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Review Article

A Review on Ophthalmoplegia Through Patient Case Studies: A Comparative Analysis

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Abstract

Ophthalmoplegia, a condition marked by paralysis or weakness of extraocular muscles, leads to impaired eye movement and associated visual disturbances. This comparative review focuses on ophthalmoplegia through detailed case studies, aiming to deepen our understanding of the diverse presentations, underlying causes, and treatment responses of the condition. By examining cases of different types of ophthalmoplegia, such as isolated oculomotor nerve palsy, progressive chronic external ophthalmoplegia, and ophthalmoplegia associated with systemic or genetic conditions, this review highlights the range of patient outcomes. The emphasis is on diagnostic strategies, treatment approaches, and patient-centered care. The findings suggest that customized treatment, based on a precise etiological diagnosis and severity, can significantly improve prognosis and quality of life. The review concludes with recommendations for optimizing diagnostic tools and exploring future therapeutic options, including advancements in gene therapy and neurorehabilitation.

1. Introduction

Ophthalmoplegia is an eye disorder that causes weakness or paralysis of the eye muscles, making it difficult to control eye movements. Restrictive, paretic, neurologic and myasthenia could be considered various etiologies that can reduce the eye mobility at first glance [1]. Examiners suggest various scans and lab test to reach out the assessment of diagnosis of ophthalmoplegia by clinical examination. Diabetis Mellitus one of the most associated disease through which ophthalmopegia can cause due to high blood sugar levels which affect cranial nerves, it is associated with great anxiety for the patients and often appears to be a serious problem from a diagnostic and therapeutic point of view [2]. Ophthalmoplegia can be painless or painful depending upon types and disease. In the painful unilateral ophthalmoplegia the pain may be focused in or around the orbit that is accompanied with ipsilateral ocular motor paresis. There are many etiologies with different categories, Horner syndrome (opthalmic division of the 5th cranial), inflammatory and infectious disorder (Tolosa Hunt syndrome, orbital pseudo tumor, sarcoidosis, systemic lupus erythematosus and cranial trauma). In majority of cases diabetes mellitus is the main etiology [3]. The physicians refer the patients to neurologists and ophthalmologist for neuro-ophthalmic evaluation. Botulinum Toxin injection been used in the treatment of ophthalmoplegia. It is produced by bacterium Clostridium botulinum which produces seven antigen-specific neurotoxins i.e. A, B, C, D, E, F, and G. Botulinum neurotoxin type A is most utilized for ocular purposes. Thus when injected in at therapeutic doses, botulinum toxin produces a partial chemical denervation of the muscle resulting in localized muscle paralysis [4].

