Original article

A Systematic Approach to Cranial Nerve III (Oculomotor) Lesions: a Case Report

Dr Daniel A Erasmus MBBCh (Wits); BEngSc(BME) (Wits)
Community Service Medical Officer, Department of Ophthalmology, Klerksdorp/Tshepong Hospital Complex, North-West Province, South Africa. Contact details: Tel. number: +27 738704622, Email address: daerasmus@icloud.com

Dr C. Chiwara MBcHB (Zimbabwe), Dip (Opthalmology) (South Africa), MMed (Opthalmology) (Zimbabwe)
Consultant, Department of Ophthalmology, Klerksdorp/Tshepong Hospital Complex, North-West Province, South Africa. Tel. number +27 83 292 8022, Email address: cchiwara18@gmail.com

ABSTRACT

Cranial nerve III (Oculomotor) pathology is a relatively common presenting complaint in general Ophthalmology practice. Lesions can be broadly classified into ischaemic or intracranial causes - with the latter mandating urgent neuro-imaging to exclude a potentially life-threatening aneurysm. By combining a relevant clinical history together with a structured anatomical approach to the general, neurological and ophthalmological examination the clinician is able to localize a likely level and thus guide optimal investigation and management. Classifying the lesion according to various patterns of involvement focuses the differential as well as highlights potential warning signs. We propose adopting a system of classification that differentiates between single-nerve involvement (isolated) versus multiple cranial nerve, peripheral nerve and cerebellar involvement (complex). **The presence of pupillary involvement assumes paramount importance in this classification system as the presence thereof is almost pathognomonic of intracranial pathology while pupil sparing pathology is *conversely* almost always ischaemic in origin.** The deficit at the orbit itself may be divided into a single-muscle involvement (partial) or diplopia with an abducted, hypotropic eye plus ptosis of the associated lid (complete).

Mr J.S. a 49 year old African male from Taung, North West Province was urgently referred to the Ophthalmology clinic at Klerksdorp Hospital with a two week history of constant, severe, diffuse headache over the left side of his head with an associated drooping upper eyelid on the same side. He furthermore complained of a left outward and downwardly deviated eye with horizontal double vision in both eyes, especially prominent on right lateral gaze. The patient denied any symptoms of nausea, vomiting, photophobia or stiff and painful neck.

Mr J.S. was diagnosed with HIV at his local clinic 3 years ago and initiated on anti-retroviral medication - with a most recent CD4 count of 179. He is otherwise healthy - with no other medical, surgical or ophthalmological history.

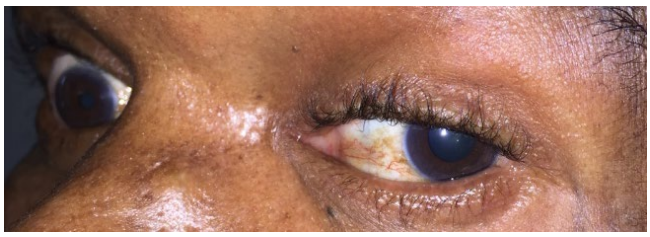

Figure 1: Close up of pupillary involvement. Eyelid held open superiorly (not shown)

He gives no history of any previous visual assessment or of wearing spectacles. He denies any smoking, and volunteers that he consumes between 6-8 units of alcohol per week. He is currently unemployed, not receiving social assistance and stays with his wife and 3 teenage children in the backroom of a friend's house.

On examination the patient was stable with a blood pressure of 133/77, a pulse rate of 87, a random blood sugar of 5.9 and temperature of 36.9 ºC. Mr J.S. did not appear acutely unwell although he exhibited marked temporal wasting. Central nervous system examination revealed no evidence of meningism. The left pupil was non-pharmacologically dilated and very poorly responsive to light **(*Figure 1*).** Furthermore there was severe ptosis with an abducted and hypotropic eye on the ipsilateral side ***(Figure 2).***

Auscultation of the chest revealed mild crackles bi-basally. Neurologically there was no other cranial nerve involvement evident, reflexes, power and tone were globally normal and gait was unaffected. There was no cerebellar deficit clinically. The remainder of the general examination was unremarkable.

Visual acuity was 6/30, improving with pinhole to 6/12 in the right eye and 6/120 with no improvement in the left eye. Intraocular pressure was 12 and 15 in the right and left eye, respectively.

