Corneal Involvement in Wallenberg Syndrome: Case Report and Literature Review

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ABSTRACT

A 47-year-old man with Wallenberg syndrome after a stroke in the territory of the left vertebral-basilar artery and posterior inferior cerebellar artery, presented a week later complaining of visual loss in the left eye. Examination showed corneal anaesthesia associated with a neurotrophic corneal epithelial defect. Corneal involvement secondary to trigeminal neuropathy in Wallenberg syndrome is not frequently reported and may lead to epithelial erosion and neurotrophic keratopathy. Clinicians should be aware that visual loss can occur from a neurogenic basis (e.g., Wallenberg syndrome) due to neurotrophic keratopathy. The use of cocaine, a potential cause of neurotrophic keratopathy, should also be suspected in the appropriate clinical scenario.

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Case report

A 47-year-old man was admitted with acute onset of vertigo and vomiting. He had had chronic cocaine addiction for the previous five years. His past ocular history, medical history, and family history were non-contributory. He was not taking any medications.

On neurological examination, he had left-sided cerebellar signs including gait ataxia, dysmetria, and dysidiadokokinesia. Sensory examination revealed deficits in pain and temperature sensation including hypoalgesia and thermoanaesthesia on the right side of the body. A left Horner syndrome (Figure 1) and left-sided facial anaesthesia were noted. Magnetic resonance imaging (MRI) of the brain showed hyperintensity in the left dorsolateral medulla and left inferior cerebellar peduncle (Figure 2) consistent with Wallenberg syndrome (WS). A full stroke workup was negative, as was a urine drug search (UDS)

One month after discharge from the hospital, he reported progressive visual loss in the left eye (OS). On examination, the best corrected visual acuity (BCVA) was 20/20 in the right eye (OD) and 20/40 OS. Ptosis and miosis consistent with

the previously described Horner syndrome were present OS. Slit lamp examination was normal OD but showed a central corneal epithelial defect OS (Figure 3). There was corneal anaesthesia OS. Fundus examination was normal OU. Artificial tears, ointment, and ofloxacin ointment were given hourly OS. At one month follow up the clinical picture was improved with residual superficial punctate keratopathy OS and improved neurotrophic keratopathy OS (Figure 4).

Discussion

Wallenberg syndrome (WS), also known as lateral medullary syndrome, is characterised by a variety of symptoms that occur as a result of damage to the lateral segment of the medulla posterior to the inferior olivary nucleus. An acute WS is most commonly due to a posterior circulation ischaemic stroke syndrome, i.e., due to vertebralbasilar artery disease and posterior inferior cerebellar artery (PICA) ischaemic infarction.¹ The presence of “crossed” sensory symptoms (e.g., left face and right body) and ipsilesional Horner syndrome are

Figure 1. External patient appearance (infrared image) when admitted, showing left-sided Horner syndrome.

characteristic presentations of WS. In fact, the most common acute cause of a central Horner syndrome is WS² and it is present in up to three quarters of WS cases.³ Lateropulsion of saccades is also a common ocular finding in WS.⁴ Smooth pursuits may also be affected, with impairment for targets moving away from the side of lesion.⁵

Spontaneous primary position nystagmus and ocular tilt reaction may be present. Rare patients report an unusual sensation of environmental tilt (upside down vision or 90 degrees tilted vision) and this can be misinterpreted as a nonorganic symptom.⁶ Spinal trigeminal nucleus and tract lesions occurring in WS are also responsible for ipsilateral loss of pain and temperature sensation in the face.

An under-recognised ophthalmic problem caused by central trigeminal involvement in WS is corneal hypoaesthesia or anaesthesia leading to neurotrophic keratopathy (NK) and poorly healing corneal epithelial ulceration. Damage to the lower part of the dorsolateral medulla may injure the corneal sensory nerve that comes from the lowest part of the spinal trigeminal nuclei resulting in interruption of the corneal sensory nerve pathway and NK.

The corneal nerves (from the ipsilateral trigeminal nerve) play an essential role in tear production and preservation of the normal metabolism and function of the ocular surface and have a key role in maintaining a healthy ocular surface, both by triggering

Figure 2. MRI of the brain without contrast – Axial T2-weighted image showing a left-sided stroke at the level of the lateral medulla and inferior cerebellar peduncle (arrow).

Figure 3. Slit lamp examination of the left eye. a. At presentation, there is paracentral inferior corneal epithelial sloughing and an epithelial defect. b. At one month follow up, residual superficial punctate keratopathy and moderate stromal haze are evident.

protective reflexes after injury and by providing trophic factors to the corneal cells.^{7,8} In fact, the corneal nerve fibres release growth factors that provide trophic support and regulatory action in the corneal epithelium, maintaining the physiological renewal, anatomical integrity and stimulating corneal wound healing.⁹ Corneal denervation reduces vitality, metabolism and mitosis of epithelial cells leading to intracellular oedema, loss of microvilli and abnormal development of the basal lamina.⁹ Moreover, damage of sensitivity may affect corneal wound healing producing epithelial impairment such as punctate epithelial keratopathy, persistent epithelial defects and finally corneal ulceration.¹⁰

Corneal innervation is provided by trigeminal nerve bundles that lose their perineurium and myelin sheaths and penetrate into the corneal stroma at the corneoscleral limbus, branching into the stromal plexus and then into the subepithelial and subbasal nerve plexus that provide sensitivity to the corneal epithelium.^{9,10}

