IMMUNOMONITORING FOLLOWED BY OPTIMAL DEC THERAPY FOR SUCCESSFUL MANAGEMENT OF CLINICAL FILARIASIS IN AN ENDEMIC AREA.

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ABSTRACT

Lymphatic filariasis continues to be the major cause of clinical morbidity in India and other developing tropical countries. One of the major lacunae in the effective management of clinical filarial cases is the non-availability of a suitable diagnostic test for confirming filaria aetiology in acute, chronic and occult clinical cases where microfilariae (mf) are not usually seen in peripheral circulation. Studies in our laboratory have shown the usefulness of filarial antibody and antigen assays using microfilarial excretory-secretory (mf ES) antigen in detecting microfilaraemic, acute and chronic filarial cases and in confirming filarial aetiology in occult infections. Diethylcarbamazine citrate (DEC) is the drug of choice for lymphatic filariasis. Different regimens of DEC have been explored in the treatment of microfilaraemic cases. Immunomonitoring has shown that the seroconversion of antigen and antibody positivity was found to be very helpful in determining appropriate period of DEC treatment for clinical relief and cure in clinical filarial patients and further they did not have recurrence in most of the cases. Optimal DEC (6mg/kg body wt/day for 21 days each month for 3-12 months) therapy was found to be very effective in acute and atypical clinical manifestations such as asthmatic bronchitis, pulmonary eosinophilia, monoarthritis, recurrent upper respiratory tract infections (URI), pneumonia (super imposed infections) in children and minimal hydrocele, epididymoorchitis, lymphangitis, lymphadenitis, acute abdomen, central serous retinopathy, tenosynovitis, pain and swelling in limbs and joints in adults living in filaria endemic areas.

KEY WORDS : Filariasis, immunodiagnosis, immunomonitoring, DEC therapy.

FILARIASIS - A MAJOR PUBLIC HEALTH PROBLEM

Human lymphatic filariasis is caused by

the nematode parasites *Wuchereria bancrofti* and *Brugia malayi*. Filariasis is a mosquito borne disease with infected man serving as a reservoir.

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The microfilariae in blood of infected man (carrier) are picked up by mosquito to get developed into infective larvae and are then deposited on the skin of a fresh host during mosquito bite. The infective larvae reach lymphatics, develop into adult worms, fertilize and deliver microfilariae into blood circulation and thus the life cycle is complete (Fig.1).

Fig. 1 : Life cycle of filarial parasite.

About 120 million people are infected all over the world of which 43 million are affected with overt physical disabilities (1). In India about 27 million are estimated to be harbouring microfilariae and about 21 million people suffer from clinical manifestations of the disease, with 7.5 million of lymphoedema cases and 13 million of hydrocele cases (2). Microfilariae are not normally observed in peripheral blood in clinical cases making it difficult to diagnose for successful treatment. Further millions of people suffer with occult filarial infection in endemic areas without diagnosis.

The clinical manifestations of the disease

which are crippling physically, socially and economically cause considerable psychological trauma to the affected individuals. It is the worst thing to happen to unmarried men and women.

IMMUNODIAGNOSIS OF FILARIAL INFECTION

Penicillinase ELISA system (SEVA FILACHEK) has been explored in several ways at our institute using microfilarial antigen and filarial antibodies in diagnosis of filarial infection at different stages. The detection of antibodies against specific microfilarial antigen by Indirect ELISA was found to be useful for detecting microfilaraemic and clinical filarial cases with active infection (3-8). The results of antibody and antigen analysis in different clinical groups of filariasis are summarized in Table 1. Further, antigen assay by inhibition ELISA was found to be more useful in occult filarial infections such as tropical eosinophilia (5,8). The stick penicillinase ELISA test system showed a sensitivity and specificity of more than 80% in comparison with night blood parasite examination in carriers (9). Lalitha et. al. (10) reported that the recently introduced monoclonal antibody Og4C3-based ELISA kit in the market (by Tropical Biomedical Institute, Queensland University, Australia) detects circulating filarial antigen only in mf carriers but none of the clinical cases.

