Typical or surprisingly uncharacteristic presentations of neuro-ophthalmic emergencies

Irrespective of geographical location or patient cohort, emergency departments are high risk locations capable of inspiring extreme anxiety and dread in patients and doctors alike.

The stress multiplies when a walk-in or referred case is suspected of underlying neurological pathology. Often, panic motivates on-duty clinicians to investigate the patient using all modalities available with little to show for it.

Potentially grave conditions are missed due to the variability of their presentation rather than complexity of these cases. Neuro-ophthalmic emergencies exhibit signs that range from subtle and non-specific headaches, to dramatic, such as total blindness. Though such symptoms may appear random, there are clues and characteristic signals which may help in devising a guided pathway based on clinical suspicion.

Discussion

Targeted investigations carry higher probability of a positive result than generic testing (like looking for a needle in a haystack). Once nudged towards the correct diagnosis, the following imaging and haematological investigations may be applied for confirmation of the working diagnosis.

GCA induced anterior ischaemic optic neuropathy (AAION)

C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) elevation (in absence of steroid / immune suppressive therapy) with thrombocytosis, normocytic anaemia and leukocytosis carry high level of sensitivity. Temporal artery biopsy (TAB) is the accepted universal standard. A negative TAB generally rules out giant cell arteritis (GCA). However, GCA is a clinical diagnosis and if clinical suspicion is high then patients can be treated with the support of rheumatology colleagues' opinion. ESR and CRP might be normal in up to 14% of TAB positive cases. Colour Doppler imaging is an emerging noninvasive diagnostic tool that can provide some help in diagnosis [1].

Pituitary apoplexy

Most patients have a history of known pituitary lesion but some present acutely with the apoplexy. Magnetic resonance imaging (MRI) is the investigative tool of choice though occasionally in cases of pituitary haemorrhage it may fail to delineate the lesion. If clinical suspicion index is high, MR angiogram should be performed [2].

Orbital apex syndrome (rhino orbital mucormycosis / rhino cerebral mucormycosis)

Orbital apex syndrome carries variable presentations and aetiologies. It can be inflammatory, infectious, neoplastic, traumatic or vascular. Presenting features also vary but usually involve optic nerve dysfunction as well as ophthalmoplegic features such as III cranial nerve (CN) palsy, IV CN palsy and VI CN palsy.

For infectious cases such as rhino-orbital mucormycosis (ROM), diabetes is a major driving factor with, ketoacidosis recorded in half of the cases. Computed tomography (CT) scan and MRI (fat suppression) carry high sensitivity. Rarely imaging may be negative and diagnosis requires paranasal sinus biopsy as the condition seldom occurs without ethmoidal sinusitis [3].

Cerebral sinus vein thrombosis (CSVT)

Headaches are usually a feature and most patients will have papilloedema in CSVT. High-resolution contrast-enhanced CT and / or MRI are ideal investigations. Serial imaging may be required as initial scans are generally normal. Haematological parameters are useful in diagnosis of septic cases.

Important differentials: idiopathic intracranial hypertension (IIH), orbital cellulitis and direct high-flow carotid-cavernous fistula (cavernous sinus thrombosis) [4].

Third nerve palsy from PCA

Digital subtraction angiography (DSA) is the gold standard diagnostic test, especially for aneurysms below 3mm, although it carries risk of neurologic morbidity.

Current neuro-ophthalmic opinion is to investigate all III CN palsies as posterior communicating aneurysm (PCA) unless proven otherwise. MR angiography and CTA are still the most widely used tests, carrying sensitivity of up to 95% [5].

Demyelinating optic neuritis

MRI (indicative of white matter plaques) is the gold standard for diagnosis. Additional evidence may be garnered by cerebrospinal fluid (CSF) analysis (oligoclonal bands on protein electrophoresis; sensitivity 95%). Neuro-myelitis optica spectrum disorders (NMOSD) exhibit antibody response against Aquaporin-4 and myelin oligodendrocyte glycoprotein (MOG). It is really key to identify cases of NMOSD early as they carry worse prognosis and they are usually steroid responsive, hence the need for urgent evaluation and treatment [6].

Fulminant IIH

It is really important to recognise these cases urgently and refer to neuro-surgery for CSF shunting procedures if there is evidence of visual function loss or rapid deterioration. Milder cases of IIH can present with subtle optic nerve swelling and in these cases further investigations such as ultrasound B-scan (Crescent sign, optic nerve sheath extension) and MRI (tortuosity of optic nerve with sheath extension) can be useful [7].

Examples

These are some cases seen in our emergency department with uncharacteristic presentations or investigative profiles where it was important to recongnise the variability in presenting features in order to reach the correct diagnosis:

Case 1

36-year-old Afro-Caribbean female (Figure 1)

- First presentation: VA 0.1 (R) /NPL (L) (log MAR)
- Normal optic disc retinal nerve fibre layer (RNFL) and normal central and peripheral fundus
- Left relative afferent pupillary defect (RAPD)
- Diagnosed as atypical optic neuritis

Table 1: Elements of initial presentation and work-up with possible variations of major neuro-ophthalmic emergencies.

