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Review Article

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Then…ophthalmoplegic migraine now…recurrent painful ophthalmoplegic neuropathy (rpon)- a detailed review

Abstract

Ophthalmoplegic migraine (OM) is an uncommon type of migraine that is challenging to diagnose, marked by temporary ophthalmoplegia and typical migraine headache symptoms.

Ophthalmoplegic migraine is now more commonly referred to as recurrent painful ophthalmoplegic neuropathy (RPON) by the International Headache Society. This systematic review seeks to summarize the existing literature on OM, covering its prevalence, evolving causes, clinical characteristics, and treatment strategies.

Volume 10 Issue 3 - 2025

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Received: August 05, 2025 | **Published:** August 19, 2025

Introduction

Migraine is a prevalent neurological disorder with various clinical manifestations. OM is a rare condition that presents diagnostic challenges due to its resemblance to other serious neurological disorders. Ophthalmoplegic migraine (OM) is identified by the occurrence of temporary ophthalmoplegia, most often affecting the third cranial nerve in individuals with migraine headaches. This review aims to provide a comprehensive overview of the current understanding of this particular migraine form.

Epidemiology: OM is infrequent, resulting in limited epidemiological data. OM is a rare condition, with most research consisting of case reports or small series. Evidence suggests that the pediatric population is more affected than adults, although comprehensive data from population surveys is lacking. There is no consistent information on gender preference in the literature; some studies suggest OM is more common in women, while others find no gender difference. The incidence and prevalence of the disease are not well-documented due to diagnostic challenges and potential under-recognition.

Pathophysiology: Unraveling the Enigma: The precise cause of OM remains unknown, with ongoing research exploring potential causes. Neural Dysfunction: The involvement of the oculomotor nerve suggests central nervous system involvement. Cortical spreading depression, a key element of the migraine process, may lead to temporary dysfunction of the oculomotor nuclei in the brainstem. Recent studies focus on trigeminal ganglion activation and its possible impact on the brainstem nuclei controlling oculomotor functions.

Vascular involvement: Previously considered a primary cause, there is little evidence supporting a purely vascular origin. Neuroimaging studies show no evidence of higher-level vascular lesions. However, microvascular changes or brief vasospasm within the vasa nervorum supplying the oculomotor nerve cannot be entirely dismissed. Ongoing research is investigating the role of CGRP.[1,2]

Inflammatory mechanisms: Dysfunction of the oculomotor nerve may be caused by proinflammatory substances released during migraine episodes. Research is ongoing to determine the involvement of cytokines and other inflammatory markers in the onset of OM. Channelopathies: The potential for ion channel dysfunction, similar to other migraine types, is under investigation. Specific channels related to oculomotor nerve function are being evaluated for their potential contribution to OM.

Mitochondrial dysfunction: The involvement of mitochondria, especially in paediatric OM, is currently being explored. The high metabolic demands of the oculomotor nuclei may make them susceptible to mitochondrial dysfunction. Mutations in mitochondrial DNA and their connection to OM are being studied.[3]

Clinical presentation: A Range of Symptoms. OM is generally characterized by recurring headache attacks accompanied by ophthalmoplegia. Headache Characteristics: The headache is typically unilateral, throbbing, and ranges from moderate to severe, resembling a migraine headache. However, atypical headache features may also be present.

Ophthalmoplegia features: The third cranial nerve is most commonly affected, leading to ptosis, double vision, and restricted eye movements. Pupillary involvement varies. Less frequently, other crania nerves, particularly the fourth and sixth, may also be involved. Aura Phenomena: Migraine aura, including visual, sensory, and speech disturbances, may occur before, during, or after the headache and ophthalmoplegia. Duration and Recurrence: Ophthalmoplegia

usually resolves within days to weeks, but some deficits may persist. Recurrence is common, with varying intervals between episodes.

Pediatric OM specificities: Pediatric OM is characterized by more frequent attacks, increased pupillary involvement, and longer-lasting ophthalmoplegia compared to adult OM.[4]

Differential diagnosis: Navigating Diagnostic Challenges: Diagnosing OM is complex due to the numerous potential conditions to consider. Third Nerve Palsy (Non-Migrainous): An aneurysm, tumour, or inflammatory disease must be ruled out. Neuroimaging is essential.

Tolosa-hunt syndrome: Inflammation of the cavernous sinus or superior orbital fissure causes a painful ophthalmoplegia syndrome. Responsiveness to corticosteroids is a key differentiator.

Myasthenia gravis: This neuromuscular disorder can cause fluctuating ophthalmoplegia but lacks the typical headache association.

Giant cell arteritis: This type of vasculitis can lead to headaches and ophthalmoplegia, particularly in older adults. High levels of inflammatory markers are indicative.

Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (melas): This mitochondrial condition can resemble OM but is linked with additional neurological symptoms. Genetic testing is crucial.

Cavernous Sinus Thrombosis: This uncommon disorder results in painful ophthalmoplegia, proptosis, and chemosis. Neuroimaging is used for diagnosis. Neuropathic Ophthalmoplegia: This form of ophthalmoplegia is progressive and not linked to migraine headaches.

Brain tumors: Tumors located in the brainstem can lead to ophthalmoplegia and other cranial nerve palsies.[5,6]

Diagnostic evaluation: A Comprehensive Approach: A thorough diagnostic evaluation is essential to confirm OM and exclude other conditions. Neuroimaging (MRI/MRA): Magnetic resonance imaging (MRI) of the brain and orbits is vital to exclude structural lesions. Magnetic resonance angiography (MRA) can assess vascular abnormalities. Functional MRI and diffusion tensor imaging are being explored as advanced imaging methods.

Lumbar puncture: Examining cerebrospinal fluid may be conducted to rule out inflammatory or infectious processes.

Electrophysiological Studies (EMG/NCS): Electromyography (EMG) and nerve conduction studies (NCS) can help distinguish OM from other neuromuscular disorders. Blood Tests: A CBC, ESR, CRP, and other pertinent blood tests can assess systemic inflammation.

Genetic testing: Genetic testing is essential if mitochondrial disorders are suspected. Ophthalmological Examination: A comprehensive ophthalmological examination is crucial to determine the specifics of the ophthalmoplegia.[7,8]

Management: Symptomatic Relief and Prevention: OM management involves addressing symptoms during acute episodes and preventing future attacks.

Acute treatment: Triptans and nonsteroidal anti-inflammatory drugs (NSAIDs) like acute migraine medications may be used for headache relief. The use of corticosteroids in ophthalmoplegia lacks strong evidence but may be considered for severe or prolonged cases.

Preventive treatment: Preventive migraine medications such as beta-blockers, tricyclic antidepressants, and anticonvulsants may be prescribed to reduce the frequency and severity of attacks.

Botulinum toxin injections: Botulinum toxin injections have proven beneficial in certain cases, particularly for ptosis.

Supportive care: Supportive measures like eye patching and prism lenses may be necessary to manage diplopia.

Treatment of underlying conditions: If an underlying condition is identified, management should focus on that condition.

Considerations in the management

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Citation: Khardenavis S, Godse G, Khardenavis V, et al. Then…ophthalmoplegic migraine now…recurrent painful ophthalmoplegic neuropathy (rpon)- a detailed review. *MOJ Biol Med.* 2025;10(3):122–124. DOI: 10.15406/mojbm.2025.10.00252

Treatment of underlying conditions: If an underlying condition is identified, management should focus on that condition.[9,10]

Acknowledgements

I work in the capacity of a Consultant at Altnagelvin Hospital in the Department of Care of the elderly & Stroke and am the guarantor for the authenticity & originality of this manuscript.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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