Case report

Atypical Herpes simplex keratitis (HSK) presenting as a perforated corneal ulcer with a large infiltrate in a contact lens wearer: multinucleated giant cells in the Giemsa smear offered a clue to the diagnosis

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Abstract

Purpose: To report a case of atypical herpes simplex keratitis initially diagnosed as bacterial keratitis, in a contact lens wearer.

Results: Case report of an 18-year-old woman using contact lenses who presented with pain, redness and gradual decrease in vision in the right eye. Examination revealed a paracentral large stromal infiltrate with a central 2-mm perforation. Corneal and conjunctival scrapings were collected for microbiological investigations. Corneal tissue was obtained following penetrating keratoplasty. Corneal scraping revealed no microorganisms. Giemsa stained smear showed multinucleated giant cells. Conjunctival, corneal scrapings and tissue were positive for herpes simplex virus - 1 (HSV) antigen. Corneal tissue was positive for HSV DNA by PCR.

Conclusions: Atypical HSV keratitis can occur in contact lens wearers. A simple investigation like Giemsa stain may offer a clue to the diagnosis.

Introduction

Herpes simplex keratitis (HSK) often presents either as dendritic or geographic ulcers [1]. Atypical presentations of HSK have been reported [1,2]. The diagnosis of this condition can pose difficulties if patients present at later stages of the disease, especially when associated with corneal perforation. We report here an unusual case of perforated corneal ulcer with a large infiltrate, caused by HSV-1 in a contact lens wearer, initially diagnosed as bacterial keratitis. A simple investigation such as microscopic examination of Giemsa stained corneal scraping provided a clue to the diagnosis.

Case Report

An eighteen-year-old female student presented to us with complaints of pain, redness and gradual decrease in vision in the right eye of 20 days duration. She was treated with 0.3% ciprofloxacin eye drops, by a local ophthalmologist. She had discontinued using the medication prior to presentation to us. She was not treated with ster-