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History

Internuclear ophthalmoplegia one of the type of first described by the German Ophthalmologist Anton Lutz in 1923. A 22-year-old female patient with an one year history of relapsing remitting multiple sclerosis (MS) complained of difficulties focusing and brief episodes of horizontal gaze evoked diplopia. Symptoms occurred intermittently in rest, and increased whilst walking or cycling in busy environments. Her past medical and family history were unremarkable and she was not taking any medication. On examination extraocular eye movements were full and convergence was normal. There was no abducting or adducting nystagmus, and no convincingly reproducible slowing of saccades on repeated testing and no oscillopsia. The reminder of her cranial nerve examination was normal. Her vestibuloocular reflex was normal. The optokinetic nystagmus was not tested. The possibility of an internuclear ophthalmoplegia (INO) and recorded the eye movements with high-frequency infrared oculograph. The girl was diagnosed by posterior INO [5]. A brainstem lesion of any type that involves the medial longitudinal fasciculus (MLF) can cause internuclear ophthalmoplegia (INO). The case series of 410 patients, the cause of INO was infarction in 157 patients (38%), multiple sclerosis in 139 (34%), and unusual causes in 114 (28%). Unusual causes included trauma (20 cases), tentorial herniation (20 cases), infection (17 cases), tumour (17 cases), iatrogenic injury (12 cases), haemorrhage (13 cases), vasculitis (7 cases), and miscellaneous (8 cases). Internuclear ophthalmoplegia was unilateral in 136 of the infarct cases (87%), 38 of those with multiple sclerosis (27%), and 48 of the unusual cases (42%) [6]. Another series of 65 consecutive cases where, in young patients it is closely related with multiple sclerosis and considered as a clinical pathognomonic sign. Vascular etiology is also usually associated with unilateral INO, most of the patients were older than 45 years of age. In regard to the one and-a-half syndrome, approximately 60% of the patients also had a vascular cause. It was common to find several neurological syndromes in all types of INO, mainly the cerebellar syndrome. The involvement of V and VII cranial nerves was not uncommon in fact, the association of one-and-a-half syndrome with VII cranial nerve palsy is known as eight-and-half syndrome [7]. Eleven patients (eight women, three men; ages 18-80 years) with INO were evaluated with MR. Nine of the 11 were also evaluated with CT, which was performed on a high-resolution scanner (GE 9800) using 5-mm contiguous axial sections through the brainstem in all cases. Two patients had noncontract CT only. Seven patients had high-iodine CT with intravenous infusion of 88.1 gi l. MR was performed with spin-echo techniques on a GE 1.5- T Signa scanner. Spin-echo images were obtained by using repetition time (TR) = 600 msec with echo time (TE) = 20-25 msec (short TRfTE), and TR = 2000-2500 msec with TE = 20-80 msec (short-long TE). Four patients had MR performed both before and after intravenous gadolinium (Gd)-DTPA (0.1 mmol/kg). MR images were obtained in axial, coronal, and sagittal planes. Four of 11 patients had a clinical diagnosis of ”definite MS” on the basis of the presence of clinical signs and symptoms localized to at least two anatomic regions of the CNS and am course of relapses and remissions separated by at least 1 month. Five other patients had a clinical diagnosis of probable MS. Two patients were diagnosed as having had infarctions. Of the nine patients with definite or probable clinical MS, six had bilateral INO and three had unilateral INO. The two patients with infarctions both had unilateral lNO. In these cases, long TR images showed focal or nodular regions of high signal intensity in the area of the MLF [8].

External Ophthalmoplegia now called as Chronic Progressive External Ophthalmoplegia. Albrecht von Graefe first discovered the disorder in 1868. It has often been referred to as von Grafe’s disease. Mobius named the condition ”chronic progressive nuclear ophthalmoplegia,” and this term, or variants implying its nuclear etiology, was the most frequently used until 1951, when Kiloh and Nevin4 in their classic article showed that the disease is really a myopathy and suggested the term ”ocular myopathy.” Other terms used are ”progressive paralysis of the extraocular muscles,” ”hereditary ophthalmoplegia,” ”symmetrical paralysis of the extraocular muscles,” ”familial ptosis with ophthalmoplegia,” ”hereditary congenital ophthalmoplegia,” ”infantile nuclear atrophy,” ”double ophthalmoplegia externa,” and ”abiotrophic ophthalmoplegia externa.” The disease is generally recognised as Ocular Myopathy. The first description of CPEO was bt Hutchinson in 1879. He wrote “Drooping of the eyelids, so as to give to the face a half-asleep expression, is usually the first, and it is soon accompanied by weakness of all the muscles attached to the eyeball, so that the movements of the latter become much restricted, or even wholly lost. The condition is usually bilateral, though it is not always exactly the same in degree on the two sides. Its symmetry probably denotes that it is of central origin”. Hutchinson suggested that this disease is a close parallel to so-called bulbar paralysis. He also suggested that the initial lesion might be an inflammation of nuclei of the affected nerves. He presented the case history of 17 patients. Syphiliswas thought to be the cause in eight of Hutchinson’s cases. Gowers performed necropsy in one of Hutchinson’s cases and said that the state of the nuclei of the ocular nerves was nearly the same as that of the gray matter of the spinal cord in progressive muscular atrophy. The roots of the ocular nerves outside and inside the brain were gray and small, and contained scarcely any normal fibers. In the nuclei a few nerve cells of normal size were seen, but these had mostly lost their processes, and a large number of the cells had been reduced to small angular bodies or had disappeared. This necropsy helped to perpetuate the idea that chronic progressive ophthalmoplegia was nuclear in origin [9].

