Neuroparalytic keratopathy as the first sign of a cerebral meningioma

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ABSTRACT

We report a case of a cavernous sinus meningioma in a young woman presenting with a neuroparalytic corneal ulcer as the only sign of the tumour. Clinical ophthalmic examination revealed a trophic corneal ulcer in the left eye of the patient accompanied by corneal anaesthesia and loss of sensation to touch and pain stimuli in the ipsilateral dermatomes supplied by the ophthalmic and maxillary divisions of the trigeminal nerve. A MRI scan of the head revealed a left cavernous sinus meningioma. Neuroparalytic keratopathy or corneal ulcer is an infrequent presenting sign of intracranial pathology. The diagnosis can be missed if the neuroparalytic nature of corneal condition is not detected by the ophthalmologist.

SAMENVATTING

We stellen een patiënte voor bij wie een neuroparalytisch ulcus het eerste teken was van een cerebraal meningioom. We stelden een cornea ulcus vast in het linker oog met een gevoelloze cornea en verlies van gevoeligheid en pijnsensatie in de dermatomen bezenuwd door nervus ophthalmicus en maxillaris. Neurologisch onderzoek en NMR-beeldvorming toonden een meningioom in de linker sinus cavernosus. Aangezien een neuroparalytisch cornea ulcus zelden als eerste teken van een cerebrale pathologie voorkomt, wordt deze diagnose snel over het hoofd gezien. Een uitgebreide anamnese en een grondig klinisch oftalmologisch en neurologisch onderzoek brengen echter de diagnose aan het licht.

RÉSUMÉ

Nous présentons une patiente avec une kératite neuroparalytique comme premier signe d'un méningiome cérébral. Nous avons constaté un ulcère cornéen à l'oeil gauche, une cornée insensible et la perte de la sensibilité au contact et à la douleur dans les dermatomes du nerf ophtalmique et du nerf maxillaire. L'examen neurologique et l'IRM ont montré un méningiome du sinus caverneux gauche. Étant donné la basse prévalence d'un ulcère cornéen neuroparalytique comme premier signe d'une pathologie cérébrale, ce diagnostic est souvent ignoré. Une anamnèse détaillée et un examen ophtalmologique et neurologique rigoureux révèlent quand même le diagnostic.

KEY WORDS

Neuroparalytic keratopathy - meningioma

MOTS-CLÉS

Kératite neuroparalytique - méningiome

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INTRODUCTION

The cornea is richly supplied by sensory nerve fibres derived from the ophthalmic division of the trigeminal nerve and axons from the sympathetic ganglion (4, 21). Corneal sensory denervation results in decreased epithelium thickness, poor epithelial wound healing, and decreased mitosis of epithelial cells (2, 12, 20, 25). Similarly, sensory denervation of the conjunctiva in monkey eyes induces an inflammatory response characterized by infiltration of the epithelium by neutrophils and macrophages, and conjunctival tissue disorganization (22). Degenerative changes in the corneal epithelium and conjunctiva after traumatic or surgical lesions of the trigeminal nerve (11, 23) manifest in a clinical condition known as neurotrophic keratitis or keratopathy. Other conditions commonly associated with neurotrophic keratitis are infections by herpes simplex virus or varicella-zoster virus, diabetes mellitus, multiple sclerosis, contact lens wear, chemical burns, trauma, corneal surgery, radiotherapy, leprosy, tumours of the nerve (neurofibroma and meningioma), aneurysms and cerebrovascular accidents (1, 10) .

In most patients the general medical history and associated systemic signs and symptoms are helpful in the diagnosis of neurotrophic nature of the corneal condition. However, in the absence of any relevant medical antecedents, neurotrophic keratitis can be a major diagnostic challenge to the ophthalmologist. A meticulous medical history and a thorough ophthalmic examination, followed by a neurological and neuroradiologic evaluation, are necessary to detect the causative lesion. In this report we describe a patient with neurotrophic keratitis caused by a cerebral meningioma of the cavernous sinus. This young patient had no other systemic symptoms or signs.

