Further observations on the relationship between ocular onchocerciasis and the head nodule, and on the possible benefit of nodulectomy

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SUMMARY From the examination of 197 patients who presented with one or more head nodules in the Sudan savanna in Cameroon, and from previous examinations of patients with ocular onchocerciasis, it is concluded that in this part of Africa the formation of a head nodule is often preceded by the development of ocular lesions. Head nodulectomy is therefore of limited prophylactic value.

Head nodules were removed from 107 of these patients, of whom 17 also received diethyl-carbamazine citrate (DEC), and 20 received both DEC and suramin. Fifteen other patients received DEC as the only treatment, and 4 suramin alone, while 5 received both DEC and suramin. From the follow-up examinations at 9, 12, and 24 months after treatment it was concluded that removal of the head nodule was of some benefit to lesions of the anterior segment, but that the procedure should be combined with efficient micro- and macrofilaricidal therapy in patients at risk of developing ocular pathology, that is, those with 15 or more microfilariae per skin snip near the outer canthus. This index can be measured by paramedical personnel and is therefore of great public health importance in the early detection of 'at risk' patients.

In a previous paper (Fuglsang *et al.*, 1976) we reported a prevalence of head nodules of 5.5 and 5.0% in villages with hyperendemic onchocerciasis in rain forest and savanna areas of Cameroon respectively, and we demonstrated a strong association between the presence of these nodules and lesions of both the anterior and posterior segments of the eye. The relative risk of having an eye lesion in patients with head nodules compared with those without was 2.9 in the rain forest and 7.5 in the savanna. Furthermore, in a group of 483 clinic patients with ocular onchocerciasis in the savanna palpable head nodules were detected in 23.6%, and in another 140 selected patients with posterior segment ocular lesions head nodules were detected in 31.4%.

We have also shown (Anderson *et al.*, 1975) that the presence of a head nodule was associated with a high concentration of microfilariae in the skin near the eye, and this in turn with a high microfilarial invasion of the cornea and anterior chamber of the eye.

Since 1933 removal of head nodules at yearly intervals has been the major intervention in the attempt to control blindness due to onchocerciasis in Guatemala. Diaz (1957) reported that the blindness rate fell from 5 per 1000 inhabitants to 1 per 1000 between 1935 and 1945. These nodulectomy campaigns were soon extended to include removal of body nodules as well (Aguilar and Bernhard, 1967). These procedures have not reduced the prevalence of onchocerciasis in Guatemala (Figueroa-Marroquin and Guilliolli, 1971), but it is claimed that blindness has decreased as a result (Figueroa-Marroquin, 1974).

In Guatemala as many as 70% of nodules are found on the head (Diaz, 1957; Lagrault *et al.*, 1964; Brandling-Bennett *et al.*, in preparation). Tada *et al.* (1977) have shown that in some villages in Guatemala 'the nodule rate was somewhat higher than the microfilarial rate, especially in children'. This indicates that the nodule is a much earlier manifestation of onchocerciasis in Guatemala than in Africa. Apart from raising important questions concerning the immunopathological processes behind encapsulation of the adult parasite, these geographical differences suggest that removal of head nodules

would be expected to give better results in the control of ocular lesions due to onchocerciasis in Guatemala than in Africa.

In Guatemala, in a survey of 1025 people, we also found that all persons with onchocercal eye lesions and blindness either had or gave a history of a palpable head nodule (Brandling-Bennett *et al.*, in preparation). By contrast, in Cameroon only 25% of patients with onchocercal eye lesions had a palpable head nodule (Fuglsang *et al.*, 1976). They were seen in only 4 of 44 patients blinded by onchocerciasis in the Cameroon savanna and in none of the corresponding 16 patients in the rain forest (Anderson *et al.*, 1974). In sequential observations on untreated persons in Cameroon (unpublished data) 3 of 9 patients with high concentrations of microfilariae near the outer canthus and onchocercal eye lesions first developed a palpable head nodule after 3 years of observations.

From the preceding paragraph it can be deduced that the removal of head nodules in Cameroon would be of limited prophylactic value, as it would prevent neither the development of eye lesions nor blindness due to onchocerciasis. However, the question of the curative value of head nodulectomy in Africa remained unanswered.

