A CASE OF HERPETIC DISCIFORM KERATITIS COMBINED WITH NEUROTROPHIC ULCER AND TRABECULITIS

***Kalina Trifonova, **Kiril Slaveykov**

**Medical Faculty, Trakia University, Department of Ophthalmology and Otorhinolaryngology, 2 Gen. Stoletov Str, Stara Zagora, 6000, Bulgaria, e-mail: kalina.trifonova@trakia-uni.bg*

*** Medical Faculty, Trakia University, 1st Department of Internal disease and General medicine, 11 Armeiska Str, Stara Zagora, 6000, Bulgaria, e-mail:kirilslaveykov@gmail.com*

Abstract

Background: Endotheliitis is an immune-mediated condition that occurs as an immune reaction to a viral antigen or non-replicating viral particles and manifests as localized, diffuse, and linear forms. The localized form is called Disciform keratitis and manifests as central disc-shaped stromal edema with focal keratic precipitates.

Aim: To present a difficult to treat and diagnose clinical case of disciform herpetic keratitis

Methods and material: A case report with short literature review

Results: A 60-year-old male presented with complaints of pain, redness and severely blurred vision. At the time of presentation, the best corrected visual acuity in the left eye was hand movement and the intraocular pressure was 50 mmHg. The cornea had diffuse microcystic edema and there was a round 2-mm superficial ulcer slightly left to the center of the visual axis. We suspected Herpes simplex viral keratitis even though the superficial ulcer did not have characteristics of a herpetic lesion. We started treatment with Valacyclovir and epithelizing gels for the ulcer. The topical corticosteroid was postponed for a few days. Therapy for lowering the intraocular pressure was also started. Slow but significant improvement was demonstrated. On day 40 a small macula had formed in the place of the superficial ulcer. The final visual acuity was 20/40.

Conclusion: Even though herpetic keratitis is a common disease some of its more complicated forms can still be challenging for diagnosis and treatment.

Key words: *endotheliitis, immune-mediated, intraocular pressure, superficial ulcer, challenging*

Background

Herpes Simplex Virus (HSV) is the most common virus that causes eye disease. Although around 60% of the world's population are seropositive for HSV antigens, fortunately, it is estimated that only 1% of seropositive individuals develop eye disease (2).

Herpes simplex virus keratitis presents in 4 distinct ways. Epithelial keratitis manifests as corneal epithelial ulceration with a distinctive dendritic or geographic pattern and is the result of epithelial infection and cell death. HSV stromal keratitis without ulceration presents as stromal inflammation with an intact overlying epithelium and is thought to represent an immune-mediated process related only indirectly to viral reactivation. Herpes simplex virus stromal keratitis with ulceration, often referred to as necrotizing keratitis, is less common. It is induced upon viral reactivation and subsequent infection of stromal keratocytes (6). Endotheliitis is an immune-mediated condition that occurs as an immune reaction to a viral antigen or non-replicating viral particles and manifests as localized, diffuse, and linear forms. The localized form is called Disciform keratitis and manifests as central disc-shaped stromal edema with focal keratic precipitates (8). This entity occurs even less commonly than other forms of HSV keratitis (6).

Intraocular pressure could be elevated (1) when the infection causes trabecular meshwork inflammation. HSV might be secreted from the trabeculum, innervated by the trigeminal nerve (5).

Herpes Simplex is usually diagnosed clinically and requires no laboratory confirmation.

Results

A 60-year-old male with complaints of pain, redness and severely blurred vision in his left eye was admitted to the Ophthalmology Department of the University Hospital in Stara Zagora, Bulgaria. He had no past history of eye disease or traumatic eye injury. He confessed to rubbing the same eye for quite some time because of a bothering sensation, however, he did not look for an ophthalmologist until more serious complaints had started. He had accompanying systemic diseases: Hypertension grade 2, a stroke 2 years ago and arthrosis. He had no family history of ocular diseases. He was retired but still working in agriculture (self-employed).

