



Isolated third cranial nerve palsies—modern management principles

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To the Editor:

The risk of death or severe morbidity from aneurysm rupture ranges from 33 to 77% [1]. Historically, the gold standard for diagnosis was with invasive catheter digital subtraction angiography (DSA), carrying a stroke risk of 2% [2]. Classification systems of third nerve palsies were developed to identify those with a higher risk of aneurysm and justify undergoing DSA. These describe the palsy as complete, partial, pupil-involving or pupil-sparing and are based on cohort studies over 60 years old where many were undetermined in aetiology. Furthermore, there have been a handful of reports to contradict the “rule-of-the-pupil” [3–7]. We therefore cannot state that a pupil sparing third is absolutely not compressive.

Non-invasive neuroimaging has replaced DSA in the detection of intracranial aneurysms, with magnetic resonance angiography (MRA) and computer tomographic angiography (CTA) being of comparable sensitivity to DSA [8, 9]. The modern concern is no longer the stroke risk of DSA, but the risk of an overlooked aneurysm that may rupture.

We reviewed our cohort of isolated third nerve palsies to determine the diagnostic yield of neuroimaging at presentation and to find whether this removes the need for classifying isolated third nerve palsies. We found that of 47 isolated third nerve palsies between 2010 and 2019, 28 (60%) had causative pathology on neuroimaging. Nineteen (40%) of these were caused by an aneurysm, 9 (19%) were other causes. Nineteen (40%) were presumed microvascular with negative neuroimaging and later confirmed with partial or total resolution. The presenting features are shown in Table 1.

Our findings match previous studies showing that complete palsy, anisocoria and pain are frequent presenting features of aneurysmal third nerve palsies [10, 11]. We also show these features are not uncommon in microvascular cases. Therefore, decisions to investigate should not be based on clinical features.

Neuroimaging identified a diagnosis in 60%. The remaining 40% were presumed microvascular and later confirmed with total/partial recovery. Thus, neuroimaging provides diagnostic information in almost all cases. Forty percent had an aneurysm. Other reports suggest 10–60% of isolated thirds are aneurysms [3, 12]. If the true incidence is as low as 10%, we consider this too high to miss while morbidity of rupture is up to 77%. On this basis, we suggest all patients with isolated thirds undergo neuroimaging at presentation, given that there is a very high chance of providing a diagnosis.

Classifications were developed to determine who should undergo DSA. Modern neuroimaging does not carry a stroke risk and so classifying thirds is no longer useful. In 1999, Jacobson and Trobe estimated that MRA will overlook 1.5% of aneurysms liable to rupture over 8 years [13]. The true value is now likely lower, given the advances in image resolution. CTA and MRA are readily available, cost-effective and are as sensitive as DSA.

Whether CTA or MRA is better depends upon patient suitability and the experience and preference of the local neuroradiologist. A recent meta-analysis concluded that MRA is comparable to CTA in sensitivity [14]. We agree with Elmaleh, et al., that the most important factor in scan interpretation is the experience of the neuroradiologist [15].

Overall, we recommend that (1) all isolated thirds undergo neuroimaging at presentation, (2) the decision to investigate should not depend upon the classification, (3) we no longer teach the classification of thirds (4) all imaging should be reviewed by an experienced neuroradiologist and (5) patients with treated aneurysms undergo long term follow up. It must be stressed that this should not apply to

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Table 1 Presenting Features of Isolated Third Nerve Palsies.

	Aneurysm (n = 19)	Non-aneurysm (n = 28)
Complete	12 (63%)	11 (39%)
Partial	3 (16%)	12 (43%)
Unknown completeness	5 (26%)	5 (18%)
Anisocoria	15 (79%)	5 (18%)
Complete and pupil sparing	0	8 (29%)
Complete and pupil involving	11 (58%)	2 (71%)
Partial and pupil sparing	1 (5%)	8 (29%)
Partial and pupil involving	2 (11%)	2 (7%)
Pain	15 (83%)	14 (50%)
Vascular risk factors	3 (17%)	22 (79%)

third nerve palsies that are not isolated (i.e., have other neurological features).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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