

Aspects of corneal changes in onchocerciasis

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SUMMARY The distribution of living and dead microfilariae in 160 cases of ocular onchocerciasis has been studied. A model for coding the densities in 9 different areas of the cornea has been used. The average numbers of microfilariae and onchocercal punctate opacities per square millimetre were assessed. The highest densities were found in the superficial one-third of the corneal stroma at the periphery of the nasal and temporal parts of the cornea. Sclerosing keratitis was also recorded, and the average age of the patients in this group was significantly higher than in the group with non-sclerosing onchocercal involvement. Corneal thickness measurements showed that the presence of microfilariae or onchocercal punctate opacities or a faint uveitis did not influence the values. In sclerosed areas the corneal thickness varied greatly and was dependent on the degree of the vascularisation. The routes of entry of microfilariae into the eye are discussed on the basis of the distribution patterns of microfilariae and onchocercal opacities.

Invasion of microfilariae of *Onchocerca volvulus* into the eye causes lesions in both the anterior and the posterior segments. Dead and living microfilariae are readily recognised in the cornea with the slit lamp (Anderson and Fuglsang, 1973), and onchocercal opacities, which are the results of disintegrated microfilariae, are also easily seen. These opacities have been named 'snow-flake' or 'fluffy' opacities, or 'onchocercal punctate keratitis'. In advanced cases sclerosing keratitis is seen, varying from small areas adjacent to the limbus nasally and temporally to an involvement of the entire cornea. Optic atrophy, choroidoretinal lesions, iritis, complicating cataract, or secondary glaucoma are other important causes of visual impairment in ocular onchocerciasis. The corneal changes are mostly found in the interpalpebral part, but a detailed study of the distribution of microfilariae and onchocercal opacities in the cornea is lacking. The route of entry into the eye and the cornea is still a controversial problem.

The purpose of the present paper is to describe the distribution pattern of microfilariae and their consecutive opacities in the cornea, and to report on corneal thickness measurements in eyes with and without signs of ocular onchocerciasis.

Material and methods

This study was done during an epidemiological field survey in Niger and Togo for the WHO Oncho-

cerciasis Control Programme in the Volta River basin area.

A total of 160 persons who had onchocerciasis with corneal involvement were included. The ophthalmological examination was done in a dark-room using a Haag-Streit 900 slit lamp with 16 and 25 times magnification in direct and reflected light. Ophthalmoscopy was done after dilatation of the pupil with tropicamide 1%. The Haag-Streit equipment for corneal thickness measurements was used in a sample of 324 persons as seen from Table 1.

Table 2 shows the distribution by age and sex of those with corneal lesions due to onchocerciasis.

The observations reported here refer to the right eye of each person.

The cornea was divided into 9 areas (Fig. 1). The numbers of living microfilariae (LMFC) and dead

Table 1 *The corneal thickness of the right eye of 236 persons with onchocercal ocular involvement and of 86 controls. MFAC: microfilariae in the anterior chamber. OPO: onchocercal punctate opacities. SK: sclerosing keratitis. MF: microfilariae, living or dead. n: number of eyes. \bar{x} : mean value. SD: standard deviation. SEM: standard error of the mean*

	MFAC \pm iritis		Mf \leq 5	Mf $>$ 5	OPO \leq 5	OPO $>$ 5	SK	Controls
n	27	52	48	45	44	20	86	
\bar{x}	0.576	0.570	0.561	0.557	0.555	0.581	0.561	
SD	0.040	0.042	0.046	0.038	0.037	0.061	0.038	
SEM	0.008	0.006	0.007	0.006	0.006	0.014	0.004	

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Table 2 *Distribution by sex and age of 160 persons with corneal involvement of onchocerciasis*

Age	Males	Females	Total
0-9	14	3	17
10-19	28	16	44
20-29	16	18	34
30-39	17	16	33
40-49	10	4	14
≥50	16	2	18
Total	101	59	160