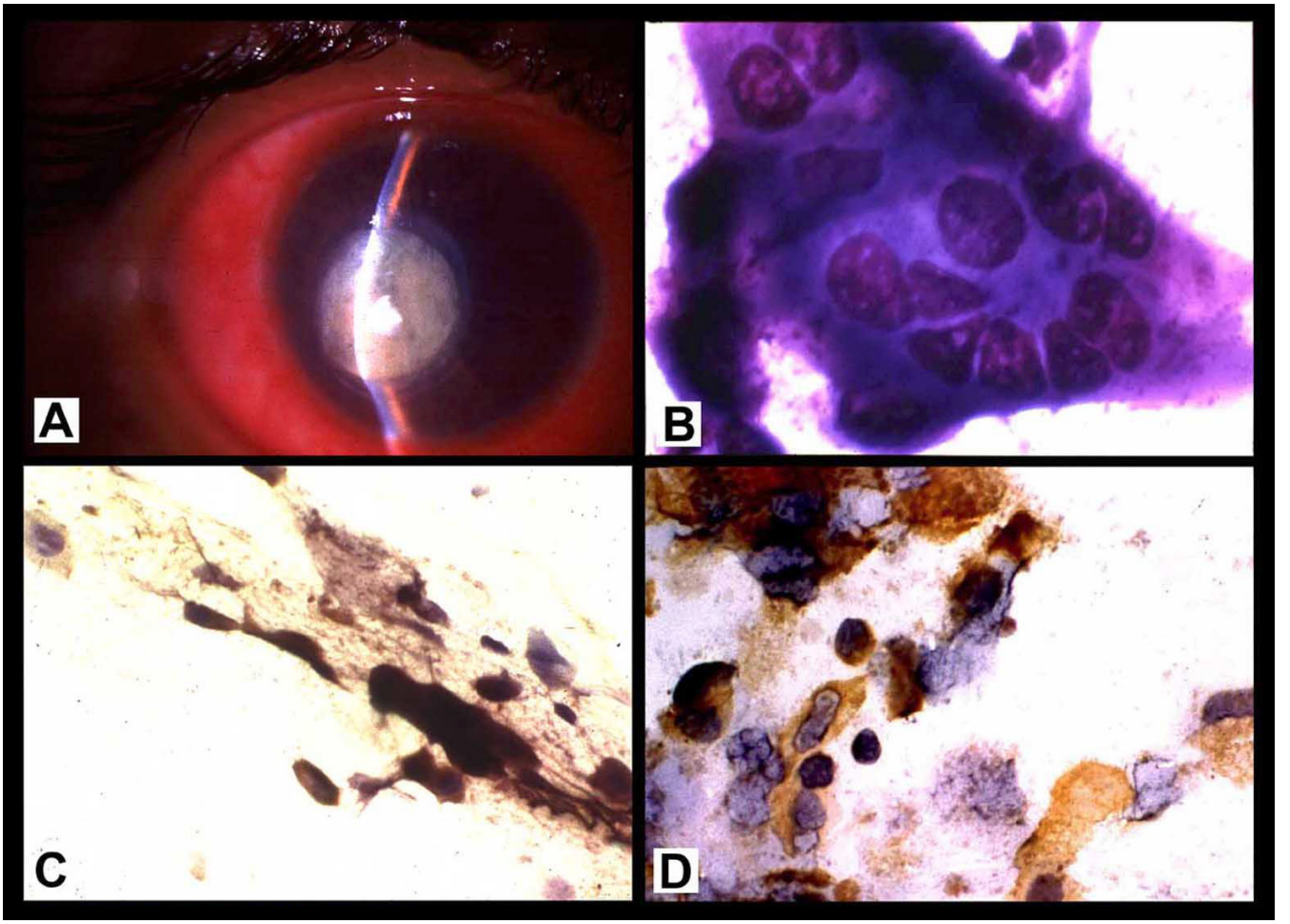

Figure 1
Clinical and virological investigations: **A**. Slit lamp biomicroscopy under optical section of the right eye showing a solitary paracentral, well circumscribed, large, full thickness stromal infiltrate, collapsed anterior chamber and a central area of perforation. X 16. **B**. Giemsa stained corneal scraping showing a multinucleated giant cell with characteristic molding of the nuclei. X 1250. **C**. Conjunctival scraping from lower palpebral conjunctiva showing epithelial cells positive for HSV-1 antigen (Indirect immunoperoxidase, X 500). **D**. Corneal scraping showing many cells positive for HSV-1 antigen (Indirect immunoperoxidase, X 500).

oids at any point of time. She was a myope using daily wear monthly disposable hydrogel contact lenses since eight months which she discontinued wearing with the onset of the present symptoms.

On examination, her visual acuity was restricted to perception of light and accurate projection of rays in the right eye and 20/20 in the left eye. Slit lamp examination of left eye was within normal limits. The right eye showed congestion of bulbar conjunctiva. Cornea showed a paracentral solitary, large, well circumscribed, full thickness, and yellowish white stromal infiltrate measuring 4.5 mm × 5.5 mm with a central 2-mm perforation. Anterior chamber was shallow (Fig. 1A).

Based on the history and clinical findings a clinical diagnosis of perforated corneal ulcer, probably of bacterial origin (*Pseudomonas* spp.) was made. Corneal scrapings were collected for microscopic examination, bacterial, fungal and acanthamoeba cultures as described elsewhere [3]. Contact lenses and the cleaning solution were also collected for microbiological investigations. Gram, Giemsa stained smears and the potassium hydroxide preparation of the scraping did not reveal any organisms. However, Giemsa stained smear showed the presence of multinucleated giant cells, with characteristic molding of nuclei (Fig. 1B), suggesting infectious keratitis, probably of a viral etiology. Scrapings obtained from the lower palpebral conjunctiva, on the following day (corneal scrapings could not be collected due to the application of

