF) and the contralateral MLF is located within the abducens nerve nucleus. Accordingly, nuclear lesions of the abducens nerve frequently cause ipsilateral horizontal gaze palsy. The long intracranial course contributes to the greater susceptibility of the abducens nerve to injury by a variety of abnormalities. Ischemia and trauma (Fig. 7) cause isolated abducens nerve palsy most commonly in adults, while viral neuritis and trauma cause it most commonly in children. Its other causes include neoplasm (Fig. 8), either primary or secondary, multiple sclerosis, aneurysm, increased intracranial pressure, iatrogenic complications from surgery or lumbar puncture, carotico-cavernous fistula, meningitis, and otitis (1, 2, 4, 6, 7, 10).

Complex oculomotor, trochlear and abducens nerve palsy

Complex neuropathy involving one or more ocular nerves can occur either through a pathological process involving the sites where specific ocular motor nuclei or

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Fig. 10. Gradenigo's syndrome. Enhanced axial T1-weighted MR image shows a marked enhancement in the right nasopharynx and adjacent skull base (arrows). Note enhancement of inflammatory tissue within the right mastoid area (arrowheads).
Fig. 11. Tolosa-Hunt syndrome. Axial fat saturated T1-weighted MR image shows high signal
intensity lesion (arrow) in the left orbital apex. The ipsilateral cavernous sinus was also enlarged (not shown).
Fig. 12. Complex cranial neuropathy due to meningioma in the cavernous sinus. Enhanced axial T1-weighted MR image shows a well enhancing mass in the left cavernous sinus. Note the dural tail on its posterior aspect (arrow).
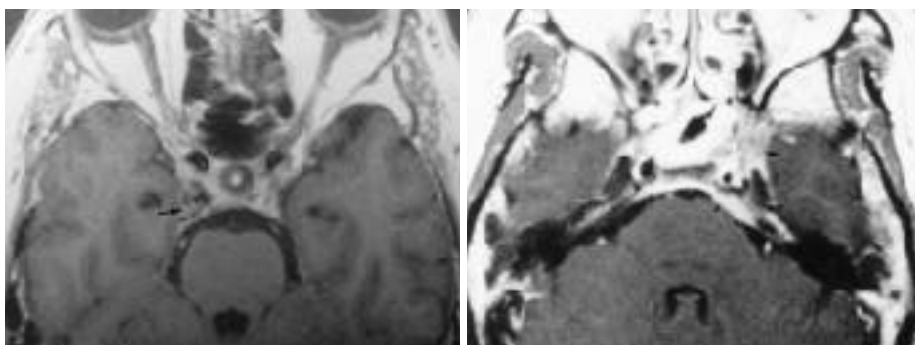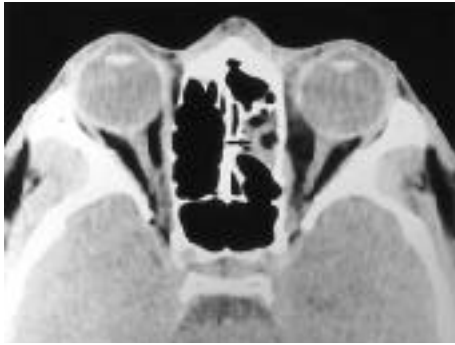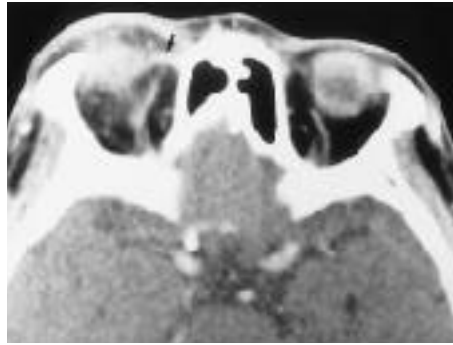

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Fig. 13. Complex cranial neuropathy due to cavernous dural arteriovenous malformation. Enhanced axial T1-weighted MR image shows an irregular signal void area (arrow) within the right cavernous sinus. Subsequent MR and conventional angiography confirmed the diagnosis.
Fig. 14. Complex cranial neuropathy due to aggressive sphenoid sinusitis. Enhanced axial
T1-weighted MR image shows a circumscribed mucosal enhancement of
the sphenoid sinus with associated enlargement and irregular enhancement of left cavernous sinus (arrow). Also noted is a dural enhancement posterior to the clivus (arrowheads).

Fig. 15. Ocular motor pseudopalsy due to orbital medial blow-out fracture. Axial CT shows an entrapped left medial rectus muscle (arrow) within the ethmoid sinus.
Fig. 16. Ocular motor pseudopalsy due to acquired Brown's syndrome resulting from pseudotumor. Axial CT scan shows a thickened right superior oblique muscle at its tendinous reflection (arrow).

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fascicles are close to various neural tracts, as in the brain stem, or by diseases involving areas where ocular nerves are closely related in space, as in the cavernous sinus or orbital apex (2, 4). It may result from pathology in the subarachnoid cistern large enough to involve multiple cranial nerves, being caused, for example, by a tumor or dolichoectasia, or by a systemic, infectious, or traumatic disease.

Numerous eponyms are used to characterize complex neuropathies of cranial nerves III, IV, and VI, according to the location of involved brain stem nuclei, fascicles and tracts (2, 4). Any pathological process can produce the same clinical manifestations, once it involves the same location (Fig. 9).

Outside the brain stem, complex neuropathy can be produced by a lesion localized to the subarachnoid cistern, cavernous sinus, orbital fissure, or orbital apex. Although there may be diseases which more frequently affect a specific locus, any pathology located at or near the above sites can produce the same constellation of clinical manifestations. Gradenigo's syndrome is an uncommon cause of petrous apex syndrome caused by ear infections (1) (Fig. 10). Tolosa-Hunt syndrome, which is usually steroid responsive, is an uncommon cause of superior orbital fissure or orbital apex syndrome secondary to idiopathic granulomatous inflammation of the cavernous sinus or superior orbital fissure (11) (Fig. 11). The cavernous sinus houses cranial nerves III, IV, V1 and VI as well as the internal carotid artery and postganglionic sympathetic fibers. As expected, various conditions can involve the cavernous sinus, resulting in complex neuropathy (Figs. 12-14).

Ocular Motor Pseudopalsy

A variety of diseases involving the orbit or extraocular muscles can lead to disturbed eye movements, though these are not true palsies, because they do not involve the nerves, tracts, or nuclei (2). Restrictive myopathy due to an infiltrative or inflammatory disease such as Graves disease, pseudotumor, lymphoma, tumor, sarcoidosis, or infection and diseases affecting neuromuscular junction (myasthenia gravis, for example) are responsible for the majority of these conditions. Restrictive myopathy can often be distinguished from neuropathy by a forced duction test (12). Orbital trauma is another common cause of restriction of muscle by way of entrapment between the fractured bones (Fig. 15). Brown's superior oblique tendon sheath syndrome may be either congenital or acquired. In this condition, there is an impaired ability to raise the eye in adduction, simulating inferior oblique palsy, and resulting from failure of the superior oblique tendon to slide through the trochlea (12) (Fig. 16). Other less common causes of ocular motor pseudopalsy are progressive external ophthalmoplegia, myotonic dystrophy, ocular neuromyotonia, craniosynostosis, Duane's retraction syndrome, congenital double elevator palsy and convergence spasm (1, 2, 12).

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