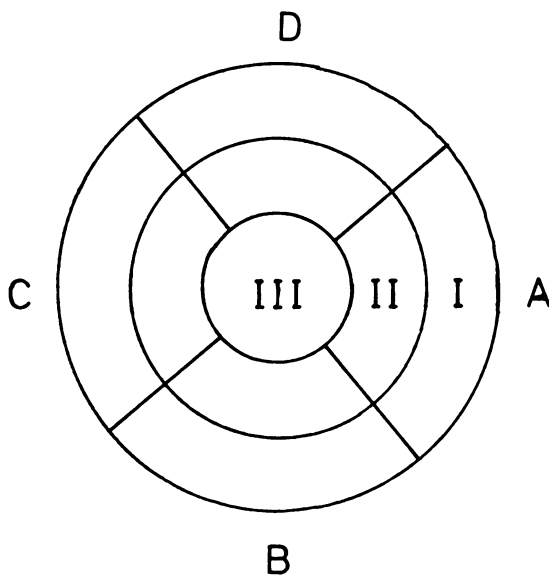


Fig. 1 *The corneae were divided into 4 quadrants by diameters through 45° and 135° from the 12 o'clock position and by circles into a peripheral, intermediate, and central zones, altogether 9 areas. The densities of living and dead microfilariae and of onchocercal punctate opacities were calculated as the average numbers per square millimetre of the 9 different areas among the 160 cases with onchocercal corneal involvement*

microfilariae (DMFC) and of onchocercal punctate opacities (OPO) were counted and plotted for each area. The average densities for each of these elements in the 9 areas were calculated as the average number per square millimetre, with the approximation that the cornea had an average diameter of 11.5 mm and was flat. The orientation of the straightened DMFC was also recorded. Sclerosing keratitis (SK) was recorded as grade I when present in the nasal and/or the temporal quadrant, grade II when a

continuous band along the lower part of the limbus was present, and grade III when the pupillary area or even the entire cornea was involved.

Observations

Microfilariae and onchocercal punctate opacities.—The LMFC were transparent and curled and were sometimes seen to move. The DMFC were straightened and most often less transparent. They had a fairly typical orientation in the nasal and the temporal quadrants, where they lay vertical, or parallel to the limbus. In the upper and lower quadrants, where they were relatively fewer, this orientation was not so typical. Some of the DMFC were surrounded by opacification of varying degrees, obviously starting from the ends. The disintegration was assumed to be the precursor to the onchocercal punctate opacities (OPO). These were greyish, with a diameter of 0.5 to 1.5 mm, and had diffuse demarcations. There were only faint signs of inflammation caused by these elements, without conjunctival and ciliary hyperaemia. They were found in all layers of the stroma, but most frequently in the superficial one-third. The epithelium was intact and in no case were elevations of the surface corresponding to the microfilariae or the OPO observed. There was no sign of neovascularisation or cellular infiltration.

Sclerosing keratitis.—This was present in 30 individuals, 19 of grade I, 9 of grade II, and 2 of grade III. Grade I was confined to the peripheral zone of the nasal and the temporal quadrants except for 4 cases in which the changes extended into the lower quadrant. The average age of those with sclerosing keratitis was 41.2 years, whereas those without had an average age of 24.6 years; 26 were males and 4 were females.

The densities of LMFC, DMFC, and OPO are given in Table 3 and in Fig. 2a, b and c. The highest densities were found in the peripheral zones of the nasal and temporal quadrants. However, considerable numbers of microfilariae had traversed the corneal stroma even to the central zone. In the central zone the OPO was the element which had the highest density.

The corneal thickness given in Table 1 refers to the central zone of the cornea. In this sample there was no significant difference between the groups with LMFC and DMFC, OPO, uveitis with and without microfilariae in the anterior chamber, and the control group. In cases with sclerosing keratitis the thickness of the corneae outside the sclerosed parts was normal. In the sclerosed areas of the corneae the thickness varied, but mostly it was greater than normal, the thickness apparently

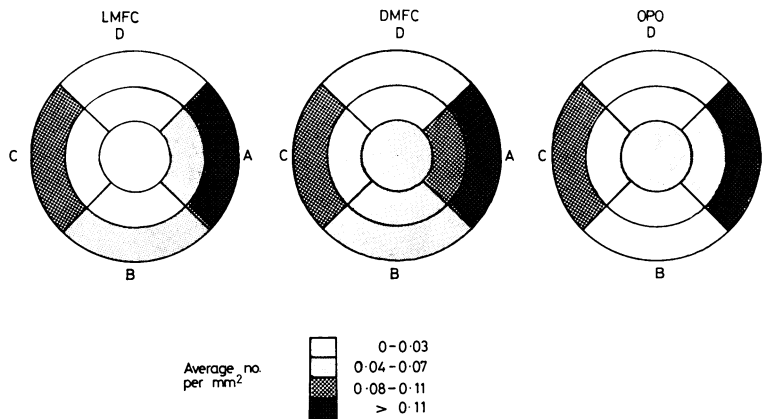


Fig. 2 The distribution pattern of living (LMFC) and dead (DMFC) microfilariae of *Onchocerca volvulus* and onchocercal punctate opacities (OPO) in the right cornea of 160 persons with onchocercal corneal involvement. The densities are the mean values per square millimetre in each area