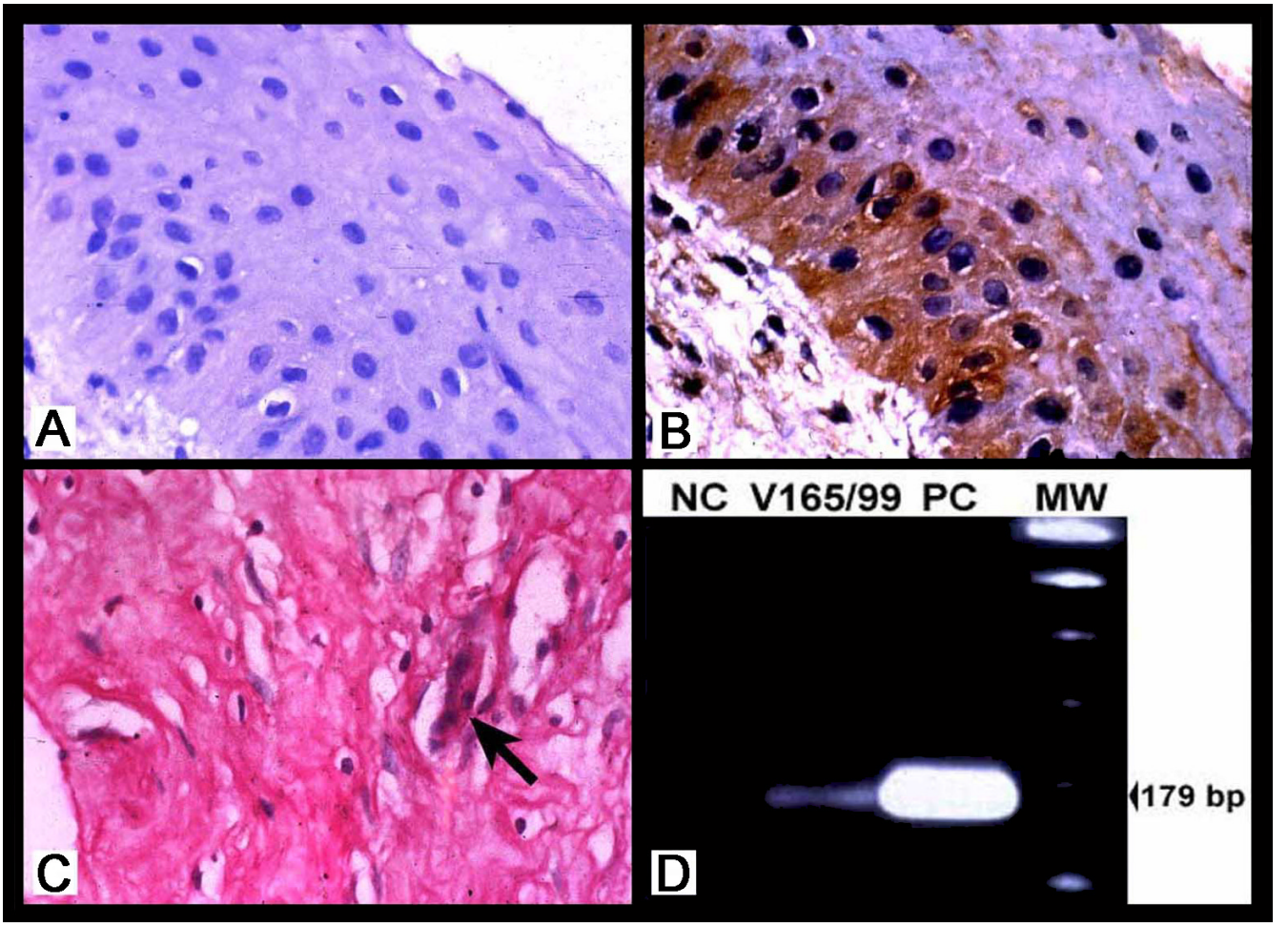

Figure 2
A. Corneal tissue section showing absence of HSV-1 antigen in the epithelium (Negative control, Immunohistochemistry, X 500). **B**. Corneal tissue section showing presence of HSV-1 antigen in the epithelium (Immunohistochemistry, X 500). **C**. Corneal tissue section showing a multinucleated giant cell (arrow) (PAS, X 500). **D**. Agarose gel electrophoresis stained with ethidium bromide showing PCR amplified products using primers for a 179 bp sequence of the DNA polymerase gene specific for HSV-1/2. Lane 1: Negative control (NC); Lane 2: Patient's corneal tissue (VI 65/99); Lane 3: Positive control (PC); Lane 4: Molecular weight markers (MW).

