A PRELIMINARY STUDY OF FILARIASIS RELATED ACUTE ADENOLYMPHANGITIS WITH SPECIAL REFERENCE TO PRECIPITATING FACTORS AND TREATMENT MODALITIES

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Abstract. Episodic adenolymphangitis (ADL) is one of the important clinical manifestations of lymphatic filariasis. Recurrent ADLs contribute to the progress of the disease and also have important socioeconomic implications since they cause significant loss of man days. The present study was conducted in order to identify the precipitating factors responsible for ADL attacks and also to examine the different modalities of treatment. Sixty-five individuals with filariasis related ADL attacks, who are residents of Alleppey district (endemic for *Brugia malayi*) were studied. All efforts were taken to identify the precipitating factors for ADLs in these individuals. They were hospitalized for a period of five days or more. All of them received symptomatic antipyretic/antiinflammatory therapy and topical antibiotic/antifungal treatment of the affected limbs. They were then randomly allocated to one of the following four regimens: group I - symptomatic alone; group II - symptomatic plus antibiotics; group III - symptomatic followed by diethylcarbamazine citrate (DEC) and group IV - symptomatic plus antibiotic followed by DEC. Patients in groups III and IV received DEC every three months up to one year. There was a significant relationship between the number of ADL attacks and the grade of edema. Presence of focus of infection in the affected limb could be identified in 28 of the 65 patients. In the majority of patients (48) response to treatment was rapid (resolution in less than five days). Neither antibiotics nor DEC (given at intervals of three months) appeared to alter the frequency of ADL attacks. On the otherhand simple hygienic measures combined with good foot care and local antibiotic/antifungal cream application (where required), were effective in reducing the number of ADL attacks.

INTRODUCTION

Lymphatic filariasis is a major health problem in India with over 22 million microfilaria carriers, 16 million clinical cases of filariasis and 6 million cases of acute filarial disease per year. Adenolymphangitis (ADL) is the single most common event that brings a patient with lymphatic filariasi to the physician. It is a well recognized actue clinical manifestation of lymphatic filariasis. ADL attacks are characterized by pain, lymphadenitis and retrograde lymphangitis resulting in inflammation of the part of body affected (WHO, 1984). Attacks of ADL can recur at a variable rate per year for the given patient and recurrent episodes in the same limb hasten the progression of obstructive lymphatic disease culminating in elephantiasis (Pani *et al.*, 1990; Rajagopalan, 1990). They may be associated with cellulitis, abscess formation and rarely septicemia with serious consequences.

The etiology of ADL in lymphatic filariasis is unknown. There are at least two views regarding the causation of ADL. The first of these supposes ADL to be the result of a reaction to parasite products released either by the adult worm or by microfilariae (Chan *et al*, 1984; Ottesen, 1984; Partono, 1987). However, many workers believe that ADL is a consequence of secondary bacterial infection which occurs on the background of damaged lymphatics (Jamal and Pani, 1990; Rajagopalan, 1990).

The management of ADL in filariasis also has posed several problems. Conventionally these attacks have been treated with diethylcarbamazine (DEC) or antibiotics or a combination of both. These therapeutic choices reflect the belief of the individual physician as to the etiological basis of ADL. It is also recognised that simple measures of hygiene such as cleaning the affected part and protection from injuries by the use of foot wear greatly decrease the frequency of ADL attacks, although there have been no controlled clinical trials to confirm these observations.

The present study was designed to identify factors precipitating ADL attacks in patients with lymphatic filariasis and to compare the efficacy of various

treatment modalities in the management of these attacks.

PATIENTS AND METHODS

The study population consisted of 65 individuals (age range 13 - 69 years) who were residents of Shertallai Taluk of Alleppey District, Kerala, South India, an area endemic for *Brugia malayi*. They were admitted with a diagnosis of acute ADL associated with filariasis, in the Department of Medicine, TD Medical College Hospital, Alleppey during the period April 1991 to January 1993. The inclusion criteria for admission to this study are summarized in Table 1. All patients underwent a detailed clinical examination. Lymphoedema was graded according to Brunner's classification as Grade I, II or III (Jamal, 1988). Local examination of the affected part included search for any points of entry of infection as evidenced by discontinuity of skin due to either injury, fungal infection or other causes. Routine laboratory investigations such as complete hemogram, urinalyses and serum chemistry were carried out on all patients. Night blood examination for the presence of parasites was carried out using the membrane filtration method. In order to identify the involvement of bacterial or fungal agents, special investigations such as blood culture, pus culture (wherever available) and skin scrapings for fungi were carried out. All organisms isolated were characterized up to the species level and antibiograms were constructed. Indirect evidence of bacterial infection was also sought by measuring ASO titers in all cases.