Progressive external ophthalmoplegia (PEO, also known as chronic progressive external ophthalmoplegia [CPEO]) is a clinical syndrome that was defined by Lewis P. Rowland in the 1992 *Handbook of Clinical Neurology* [10], the following features are progressive ptosis and impaired mobility of the eyes, bilaterally, affected muscles are innervated by more than one nerve, pupils are spared, gradual progression over months or years and there are no remissions or exacerbations [11]. Certain case reports were their. Case 1, a female aged 40, attended in March, 1955, complaining of increasing ptosis during the previous 12 months. She stated that her mother (Case 2) had worn ptosis props for years and that her maternal grandfather and great-grandfather had had similar drooping of the lids as well as a maternal uncle who had had an operation on his eyes some years previously. Examination.She was found to have a moderate degree of ptosis, the orbicularis muscles being of normal strength. The eyes were in visual alignment, but there was an absence of elevation of the eyeballs, and downward and lateral gaze was restricted to about half of the normal amplitude; diplopia had never been a symptom. Intramuscular injection of prostigmine had no effect on the eye movements. The pupil reactions were normal and the eyes were otherwise healthy. Visual acuity varied but could never be improved beyond 6/18 in either eye and the fields were concentrically contracted; this contraction altered from time to time, suggesting the possibility of a functional element. Case 2, a female aged 64, mother of Case 1, gave a history of increasing ptosis for 14 to 16 years. She had had an operation for the correction of the left ptosis some years ago, but had been in excellent health otherwise. Examination in April, 1955, showed well-developed ptosis, more marked on the right side where the pupil was practically obscured. Her eyes were in alignment for distance and, although converging power was absent, she experienced no diplopia. There was no elevation of the eyeballs, and depression and lateral movements were very restricted. The pupils were moderately sluggish. There was some calcareous change in the left cornea, resulting from an injury by a pillow-slip some years earlier, which reduced vision in this eye to 6/36. Visual acuity in the right eye (corrected) was 6/6. The eyes were otherwise healthy. Case 3, a female aged 64, stated that her eyelids had drooped since childhood and that her mother had been similarly affected. Examination in August, 1955, showed that the ptosis did not interfere markedly with her vision, the eyelid

margins clearing the visual line by about 2 mm. The eyes were in alignment, but movements in all directions were defective, with no power of elevation above the horizontal. There was no diplopia. Intramuscular injection of prostigmine failed to influence the ocular movements. The visual acuity and pupils were normal, and there was no other apparent ocular disease apart from some retinal arteriosclerosis. The patient was quite fit for her age and general physical examination revealed no abnormality. Her intelligence was within normal limits. Case 4, a male aged 42, gave a history of drooping eyelids for 4 or 5 years, though he was not very certain about the time of onset. On June 15, 1956, he had bilateral ptosis, the lid margins half obscuring the pupils of each eye. The ocular movements were restricted to approximately one sixth of the full amplitude, elevation being the most markedly affected. There were fine oscillating movements of the eyes in the primary position, and the patient was conscious of diplopia " only when he stared at an object for a considerable length of time The pupil reaction was somewhat sluggish to light stimulation the left pupil reacting less briskly than the right. Visual acuity was 6/18 in each eye, with correction for myopia, the reduced vision being due presumably to the fine oscillations. General physical examination did not disclose defective action of any other muscles [12].