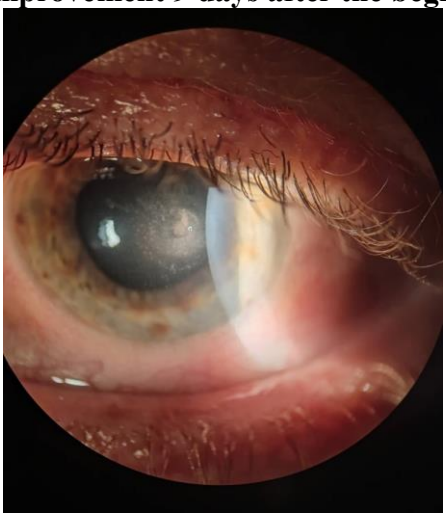
At the time of presentation, the best corrected visual acuity (BCVA) in the left eye was hand movement (HM) and the intraocular pressure (IOP) was 50 mmHg (measured with a hand-held tonometer). There was hyperemia of the conjunctiva with ciliary injection. The cornea had diffuse microcystic edema and there was a round 2-mm superficial ulcer slightly left to the center of the visual axis. The borders of the ulcer looked clear, and it seemed like a foreign body had been recently removed. There was a ring-shaped haze around the ulcer, which wasn't clearly observed due to the diffuse edema.

We suspected Herpes simplex etiology due to the combination of severely increased IOP and keratitis. What did not fit the clinical picture was the superficial ulcer that did not have characteristics of a herpetic lesion. A PCR assay for the detection of HSV DNA using aqueous humor would have provided supporting evidence (3).

Initially, we started treatment with Mannitol 10 % i.v. infusions q.d. and Azarga (Brinzolamide/Timolol) b.i.d. in order to decrease the IOP and stop further damage to the optic nerve. Since herpetic keratouveitis was suspected Unitropic (Tropicamide) 1% was started t.i.d. and Valtrex (Valacyclovir) 500 mg t.i.d. Vigamox (Moxifloxan) drops were also prescribed because of the corneal ulcer with unknown origin (suspected trauma) and Corneregel (dexpanthenol) both 5X a day. Local corticosteroids were postponed until the third day to see initial epithelization of the ulcer and eventually some reduction of the microcystic corneal edema. Due to the lack of significant change in the clinical picture treatment with Flarex (Fluorometholone acetate) 5X a day was started. On day 5 we prescribed Hydramed night (Vitamin A palmitate, Liquid paraffin) ointment before bedtime and Terso (Ophthalmic Solution with Osmotic Action) b.i.d. and reduced the Corneregel to t.i.d. The lack of further epithelization of the ulcer was the reason for this change in the treatment. On day 6 the patient was discharged with the same treatment continued at home and Diazomid 250 mg (Acetazolamide) to substitute the Mannitol infusions for five more days.

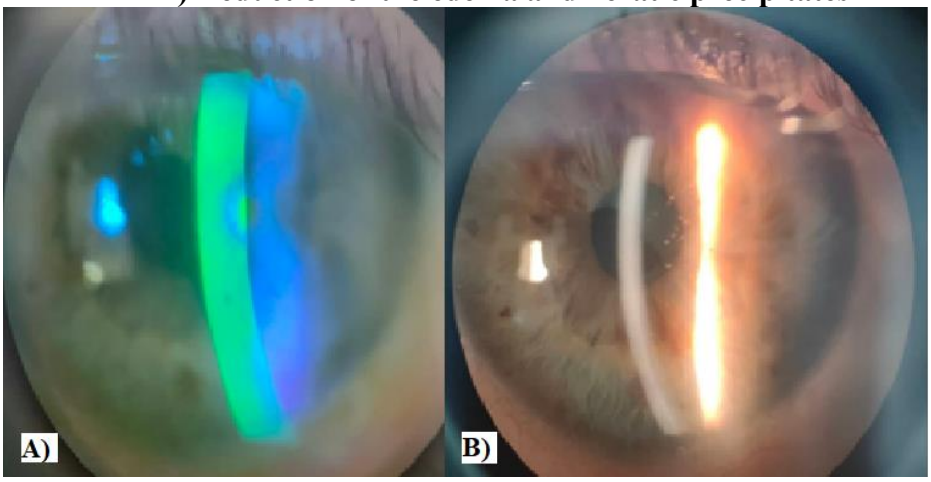
The patient came for follow-up on the 9th day. The diffuse edema had resolved and we could easily observe slightly paracentral epithelial edema with haze in a round distribution, associated with keratic precipitates underlying the zone of the edema (fig.1). The patient's complaints had already decreased. We decided to stop the antibiotic drops.

