Introduction
The oculomotor nerve has two components—outer parasympathetic fibers and inner somatic fibers. The outer parasympathetic fibers supply the ciliary muscles and the sphincter pupillae. The inner somatic fibers supply the levator palpebrae superioris and the four extraocular muscles (superior rectus, medial rectus, inferior rectus and inferior oblique). The oculomotor nucleus complex is present in the midbrain at the level of the superior colliculus. It consists of the main motor nucleus and an accessory parasympathetic nucleus (Edinger-Westphal nucleus). Compressive lesions (aneurysm or tumor) affect the superficial pupillomotor fibers and their blood supply. Medical lesions (diabetes mellitus or hypertension) on the other hand affect the vasa vasorum and thus spare the pupillary fibers. Compressive or traumatic lesions also cause aberrant regeneration of third nerve.\(^1\)

Etiology
Third nerve can be affected anywhere along its path. The lesions can be nuclear, fascicular, basilar, intracavernous or intraorbital (Figure 1). A complete third nerve palsy presents with ipsilateral mydriasis, bilateral ptosis, contralateral elevation deficit, and ipsilateral adduction and depression deficits.\(^2\)

The nuclear complex lies in the midbrain at the level of the superior colliculus. The central caudal nucleus innervates bilateral levator palpebrae superioris (LPS). Contralateral Superior rectus is supplied by the decussation of the fibers in the nuclear complex. Ipsilateral medial rectus, inferior rectus, inferior oblique and parasympathetic pathways are supplied by the paired subnuclei (Table 1). Lesions causing nerve palsy in this region are tumors, inflammation, infarction and metastasis.

A fascicular palsy affects the ipsilateral eye and is associated with other neurological deficits because of the presence of red nucleus and cerebral peduncle in the brainstem. The leading causes are vascular, inflammatory and infiltrative. Multiple sclerosis can also be a cause as the fascicles are a part of white matter (Table 2).

In the basilar portion, isolated nerve palsy is very common. Aneurysm of the posterior communicating artery and posterior cerebral artery or a subarachnoid hemorrhage can cause painful third nerve palsy. Severe trauma leading to skull fracture and loss of consciousness tend to damage third nerve. However, minor trauma causing the same should arouse suspicion of an underlying mass or aneurysm.

The nerve divides into superior and inferior divisions in the

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Table 1: Daroff’s rule for nuclear third nerve palsy

| Conditions that obligate nuclear involvement | Bilateral IIIrd nerve palsy without ptosis (bilaterally spared LPS function) |
|--------------------------------------------|------------------------------------------------------------------|
|                                              | Unilateral IIIrd nerve palsy with contralateral superior rectus weakness |
|                                              | Bilateral partial ptosis                                          |

| Conditions that exclude a nuclear lesion    | Unilateral ptosis                                                              |
|---------------------------------------------|--------------------------------------------------------------------------------|
|                                              | Unilateral internal ophthalmoplegia                                            |
|                                              | Unilateral external ophthalmoplegia associated with normal contralateral superior rectus function |

| Conditions that neither exclude nor obligate a nuclear lesion | Bilateral total IIIrd nerve palsy | Bilateral ptosis | Bilateral internal ophthalmoplegia | Bilateral medial rectus ptosis |
|-------------------------------------------------------------|----------------------------------|-----------------|-----------------------------------|------------------------------|

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Figure 1: Course of third nerve
region of the anterior cavernous sinus and superior orbital fissure. In the anterior part of the cavernous sinus, superior or inferior divisions of the third nerve may be selectively involved. The superior division innervates the superior rectus and levator palpebrae superioris. The inferior division supplies the inferior rectus, medial rectus and inferior oblique muscle. It also transmits parasympathetic fibers to the ciliary ganglion. Multiple nerve palsies are common in the cavernous sinus due to close proximity of cranial nerves IV, V and VI in this region. Common causes include caroticocavernous fistula, pituitary apoplexy, neoplasms (pituatory tumors, craniohypophyngioma, meningioma, nasopharyngeal carcinoma, metastasis), Tolosa-Hunt syndrome, sarcoidosis, aneurysmal compression, ischemia, cavernous sinus thrombosis and arteriovenous fistula.

Orbital lesions are associated with proptosis and sometimes optic neuropathy, (Figure 2). Orbital tumors have been classified into five types: (1) INFLITRATIVE- restriction of motility, firm orbit, ptosis and enophthalmos (2) MASS-proptosis, displacement of globe and palpable orbital mass (3) INFLAMMATORY – pain, chemosis, erythema & periorbital swelling (4) FUNCTIONAL – ocular motility disproportionate with the degree of orbital involvement (5) SILENT – orbital metastatic lesions detected by MRI/CT but asymptomatic (4). Isolated third nerve palsy in children has various causes - congenital (43%), trauma (20%), inflammation (13%), aneurysm (7%) and ophthalmoplegic migraine.

| Syndrome                  | Site Involved       | Neurological Signs                                      |
|---------------------------|---------------------|--------------------------------------------------------|
| Benedikt’s Syndrome       | Red Nucleus         | Contralateral Tremor, Hemichorea, Hemiamyotrophy, Or Hemiplegia |
| Weber’s Syndrome          | Cerebral Penduncle  | Contralateral Hemiparesis Or Hemiplegia                 |
| Nothnagel’s Syndrome      | Superior Cerebellar Peduncle | Ipsilateral Cerebellar Ataxia                        |
| Claude’s Syndrome         | Red Nucleus & Superior Cerebellar Peduncle | Contralateral Tremor And Ipsilateral Cerebellar Ataxia (Benedikt + Nothnagel) |