External examination of the brow and orbit revealed no evidence of temporal swelling, pulsations or tenderness. As noted above, the left eyelid exhibited moderate/severe ptosis although the Bell's sign was completely preserved. The lid crease height was increased to 12 mm (normal 6-8mm), while the palpebral fissure height (MRD1 of 1mm + MRD2 of 4mm) was decreased to only 5mm (normal 9-10mm). Elimination of the frontalis muscle assistance revealed very poor levator function with displacement of the upper lid with downward and upward gaze reduced to only 5mm (13-17mm). There

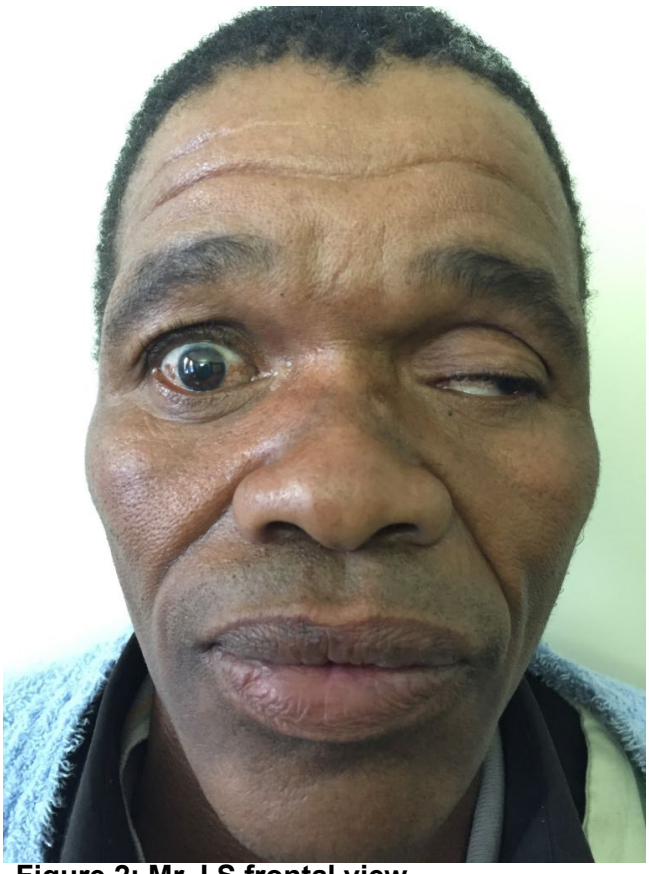

Figure 2: Mr J.S frontal view

was no Marcus Gunn Jaw Winking present.

The left eye was abducted and hypotropic with very limited ability to adduct, elevate or intort and was noted not to be able to cross the midline in neutral forward gaze. The left pupil was 7mm, compared with 4mm on the right, centrally placed with very poor direct and consensual light response.

Funduscopy was within normal limits bilaterally with mild degenerative changes at the macula - more pronounced on the left than the right. The optic disc was salmon-pink with normal vasculature and crisp edges nasally. The remainder of the retina was unremarkable with no evidence of hard exudates, cotton wool spots or haemorrhages.

Thus our working assessment was that of an isolated, complete cranial nerve III (Oculomotor) lesion with neurogenic ptosis and pupil involvement.

This was most likely due to posterior communicating aneurysm (PCA) - especially considering the presence of pupillary involvement, the severe headache and acute onset of symptoms. Additional differential diagnoses included **giant cell arteritis and intracranial pathology.**

Biochemistry was within normal limits for full blood count (FBC), urea and electrolytes (U&E) and infective markers although the erythrocyte sedimentation rate (ESR) was elevated to 48. An LP was deferred at this time.

An urgent contrast CT scan of the brain and orbits revealed a 10 x 9 mm left supraclinoid internal carotid aneurysm (ICA) with a 3mm long neck arising adjacent to the origin of left PCA.

The aneurysm was noted to be partially thrombosed and causing medial displacement of the PCA with associated pressure erosion of the underlying clinoid. The rest of the scan was normal.

The patient was immediately referred to neurosurgery for intervention where he, together with his family, was counselled for clipping of the aneurysm.

