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RESEARCH ARTICLE

A CASE REPORT OF NEUROTROPHIC KERATITIS

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Abstract

Introduction: Neurotrophic keratitis (NK) is a rare corneal disease caused by damage to trigeminal nerve supply, leading to poor corneal healing and epithelial breakdown. Its key feature is reduced or absent corneal sensation, which can progress to ulcers, corneal melting, or perforation.

Material and Methodology: This case report describes a 55-year-old male presented to Maharani Laxmi Bai Medical College with Neurotro phic keratitis in the left eye.A detailed ocular and systemic examination was performed. The patient was admitted for conservative management with conventional treatment modalities and post treatment, the patient's condition showed improvement.

Management and Treatment: There is no definitive pharmacological treatment available for neurotrophic keratitis (NK), and management mainly focuses on supportive care and prevention of complications. Growth factors and metalloprotease inhibitors are two new and promisi ng treatments for NK, according to certain experimental and clinical data.

Conclusion :NK is challenging for ophthalmologists to diagnose and treat, with current therapies mainly focused on preventing corneal perfo ration, promoting healing, and halting disease progression. However, no available treatment reliably restores corneal sensitivity or improves visual acuity. Emerging therapies, including growth factors, and ongoing clinical trials offer hope for more effective future treatments.

Introduction:-

Neurotrophic keratitis (NK) is a rare degenerative corneal disease caused by impairment of trigeminal innervation leading to corneal epithelial breakdown, impairment of healing, and development of corneal ulceration, melting, and perforation. The hallmark of NK is a decrease or absence of corneal sensation. [1]

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Magendie first identified NK as "neuroparalytic keratitis" and conducted experiments to support his theory that trophic nerve fibers in the trigeminal nerve regulate the tissue metabolism. [2] It is now known that the trigeminal nerve plays a crucial role in preserving the anatomical integrity and functionality of the ocular surface by supplying the cornea with trophic nutrients and corneal sensibility.[3]Through the secretion of cytokines, neuropeptides, and neuromediators, the ocular surface epithelium, tear gland, and sensory and autonomic nerve fibres regulate each other's structures and functions.[1, 3]

Impairment of corneal trigeminal innervation causes morphological and metabolic epithelial disturbances and leads to development of recurrent or persistent epithelial defects. Recurrent or permanent epithelial deficiencies emerge as a result of morphological and metabolic epithelial changes brought on by impairment of corneal trigeminal innervations

Grading:-

Stage I(Mild): Characterized by decreased tear break-up time and irregular surface cells (punctate keratopathy), often closely mimicking standard dry eye disease.

Stage II(Moderate): Defined by the development of persistent, recurrent open wounds (epithelial defects) on the cornea. These wounds often have smooth edges because the cornea's natural healing ability is hindered.

Stage III(Severe): The most advanced phase, involving corneal melting, deep ulcers, and a high risk of corneal perforation.

Causes:-

NK may arise as a result of ocular and systemic disorders linked to injury at any level of the fifth cranial nerve (trigeminal nerve), from the corneal nerve endings to the trigeminal nucleus. Herpetic keratitis, cerebral space-occupying lesions, and/or neurosurgical procedures that harm the trigeminal ophthalmic branch are the most frequent causes of impaired corneal sensation. Chemical burns, physical trauma, corneal dystrophy, long-term topical drug use, and anterior segment surgery involving nerve transection are additional ocular reasons of corneal sensitivity degradation. Corneal anaesthesia is also linked to a number of systemic illnesses, such as leprosy, multiple sclerosis, diabetes, and congenital abnormalities.[1]