CASE REPORT

A young woman, 26-years of age, with a history of corneal ulcer in the left eye for one month, was referred to us by an ophthalmologist in the last week of October 2003. The only relevant ophthalmic history was slight redness of the left eye without any irritation which was treated by an ophthalmologist. She had suffered from fibromyalgia in the past. In July 2003 her first full term healthy child was born by caesarean section. The gestation period was uneventful. At the first consultation the best-corrected visual acuity was 10/10 RE and 5/10 LE. Ocular examination of the right eye was normal, and it remained so during the follow-up period. Slitlamp examination of the left eye showed a paracentral corneal ulcer with undermined edges, but without conjunctival hyperaemia or aqueous flare. The left cornea was insensitive to touch by a cotton tip applicator. The skin dermatome supplied by the first branch of the left trigeminal nerve was insensitive to touch and pain stimuli, and hypoesthesic in the dermatome supplied by the second branch of the trigeminal nerve. Explicit questioning revealed that epilation of the left eyebrow was painless for about one year, and that she had noticed a transient painless redness of the left eye, and a smaller left palpebral fissure, soon after her child was born. The ocular motility, pupil size and pupil reflexes, anterior chamber structures and the ocular fundus were normal. The central and peripheral visual fields were intact. A tentative diagnosis of neuroparalytic keratitis was made. Since the patient declined immediate admission to the hospital and further investigations, she was put on Delcol® eye drops 3 times a day and VitA-pos® ointment twice a day. During the following month the corneal ulcer persisted (Figure 1) with deterioration of vision to 25/100. The left eye had also become slightly red but there was no discharge. Our patient now agreed for admission to the hospital and the topical treatment was changed to Trafloxal® ointment once a day, Hylo-comod® eye drops 5 to 6 times a day and an eye patch. The

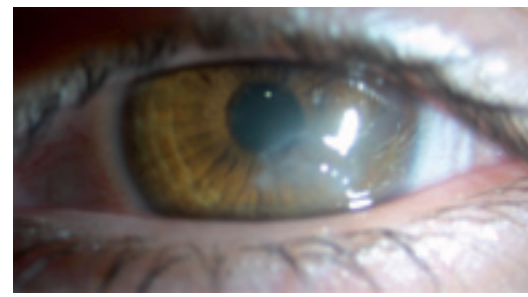

Figure 1: Slit lamp photograph of the neuroparalytic ulcer on the left eye of our patient.

corneal ulcer healed in 6 days with vision improving to 7/10. The topical treatment was further continued to protect the ocular surface.

In the meantime, clinical neurological examination suggested a partial sinus cavernous syndrome with anaesthesia of V1, hypoesthesia of V2. Nuclear magnetic resonance imaging confirmed the presence of an intracranial mass, measuring 3,1 x 2,9 x 1,9 cm, in the left cavernous sinus suspected to be a meningioma, (Figure 2). The patient was transferred to the department of neurosurgery. In the first week of December 2003 a partial resection of the intracranial mass was carried out. The tumour was not removed in toto because this would have involved sacrificing the left trochlear and the ophthalmic nerves. Histopathological examination confirmed the mass to be a WHO stage 1 fibrous meningioma. Our patient was discharged from the hospital on 9 December 2003 with topical Trafloxal® ointment once daily and Hylo-comod® eye drops 4 times and a day. Two weeks later the patient reported a worsening of the vision of the left eye for a couple of days which was again reduced to 3/10 with recurrence of the corneal ulcer at the same site where the ulcer had been previously. The eye was now red. Patching of the eye was restarted and the frequency of Hylo-comod® instillation was raised to 6 times a day. This treatment was successful in healing the ulcer again quickly. On 19 January 2004, a fluoresceine-positive epithelial defect was detected again on the previous ulcer site. We decided to induce upper eyelid ptosis by botulinum A toxin injection. It was done on 9 February 2004. The ptosis induction was incomplete and short lived but it lead to the healing of the ulcer rapidly with visual recovery to 6/10. To achieve longer protection of the corneal surface, a second botulin injection was given in March, but there was hardly any response in terms of ptosis induction and the corneal lesion again started to stain with fluoresceine. The patient started to become fed up with patching. In the middle of June 2004 a bandage soft contact lens was applied with Predmycine P® eye drops 3 times a day. Initially this therapy was effective but the patient reported intolerance to the lens. She started taking the lens out before retiring to bed at night. Several lenses were lost. By mid November 2004 the patient was not wearing the bandage lenses anymore. The corneal ulcer had increased in size with peripheral neovascularisation. The patient insisted upon some kind of permanent solution to her problem. On 1 December 2004 a conjunctivoplasty by Gunderson flap was done to cover the left cornea because of the uncertainty of results by the newer treatment options. There has been no corneal ulceration since then. The vision is hand movements nearby. Regular neurological and neuroradiological checkups have not shown tumour growth.