	Visual acuity	Colour vision	Pupil reaction	Optic disc	Visual fields	Associated symptoms
Giant cell arteritis	• Unilateral in 70% of cases • Sudden, profound loss in 50% • Transient obscurations followed by complete loss in 30%	Severely impaired	RAPD in unilateral or asymmetric cases	Pallid 'chalky white' swelling but could be less dramatic with mild swelling	Central, arcuate, or altitudinal pattern	• Jaw claudication, neck pain, headache, scalp tenderness, weight loss, anorexia, myalgias, malaise • Temporal artery tortuosity, prominence and / or tenderness • 20% are asymptomatic
Pituitary apoplexy	Normal	Normal	Fixed, mid-dilated if associated with III cranial nerve palsy	Normal	Bi-temporal defects	• Unilateral or bilateral ophthalmoplegia (III followed by IV and VI involvement) in 50% • Sudden, severe headache and neck stiffness • Reduced level of consciousness, thermoregulatory and / or cardiorespiratory dysfunction
Rhino-orbital mucormycosis	Unilateral profound, painful loss	Severely impaired	RAPD	Normal to pale	• Central loss • Complete blackout	• Complete painful ophthalmoplegia, ptosis / proptosis • Fever, nasal-mucosal ulceration / necrosis, sinusitis, headache • Black eschar in 20% • Suspicion: uncontrolled diabetes
Cavernous sinus thrombosis	• Normal in > 50% • Diminution may develop later due to secondary pathologies	Normal	Involved in cases of secondary AION or asymmetric	Bilateral but could be asymmetrical optic disc swelling	• Enlargement of blind spot • Temporal wedges defects	• Proptosis, chemosis, ptosis, ophthalmoplegia in cases of cavernous sinus involvement • Most common presentation is with VI CNP • Fever, headache, lethargy, altered sensorium. • Rarely, seizures and hemiparesis secondary to venous infarction
Posterior communicating aneurysm	• Normal • Diminution in late stages, if there is cortical involvement	Normal	• Fixed mid-dilated • Anisocoria worse in bright light • Sluggishly reactive or uninvolved in few	Normal		• Ptosis with supra, infra, and adduction deficits • Suspicion: non-diabetic patient with III CN palsy
Retrobulbar neuritis	Unilateral, could be profound with mild pain on ocular motility	Severely impaired	RAPD	Normal	Central / centro-caecal, arcuate, or altitudinal pattern	Typical in young / middle aged women with possible demyelination
Idiopathic intracranial hypertension	• Variable • Transient obscuration of vision	• Variable • Normal in majority	Normal in majority	Papilloedema, asymmetrical, with or without pre-papillary haemorrhages	• Enlargement of blind spot • Temporal wedges defects	• Severe debilitating headaches • Transient obscuration of vision • Tinnitus or whooshing sound in the head • Associated chronic migraine • VI CN palsy

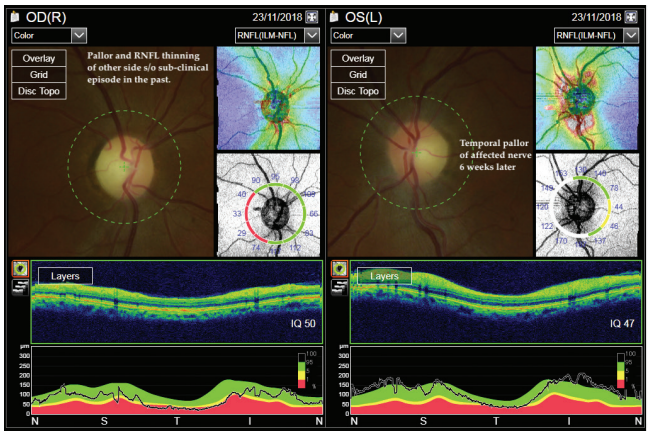
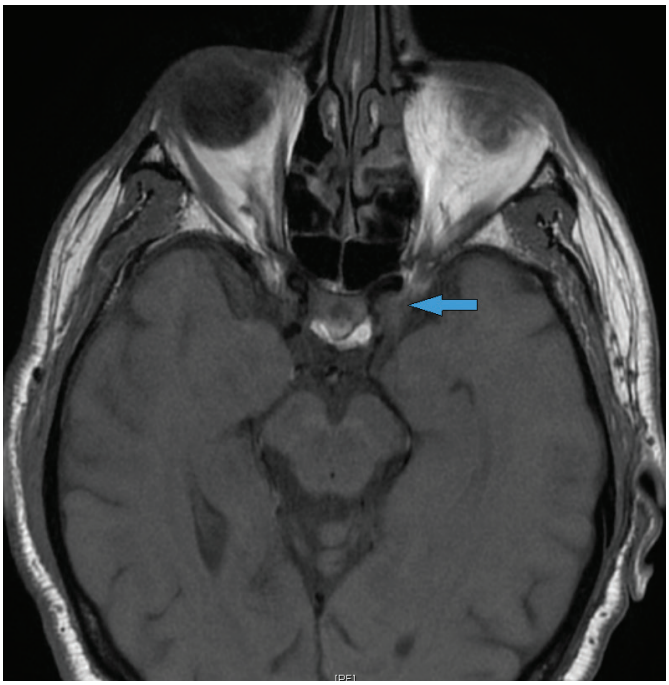