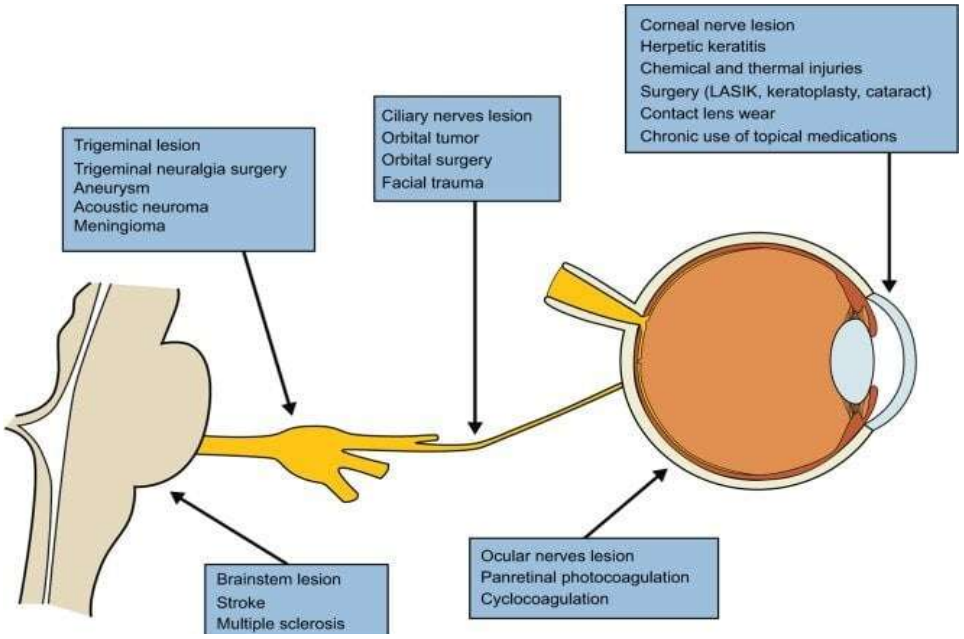

Figure 1 : Causes of Neurotrophic Keratitis

Material and Methodology:-

This is a case report of a 55 years old male patient who came to Maharani LaxmiBai Medical College, Jhansi, with Neurotrophic Keratitis in left eye and immature senile cataract in right eye. Detailed ocular and systemic examination were done to rule out any other abnormalities, which included history of the presenting illness, visual acuity using Snellen's chart, corneal sensitivity, complete ocular examination using slit lamp, intra-ocular pressure using non-contact tonometer. Blood was sent for routine laboratory investigations. Patient is admitted for conservative management using conventional treatment options and the condition of patient is improved.

Case Report:-

A 55 years old male presented with complaints of Diminution of vision in left eyefrom past 3 months which was insidious in onset and gradually progressive in nature. It was associated with watering, redness and photophobia.He has a past history of chronic use of multiple topical medications. No past history of pain, headache or trauma. No prior history of wearing spectacles. There is no known instance of ischemic heart disease, diabetes, asthma, chronic obstructive pulmonary disease [COPD], or hypertension.

Ocular Examination

Table 1 : Ocular findings of patient

O/E	RIGHT EYE	LEFT EYE
Vision (using snellen's chart)	6/24	Hand movement +ve
Best Corrected Visual Acuity	6/12	Hand movement +ve
Perception of light	Present	Present
Projection of rays	Present in all 4 quadrants	Present in all 4 quadrants
Orbital Margins	Intact on palpation	Intact on palpation
Extraocular Movements	WNL in all directions of gaze	WNL in all directions of gaze
Eyelid/Eyebrow	WNL	WNL
Intraocular pressure (non-contact tonometry)	14 mmhg	11 mmhg

Slit Lamp Examination

Table 2 : Slit Lamp Findings of patient

O/E	RIGHT EYE	LEFT EYE
Cornea	WNL	• Stromal ulceration/melting characterised by crater-like defect • Stromal edema • Sterile stromal necrosis • Stain positive persistent epithelial defect • Neovascularization • Reduced corneal sensations
Conjunctiva	WNL	Diffuse congestion
Anterior Chamber	Normal depth (VH4)	Shallow (VH2)
Iris	Normal colour/normal pattern	Normal colour/normal pattern

Pupil	Round/Regular/Reactive	Round/Regular/Reactive
Lens	Greyish white reflex	Glassy Reflex
Fundal glow	Fair	Poor