The present paper first analyses results from the examination of 197 patients with 1 or more head nodules. It gives the nodule distribution on the head and comments on the diagnostic problems and the association with microfilarial load and ocular disease. It also describes the effects of head nodulectomy as the only treatment in 70 of these patients, of head nodulectomy combined with the microfilaricide diethylcarbamazine (DEC) in 17, and combined with the macrofilaricide suramin in 20 others. The effects of treatment were measured by the concentration of microfilariae in the skin near the eye, as well as in the cornea and anterior chamber, and on changes in clinical ocular disease. A comparison was made with a group of 15 similar patients who received DEC as the only treatment and another group of 9 who received suramin.

I. The head nodule and ocular onchocerciasis

MATERIALS AND METHODS

The 197 patients all came from the area near Touboro, a Sudan savanna village in north Cameroon. Either they had been encouraged to come to our field clinic because they were found to have a head nodule during our village and school surveys, or they came spontaneously with or without eye lesions, some unaware of the presence of a head nodule, others having heard about its possible danger to the eye. The methods used in the examinations

of the patients were the same as those described by Anderson and Fuglsang (1978).

RESULTS AND COMMENTS

In the majority of the patients (47%) the nodules lay over the temporal bone. In 14% they were situated in the groove behind the pinna of the ear, sometimes so deep as to be almost impalpable, while in 2% they lay below the mastoid process hidden deep to or in the sternomastoid fibres. The nodules were parieto-occipital in position in 29% and frontal in the remaining 24%.

Postauricular and occipital lymph nodes were often enlarged in these heavily infected patients, and in a few cases it was impossible to distinguish them from nodules by palpation alone. Small lipomas and cysts gave rise to similar diagnostic difficulties.

Fig. 1 shows the age and sex distribution of the 197 patients with head nodules, 139 males and 58 females. The highest proportion of both males and females with head nodules was between 10 and 19 years of age; 112 of the 139 males (81%) had 15 or more microfilariae per snip near the outer canthus, while only 33 of the 58 females (57%) fell in the same group.

An overall 77% of the 112 males and 82% of the 33 females with 15 or more microfilariae near the

Fig. 1 Above: age and sex distribution of the 197 patients presenting with head nodule(s). The dark areas indicate the percentage with 15 or more microfilariae in a skin snip near the outer canthus. Below: age and sex distribution of the population of 8 villages in the Touboro area

eye already had an eye lesion, and this percentage was high from the age of 10. In the 5 to 9 year age group only 36% and 43% of boys and girls respectively had eye lesions, and it is especially in these young patients that head nodulectomy might be of prophylactic value, as well as being easy to arrange. Lesions of the anterior segment alone (sclerosing keratitis and iritis) were commoner than lesions of the posterior segment alone (choroidoretinitis and optic atrophy), and more so in the males (29% anterior, and 10% posterior) than in the females (39% anterior, 27% posterior). Combined anterior and posterior segment lesions were commoner in males (38%) than females (15%).

Only 30% of the 27 males and 20% of the 25 females with less than 15 microfilariae in the skin near the eye showed eye lesions, and these lesions were not present in children under the age of 10. There were no marked differences in prevalence between lesions of the anterior and posterior segment, and combined lesions were seen in 15 and 8% of males and females respectively. These less heavily infected patients consisted mainly of children (Fig. 1), in whom the nodules often had a thick capsule and usually showed obvious signs of degeneration of the worm when they were cut open.

Six of the 197 patients were known to suffer from epilepsy, a condition which has been associated with onchocerciasis.

II. Effects of head nodulectomy, DEC, and suramin treatment, alone and in different combinations

MATERIALS AND METHODS

The study was carried out between 1972 and 1977 during field visits to the Touboro area. For practical reasons it was not possible to allocate the patients randomly to the different groups, which were as follows:

- Group A: 45 patients—removal of head nodules.*
- Group B: 25 patients—removal of head nodules.*
- Group C: 17 patients—removal of head nodules + DEC.
- Group D: 20 patients—removal of head nodules + DEC + suramin.
- Group E: 15 patients—DEC alone.
- Group F: 4 patients—suramin alone.
- Group G: 5 patients—DEC and suramin.