tissue adhesive and a bandage contact lens), was positive for HSV-1 antigen (Fig. 1C) by an immunoperoxidase assay. Patient was prescribed 3% acyclovir ointment application 5 times daily. None of the cultures yielded any growth.

She returned to the clinic after a week. On examination, the tissue adhesive and bandage contact lens were dislodged. Repeat corneal scrapings were obtained for microbiological investigations. HSV-1 antigen was detected by an immunoperoxidase assay (Fig. 1D) in the repeat corneal scrapings while bacterial and viral cultures (shell vial and conventional tube cultures for HSV-1) were negative.

Clinical condition did not improve during the subsequent week. Hence, the patient underwent a therapeutic penetrating keratoplasty (PK). Corneal tissue was obtained at PK. She received oral acyclovir 400 mg, 5 times a day and 1% prednisolone acetate eye drops, 6 times a day. Corneal tissue was positive for HSV-1 antigen by immunohistochemistry (Fig. 2A, B) and for HSV DNA by PCR (Fig. 2D). Histopathological examination of the formalin fixed corneal tissue revealed polymorpho nuclear neutrophils admixed with mononuclear cells, multinucleated giant cells in H & E and PAS (Fig. 2C) stained sections. Stromal melting was seen in the central cornea. The visual acuity improved to 20/20. There was no recurrence and the graft was clear (14 months post PK).

Discussion

Clinical diagnosis of atypical HSV keratitis can often be difficult. This case was diagnosed initially as bacterial keratitis considering the rapid progression of the symptoms and a history of contact lens wear. A simple stain like Giemsa revealed the presence of multinucleated giant cells in the corneal scraping. The presence of multinucleated giant cells with characteristic nuclear morphology (molding), may suggest a viral etiology. It may be seen in infections caused by HSV- 1, HSV-2 and VZV. However, this staining technique is not as sensitive as other methods like viral antigen detection, culture or rapid assays like HerpChek . Subsequent virological investigations confirmed the etiology (HSV-1) in this case. Virus cultures were negative probably because the specimens were collected following antiviral therapy.

We performed the PCR to confirm the presence of HSV DNA, since all viral cultures were negative. PCR for HSV has been shown to be most useful to the clinician in atypical presentations of herpetic ocular disease [1,4,5]. Predisposing factor for an atypical presentation as seen in this case could be due to the contact lens wear, for poor fitting lenses, poor lens hygiene and micro-trauma may all lead to the reactivation of herpetic keratitis.

It is interesting to note that it is very unusual for a herpes ulcer alone to present with a large yellowish-white infiltrate. Concurrent bacterial infection could have contributed to such a presentation. The possibility of a mixed infection (Bacterial: Herpetic infection) cannot be ruled out entirely in this case since the patient had received topical antibiotics elsewhere before presenting to us. The negative bacterial cultures may be attributed to this finding.

This case highlights the following: Atypical HSK can present as a perforated corneal ulcer associated with a large infiltrate. A "Low Tech" method like "Giemsa stain" of corneal scraping may offer a clue to the diagnosis. Nevertheless, other tests like viral antigen detection, culture or HerpChek should be done if HSV is specifically suspected. Conjunctival scrapings may be useful for the detection of viral antigen where corneal scrapings cannot be collected. PCR may be useful in the laboratory diagnosis of such an atypical presentation of HSK.

We believe that diagnosis of such cases would be beneficial in the prompt institution of prophylactic antivirals, especially following penetrating keratoplasty to prevent complications.

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