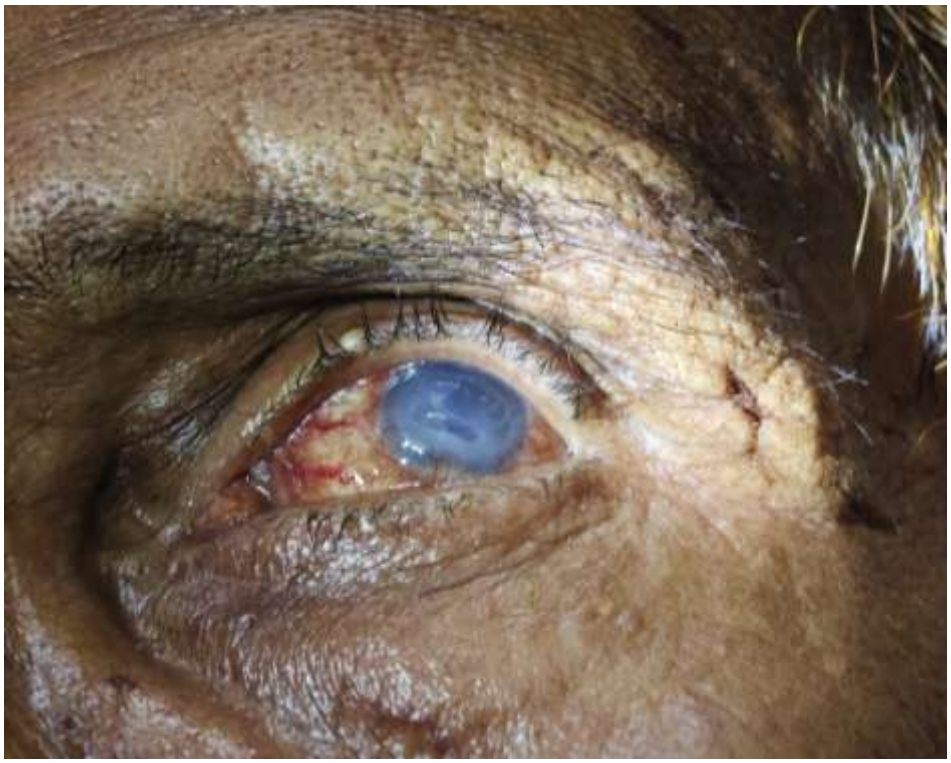

Figure 2 : Patient's eye on the day of presentation (day 0)

Provisional Diagnosis:-
On the basis of history and ocular examinations, the provisional diagnosis is Left eye Neurotrophic Keratitis (stage III)

Management and Treatment Options:-
There are no pharmacological therapies for NK. However, at every level of the severity of the disease, the corneal surface may be improved by using artificial tears without preservatives. Although topical steroids have been suggested for NK to manage ocular inflammation (if it exists), their usage should be carefully examined as they may raise the risk of corneal melting and perforation by preventing stromal repair.[1, 4, 5] Topical nonsteroidal anti-inflammatory medications should be avoided as they may also impede the healing process. [6]Short-acting cycloplegic and mydriatic agent can also be used as an adjunctive, supportive therapy rather than a primary treatment. It relieves pain caused by ciliary muscle spasm and helps prevent iris adhesions (synechiae) when secondary inflammation occurs. Antivirals are essential as prophylaxis or suppressive therapy against viral reactivations, but they do not directly treat neurotrophic keratitis. Antivirals stop quiet, recurrent viral infections from seriously harming an already weakened cornea when neurotrophic keratitis is brought on by herpes simplex or herpes zoster.In order to prevent infection in eyes with NK at stages 2 and 3, topical antibiotic eye drops are advised.
℞

Patient was started with following medications :-
- E/d Carboxymethyl Cellulose 1% 1d 1 hrly
- E/d Moxifloxacin 0.5% 1d QID
- E/d Prednisolone 1% 1d QID

- E/d Homatropine 2% 1d TDS
- Tab Acyclovir 400mg x 5times/day

Figure 3 : Patient's eye on 3rd day post treatment

Follow Up:-

Patient was discharged with following medications and called for follow up after 1 week

- E/d Carboxymethyl Cellulose 1% 1d 6times/day
- E/d Moxifloxacin 0.5% 1d QID
- E/d Prednisolone 1% 1d 3/2/1 times/day/week
- E/d Homatropine 2% 1d TDS
- Tab Acyclovir 400mg x 5times/day

Slit Lamp Examination:-

- Corneal sensations got back to normal
- Fluorescein stain negative
- Stromal ulcerations resolved
- Mild stromal edema present
- Neovascularisation resolved
- Conjunctival congestion resolved