Disease

Kugelberg-Welander Disease is the juvenile form of spinal muscular atrophy [13]. Metabollic Diseases in a newborn as a sign of ophthalmoplegia [14]. Diabetic ophthalmoplegia occurs in adult patients with diabetes of long duration, usually under poor control. In contrast, other causes of eye palsy affect all age groups [2]. Whipple's disease (WD) is a rare disorder that is more common in males than females [14]. Motor Neuron disease, abnormal eye movements are not common [15]. Myasthenia gravis or Graves ophthalmopathy, these disease can cause ophthalmoplegia, proptosis, optic neuropathy, and eyelid retraction [16]. Herpes Zoster Ophthalmicus (HZO), also known as ophathlmic zoaster is shinhles involving the eye or the surrounding area [17]. Vitamin E deficiency, cause progressive ophthalmoplegia (PEO), ptosis, and pigmentary retinopathy [18]. Sarcoidosis is a multisystem disease of unknown etiology, characterized by the presence of noncaseating epithelioid granulomas and accumulation of T lymphocytes and mononuclear phagocytes, which damages the normal structure of tissues. It is the underlying etiology of painful ophthalmoplegia, even without systemic manifestation of the disease [19]. The Neurovisceral storage disease related to spranuclear ophthalmoplegia [20].

Types

• Internuclear Ophthalmoplegia:- Internuclear Ophthlmoplegia a brainstem lesion of any type that involves the medial longitudinal fasciculus (MLF), [21, 22].
• Progressive External Ophthalmoplegia [23].
• Total Ophthalmoplegia
Total ophthalmoplegia is defined as total paralysis of all the muscles of the eye, which in turn results in ptosis, dilated non reacting pupil, immobility of the eye and total loss accomodation [24].

Classification in Figures

Internuclear ophthalmoplegia:

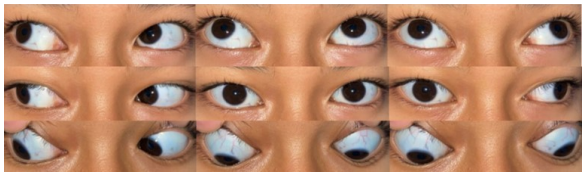

Figure 1: Internuclear Ophthalmoplegia [25]

External Ophthalmoplegia/Progressive Ophthalmoplegia/ Chronic Progressive External Opthalmoplegia:

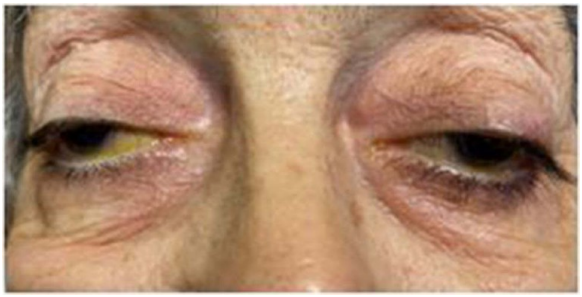

Figure 2: External Ophthalmoplegia [26]

Total Ophthalmoplegia:

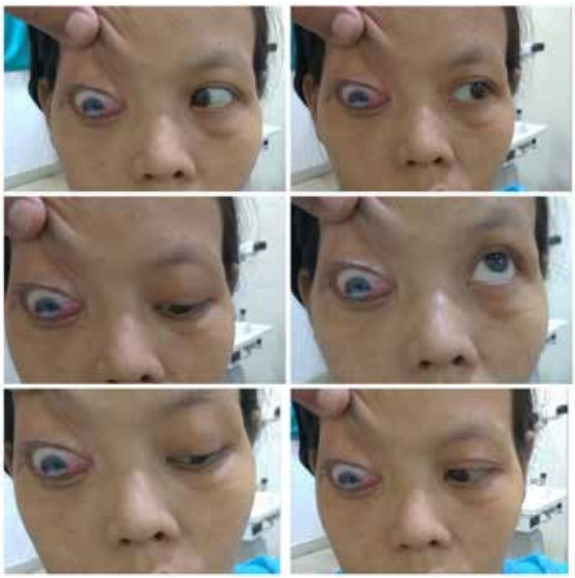

Figure 3: Total Ophthalmoplegia [24]

Dosage Form

Reviewed from references there is parentral dosage form of ophthalmoplegia is available. Rather references show side use or not exact use of solid dosage form.