Study design

All the 65 patients were initially hospitalized for a minimum period of five days. All patients received symptomatic therapy in the form of analgesics (Ibuprofen), antipyretics (Paracetamol) and antihistamines (Chlorpheniramine maleate). Topical application of antibiotic/antifungal creams was initiated wherever necessary. In addition, patients with grade II and grade III edema were advised to apply a pressure bandage on the affected limb, when they were ambulant.

Based on simple randomization, patients were allocated to one of four regimens. Group I symptomatic treatment only (as outlined above); group II symptomatic treatment along with antibiotics (Ampicillin, cotrimoxazole) for five days or more where required; group III symptomatic treatment followed by DEC (100 mg 3 times/day for 12 days repeated every three months for one year) and group IV symptomatic treatment along with antibiotics followed by DEC as above. Antibiotics were added or changed if there was clinical deterioration due to infection during the hospital phase.

After the hospitalization period patients were advised to report back to the clinic every three months and also whenever there was an ADL attack. They were also advised to continue foot care and where necessary topical applications of antibiotic/antifungal creams while at home. At each follow up examination, detailed investigations were carried out

Table 1

Criteria for inclusion into the study.

A. Definite criteria

Acute ADL-Episodes of brief duration characterized by pain, lymphadenopathy, retrograde lymphangitis and inflammation of part affected.

B. Additional criteria
- i) Presence of associated lymphoedema
- ii) Past history of recurrent attacks of ADL
- iii) First episode of ADL where no obvious precipitating cause is detected

Patients with A plus one or more of B alone were included.

to assess the size of the limb and the presence of any focus of infection.

RESULTS

There were 33 males and 32 females in the study. Thirty-three of the patients had grade I edema while 19 had grade II edema. The remaining 13 had grade III edema. Table 2 shows the relationship between the number of ADL attacks in the immediate past year before treatment and the grade of edema. Twelve of the 65 patients did not experience any ADL attacks in the past one year. Nearly one third of the patients (25/65) had one to two attacks in the previous year. It is seen that the number of attacks increased with the grade of edema, 12/13 individuals with grade III edema having more than three ADL attacks in the past year. From the same table it can be seen that a point of entry of infection could be identified in the majority of patients with grade III edema.

In all, a portal of entry of infection was identified in 28 patients (Table 2). In 12 of these patients, these were identified as due to minor injuries, while in others fungal infection (9) and miscellaneous skin disorders (7) such as pyoderma, eczema *etc* were the causes.

The relationship between elevated ASO titer (> 200 IU) and the grade of edema is also illustrated in Table 2. It is obvious that a significant proportion of patients with grade III edema had elevated levels of ASO titers. However ASO titers > 200 IU were found in only 40% of patients in whom a portal of entry for infection was detected. Only one patient had circulating microfilaria and *Streptococcus pyogenes* was isolated in one blood culture. In five cases where pus was cultured *Staphylococcus aureus* was identified in two of the specimens. Two patients developed subcutaneous nodules which were biopsied. In one a definitive diagnosis of parasitic granuloma was made, while the other showed only chronic inflammatory mass.

Table 3 illustrates the response to therapy in the hospitalization phase. For the purpose of this analysis patients were classified into two groups; group A (group II and IV, *ie* those who received antibiotics) and group B (group I and III, *ie* those who received only symptomatic therapy while in hospital). The majority of the patients responded to treatment rapidly (within five days) irrespective of the group to which they belonged.

Fifty patients were followed up for six months and only 35 could be followed up for one year. Fifteen

Table 2

Number of ADL attacks in the past year, presence of infection and ASO titer in relation to grade of edema.

Grade of edema	No. of ADL attacks in the immediate past year				Presence of infection	ASO > 200 IU
(n=65)	None (n=12)	1-2 (n=25)	3-4 (n=16)	> 5 (n=12)	(n=28)	(n=30)
I (33)	12	17	2	2	8	10 (30%)
II (19)	0	7	8	4	11	10 (52%)
III (13)	0	1	6	6	9	10 (77%)

Table 3

Response to antibiotics *vs* symptomatic treatment.

Response	A. Antibiotic group Group II and IV n=36	B. Symptomatic Group I and III n=29
Rapid < 5 days	25	23
Delayed > 5 days	11	6

Table 4

Recurrence of ADL in relation to treatment regimen at 6th month and one year follow up.

