

Chronic hepatitis C virus infection is not associated with Mooren's ulcer

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CLINICAL STUDY

Abstract

Aim To investigate the association between chronic hepatitis C virus (HCV) infection and Mooren's ulcer.

Methods Eight patients from different parts of China who were diagnosed with Mooren's ulcer at the Zhongshan Ophthalmic Center, Guangzhou (China) were screened for chronic HCV infection. Mooren's ulcer was diagnosed by the typical ulcer morphology, detailed case history, physical examination, and comprehensive laboratory tests. All patients had serological screening for HCV infection.

Results Six male and two female patients were enrolled in the study. Their ages ranged from 31 to 65 years (mean 43.6 ± 13.7). None of them was reported to have any clinical evidence of chronic HCV infection before enrolment and all were negative for HCV serology.

Conclusion There was no association between chronic HCV infection and Mooren's ulcer in this limited case series study.

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Keywords: hepatitis C virus; Mooren's ulcer; cornea

Introduction

Mooren's ulcer is a chronic and painful corneal ulceration that typically begins in the peripheral cornea and usually progresses centrally or circumferentially. It is very difficult to manage and can cause blindness. The incidence of Mooren's ulcer in China has been reported to be 0.03%.¹ Our previous work described the clinical characteristics of patients with Mooren's corneal ulcer in China and demonstrated the effectiveness of treatment with lamellar keratoplasty plus 1% cyclosporine A eye drops.² The etiology of Mooren's ulcer remains unclear.

Autoimmunity may play an important part in its pathogenesis.^{3–5} Chronic hepatitis C virus (HCV) infection has been associated with Mooren's ulcer in some case reports,^{6–9} although other studies have not supported this observation.^{10–12} The objective of our study was to determine whether chronic HCV infection is associated with Mooren's ulcer in a series of eight patients.

Subjects and methods

Eight patients from different parts of China who had been treated for Mooren's ulcer at the Zhongshan Ophthalmic Center within the past 6 months were recruited to the study. The diagnosis of Mooren's ulcer had been established on the basis of typical ulcer morphology, detailed case history, physical examination, and comprehensive laboratory tests. All of the patients showed peripheral corneal ulceration without involvement of the sclera (Figure 1a). There was clear corneal ulceration with a prowling edge that began at the junction of the cornea and the sclera and progressed centrally and circumferentially. There were no clear or relatively normal corneal bands between the corneal ulceration and the corneal limbus (Figure 1b). None of the patients had arthralgia, chest pain, cough, erythema, or other systemic symptoms. Erythrocyte sedimentation rate, anti-streptolysin O and rheumatoid factor were checked to exclude peripheral corneal ulcers associated with rheumatoid arthritis (Figure 1c) or systemic lupus erythematosus. Antinuclear antibody tests were carried out and chest and nasopharyngeal X-rays taken to screen for Wegener's granulomatosis (Figure 1d).

Patients' blood samples were drawn into collection tubes with potassium ethylenediamine tetra-acetic acid and immediately transported to the clinical laboratory of Zhongshan Ophthalmic Center at Sun Yat-sen University, where serological tests

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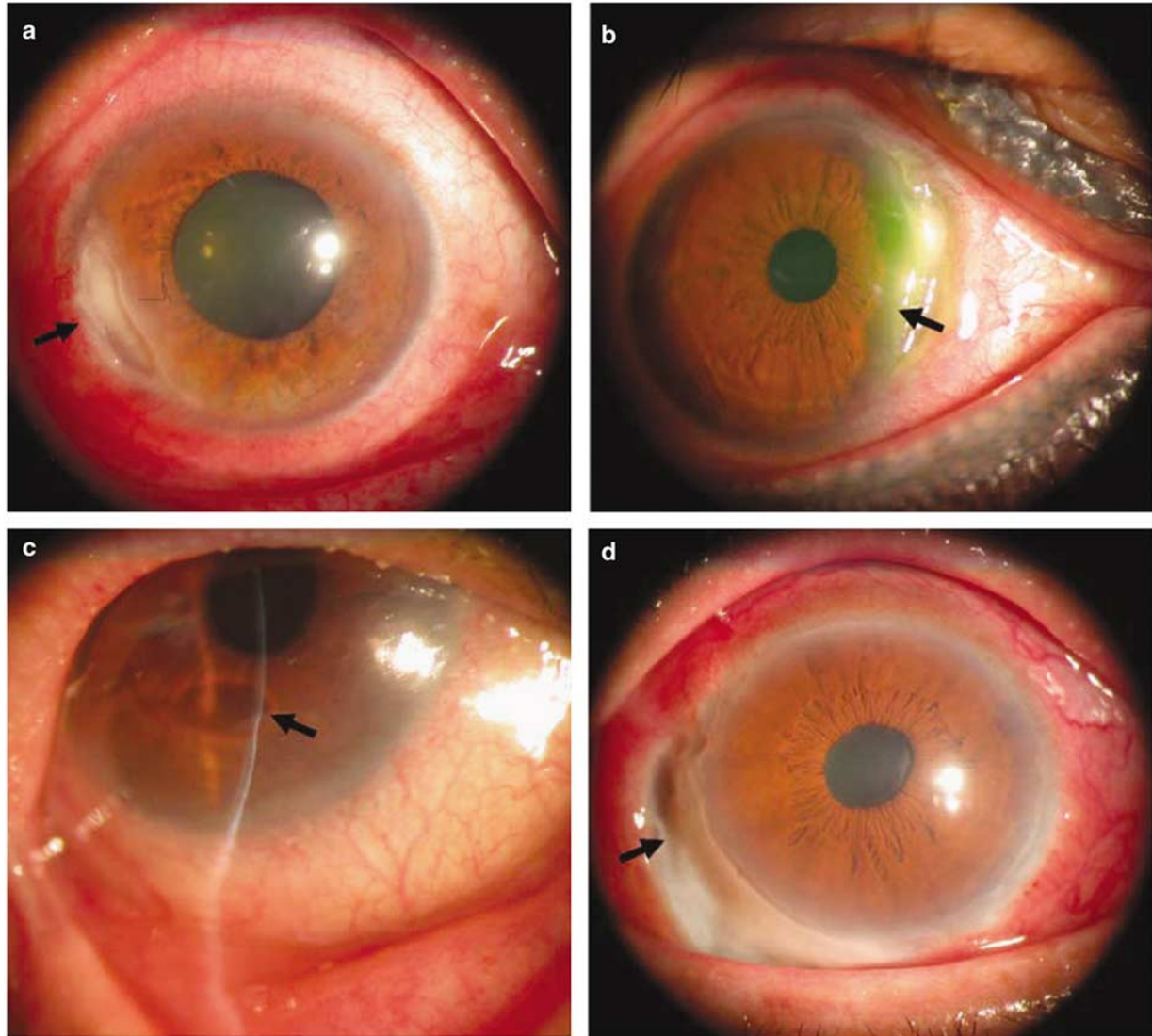