Discussion

In order to tease out the likely cause of pathology it is essential to understand the relevant clinical anatomy and complex course of the third cranial nerve (the oculomotor nerve (CN III). CN III consists of **motor fibres** (levator palpebrae superioris and all the extraocular muscles of the eye excluding the superior and lateral rectus), **parasympathetic fibres** (sphincter pupillae and the ciliary muscles of the eyes) as well as **sympathetic fibres** (innervation superior tarsal muscle) [1].

TABLE 1: PATTERN OF CN III NEUR		TABLE 1: PATTERN OF CN III NEUROLO		
Nuclear, fascicular or Peripheral (nerve palsy)	*Nuclear:* - Ipsilateral CN I rectus paresis A - Bilateral palsy	***Complete***	1. Monocular diplopia (a vertical al superior 2. **OR** s. Complete ptosis with	
	Fascicular: A. Red-nucleus - Ipsilateral CN III palsy + Contralateral intention tremor + ataxia +/- contralateral anaesthesia (Benedikt's syndrome) B.Cerebral peduncle (anterior midbrain) - Ipsilateral CN III palsy + contralateral hemiparesis (Weber's syndrome)	***Partial***	1. Single muscle paresis involvement, **OR** 2. Aberrant regeneration	
Isolated	Single nerve involvement			
Complex	Involvement other cranial nerves, cerebellum or peripheral nervous system - these may be local or disseminated findings			
Pupil involving (cf Pupil sparing)	1. Mydriasis (no pupillary light reflex or accommodation reflex) 2. Poor focusing			

Fascicles from the cranial nerve III nucleus in the midbrain traverse the subarachnoid space before passing between the posterior cerebral and superior cerebellar arteries [1]. It then pierces the arachnoid and comes to lie between the layers of the tentorium cerebri [1]. Laterally to the posterior clinoid process, above the clivus, the nerve then pierces the dura mater and thus comes to lie in the lateral wall of the cavernous sinus above the trochlear nerve [1]. CN III then receives sensory communicating branches from the ophthalmic division of the trigeminal nerve before dividing into a small inferior and a large superior division which (in addition to the abducent, trochlear and multiple branches of the V1 division of trigeminal nerve) enter the superior orbital fissure and Circle of Zinn where they supply the extraocular muscles of the eye as described above [1].

CN III pathology presents a diagnostic challenge to the clinician, which is compounded by the fact that many aspects of the workup and treatment remain controversial [2]. In addition, the aetiology ranges from the imminently

life-threatening to that of the relatively benign. Fortunately, a comprehensive general and ophthalmological history combined with a good neurological and ophthalmological examination, are sufficient to arrive at a focused working diagnosis.
In order to localize the level it is important to classify the lesion according to the following patterns of involvement **(Table 1)**