Fig 1. Significant improvement 9 days after the beginning of treatment



On the next follow-up (day 12) we reduced the Valtrex dosage to b.i.d. The patient stopped using Terso and Unitropic 1% drops. On the next visit 25 days after the beginning of treatment the BCVA had significantly improved to 20/40 and the IOP was 11 mmHg. The patient acknowledged improvement of the corneal sensation examined with a cotton bud. The ulcer had almost healed with mild loss of transparency and edema around it. It still stained with fluorescein (fig. 3 A). There was significant reduction in the corneal haze and edema and the keratic precipitates were resorbed to small pigmentary lesions(fig.3 B). We stopped the instillation of Azarga, reduced the Valtrex to q.d. We gradually reduced Flarex to t.i.d. for 7 days and b.i.d. for 7 days.

fig. 3 A) Almost epithelized ulcer but still staining with fluorescein
B) Reduction of the edema and keratic precipitates

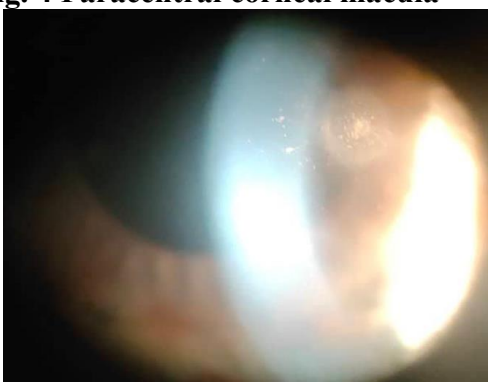


The slow healing of the ulcer confirmed our suspicion that the ulcer was neurotrophic. Our hypothesis was that the patient created it by the constant rubbing to which he confessed and it couldn't heal properly due to the damaged corneal sensory innervation by the virus (13). When the corneal sensitivity started to recover the wound finally started to heal. The patient was advised to continue instillation of Corneregel b.d. during the day and Hydramed night before bed.

On the next follow-up (40 days after the beginning of treatment) the BCVA was still 20/40. A paracentral macula (fig. 4) had formed in the place of the ulcer with no signs of inflammation. There was initial cataract that couldn't explain the decreased visual acuity. On fundoscopic examination we

found a small optic disk which was vital with clear margins. The blood vessels were in stage 2 hypertensive retinopathy and there were no changes in the retina and macula. The visual acuity was decreased due to astigmatism created by the cicatricial changes in the cornea. The patient would continue with Hydramed night every evening for a month and Valacyclovir 500 mg q.d. for at least two more month. Since this was the first incident of herpetic keratitis for this patient, we did not recommend prolonged prophylaxis.

Fig. 4 Paracentral corneal macula



Discussion

In the treatment of disciform keratitis the use of topical steroids is mandatory as there is an active immunological process. The use of systemic antiviral medication is necessary at the same time in order to avoid reactivation of viral replication (7).

Acyclovir has a few downsides as treatment of ocular HSV-1 infections. The first is that it affects only newly synthesized viral DNA, and therefore it does not cure infected cells of the virus, but it does prevent new viruses from being produced (4). Secondly, acyclovir is susceptible to drug resistance. Many cases of drug resistance have been reported, and immunocompromised patients appear especially vulnerable to developing resistant HSV-1 infections (10). In addition, acyclovir has poor bioavailability, so that high doses and increased frequency of administration are required (4). On the other hand, valacyclovir, a prodrug of acyclovir, has better bioavailability than oral acyclovir and produces higher acyclovir tissue and serum concentrations (12).

Long-term administration of low-dose oral antivirals as prophylaxis has demonstrated a significant decrease in recurrence of all forms of herpetic eye disease (14). The HEDS (Herpetic eye disease study) study and other recent studies have shown that 400 mg of oral acyclovir twice daily reduced the 1-year ocular HSV recurrence rate by approximately 45% (9)**.** Additionally, patients treated with oral antivirals for only 12 months showed higher rates of recurrence and shorter disease-free intervals as opposed to those treated longer than 12 months, suggesting a benefit of treatment with oral acyclovir beyond 1 year (14). Moreover, the addition of oral ascorbic acid in prophylactic treatment was associated with further reduced risk of herpes simplex keratitis recurrence (9).

Conclusion

Even though herpetic keratitis is a common disease some of its more complicated forms can still be challenging for diagnosis and treatment. Patients with a history of HSV keratitis should be educated about their relative risk of recurrence, acquainted with the signs and symptoms of recurrence, and informed that they should consult an ophthalmologist promptly if they experience warning signs or symptoms (11).

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