* The patients in group A all had 15 or more microfilariae per snip near the eye, while those in group B all had less than 15, as had 1 in D, 2 in E, and 1 in F.

The methods used in the examinations of the patients before and after treatment were the same as those already referred to, and the same paper describes the DEC and suramin course.

RESULTS

Despite the lack of random allocation there was

little or no difference between the groups with respect to ocular disease and microfilarial concentration in the skin and eye, group B excepted as stated above.

Microfilariae in the skin. Table 1 shows the mean concentration of microfilariae in the skin near the eye before treatment, and changes following treatment in groups A–G. It is obvious that the removal of the head nodule had little influence on this concentration. The additional course of DEC (group C) lowered the concentration considerably, and maintained it at 26% of the original value even after 24 months. A DEC course without nodulectomy (group E) also kept the skin concentration near the eye under 50% of its original value for 24 months. However, the corresponding value in the patients who received suramin (groups D, F, and G) was near zero at 24 months.

Microfilariae in the cornea. Table 2 shows the number of patients with reduced, unchanged, and increased numbers of microfilariae in the cornea at 12 and 24 months after treatment. In groups A and B (nodulectomy alone) a reduction was commoner than an increase, but about a third continued to show the same number. The additional DEC course (C) reduced the numbers considerably, while the course of DEC without nodulectomy (E) was less effective than nodulectomy alone. Again the largest reduction was seen in the patients who received suramin, many of whom became free of corneal microfilariae.

Microfilariae in the anterior chamber. Table 2 also gives the number of patients with reduced, unchanged, and increased numbers of microfilariae in the anterior chamber at 12 and 24 months.

Table 1 *The mean number of microfilariae per skin snip near the outer canthus before treatment, and at 9, 12, and 24 months after treatment (expressed as a percentage of the pretreatment value). The numbers in parentheses indicate the number of persons seen at each examination*

Group	Before treatment	After treatment		
		9 months	12 months	24 months
A (N)	70 (45)	67 (14)	110 (28)	91 (22)
B (N)	5 (25)	100 (10)	125 (14)	71 (17)
C (N+D)	88 (17)	13 (12)	18 (8)	26 (5)
D (N+D+S)	119 (20)	5 (8)	9 (11)	2 (11)
E (D)	78 (15)	30 (4)	29 (13)	46 (11)
F (S)	84 (9)	20 (44)	5 (7)	1 (9)
G (D+S)				

(N) = nodulectomy (head nodules only). (D) = DEC course. (S) = suramin course.

Table 2 Number of persons showing decreased, unchanged, or increased concentrations of microfilariae in the cornea and anterior chamber at 12 and 24 months after treatment

Group	Microfilarial concentration in the cornea						Microfilarial concentration in the anterior chamber					
	12 months			24 months			12 months			24 months		
	Decreased	Unchanged	Increased	Decreased	Unchanged	Increased	Decreased	Unchanged	Increased	Decreased	Unchanged	Increased
A (N)	18	7	3	14	5	3	4	15	9	8	7	7
B (N)	7	5	2	9	7	1	6	7	1	6	11	0
C (N+D)	8	0	0	4	1	0	6	2	0	2	1	2
D (N+D+S)	10	0	1	11	0	0	10	0	1	10	1	0
E (D)	6	5	2	4	3	4	4	6	3	4	1	6
F (S)	7	0	0	9	0	0	5	2	0	6	2	0
G (D+S)												

(N) = nodulectomy (head nodules only). (D) = DEC course. (S) = suramin course

Table 3 Number of patients with anterior and posterior segment lesions which became better or worse or remained unchanged after treatment. New lesions = Number of patients with new lesions/number of patients at risk

Group	Anterior segment lesions				Posterior segment lesions			
	Better	Same	Worse	New lesions	Better	Same	Worse	New lesions
A (N)	5	13	7	1/20	0	9	10	1/26
B (N)	1	2	1	1/21	0	5	1	0/19
C (N+D)	6	5	0	0/6	0	5	4	0/8
D (N+D+S)	7	7	1	0/5	0	7	2	0/11
E (D)	3	5	4	1/3	0	0	3	0/12
F (S)	6	1	0	0/2	0	1	5	0/3
G (D+S)								

(N) = nodulectomy (head nodules only). (D) = DEC course. (S) = suramin course

In groups *A* and *B* the majority remained unchanged, though at 24 months a reduction was slightly commoner than an increase. Nodulectomy combined with DEC (*C*) caused a bigger reduction at 12 months but showed no additional effect at 24 months. Again a single DEC course (*E*) was less effective than nodulectomy alone (*A* and *B*), and the greatest reduction was obtained in patients who received suramin.