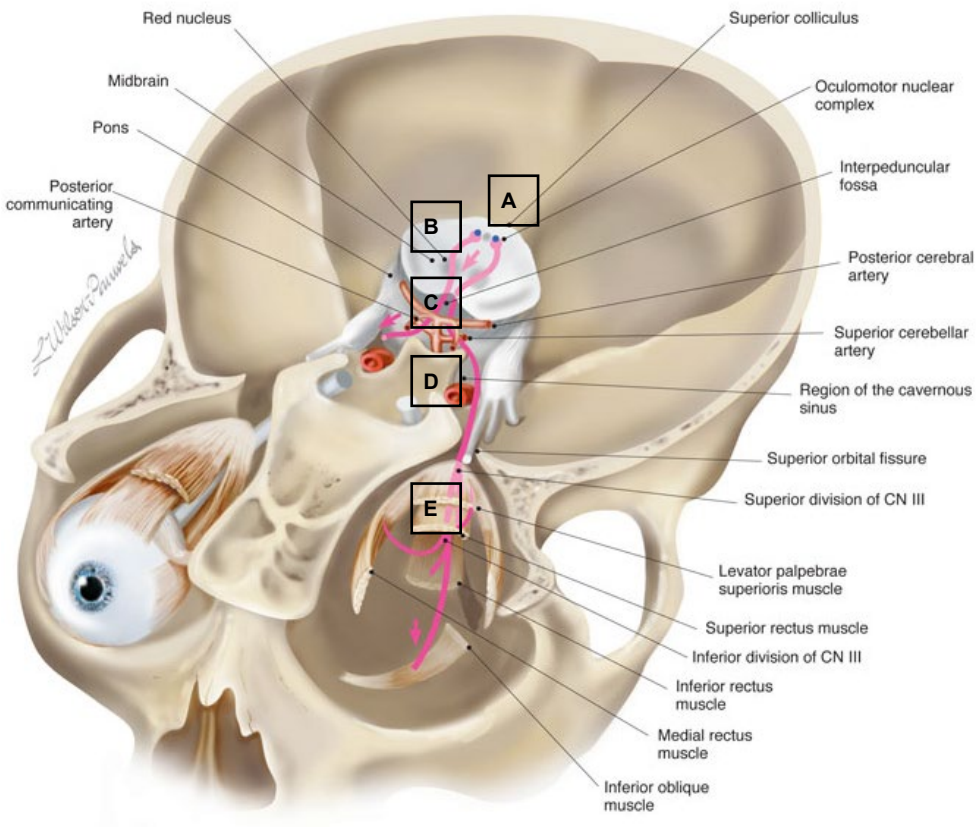

Figure 3: Anatomical path of Cranial Nerve III (Oculomotor nerve)

Nuclear lesions ***(Figure 3 "A"***) at the midbrain are associated with **isolated, complete** or **partial** bilateral, asymmetrical pathology due to the fact that certain sub-nuclei (for instance of the superior rectus) receive contralateral innervation [4,10,11]. Conversely the levator palpebrae superioris receives innervation from a single central caudal nucleus and thus produces bilateral ptosis [4]. Lesions in the oculomotor-nucleus complex are variably **pupil-involving** on the ipsilateral side but when present indicate dorsal rostral damage. Fallout at this level is usually the result of ischaemia of the small, dorsal perforating branches of the mesencephalic component of the basilar artery [4,5].

Fascicular involvement **(Figure 3 "B")** results in **isolated, complete** palsies that are often difficult to distinguish from midbrain lesions except when they result in one of the eponymous syndromes [3-5] **(Table 1).**

Lesions in the subarachnoid space **(Figure 3 "C")** (interpeduncular fossa) are **isolated** and **complete** with either **pupil-involvement** or **sparing**. This is vital to note as pupillary fibres are carried peripherally with a large collateral supply component compared with the centre of the nerve. The clinical implications of this are that **pupil-involvement** almost always indicates a compressive lesion such as an aneurysm, which constitutes a medical and surgical emergency [4].

While digital subtraction cerebral angiography remains the gold-standard for neuroimaging it is invasive and contra-indicated in patients with severe hypertension, the elderly and infirm, known contrast sensitivity, renal failure, coagulopathy and in the presence of severe subarachnoid haemorrhage [6].

An alternative is CT Angiography (CTA) or Magnetic Resonance Angiography (MRA), which has a sensitivity rate of 95-98% [6] **in the setting of aneurysms associated with CN III palsies** - although it is still contraindicated in known contrast sensitivity or patients with poor renal function [6]. Conversely **pupil-sparing** lesions are almost uniformly due to ischaemia as a result of diabetes, atherosclerosis or cardiovascular disease [6,7].

In patients older than 55 years a diagnosis of giant cell arteritis should be explored - especially if symptoms of headache, jaw or tongue claudication, polymyalgia or visual loss are present. Such patients are worked up with inflammatory markers, including CRP and ESR, and possibly temporal artery biopsy [8].

The benefit of neuroimaging and LP **in those patients younger than 55,** whose pathology does not improve within 6 - 12 weeks or who develop signs of aberrant regeneration is unclear currently but is likely to be beneficial [9].

Pathology within the cavernous sinus (Figure 3 "D") and superior orbital fissure is almost impossible to distinguish clinically and is thus considered together as a combined syndrome for practical purposes.

Lesions at this level are **complex** and **complete** with space occupying lesions **(especially meningiomas)** being mainly responsible [4,5]. The clinical picture is that of paresis of the oculomotor, trochlear and abducent nerves with associated pain from the maxillary division of the trigeminal nerve.

Other causes include vasculitic processes such as cavernous sinus thrombosis, carotid-cavernous fistulas, syphillis and autoimmune/connective tissue diseases.