At 6 months follow up n=50	No. with recurrence n=14	Injury	Moniliasis
Group I (14)	5	1	3
Group II (12)	4	1	3
Group III (9)	4	1	2
Group IV (15)	1	1	0
At 1 year follow up n=35	n=8		
Group I (9)	2	1	2
Group II (8)	3	1	2
Group III (6)	2	1	-
Group IV (12)	1	1	-

patients were lost for follow up. Table 4 shows the pattern of recurrence of ADL attacks in the various treatment groups at six months and one year of follow up. At six months 14 patients had recurrence of ADL which was similar in the first three groups. In 12 of these patients a local source of infection could be demonstrated. An identical pattern was observed at one year also. Of the patients who had recurrence of ADL attacks roughly 1/3rd were receiving repeated doses of DEC.

DISCUSSION

Brugian filariasis is a major health problem in parts of Kerala State in India. This disease is endemic in Shertallai Taluk of Alleppey District. It imposes a significant burden on the socioeconomic front of the population. Acute ADLs occur at a frequency of 2 - 6 episodes per year and there is a higher incidence in the low socioeconomic class (Pani *et al*, 1989).

The present study has clearly shown that infections which gain entry through easily overlooked points in the affected limb, especially web spaces and soles of feet contribute significantly to the occurrence of ADL. Such a point of entry could be identified in 28 of 65 patients in the present study. It is important to note that these sites of infection were easily identifiable and treated. As in previous studies, the present study has also shown a relationship in the number of ADL attacks and the grade of edema reaching statistical significance with grade III edema (< 0.05). This is also confirmed by the indirect evidence of infection *ie*, high titers of ASO in individuals with higher grades of edema ($p < 0.05$).

The therapeutic response of individuals admitted to this study allows us to make some interesting observations, regarding the choice of treatment, for the management of ADL. Table 3 clarly demonstrates that an effective response could be achieved just as well by symptomatic therapy, as by antibiotics. The role of DEC in the management of acute attacks of ADL has been emphasized in previous reports (Pani *et al*, 1990; WHO, 1984). These reports have claimed a decrease in the number of ADL attacks in individuals who received prophylactic DEC. In the present study however no such beneficial effect was seen among individuals who received DEC at three months intervals. It is also interesting to note that nearly half of them had received some form of DEC therapy prior to admission to this study. Significantly acute attacks of ADL continued to occur in all the four treatment groups although there was a general decline in the number of such attacks. It is likely that the bulk of the reduction in ADL attacks may have been achieved through the institution of simple measures of hygiene rather than due to any therapeutic measures.

The findings of the present study have important implications not only for clinicians but also for health planners. It also has shown that ADLs were commonly seen in the lower socioeconomic strata of society (57 of 65 patients - 88%) and possibly poor personal hygiene of the limbs. The observations that mere improvement of hygiene and better foot care is all that is required to decrease the frequency of ADL attacks ought to simplify the clinical management of ADL attacks. It will also have the added advantage of eliminating the repeated use of either antibiotics (with their associated side effects) or DEC. Naturally, this would decrease the cost of health care in the management of lymphatic filariasis. Needless to say, better emphasis needs to be placed on patient and health personnel education on the value of simple hygienic measures in the prevention of ADL attacks. We believe that adoption of these measures will go a long way in our efforts to control the morbidity associated with lymphatic filariasis.

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REFERENCES

Annual Report. Vector Control Research Centre, Pondicherry, India. 1991.

Chan SH, Dissanayake S, Mak JW, *et al.* HLA and filariasis in Srilankans and Indians. *Southeast Asian J Trop Med Public Health* 1984; 15 : 281-6.

Jamal S. Grading of lymphoedema - further refinement proposed: *Progr in Lymphol* 1988; 9 : 505-8.

Jamal S, Pani SP. The clinical perspectives and research needs in lymphatic filariasis. *Misc Public VCRC* 1990; 16 : 29-41.

Ottesen EA. Immunopathology of lymphatic filariasis in man. *Springer Semin Immunopathol* 1980; 2 : 373-85.

Pani SP, Das K, Balakrishnan N, *et al.* A study of the clinical manifestations of Brugian filariasis in Pondicherry, South India. *Indian Med Gaz* 1989; 123 : 111-5.

Pani SP, Krishnamoorthy K, Rao AS. Clinical manifestations in Malayan filariasis infection with special reference to lymphoedema grading. *Indian J Med Res* 1990; 91 : 200-7.

Partono F. The spectrum of diseases in lymphatic filariasis. *Ciba Foundation Sym* 1987; 127 : 15-31.

Rajagopalan K. Filariasis in India. *Nat Med J India* 1990; 3 : 1-4.

World Health Organisation. Lymphatic Filariasis: Fourth Report: *WHO Tech Rep Ser* 1984; 702 : 3-112.