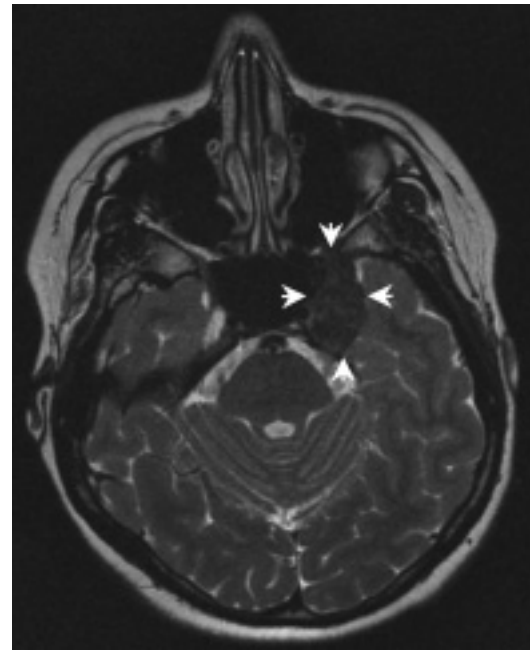

Figure 2: NMR of the brains showing a meningioma in the left cavernous sinus.

DISCUSSION

The characteristic clinical feature of neurotrophic keratopathy is a breakdown of the corneal epithelium resulting in an epithelial defect surrounded by a rim of loose epithelium with rolled up edges and oedema. The defect usually persists despite of treatment and becomes oval or circular in shape. With continued progression necrosis, stromal melting and perforation may ensue. Lack of redness, pain, discharge, and in early stages, absence of stromal infiltration

should make one suspect the presence of corneal anaesthesia (9) as the cause of the corneal changes.

Reviewing the literature on the pathogenesis of neurotrophic keratopathy, Müller et al (21) upheld mainly three hypotheses that may explain the corneal changes after corneal denervation. Firstly, corneal desiccation may ensue due to decreased lacrimal secretions and diminished blink reflex (14, 16) resulting from impaired corneal sensitivity. Secondly, an abnormal epithelial cell metabolism may be responsible for the failure of epithelial cells to resist the effects of trauma, drying and infection, as epithelial cell metabolic activity decreases after corneal denervation (26). Finally, the absence of the trophic influence of sensory nerves mediated by neuropeptides like substance-P or vasointestinal protein (VIP) may initiate neurotrophic changes. It is believed that the neurotrophic deficit plays the main role in destroying the denervated cornea, the cellular metabolic change and increased desiccation having a less important deleterious effect (9, 15, 17, 21).

Morphological and metabolic epithelial changes after corneal denervation have been studied in a large number of experimental animals (3, 5, 16, 24). The first change to occur is the loss of cytoskeletal structures in the superficial squameous epithelial cells accompanied by the loss of cellular adhesions and the loss of cell migration direction, and intercellular oedema (3, 5). Consequently increased cell desquamation occurs due to the weakened cellular attachments which result in a stippled corneal surface with multiple punctuate epithelial defects, and the accumulated epithelial defects may contribute to the tendency to form recurrent erosions (3, 5). Interruption of the epithelial nerve supply causes a reduction in the metabolic activity of the cells (26) with subsequent decreased oxygen uptake rate and altered hypoxic swelling response (13, 21). All these factors contribute to a decreased repair capability following a standardized epithelial abrasion. In addition, exposure and drying may enhance the chances of corneal ulceration (5).