Any condition that impairs trigeminal innervation at any level can cause NK.¹¹ Among these, herpes simplex virus (HSV) and Varicella-zoster virus (VZV) keratitis are the most common causes of corneal anaesthesia and of NK associated with a severe reduction of sub-basal nerve plexus density.¹² Corneal surgeries like laser-assisted in-situ keratomileusis (LASIK), keratoplasty, and corneal incisions for cataract may compromise corneal innervation and cause NK due to the distal nerves degenerating after nerve transection at the peripheral cornea, with an immediate loss of sensation to the corresponding region.¹³ Nerve regeneration occurs gradually over months with the variable and sometimes incomplete return of corneal sensitivity.¹³ Other ocular surface conditions associated with NK are corneal injuries, corneal dystrophies, and long-term wearing of contact lenses in addition to the chronic use of topical medications such as antivirals, glaucoma medications, antibiotics, and nonsteroidal anti-inflammatory drugs.^{14,15}

Diabetes mellitus and multiple sclerosis may impair corneal sensitivity and lead to NK. In particular, neuropathy is one of the most common complications of diabetes mellitus and results from microvascular damage of myelinated nerve fibres.¹⁶

Long-term systemic therapy with antipsychotics and antihistamines may also cause NK, as well as very rare congenital conditions like Riley-Day

syndrome, Moebius syndrome, Goldenhar–Gorlin syndrome, and congenital corneal anaesthesia.¹⁵

Neurotrophic keratopathy caused by the systemic use of crack cocaine has been reported and can result in significant epithelial defects, the most well-known being the syndrome ‘crack eye’.¹⁷

It is well known that abuse of topical cocaine-derived anaesthetics can result in corneal sensory nerve impairment, and in some cases neurotrophic keratopathy.¹⁸ Similarly, systemic administration of cocaine has been found to be associated with corneal pathology. Currently, known manifestations of systemic use of cocaine in the eye include corneal epithelial defects that range from mild superficial punctate keratitis to more severe corneal epithelial defects and ulceration.

It is the authors’ opinion that a patient with unexplained corneal findings related to reduced corneal sensitivity should undergo a UDS.

Corneal involvement in WS is rare. Our review of the literature found five cases of corneal involvement in the setting of WS (Table 1). Hipps et al. in 2004,¹⁹ first described a patient with a corneal ulcer and superinfection in the setting of WS. Ciudad et al. described three cases,²⁰ all female, with corneal anaesthesia; one of them had a previous penetrating keratoplasty resulting in a low final visual acuity. Wu et al. described a 43-year-old male with a corneal epithelial defect resulting from corneal anaesthesia in WS.²¹ Females and males have been equally affected, and the ages have ranged from 43 to 77 years. The BCVA at presentation ranged from counting fingers (CF) to 0.3, while the final VA ranged from CF to 0.7. All patients were treated with topical lubricants, while three of them required topical antibiotic treatment. The patient described by Wu et al. also required amniotic membrane grafting and systemic therapy with antivirals and steroids.²¹ The patient described by Hipps et al. required surgery as well.¹⁹

In conclusion, corneal involvement is a rare but serious complication of WS. Ophthalmologists and eye care providers should be aware that visual loss due to corneal disease can occur in patients with the WS as a “false localising” symptom or sign of brainstem infarction. The presence of NK can be delayed by months in patients with a prior WS when the other neurological symptoms/signs of the brainstem infarct may be resolving or resolved. The presence of the combination of a Horner syndrome and ipsilateral

Table 1. Cases reported in the literature of corneal involvement in the setting of Wallenberg syndrome. AM amniotic membrane; BCVA best corrected visual acuity; CA corneal anaesthesia; CF count fingers; ED epithelial defect; HS Horner Syndrome; OS left eye; pPK previous penetrating keratoplasty; SPK superficiae punctate keratitis; * eye medication/therapy; ** oral medication.

Author (year)	Age (yrs)	Sex	Eye	Time after stroke	BCVA baseline	Corneal findings	Systemic association	Therapy	BCVA final
Pellegrini F. et al. (2019)	47	M	OS	One month	2/10	CA/ED	Drug addiction	Lubricants*, Ofloxacin ointment*	3/10
Cidad P. et al. (2014)	77	F	OS	Three years	3/10	CA/SPK	-	Lubricants *	5/10
	72	F	OS	One year	3/10	CA/Ulcer/SPK	-	Lubricants* Gentamicin ointment *	7/10
	58	F	OS	Eight years	CF	pPK/CA/ED/hypopion	-	Lubricants* Moxifloxacin* Tobramycin* Valacyclovir** Prednisone** Levofloxacin* Calf serum eye gel* AM*	3/10
Wu S. et al. (2014)	43	M	OS	One month	1/20	CA/ED	Hypertension	Lubricants*, Tobramycin* Ceftazidime *	3/10
Hipps et al. (2004)	48	M	OD	Two months	CF	CA/ED/ulcer/hypopion	Hypertension	Contact lens, tarsorrhaphy	CF

corneal anaesthesia or NK should prompt consideration of tWS.

Methods of literature search

A literature search was carried out looking for all relevant articles published in English between January 1950 and December 2018. The database searched was PubMed. The keywords used were “corneal involvement in Wallenberg syndrome”, “neurotrophic keratitis”, “trigeminal innervations impairment”. Data extracted from each case included age, gender, visual acuity, surgical or medical therapy, and outcome.

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