Severe herpetic keratitis. I: Prevalence of visual impairment in a clinic population

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SUMMARY We report a prevalence study of the best visual acuity in the affected eye of 100 selected patients with herpetic keratitis seen during a two-year period. Sixty-two patients retained an acuity of 6/9 or better without requiring penetrating keratoplasty (PK). The prevalence of reduced visual acuity severe enough to warrant PK was 33%. Patients requiring PK for whom full clinical records were available suffered a mean of 6.8 episodes of keratitis. In this group of patients the vision of 18 fell from 6/6 to 6/60 over a mean period of 8.5 years. Once visual acuity was permanently reduced to 6/12, 78% of patients proceeded to lose vision to 6/60. Unilateral visual impairment occurs in at least a third of patients with severe herpetic keratitis. Once vision falls permanently to 6/12, the long-term prognosis for vision appears to be poor.

Bristol Eye Hospital provides ophthalmic care for the City of Bristol and surrounding areas, a population of approximately 863 000. The Corneal Clinic has been established for 14 years, and all cases of severe herpetic eye disease are referred here. However, it should be noted that simple epithelial disease which heals readily with little or no visual loss is not routinely seen in this clinic.

We have surveyed the population with herpetic keratitis seen in the Corneal Clinic and recorded the best corrected visual acuities (VA). When penetrating keratoplasty was required, best VA prior to PK was recorded.

We wished to know what proportion of patients with severe herpetic keratitis lost significant VA, and we tried to ascertain how rapidly such loss occurred. To record rate of loss of VA we arbitrarily chose 6/12 and 6/60, and noted the time for eyes with acuities of 6/6 to fall to these levels. These levels were chosen because, if they had represented best visual acuity in the best eye, they would have prevented the patient from driving or would have allowed them to be registered as partially sighted. Since official statistics do not include unilateral loss of sight, and since the

majority of herpetic eye disease is unilateral, such patients will not appear in these statistics.

In addition we have recorded the number of recurrences of herpetic keratitis associated with a reduction in VA severe enough to warrant PK.

Materials and methods

A computerised database of all patients seen in the Corneal Clinic was begun in August 1984. It was maintained on the University main-frame Multics computer with an XOX editor. Recorded data included all diagnoses and adequate information for retrieval of hospital notes. The database was augmented and updated on a weekly basis after each clinic, and thus patients were prospectively recruited into the database.

At the end of July 1985 the database was searched for all patients with herpetic keratitis. One hundred and four patients were identified. Case notes could be located for 100 of them, and these formed the study group. The group included new patients with active keratitis during the period August 1984 to end of July 1986, old patients with recurrent keratitis, old patients with quiescent disease attending for review, pre- and postoperative patients, and those seen some time after penetrating keratoplasty.

The characteristics recorded for each patient

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Table 1 Patient characteristics recorded

<i>All patients</i>	
Sex	
Age first seen with herpetic keratitis	
History of previous attacks	
Right or left or both eyes affected	
Disease when first seen	
<i>Subpopulation with vision reduced to at least 6/12</i>	
Sex	
Age first seen with herpetic keratitis	
Time from onset to vision of 6/12	
<i>Subpopulation with vision reduced to at least 6/60</i>	
Sex	
Age first seen with herpetic keratitis	
Time from onset to vision of 6/60	
<i>Subpopulation undergoing penetrating keratoplasty (PK)</i>	
Sex	
Visual acuity when listed	
Number of recurrences prior to listing for PK	
Age at time of PK	
Initial disease	
Number of outpatient visits and days as in patient during the year before and two years after PK	

included age at onset and at various times thereafter, sex, and whether PK was required for visual rehabilitation. A full list of characteristics is shown in Table 1.

Results

There were 51 male patients and 49 females. The mean age at onset was 38.6 years for the 68 patients who had not been treated elsewhere prior to being seen in Bristol. The left eye was involved in 62 patients and the right eye in 38 ($p>0.05$). Five patients had bilateral disease. The diagnosis of herpetic keratitis was clinical in all cases (100 patients), based on observation of a dendritic or geographical ulcer, or typical stromal disease.

The disease at presentation was epithelial (dendritic or geographical ulceration) in 41 patients, stromal in eight, and mixed in 51. At the time of the survey 62 patients had a VA of 6/9 or better after medical therapy. Five patients had acuities between 6/12 and 6/24. All 33 patients whose VA had fallen to 6/36 or worse had received a PK.

The presenting keratitis in those patients who required PK had been purely epithelial in 10 patients (30.3%), purely stromal in two patients (6.1%), and mixed stromal and epithelial in 21 patients (63.6%). Details on the number of recurrences of keratitis prior to PK were available for 20 patients (60%); these patients had a mean of 6.8 recorded recurrences (range 3–15) before requiring PK.

Of the 33 patients who required PK 11 had no recorded VA better than 6/60. These included

patients referred to Bristol from elsewhere. However, 18 patients had clinical histories which recorded visual impairment from 6/6 to at least 6/60. There were 11 male patients and 7 female. The mean age at onset of herpetic keratitis was 51.0 years for male patients and 42.1 years for females. The mean time taken for vision to fall from 6/6 to 6/60 was 8.5 years.