The corneal degenerative changes generally develop within the first 6 months after lesions of the trigeminal nerve. As an immediate response to the nerve injury, conjunctival hyperaemia can sometimes be seen for 8 to 10 months, whether or not associated with iritis (9). A transient painless red eye soon after the delivery reported by our patient probably corresponded to this stage. Conjunctival hyperemia should be regarded as a forewarning of future trouble in patients with trigeminal nerve lesions. Corneal alterations may start within 24 hours after the ophthalmic or trigeminal nerve lesions. The clinical picture may resemble one of the following three stages. (1) The first stage is a significant lack of the corneal luster and the appearance of punctate keratopathy (6, 7, 9). Occasionally the process does not progress further and resolves into a picture resembling a diffuse vesicular keratitis or recurrent erosions. When there is progression, a persistent epithelial defect appears without (Stage 2) or with corneal ulceration (stage 3). The areas of degeneration are sometimes sharply circumscribed, known as Gaule's spots or Dellen when in the periphery. Otherwise a rapid and massive exfoliation of the epithelium occurs starting in the central cornea, and spreading to involve the entire corneal surface apart from a small rim of epithelium near to the limbus. The denuded surface appears dry, milky and hazy. It is surrounded by a slightly raised grey ring of proliferating epithelium. This is the typical picture of neuroparalytic keratitis. In untreated or neglected cases the entire cornea becomes opaque or a secondary infection may cause ulceration which may hasten perforation of the cornea. The course of disease is slow and chronic with many relapses. Because of associated anesthesia it is characterized by the absence of acute symptoms (9).

The management of neuroparalytic keratitis is one of the most difficult and challenging among all corneal diseases, because of the lack of specific treatment. The best options are preservative-free artificial tears, prophylactic topical antibiotic drops and eyelid closure. After a successful lid closure, a rapid improvement follows almost immediately (9, 18). Currently, ptosis induction by botulinum A toxin for temporary eyelid closure is preferred to a tarsorraphy because the later is more disfiguring. Repeated botulinum A toxin injections in our patient failed to induce adequate ptosis. Therefore, we had to resort to other management mo-

dalities like therapeutic contact lenses and conjunctival flap according to Gunderson. Although neuropeptides and growth factors have been reported to be beneficial in the management of neurotrophic disorders (6, 7, 8), we could not try them because of unavailability.

Neuroparalytic keratopathy following trigeminal nerve damage may occur after orbital or head surgery, head trauma, tumours, aneurysms, or intracranial neurological disease (9, 19). In such cases the history or associated neurological symptoms are generally helpful in suspecting an anaesthetic cornea. Diseases like herpes simplex and herpes zoster infections, chemical and physical injury, diabetes and ophthalmic surgery (LASIK, certain forms of cataract and retinal surgery, and some ophthalmic laser procedures) may induce corneal anaesthesia and neurotrophic keratitis. However, these conditions do not cause such a severe trophic alterations of the cornea as compared to neuroparalytic lesions (6, 7, 9, 18).

CONCLUSION

This case report demonstrates that a neuroparalytic ulcer can be the only sign of a brain tumour. In our patient it was a cavernous sinus meningioma that did not cause any other signs or symptoms of neurological disease. Awareness of this possibility and thorough ophthalmic and neurological examinations are mandatory to establish the diagnosis.

REFERENCES

(1) ALLEN V.D., MALINOVSKY V. – Management of neurotrophic keratopathy. Contact Lens & Ant Eye. 2003, 26: 161-165.

(2) ALPER M. – The anaesthetic eye: an investigation of changes in the anterior ocular segment of the monkey caused by interrupting the trigeminal nerve at various levels along its course. Trans. Am. Ophthalmol. Soc. 1975, 73: 323-365.

(3) ARAKI K., OHASHI Y., KINOSHITA S., HAYASHI K., KUWAYAMA Y., TANO Y. – Epithelial wound healing in the denervated cornea. Curr. Eye Res. 1994, 13: 203-211.

(4) BELMONTE C., GARCIA-HIRSCHFIELD J., GALLAR J. – Neurobiology of ocular pain. Prog. Ret. Eye Res. 1997; 16: 117-156.

(5) BEUERMANN R.W., SCHIMMELPFENNIG B. – Sensory denervation of the rabbit cornea affects epithelial properties. Exp. Neurol. 1980, 69: 196-201.

(6) BONINI S., LAMBIASE A., RAMA P., CAPRIOGLIO G., ALOE L. – Topical treatment with nerve growth factor for neurotrophic keratitis. Ophthalmology 2000; 107: 1347-1351.