IMMUNOMONITORING DURING CHEMOTHERAPY

Chemotherapy remains the main strategy in the reduction of filarial transmission and morbidity. Over the last five decades, diethylcarbamazine citrate (DEC) has been the drug of choice in the treatment of lymphatic

Table 1. Analysis of clinical and occult filarial sera for the presence of filarial antigen and antibody (1991 to 1997)

Clinical manifestation	Number screened for filarial antibodies	Positive for filarial antibodies* No. (%)	Number screened for filarial antigen	Positive for filarial antigen* No. (%)
Fever with chills and slight oedema with pain	1261	815 (65)	396	192 (48)
Lymphadenopathy				
Generalised	138	96 (70)	58	31 (53)
Inguinal	138	75 (54)	51	19 (37)
Cervical	67	47 (70)	17	8 (47)
Funiculitis	4	2 (50)	4	3 (75)
Epididymoorchitis	194	66 (34)	97	48 (50)
Chyluria/Haematuria	65	40 (62)	21	8 (38)
Hydrocele	465	351 (75)	292	138 (47)
Lymphoedema	381	253 (66)	362	143 (40)
Elephantiasis	281	230 (82)	67	35 (52)
Tropical pulmonary eosinophilia	363	165 (43)	234	115 (50)
Bronchitis, asthma & chest pain	39	18 (46)	39	15 (38)
Joints pain				
(Knee/ankle)	18	6 (33)	18	9 (50)
Monoarthritis	276	144 (52)	21	8 (38)
Polyarthritis	167	78 (47)	47	19 (40)
Tenosynovitis	71	22 (31)	16	8 (50)
Urticaria	8	3 (38)	8	3 (38)
Cellulitis	4	1 (25)	4	3 (75)
Glomerulonephropathy	139	29 (21)	17	4 (24)
Retroperitoneal lymphangitis (Acute abdomen)	83	55 (66)	15	12 (80)
Central serous retinopathy	60	38 (63)	44	6 (14)
Iridocyclitis, acute conjunctivitis, recurrent scleritis & macular oedema	109	36 (33)	4	2 (50)
Nutritional anorexia	3	3(100)	3	0
Fibrinoma	4	2 (50)	4	0
Total	4338	2566 (59)	1839	829 (45)

* Cases showing the presence of filarial antigen/antibody at a serum dilution of 1:300 are considered as positive.

filariasis. Therapeutic concentration of DEC has no effect on the microfilariae *in vitro*, but *in vivo* it causes rapid disappearance of microfilariae from the blood circulation. Recently, long term administration of DEC has been shown to be effective against adult worms as observed by ultra sound technique (11). Variety of DEC regimens have been used to treat microfilaraemic cases who were then followed up for mf in circulation and by immunomonitoring for filarial antibodies and/or antigen (12-17). Following short term DEC treatment it was observed that the filarial antibody and antigen levels were decreased and might reappear or increase with the recurrence of mf in circulation. A ten year follow up study on immunomonitoring of 27 microfilaraemic cases during DEC treatment showed that the carriers turn negative for antigen and antibodies with clearance of microfilariae thus confirming that presence of antigen/antibodies may be used as markers of active infection (18,19).

OPTIMAL DEC (OpDEC) THERAPY FOR CLINICAL FILARIASIS

Treatment of clinical disease groups i.e. acute, chronic and occult filarial cases where mf are always not visible in peripheral circulation, has been a challenging problem to the treating clinician. Hence we explored immunomonitoring for antibody and antigen in clinical cases during treatment in the absence of microfilaraemia. Long term treatment with repeated doses has been shown to be effective in reduction of early manifestations such as transient oedema and minimal hydrocele (Fig. 2 & 3) and marked improvement was observed in occult filarial cases with manifestations like TPE, monoarthritis

etc. (5,20). However for appropriate period of treatment, the main obstacles have been confirmation of filaria aetiology and determining the period of treatment for complete clinical relief and cure. Many patients referred to this hospital by General Practitioners from surrounding endemic areas, give history of DEC administration for short periods and temporary relief. The patients are also not convinced of the need for long term treatment in the absence of specific test as a marker of active infection.

Fig. 2 : Acute lymphoedema of the left foot.

Fig. 3 : Epididymo-orchitis (acute) with minimal hydrocele.

Table 2 : Immunomonitoring and clinical follow up of filarial patients during DEC therapy.