In addition to the 18 patients who lost vision from 6/6 to 6/60 a further five lost vision to between 6/12 and 6/36. We were therefore able to note the rate of visual loss to 6/12 in 23 patients. These patients lost vision from 6/6 to 6/12 in a mean of 4.8 years. Of the 23 patients who permanently lost vision to 6/12 18 progressed to 6/60 or worse (78%).

Discussion

Herpes simplex virus (HSV) causes disease not only when it first infects the eye, but also by producing recurrent disease (reviewed by Falcon¹). Recurrent disease is thought to occur when HSV, which has established latency in the trigeminal ganglion, is shed into corneal tissue via neural pathways. Recently latency (or persistence) of HSV in ocular tissue has been reported^{2,6} (Claoué *et al.*, in preparation), and clearly this may play a part in the genesis of severe recurrent disease and chronic stromal keratitis.

The pathogenic mechanisms whereby HSV produces stromal scarring and visual loss are not known. However, laboratory studies have suggested a role for T-cell mediated pathogenesis,⁷ and it is known that the cell population in corneal buttons removed for PK ‘à chaud’ contain a large proportion of cytotoxic T cells.^{8,9}

The incidence of herpetic keratitis is estimated to be five patients per 10 000 population per year,¹⁰ and 46% retain a visual acuity of 6/6 over a period of seven years.¹¹ Thus 54% had reduced vision and could be considered to have severe disease, including 17% whose vision fell to 6/18 or worse. While we do not have a precise figure for the total number of new patients with herpetic keratitis seen during the two-year period studied at this hospital (serving a population of 863 000), it is known that approximately 120 new patients with herpetic keratitis are seen per year.¹² This is less than that predicted from the experience of Norn.¹⁰

As in previous studies (reviewed by Tullo¹³) we find that the onset of disease is predominantly in the fifth decade of life. However, the male preponderance reported by other authors^{10 14–17} was not found. This could be due to a number of factors, including a reduced frequency of severe disease in males. A number of other authors have also failed to find an obvious male preponderance among patients with stromal disease^{18 19} or keratouveitis,^{20 21} and we

believe that our patients are similar to those seen elsewhere in the United Kingdom.

It is generally known that patients with herpetic keratitis may lose vision, though this particular aspect has not been extensively studied. There is no mention of the extent of visual loss in herpetic eye disease either in ophthalmic reference texts^{22,23} or in specialist texts on herpetic eye disease.²⁴ This is in part because of the problems of following up patients for the prolonged periods required to detect visual loss, a point first made by Thygeson *et al.*²⁵ in 1956. However, 17% of patients in one series had vision reduced to 6/18 or worse¹¹ and 23.4% of patients in another series lost vision to at least 6/12.²⁶ In a series of 15 patients with herpetic keratouveitis 40% had a visual acuity of 6/12 or worse.¹⁶ The prognosis for patients with disciform keratitis seems to be even worse, with 30% having visual acuities of 6/60 or worse at presentation, of whom the majority (67.5%) had the same or worse vision after treatment.¹⁹ These studies were performed by different methods from those reported here, and are also in genetically different populations. Thus it may be difficult to compare the results of other workers directly with our own.

Although we found that 33% of our patients developed visual acuities of 6/36 or worse, other patients in our study group may go on to develop visual impairment, and so this figure can represent only a minimum.

The majority of patients in this study presented originally with either purely epithelial disease or mixed epithelial and stromal disease (often a small infiltrate under an ulcer). Despite treatment many progressed to significant loss of vision. However, this treatment was not standardised, and it is possible that the latest penetrating antiviral drugs such as acyclovir may prevent progression to visual impairment or alter the recurrence rate.

Those patients who regained good vision after their initial episode were observed to lose vision to 6/12 in 4.8 years, and to 6/60 after 8.5 years despite treatment, though therapy was not identical for all the patients. The patients with loss of vision to 6/60 were on average older when first seen than the less severely affected group. It is known that stromal keratitis is commoner with increasing age.²⁷

The finding that 33% of patients with severe herpetic keratitis require PK stresses that visual loss is frequently severe. Since these patients regained good vision and did not require simultaneous or early cataract surgery, it is reasonable to attribute the visual loss exclusively to the keratitis. Moreover, since the visual loss is most often unilateral, official statistics of blindness will not show the incidence, as they are based on the best vision in the better eye.

The number of episodes of keratitis producing a degree of handicap requiring keratoplasty can be as little as 3, while the mean is only 7, stressing the need for optimal therapy each time a recurrence occurs. It is, however, worrying to note that 78% of patients who permanently lost vision to 6/12 later progressed to 6/60 or worse, suggesting that even quite mild degrees of visual loss in patients with herpetic keratitis should be considered as serious indicators of prognosis. Since this is not a closed study, the figure of 78% can be regarded as only a minimum. There is thus a clear need for optimal medical therapy for patients with severe herpetic keratitis.

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