(7) BONINI S., RAMA P., OLZI D., LAMBIASE A. – Neurotrophic keratitis. Eye 2003; 17: 989-995.

(8) BROWN S.M., LAMBERTS D.W., REID T.W., NISHIDA T., MURPHY C.J. – Neurotrophic and anhidrotic keratopathy treated with substance P and insulin-like growth factor 1. Arch Ophthalmol. 1997, 115: 926-927.

(9) DUKE-ELDER S., LEIGH A.G. – Degenerative types of superficial keratitis. In: System of Ophthalmology, volume VIII Diseases of the outer eye; edited by Sir Stewart Duke-Elder, Henry Kimpton: London, 1965. pp 801-811.

(10) FOSTER C.S. - Corneal manifestations of neurologic diseases. In: SMOLIN G., THOFT R.A. - The Cornea. Little Brown and Company. Boston/Toronto, 1987, pp 413 - 426.

(11) FRANÇOIS J., HOFFMAN G., SOLEME J. - La kératite neuroparalytique et sa fréquence après les différentes neurotomies pour neuralgie essentielle du trijumeau. Neurochirurgia 1966, 9: 81-98.

(12) FRIEDENWALD J.S., BUSCHKE W. - Some factors concerned in the mitotic and wound-healing activities of the corneal epithelium. Trans Am Ophthalmol Soc. 1944, 42: 371-383.

(13) HOLDEN B.A., POLSE K.A., FONN D., MERTZ G.W. - Effects of cataract surgery on corneal function. Invest. Ophthalmol Vis. Sci. 1982, 22: 343-350.

(14) HEIGLE T.J., PFLUGFELDER S.C. - Aqueous tear production in patients with neurotrophic keratitis. Cornea 1996, 15, 135-138.

(15) GALLAR J., POZO M.A., REBOLLO I., BELMONTE C. - Effects of capsaicin on corneal wound healing. Invest. Ophthalmol. Vis. Sci. 1990, 31: 1968-1974.

(16) GILBARD J.P., ROSSI S.R. - Tear film and ocular surface changes in a rabbit model of neurotrophic keratitis. Ophthalmology 1990, 97: 308-312.

(17) KNYAZEV G.G., KNYAZEVA, G.B., TOLOCHKO Z.S. - Trophic functions of primary sensory neurons: are they really local? Neuroscience 1991, 42: 555-560.

(18) LAMBIASE A., RAMA P., ALOE L., BONINI S. - Management of neurotrophic keratopathy. Curr Opin Ophthalmol 1999; 10: 270-276.

(19) MADHUSUDAN G.R., SHARMA R.K., NANDA V. – Neuroparalytic keratitis: a rare manifestation of posttraumatic superior orbital fissure syndrome. Annals of plastic surgery 2004; 53: 83-85.
(20) MISHIMA S. – The effects of the denervation and the stimulation of the sympathetic and trigeminal nerve on the mitotic rate of the corneal epithelium in the rabbit. Jpn J Ophthalmol. 1: 65-73, 1957.
(21) MÜLLER L.J., MARFURT C.F., KRUSE F., TERVO T.M.T. – Corneal nerves: structure, contents and function. Exp. Eye Res 2003; 76: 521-542.
(22) ODUNTAN A.O. – Cellular inflammatory response induced by sensory denervation of the conjunctiva in monkeys. J Anat. 2005: 206: 287-294.
(23) PATON L. – The trigeminal and its ocular lesions. 1926, 10: 300-342.
(24) SCHIMMELPFENNIG B., BEUERMAN R. – A technique for controlled sensory denervation of the rabbit cornea. Graefes Arch. Clin. Exp. Ophthalmol. 1982, 218: 287-293.
(25) SIEGELMAN S, FRIEDENWALD J.S. – Mitotic and wound healing properties of the corneal epithelium: effect of sensory denervation. Arch Ophthalmol. 52: 46-57, 1954.
(26) VANNAS A., HOLDEN B.A., SWEENEY D.F., POLSE K.A. – Surgical incisions alters the swelling response of the human cornea. Invest. Ophthalmol. Vis. Sci. 1985, 26: 864-868.

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