Figure 1: OCT scan of patient at six weeks follow-up indicating bilateral optic discs with temporal pallor. Surprisingly RNFL thinning is observed on the right side (rather than the affected eye) suggestive of a possible sub-clinical episode in the past.



(Above) Figure 2: MRI scan, T1 weighted image indicates hyperintensity in the orbital apex extending to medial aspect congruent with III cranial nerve involvement but no clinical features suggestive of inflammation were seen.

(Left) Figure 3: OCT scan of patient at presentation indicated mild swelling of non-crowded right optic disc with normal appearance on the left side.

- Initiated on IV methylprednisolone 1gm for three days followed by oral steroids
- MRI: no demyelination plaques
- Aquaporin-4 positive
- VA (at six weeks): 0.1 (R) / 0.3 (L) (log MAR) (Figure 1)
- Initiated on immune suppressive therapy for NMOSD under neurological and rheumatology teams.

Case 2

68-year-old Caucasian male (Figure 2)

- First presentation: Complete left ptosis with exo-hypo deviation of LE
- Visual parameters: normal
- Pupil: uninvolved
- Normal optic discs
- Non-diabetic with no systemic co-morbidities
- CTA normal
- MRI: orbital apex syndrome due to an inflammatory lesion (Figure 2)
- Initiated on Tab Prednisone 60mg OD.

Case 3

63-year-old Caucasian female with episodes of obscurations of vision in right eye for two weeks followed by complete loss of vision (Figure 3)

- VA at presentation: RE: PL in two quadrants; LE: 0.3 (log MAR)
- Jaw pain and claudication
- ESR: 105 CRP: 45
- Right optic disc swelling (Figure 3)
- Initiated on IV methylprednisolone 1gm for three days followed by oral steroids
- Temporal artery biopsy: positive for GCA
- Visual parameters at 10 days follow-up: No change.

Conclusion

Neuro-ophthalmic disorders may not always display textbook features but the basic underlying defect leaves a trail of recognisable bread crumbs.

Exhaustive history and thorough clinical work-up are required to formulate a clinical suspicion rather than indiscriminate and often unnecessary investigations which may blind-side the true diagnosis.

References

1. Hayreh SS, Podhajsky PA, Zimmerman B. Ocular manifestations of giant cell arteritis. *Am J Ophthalmol* 1998;**125(4)**:509-20.
2. Semple PL, Webb MK, de Villiers JC, Laws ER Jr. Pituitary apoplexy. *Neurosurgery* 2005;**56(1)**:65-72; discussion 3.
3. Thurtell MJ, Chiu AL, Goold LA, et al. Neuro-ophthalmology of invasive fungal sinusitis: 14 consecutive patients and a review of the literature. *Clin Experiment Ophthalmol* 2013;**41(6)**:567-76.
4. Chung JW, Chang KH, Han MH, et al. Computed tomography of cavernous sinus diseases. *Neuroradiology* 1988;**30(4)**:319-28.
5. Lee AG, Hayman LA, Brazis PW. The evaluation of isolated third nerve palsy revisited: an update on the evolving role of magnetic resonance, computed tomography, and catheter angiography. *Surv Ophthalmol* 2002;**47(2)**:137-57.
6. Weber MS, Derfuss T, Metz I, Bruck W. Defining distinct features of anti-MOG antibody associated central nervous system demyelination. *Ther Adv Neurol Disord* 2018;**11**:17562864187620883.
7. Hayreh MS, Hayreh SS. Optic disc edema in raised intracranial pressure. I. Evolution and resolution. *Arch Ophthalmol* 1977;**95**:1237-44.

"Neuro-ophthalmic disorders may not always display textbook features but the basic underlying defect leaves a trail of recognisable bread crumbs"

AUTHOR

Mr P Gupta,

Neuro Ophthalmology Fellow, Manchester Royal Eye Hospital, UK.

SECTION EDITOR

Ali Yagan,

Consultant Ophthalmic Surgeon, Neuro-Ophthalmology and Adult Strabismus Fellowship, Manchester Royal Eye Hospital, Manchester, UK.