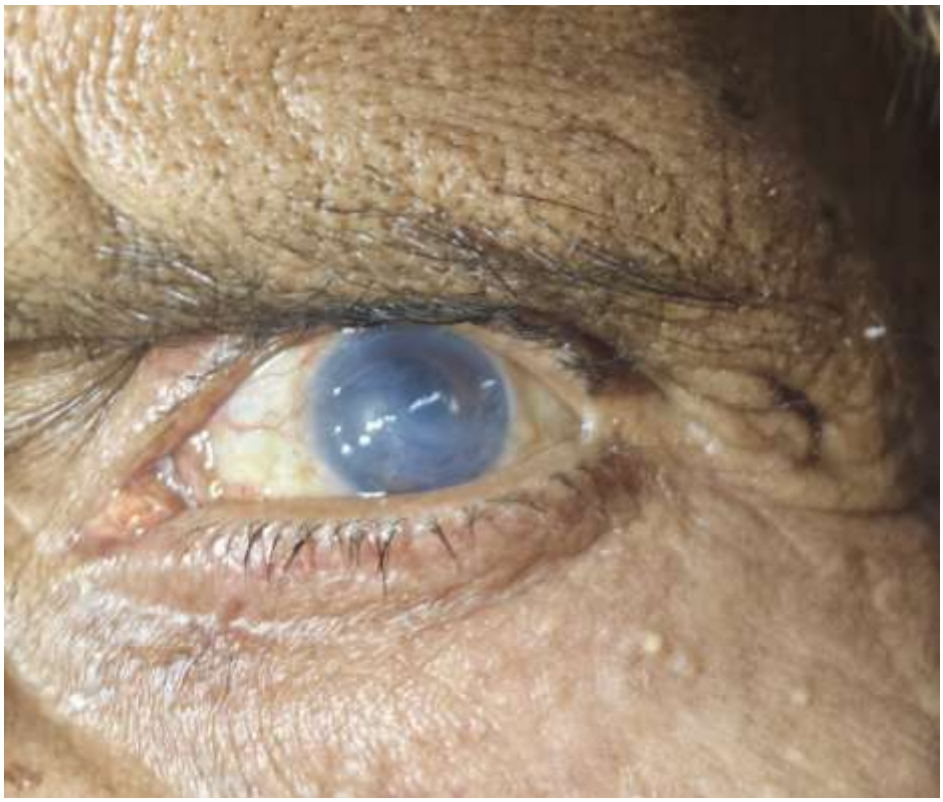

Figure 3 : Patient's eye on 7th day post treatment follow up

Future Developments:-

For NK, new medicinal and surgical interventions have been suggested and are presently being researched. [1, 4, 7] Six NK patients with unilateral facial palsy with corneal anesthesia have shown improved results following surgical operations of sensory neurotization by insertion of the contralateral supraorbital and supratrochlear nerves to the anesthetic corneal limbus. [8]

In one patient with NK brought on by herpes zoster keratitis, the use of a Boston keratoprosthesis (Boston K-Pro; Massachusetts Eye and Ear Infirmary, Boston, MA, USA) restored visual function at a 4-month follow-up. [9]Numerous pharmacological therapies have been shown to be effective in promoting the healing of corneal ulcers in NK, according to open studies. Eight out of eleven patients (73%) who received treatment with eye drops containing RGTA® (Cacicol20®; OTR3, Paris, France), a matrix agent that mimics heparansulfate, experienced full healing, with the NK ulcer closing after an average of 8.7 weeks. [10]

In another trial, eye drops containing thymosin beta-4—a synthetic version of the naturally occurring 43-amino acid G-actin sequestering molecule—were administered to nine NK patients with PED. Three of these patients had recovered by the conclusion of the 30-day follow-up period, and one patient had fully recovered by the end of the therapy period. [11]In an average of 22 days, autologous serum (50%) eye drops caused corneal healing in 23 out of 25 NK eyes.[12] Additionally, a retrospective study comparing the effectiveness of AMT with autologous serum eye drops found that multilayer AMT was superior for healing deep corneal ulcers following herpes simplex keratitis. [13] All eyes treated with topical non-gelified platelet-rich plasma for PED caused by various disorders, including NK, healed completely in 6–32 days. [14] Furthermore, after receiving umbilical cord serum eye drops for an average of four weeks, 28 NK patients had total corneal healing. [15]Neuropeptides and growth factors have been suggested for the therapy of NK in a number of studies. Larger investigations, however, could not corroborate early findings about the effective use of epidermal growth factor eye drops in NK patients. [16]

In an open research, 25 patients with NK received topical treatment with substance P and insulin-like growth factor-1; at 4 weeks, 73% of patients showed complete repair of epithelial abnormalities. [17] Eleven NK patients were

treated with PED using a combination of substance P-derived peptide, phenylalanine–glycine–leucine–methionine–amide, and insulin-like growth factor-1, which resulted in total epithelial resurfacing in 89% of instances. [18] One extremely potential future therapeutic strategy for the prevention and treatment of NK is the use of nerve growth factor eye drops. Recovery from NK may result from nerve growth factor's ability to enhance tear and nerve function as well as promote corneal epithelial and sensory nerve survival and regeneration. Patients with moderate to severe NK (stages 2 and 3) responded well to topical nerve growth factor treatment. After using nerve growth factor eye drops for 12 days to 6 weeks, 100% of 55 patients in two open, uncontrolled investigations showed complete corneal healing.

Conclusion:-

For ophthalmologists, diagnosing and treating NK can be difficult. The goals of the current medication and surgical interventions are to prevent corneal perforation, encourage healing, and stop the condition from getting worse. Nevertheless, there are currently no treatments that can enhance corneal sensitivity degradation and restore visual acuity. Numerous cutting-edge therapies, including growth factors, may enhance the therapeutic outcome of NK, according to experimental and clinical data. New treatments for this orphan disease will be made possible by the results of current clinical trials.

Disclosure:-

All the photographs used in this journal have been published after obtaining informed consent and permissions from the patient.

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Conflicts of interest:-

Nil

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