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SPECIAL REPORT

SKIN BACTERIAL FACTOR IN PROGRESSION OF FILARIAL LYMPHEDEMA

Filarial lymphedema of the extremities affecting, according to the World Health Organization, more than 300 million people, is a disease caused by nematodes Filariidea (*Wuchereria bancrofti* or *Brugia malayi*). Third-stage larvae of these parasites, after inoculation by mosquitoes, enter initial lymphatics. The worms flow with the lymph stream to the groin or axillary lymph nodes, but unable to penetrate this barrier remain in afferent lymphatic trunks and mature into adult worms of both sexes. Lymphokinetic disturbances develop due to partial obstruction, injury or dysfunction of the lymphatics. Host local immune reaction to filarial antigens and presumably accumulation of parasitic metabolic products promote destruction of the lymphatic wall. Spontaneous contractility of lymphatics ceases and lymph stasis develops with its clinical equivalence of skin edema, subsequent hyperkeratosis and fibrosis. Recurrent episodes of "filarial fever" with premonitory malaise, followed by acute lymphangioadenitis and increase in limb girth are common occurrences. They are an integral part of the clinical picture of filariasis and are supposedly caused by "activation" of the parasite.

We now challenge the view that filarial fever and progression of lymphedema are due to activation of the parasite dwelling in limb lymphatics or microfilaria circulating in the bloodstream. Our histopathologic and bacteriologic studies of skin, tissue fluid, lymph and lymph nodes, carried out in 100 patients with stage I to IV filarial lymphedema in Madras, Thanjavur and Pondicherry, India (with Drs. Dhana, Kumaraswami, Manokoran, and Pani), in a WHO TDR sponsored programme, point to bacteria as the main secondary pathogenic factor accounting for progression of the signs of lymphedema. Skin biopsies and histopathology in patients uniformly reveal a typical appearance of latent (subclinical) dermatitis, most apparent at the epidermal-dermal junction. There is an increase in number of CD1a+ Langerhans cells in the epidermis, accumulation of class II+, CD3+, CD68+ (macrophages) cells around skin blood capillaries, venules and in the intercapillary areas, but not around skin lymphatics and collecting trunks (1).

In search for a factor responsible for these integumental changes, bacteriological investigations of skin tissue fluid, afferent lymph and lymph nodes were performed. Cultures revealed the presence of bacteria in 75% of samples (100% in stage III and IV lymphedema) (2). This flora was notably different from skin surface swab cultures in which only 27% of samples revealed similar strains. The most common types were *Staphylococcus epidermidis, S. hominis,* Micrococcus species and *luteus, Streptococcus acidominus, Corynebacteria, Bacillus cereus* and *badius.* They somewhat differed from skin surface flora where primarily *Bacilli cereus, lentus, badius* and other subtypes were identified. Moreover, six patients with acute filarial fever had bacteremia. In a control group of 30 healthy European volunteers previously studied, undergoing similar

bacteriological investigations, no positive cultures of tissue fluid and lymph were found. Search for filarial antigens in skin and lymph with use of specific antibodies did not yield positive results. This finding challenges the traditional concept that filarial antigens are responsible for progressive skin changes in filarial lymphedema.

From our own and previous clinical observations, the administration of penicillin is highly effective in interrupting or preventing attacks of filarial fever. Taken together, the data suggest that after the initial injury to peripheral lymphatics by the filarial nematode, bacteria steadily colonize the dermis, lymphatics and lymph stream. Injury to the skin during strenuous exercise or walking barefoot, tooth infection with transient bacteremia are examples of precipitating factors that account for acute filarial fever and dermolymphangioadenitis (DLA). Which specific strains are primarily responsible for the acute episodes is still unclear. Perhaps these bacterial types possess special affinity for specific skin molecular structures. Nonetheless, our findings favor revising the treatment protocols of patients with filarial lymphedema with greater emphasis on control of local bacterial infection. A large double-blind placebo-controlled study on the efficacy of penicillin in preventing filarial fever is now underway.

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