**Clinical Features**

Third nerve palsy presents with the following features:

- **Diplopia**: Crossed diplopia is characteristic of third nerve palsy. In complete ptosis diplopia will be absent. However, it can be elicited on lifting the eyelid.
- **Ptosis**: Due to paralysis of LPS (levator palpebrae superioris) muscle.
- **Exotropia and hypotropia**: Because of the unopposed action of the lateral rectus and superior oblique eye in a down and out position. In case of partial third nerve or recovered third nerve palsy the deviation will depend on the affected muscles.
- **Anisocoria**: The pupil becomes fixed and dilated due to paralysis of sphincter pupillae in compressive lesions. Ciliary muscle paralysis also leads to loss of accommodation. However, in ischemic lesions, the pupil is spared, and there is no loss of accommodation.
- **Aberrant regeneration**: It is a synkinesis thought to be due to misdirection of regenerated axons in the nerve. It is not seen in microvascular 3rd nerve palsies. Signs of aberrant innervation are:
  - 1. Elevation of the eyelid during attempted adduction (Inverse Duane sign, (Figure 3).
  - 2. Elevation/Retracton of the upper eyelid when eye is looking down (Pseudo-Von Graefe’s sign, (Figure 4).
  - 3. Miotic pupils that do not constrict when exposed to bright light but do so while focusing for near (Pseudo-Argyll-Robertson pupil)
  - 4. Segmental contraction of the sphincter may be seen on eye movements (Czannecki’s sign)

**Investigations**

Diplopia charting (Figure 5) and Hess charting should be done on each visit to look for recovery of the paralysed muscles.

A complete neurological workup along with neuroimaging should be done in patients less than 40 years of age. Isolated palsies are commonly seen in basilar lesions and are idiopathic in 25%. In patients with pupil sparing third nerve palsy a vascular cause should be looked for (fasting and post-prandial blood sugar along with HBA1C and blood pressure measurement). However, giant cell arteritis should also be
ruled out in elderly patients by doing complete blood count with erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Weekly follow-ups should be done to look for pupil involvement followed by monthly assessment till the ischemic neuropathy resolves (usually takes about 3 months to start recovering). If clinical signs and symptoms cannot distinguish between a microvascular cause and compression, neuroimaging is recommended. Magnetic resonance imaging of the brain should be done immediately as it shows the entire course of third nerve and soft tissue contrast. The MRI should include T1 and T2 weighted images, MR angiography, thin slice and contrast enhanced sequences. Use of computed tomography is limited in case a subarachnoid haemorrhage, skull fracture or cerebral aneurysm is suspected. Digital subtraction angiography is only performed for carotico-cavernous fistulas.\textsuperscript{4,5}

Conservative Management
Nonsurgical options can be used to avoid diplopia in acquired palsies, which may last as long as 6 months. Occlusion of one eye with a patch (Figure 6), opaque contact lens or frosted spectacle lens is helpful in relieving diplopia. In cases with complete third nerve palsies, ptosis acts as a natural patch for relieving diplopia. Prisms have a limited role as alignment cannot be improved in all positions of gaze. In partial third nerve palsies, botulinum toxin is useful. It paralyses the antagonist lateral rectus temporarily and thus neutralizes horizontal deviation in the primary position in isolated medial rectus palsies. It also prevents contracture of LR muscle. Superior rectus should not be injected as ptosis can worsen if toxin diffuses into the levator – SR
Partial Third Nerve Palsy

Exotropia with residual function of MR

LR recession and MR resection

LR recession with small resection of vertical rectus (SR & IR) & transposition to MR

Figure 9: A-(OS) Exotropia B- Residual MR function C- Orthotropia following (OS) LR+MRc

Partial Third Nerve Palsy

Exotropia with no residual function of MR

Inferior rectus may be done in cases of isolated SR weakness. For children who are susceptible to amblyopia, appropriate refractive error correction and occlusion therapy with a close follow-up is advised. This should be followed by early surgery after any progressive condition is ruled out.5,6

Surgical Management

Surgical management is sought if the nerve does not recover in 6 months. Correction is determined on the basis of forceduction tests and force generation tests. Surgery in third nerve palsy is challenging, more in cases with complete palsy.
The aim of surgery is to relieve diplopia by correcting the deviation in primary position. It is impossible to re-gain proper motility and thus, binocular single vision in all gazes. Ptosis correction should not be performed before correction of strabismus. It should be done once the eyes are aligned and the patient is diplopia free.8

**Aberrant Regeneration**

Performing surgery on the nonparetic eye keeps the paretic eye in an adducted position. To keep the eyes in the primary position, increased innervation of the lateral rectus muscle of the nonparetic eye is needed and thus the paretic eye adducts (Figure 15). As a result of this, the levator is stimulated and the ptotic lid is elevated in the primary position. Because both MR and levator start receiving equal innervation, pseudo-Von Graefe’s sign also improves.8

**Conclusion**

The ophthalmologist should evaluate whether the palsy is complete or partial and ascertain whether life-threatening problems exist. Once the diagnosis is made, temporary measures of rehabilitation should be used. Surgery should be performed once the stability of misalignment is determined and realistic goals should be set for the patient.

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