Parenteral Dosage Form

Botulinum Toxin Injection is used in the treatment of ophthalmoplegia. The first ever use of botulinum toxin as a therapeutic agent was in the field of ophthalmology for the treatment of strabismus (misalignment of the eyes). The direct mechanism of action of botulinum toxin is to block the release of acetylcholine from the presynaptic terminal of the neuromuscular junction leading to muscleparalysis. The paralysis is transient, as muscle function is restored by the generation of new nerve terminals and reestablishment of synaptic transmission, which usually takes about 3 months. Many applications for botulinum toxin have emerged since it was first used in humans, the original therapeutic target injection into the extraocular muscles to treat strabismus. There are many techniques for injecting botulinum toxin into the extraocular muscles to treat strabismus. All involve injecting botulinum toxin into the belly of the target muscle while trying to minimize the spread of toxin elsewhere in the orbit. If the botulinum toxin injection is performed at the timeof strabismus surgery, it can be injected into the extraocular muscle under direct visualization, though some experts prefer to inject before the surgical incision out of concern that injection after incision and dissection may allow for greater spread to other sites. If the botulinum toxin is being used in isolation, the injection is generally administered transconjunctivally (typically with local anesthesia in adults and under general anesthesia in children). Botulinum toxin has shown some effectiveness in the treatment of oscillopsia secondary to acquired nystagmus. The concept is that injection of botulinum toxin into the retrobulbar space will reduce the motility of all of the extraocular muscles and thus damp the nystagmus. Hemifacial spasm (HFS) is characterized by involuntary contractions of the muscles innervated by the ipsilateral facial nerve. In contrast with BEB, contractions in HFS persist during sleep. In some cases, the orbicularis oculi muscles are believed to serve as a trigger point for spasm in the lower facial muscles. Compression of the facial nerve at its root must be ruled out by neuroimaging. A starting dose of 12.5 U botulinum toxin A to the orbicularis muscle is usually effective, and the first treatment usually targets the orbicularis oculi muscles alone [4].

Patents

Botulinum toxin injection has been patent for the use of ophthalmoplegia [4].

Future Prospects

Future prospects in treatment of opthalmoplegia can be through Nanotechnology based Drug Delivery system to deliver the drug to targeted site with therapeutic sustained dose [27]. Several ocular formulations such as nano formulations, liposomes, ocular inserts, and ocular mini-tablets are also being widely studied as future treatments to improve ocular drug delivery and as an alternative to conventional drug delivery [28]. Researchers are exploring, focusing on overcoming blood-neural barriers (BNBs). Drugs could be deliver targeted retina and vitreous humor, considering the anatomic barriers and physiologic clearance mechanisms of the eye. Through the polymers embedded drug, the drug will be delivered to targeted site without using conventional forms. Polymers should be non-reactive with drugs embedded on it [29]. If ophthalmoplegia is related to disfunction in eye muscles, then anticonvulsant drugs can be made use to it [30]. Gabapentin [31, 32] and pregablin under the class of this drug can be made use into the future through proper research and certain properties should be concerned. Minimally invasive surgeries an, ocular implant and pharmacological interventions tehnology can also be in innovations.

2. Conclusion

Ophthalmoplegia is the paralysis of eye muscle classified under Internuclear and External ophthalmoplegia. Certain case studies shown different aspects of eye muscle disease, whether it is is in young or old. Certain clinical features we can conlude that are limited or absent eye movements, diplopia, ptosis, head tilt or turn to compensate for limited eye movements, nystagmus. Compre hensive eye examination, blood tests, neuro imaging were diagnostic approaches. Botulinum Toxin Injection is used in the treatment of ophthalmoplegia which is available as parenteral dosage form. The prognosis varies ophthalmoplegia may resolve with the treatment while others may result in persistent or progressive vision loss. Better development could be done on future through Novel drug delivery system and pharmacological drugs under that anticonvulsant drugs. Certain innovations have to come forward for the development of new forms of drugs to treat ophthalmoplegia.

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