Figure 1 Mooren's ulcers. (a) Peripheral corneal ulceration in a study patient; there is no involvement of the sclera (arrow). (b) A clear corneal ulcer with a prowling edge in another study patient, showing the ulcer beginning at the conjunction of the cornea and the sclera (arrow). (c) A rheumatoid arthritis-associated peripheral corneal ulcer. The corneal ulceration is close to the central corneal area (arrow). There is a clear corneal area between the peripheral corneal ulceration and corneal limbus. (d) Peripheral ulceration in a patient with Wegener's granuloma involving the peripheral cornea and the sclera (arrow).

for HCV infection were carried out. A commercially available enzyme-linked immunosorbent assay (ELISA), the third-generation HCV ELISA test kit (InTec Products Inc., Xiamen, China), was used to quantify the specific immunoglobulin G (IgG antibody) to HCV. The specificity of this ELISA is 99.6% and its sensitivity is 81%.

Results

There were six male and two female patients. Their ages ranged from 31 to 65 years (mean 43.6 ± 13.7). Five patients came from southern China and three from

northern China. Peripheral corneal ulceration was unilateral in six patients and bilateral in two. None of the patients showed positive serum antibodies to HCV.

Discussion

Since its discovery in 1989, HCV has been recognized as a major cause of chronic liver disease. The World Health Organization estimates the global prevalence of HCV infection to be about 3%, affecting around 170 million people.¹³ Although HCV is endemic, its geographic distribution varies dramatically from east to west. The prevalence of HCV is relatively high in the United States

(1.8%),¹⁴ China (3.2%),¹⁵ and Indonesia (2.1%),¹⁶ but low in Germany (0.6%),¹⁷ France (1.1%),¹⁸ India (0.9%),¹⁹ and Brazil (1.1%).²⁰ The countries with the highest reported prevalence of HCV infection are mainly located in Africa and Asia. Pakistan has a prevalence ranging from 2.4 to 6.5%,^{21–24} whereas Egypt has the highest prevalence, at 22%.²⁵

An association between HCV and Mooren's ulcer was first suggested in 1993⁶ and five cases of Mooren's ulcer coexistent with chronic HCV infection were reported.^{6–9} In three of these cases the anti-HCV therapy, interferon, was used successfully to treat the Mooren's ulcer.^{7–9} Subsequently, it was reported that a patient with Mooren's ulcer and chronic HCV infection showed symptomatic improvement and alleviation of corneal ulceration when treated with a systemic steroid.²⁶ These observations led to the speculation that chronic HCV infection may have an important role in the pathogenesis of Mooren's ulcer.

However, other data appeared to contradict this suggestion. An investigation of three patients with Mooren's ulcer showed that only one had HCV infection,²⁷ and other authors pointed out that chronic HCV infection does not increase the prevalence of significant ocular disease in the United Kingdom.¹¹ A study carried out in India with a cohort of 50 patients who had chronic HCV infection found no evidence of Mooren's ulcer.¹² In another study in which 21 patients with Mooren's ulcer (one new and 20 recalled) were screened for evidence of chronic HCV infection, none showed positive chronic HCV infection by serology.¹⁰

The association of chronic HCV infection with Mooren's ulcer remains unproven. In the study with 21 patients cited above, 20 of the patients were diagnosed 12 months before enrolment. This retrospective design may have resulted in a selection bias in that the subjects were not typical of the hospital population with Mooren's ulcer. Moreover, some patients may have been excluded unintentionally owing to severe systemic illness, death, or failure/inability to return to the hospital. Screening for Mooren's ulcer in a large number of patients with chronic HCV infection may be necessary to determine whether there is an association between these conditions. However, studies are hampered by the relatively low rate of occurrence of Mooren's ulcer compared with that of chronic HCV infection.

Our study was a prospective investigation. Blood samples from the eight patients with Mooren's ulcer were collected and tested for HCV immediately following diagnosis. None of the patients was found to have serologic evidence of chronic HCV infection. This strongly suggests that there is no association between chronic HCV infection and Mooren's ulcer. As immune responses to HCV infection and to different strains of

HCV can vary greatly among different populations, further investigations should be considered.

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