increasing with the degree of vascularisation. However, the measuring technique is unreliable when used in the diseased periphery.

Discussion

In the present material living and dead microfilariae and onchocercal punctate opacities had the highest densities in the periphery of the nasal and the temporal quadrants. But even in the central zone of the cornea considerable numbers of these elements were present.

The stroma of the cornea is very dense, although there is a permeability difference between the periphery and the thinner central area (Tønjum, 1977). Thus IgM is normally prevented from

reaching the central area. However, the microfilariae can traverse this tissue, and in this context it may be noted that they seem to prefer to move in the corium of the skin. From a mechanical point of view migration in the looser subcutis would seem to be easier. Their choice of these particular routes may be due to the production of enzymes digesting the mucopolysaccharides and/or the collagen fibrils of the fibrous tissues, this process facilitating migration over relatively long distances.

The route of entry of the microfilariae to the eye is at present controversial. Migration of microfilariae from the skin along the subconjunctival tissue seems to be the most widely accepted theory. Blood-borne invasion has been suggested by Fuglsang and Anderson (1974). Furthermore, passage of microfilariae from the subconjunctival or periocular tissues along the sheaths of the ciliary nerves and vessels to the intraocular tissues is possible, as pointed out by Neumann and Gunders (1973). Migration from a nodule in or near the orbit, as suggested by Duke (1976) may influence the distribution of microfilariae in the ocular tissues.

We are inclined to accept the skin as the most likely route of entry. The shortest distance from the skin to the eye is from the nasal and the temporal interpalpebral angles. Furthermore, on the nasal and the temporal side there are strong fibrous ligaments of the orbital septum, and there are check ligaments attached to the tendons of the rectus muscles of the eye. Migration along these fibrous tissues seems to provide the most reasonable explanation of the distribution pattern of microfilariae and of OPO in the cornea.

Migration probably takes place in a similar way in the sclera as in the cornea. In histological sections Paul and Zimmerman (1970) found many microfilariae in the sclera. This path of migration would also explain the distribution of the posterior segment

Table 3 The densities per square millimetre of living (LMFC) and dead (DMFC) microfilariae and onchocercal punctate opacities (OPO) in 9 different areas of the right cornea of 160 persons with onchocercal corneal involvement. A: nasal quadrant. B: lower quadrant. C: temporal quadrant. D: upper quadrant. I: peripheral zone. II: intermediate zone. III: central zone

	LMFC	DMFC	OPO
A	0.14	0.16	0.14
B	0.04	0.07	0.03
C	0.08	0.11	0.11
D	0.03	0.06	0.02
I			
A	0.04	0.10	0.07
B	0.01	0.04	0.02
C	0.03	0.06	0.05
D	0.00	0.02	0.02
II			
A	0.01	0.05	0.06
B			
C			
D			
III			
A			
B			
C			
D			

lesions occurring in onchocerciasis, which will be discussed in another paper (Thylefors and Tønjum, in press).

The LMFC, DMFC, and OPO had grossly similar distribution patterns. The OPO had, however, a relatively high density in the central zone. The thinner central area of the corneal stroma, which is less permeable to large molecules than the periphery, had a relatively high density of OPO, which might be due to a slower disappearance of the remains of the disintegrated microfilariae from this part.

There was a considerable difference in the average age of the group with sclerosing keratitis and the group with non-sclerosing onchocercal involvement, 41.2 years and 24.6 years, respectively. This may indicate that sclerosing keratitis is due to corneal disease of long duration (Budden, 1957; Anderson and Fuglsang, 1973).

The corneal thickness was not influenced by the presence of microfilariae or of OPO. Neither was there any alteration in the eyes with uveitis. The

aqueous flare was most often faint, and the uveitis did not seem to interfere with transport of ions and water across the corneal endothelium.

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