Lesions within the orbit (Figure 3 "E") itself may be complex or isolated, complete or partial and are associated with visual loss, ophthalmoplegia and proptosis [4,5]. It is important to note that CN III has already divided into superior and inferior branches at this level and thus (together with the abducent and trochlear nerve) single muscle involvement may be seen. **The most common causes of pathology at this level are trauma, tumours, inflammation and infiltrative processes.**

Acquired oculomotor nerve palsies can be secondary to a vast number of aetiologies, and are primarily investigated with a basic laboratory tests (including full blood count, urea and electrolytes, calcium/magnesium/potassium, erythrocyte sedimentation rate, HbA1C and a full metabolic panel) and basic vitals (blood pressure, pulse rate and

random/fasting glucose) if said lesions are suspected to be as a result of an ischaemic problem.

Neuroimaging is indicated if intracranial pathology is suspected. LP's are usually reserved for patients with persistent/progressive symptoms and signs despite negative neuroimaging or where a septic/inflammatory process cannot be excluded [9]. Treatment is focused primarily at addressing the underlying cause, and with early intervention the prognosis for both compressive and ischaemic lesions is excellent. Neurosurgical intervention for aneurysmal lesions is aimed at preventing a catastrophic subarachnoid haemorrhage - with prophylactic clipping and/or artery embolisation, usually resulting in either full or partial recovery within 2 weeks to 4 months.

Ischaemic lesions traditionally resolve over weeks to months with appropriate lifestyle modification (including tight glucose and blood pressure control) although symptoms persisting longer than six months are thought to be permanent and are likely to require prism therapy, patching, or surgery to correct the strabismus and/or ptosis [9].

Conclusion

CN III lesions can result from a lesion at any level from the midbrain nucleus all along the path of the nerve until the innervation of the extraocular muscles. Lesions can be broadly classified into ischaemic or intracranial in origin. It is vital to classify the pattern of neurology as it will define the level as well as guide the likely clinical diagnosis and subsequent management. **Generally complete, isolated, pupil involving lesions are associated with compressive lesions and mandate urgent neuroimaging to exclude an intracerebral aneurysm.**

By comparison, lesions that spare the pupil are generally associated with ischaemic insults that can usually be managed conservatively. Treatment is guided by the underlying cause and the prognosis is generally very good if diagnosed and treated early.

References

1. Snell R, Lemp M. Clinical anatomy of the eye. 2nd ed. Malden, MA, USA: Blackwell Science; 1998.
2. Chou K, Galetta S, Liu G, Volpe N, Bennett J, Asbury A et al. Acute ocular motor mononeuropathies: prospective study of the roles of neuroimaging and clinical assessment. Journal of the Neurological Sciences. 2004; 219(1-2): 35-39.
3. Tsai J. Oxford American handbook of ophthalmology. Oxford: Oxford University Press; 2011.
4. Miller N, Walsh F, Hoyt W. Walsh and Hoyt's clinical neuro-ophthalmology. Philadelphia: Lippincott Williams & Wilkins; 2005.
5. Colon-Acevedo B, Feldman B, Mamet M, Abdullah Y. Acquired Oculomotor Nerve Palsy [Internet]. American Academy of Opthalmology. 2014 [cited 18 October 2016]. Available from: http://eyewiki.aao.org
6. Jacobson D, Trobe J. The emerging role of magnetic resonance angiography in the management of patients with third cranial nerve palsy. American Journal of Ophthalmology. 1999; 128(1):94-96.

7. Dion J, Gates P, Fox A, Barnett H, Blom R. Clinical events following neuroangiography: a prospective study. Stroke. 1987;18(6):997-1004.
8. Loffredo L, Parrotto S, Violi F. Giant cell arteritis, oculomotor nerve palsy, and acute hearing loss. Scandinavian Journal of Rheumatology. 2004; 33(4): 279-280.
9. Bruce B, Biousse V, Newman N. Third Nerve Palsies. Seminars in Neurology. 2007;27(3):257-268.
10. Bartleson J, Trautmann J, Sundt T. Minimal Oculomotor Nerve Paresis Secondary to Unruptured Intracranial Aneurysm. Archives of Neurology. 1986; 43(10):1015-1020.
11. Lee S, Lee S, Park K, Han S. Isolated oculomotor nerve palsy: diagnostic approach using the degree of external and internal dysfunction. Clinical Neurology and Neurosurgery. 2002; 104(2):136-141.

Figure 3: Linda Wilson-Pauwels. Cranial nerves illlustrated [Internet]. 2013 [cited 24 October 2016] Available from: https://bmc.med.utoronto.ca/cranialnerves/illustrations-by-chapter/oculomotor-iii