Case No.	Age & Sex	Clinical presentation (Duration)	Duration * of DEC therapy	Filarial antibody positivity		Filarial antigen positivity		Clinical progress
				Before therapy	After therapy	Before therapy	After therapy	
1.	37 M	Oedema right foot (45 days) Recurrent fever (45 days)	6	+	-	+	-	Recovered
2.	40 F	Fever, ADL and oedema right lower limb (10 days)	6	+	-	+	-	Recovered
3.	46 F	Bilateral oedema lower limb with intermittent pain (45 days)	12	+	-	ND	-	Minimal oedema persists
4.	34 M	Oedema right lower limb (15 days)	3	+	-	-	-	Recovered
5.	48 M	Bilateral vaginal hydrocele (5 yr.)	6	+	-	+	-	Minimal hydrocele persists
6.	43 M	Epididymoorchitis & Funiculitis (left) (4 months)	3	+	-	+	-	Recovered
7.	33 M	Dimness of vision right eye Macular oedema & CSR (2 months)	1	+	-	-	-	Recovered
8.	23 M	CSR with dimness of vision (3 months)	3	+	-	-	-	Recovered
9.	41 M	TPE (4 months)	6	+	-	+	-	Recovered
10.	20 M	TPE (1 month)	3	-	-	+	-	Recovered

* DEC was administered 6 mg/kg body wt./day for 21 days each month for 3-12 months. ADL - Adenolymphangitis, CSR- Central serous retinopathy; TPE-Tropical pulmonary eosinophilia; ND=not done.

Patients attending this hospital with acute, chronic and occult manifestations suspected of filariasis are examined for the presence of specific filarial antibodies and antigen. Patient with suggestive clinical history of filariasis and positivity for antibodies or antigen or both is advised DEC (6 mg/kg body wt/day for 21 days in a month) and monitored quarterly. DEC treatment is continued (3-12 months) until the blood sample showed negative reaction for antigen and antibody. The patient is also keen to observe negativity of the test and thus complies with the treatment advice. Complete clinical relief and cure (reversal in cases of minimal hydrocele secondary to epididymo-orchitis and early lymphoedema) without

recurrence were observed (Table 2). Immunomonitoring for presence of antibody and antigen helped in determining optimal DEC therapy (OpDEC therapy) of 3 to 12 months for successful management of individual clinical filarial patient for clinical relief and cure (21) as shown in the table 3.

Till the end of 1997, a total of 4338 suspected filarial cases with clinical manifestations (fever with chills, lymphoedema, lymphadenopathy, epididymo-orchitis, hydrocele, pulmonary eosinophilia, mono and poly arthritis, endomyocardial fibrosis, acute abdomen, asthmatic bronchitis etc.) attending the general

Table 3. Duration of DEC treatment in different clinical presentations of filariasis based on the results of immunomonitoring

Clinical group	No. of cases	DEC treatment	
		Duration (Months)	Percent of cases covered
Acute clinical filariasis			
Funiculitis, epididymo-orchitis (acute), minimal hydrocele (acute), ADL (acute attack), lymphoedema (<45 days duration with and without pain).	22	3	36%
		6	55%
		12	9%
Chronic clinical filariasis			
Hydrocele (grade I,II & III) & elephantoid cases, lymphoedema (I,II & III) and elephantiasis cases, chronic ADL, chronic epididymo-orchitis and fibroadenoma breast.	62	3	16%
		6	61%
		12	23%
Occult filariasis			
TPE & monoarthritis	5	3	20%
		6	80%

out patient division and speciality OPDs of Surgery, Orthopaedics, Paediatrics and Medicine of our Institute were screened for filarial IgG antibodies and antigen (Table 1). About 60% positivity for filarial antibodies and 45% positivity for filarial antigen was observed in these cases with wide variety of clinical entities confirming active filarial infection. Filarial antigen detection compared to antibody was found to be more useful in tropical pulmonary eosinophilia and acute epididymoorchitis (5,8).

Immunomonitoring followed by OpDEC (optimal DEC) therapy was found to be very

effective for clinical relief and cure, in acute and atypical clinical manifestations such as asthmatic bronchitis, pulmonary eosinophilia, monoarthritis, recurrent URI, pneumonia (super imposed infections) in children and minimal hydrocele, epididymoorchitis, lymphangitis, lymphadenitis, pain and swelling in limbs and joints in adults living in filaria endemic areas. In addition to DEC therapy, judicious use of appropriate antibiotics, analgesics, antihistaminics, diuretics, antifungals for managing secondary infections and inflammatory reactions along with physiotherapy and hygiene, help in successful management of clinical filarial cases.

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