Lesions of the anterior segment of the eye. Table 3 shows the improvement or deterioration that occurred in lesions of the anterior segment at 12 and 24 months. In groups *A* and *B* combined the majority of lesions remained unchanged, 6/29 (21%) improved, while 8/29 (28%), all cases of iritis, deteriorated. Furthermore, 2 patients developed iritis *de novo*. The additional DEC course (*C*) was beneficial to the majority of lesions, DEC alone (*E*) was of doubtful benefit, and the best results were seen in patients who received suramin (*D*, *F*, and *G*).

Lesions of the posterior segment of the eye (Table 3).

No posterior segment lesion improved in any group, and these lesions deteriorated in some patients in all groups. In groups *A* and *B* combined, and also in groups *C* and *D*, lesions which remained unchanged just outweighed those which deteriorated, but the opposite was the case in groups *E*, *F*, and *G*.

Central visual acuity. The number of eyes that showed changes of 2 or more lines on the E chart was as follows:

Group	A	B	C	D	E	F+G
Improvement	4	4	3	7	5	1
Deterioration	7	0	6	6	6	5

Discussion

Is it of curative value to remove the head nodule? The reduction of the concentration of microfilariae in the skin near the eye was questionable, and it is doubtful if it would have been more marked even if all the nodules on the rest of the body had been

removed as well. We have performed total nodulectomies in a group of 13 other patients from the same area (unpublished data). The overall concentration of microfilariae in the skin, expressed as an average of the mean microfilarial density at the outer canthus, shoulder, buttock, and calf fell to 63 and 68% at 12 and 24 months respectively, and to 71% (from 14 to 10 microfilariae per milligramme) near the eye at the corresponding examinations. Had all the adult worms been eliminated in the process, a reduction to less than 10% would have been expected at 24 months due to the natural death of the microfilariae (Duke, 1968).

Although the reduction of microfilariae in the cornea and the anterior chamber was less questionable than in the skin, it was not nearly as marked as that produced in the patients who received an additional course of suramin, which is known to be an effective macrofilaricidal drug. These facts strongly suggest that in most patients only a small proportion of the fertile worms can be located in palpable nodules. Their location is obscure; some might even find their way inside the skull, thus explaining the possible association between epilepsy and onchocerciasis.

Some lesions of the anterior segment of the eye, particularly sclerosing keratitis, did improve after removal of the head nodule, but the results were better when DEC and/or suramin were given as well. Removal of head nodules is therefore far from sufficient as a curative measure in ocular onchocerciasis.

However, owing to the seriousness of this condition with its high risk of blindness and the unsatisfactory nature of existing chemotherapy (Anderson and Fuglsang, 1977) all measures with any beneficial effect should be employed in suitable combinations. Although chemotherapy with suramin or suramin and DEC gave best responses in the small numbers of cases followed (Tables 1–3), there was consistently less rebound of microfilarial invasion of skin (Table 1), cornea, and anterior chamber (Table 2) after withdrawal of DEC therapy if in addition head nodules were excised. In conformity with this finding anterior segment onchocercal eye lesions appeared to do best when DEC or DEC and suramin therapy was combined with nodulectomy (Table 3). Posterior segment lesions tended strongly to worsen. Although this tendency appeared to be reduced by nodulectomy, the numbers observed were too small to allow definite conclusions.

In Cameroon the presence of head nodules is very often too late an indicator of a high concentration of microfilariae around the eye, a concentration which could easily have been measured much earlier by paramedical personnel (Fuglsang and Anderson,

1977). Only in this way can the majority of patients at risk of developing ocular lesions be found in time for proper micro- and macrofilaricidal treatment.

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