

Occult filarial infections

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INTRODUCTION

Bancroftian filariasis is an ancient disease known to mankind since BC 600. In 1863, the filarial parasite was first discovered by Demarquay in the hydrocoele fluid of patients in Cuba. In 1866, Wucherer demonstrated microfilariae (mf) in the chylous urine of Brazilians. In India, Lewis in 1872 identified mf in the blood of patients with filariasis. Bancroft discovered the adult female worm in 1876 and Browne the adult male in 1888.¹

Lymphatic filariasis has been reported from almost all tropical and subtropical countries in the world. It is endemic in South, Central and North America, the West Indies, Africa, Asia and Australia. Of the 2677 million people living in countries where the disease is endemic, 905 million are estimated to be at risk of infection and 90 million are carriers of mf.² Filariasis is a disease characterized by a wide spectrum of clinical manifestations (Fig. 1). The so-called 'occult' manifestations such as tropical pulmonary eosinophilia (TPE),³ glomerulopathies,⁴ nerve palsies,² endomyocardial fibrosis (EMF),⁵ arthritis,⁶ and filarial infections of the breast⁷ are often seen in populations living in endemic areas.

The term occult filariasis is commonly used to designate filarial infections in which mf are not found in the peripheral blood although they may be seen in tissues.^{8,9} However, it has now been shown that in some cases with

occult filariasis, mf may actually be found after more careful blood examination despite their low density.¹⁰ The clinical features of occult filariasis are different from those of the classical disease and resemble many non-filarial diseases from which they are sometimes difficult to distinguish. Occult filarial manifestations may help explain the aetiology of many clinical syndromes which were earlier not completely understood. For example, splenic granulomatous inflammatory reactions to mf of *W. bancrofti* have been discovered only on autopsy.¹¹ Following are some of the clinical manifestations of occult filarial infestation.

TROPICAL PULMONARY EOSINOPHILIA

This is perhaps the best example of occult filariasis. It was first formally described by Frimodt-Moller and Barton in 1940¹² although in 1939 Meyer and Kouwenaar¹³ had demonstrated mf in the inguinal lymph nodes of individuals with eosinophilia and asthma. Five years later Van der Sar and Hartz¹⁴ demonstrated mf in the lymph nodes and spleens of their patients. Ottensen *et al.*³ and Jayawardene and Wijayaratnam¹⁵ showed that TPE was a disease caused by human filarial parasites and not by animal filarial parasites as was then believed. TPE also has extrapulmonary manifestations. There are ethnic differences in its prevalence. It is more commonly seen on the Indian subcontinent although Bancroftian filariasis is endemic in many parts of the world. It can occur at any age and has been reported even in infants.¹⁶ The disease can have an acute or an insidious onset. Its clinical manifestations are usually cough, fever, chest pain, breathlessness, malaise and occasional abdominal pain. Examination of the chest reveals rhonchi and crepitations. Sometimes lymphadenitis, splenomegaly and hepatomegaly may also be observed. The natural course is marked by recurrences and relapses. Long-standing untreated cases progress to pulmonary fibrosis and respiratory insufficiency.¹⁷

These patients have blood eosinophilia, raised erythrocyte sedimentation rates and there may be evidence of diffuse miliary lesions or increased bronchovascular markings in the chest X-rays especially of children.¹⁸ Microfilariae are not demonstrable in the blood smears but can be found in the lungs, liver and lymph nodes on a thorough examination.¹⁹ There is impairment of lung function with occurrence of both obstructive and restrictive defects.²⁰ It responds to treatment with diethylcarbamazine (DEC) which is yet another indication of its filarial origin.

Various immunological methods using homologous and heterologous antigens have been employed for the diagnosis of the disease. Using an indirect fluorescent

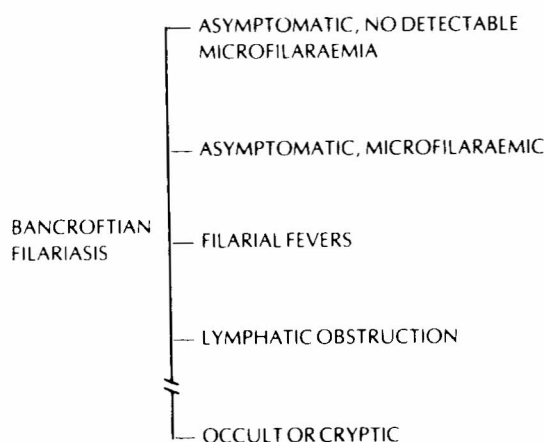


FIG 1. Clinical manifestations³

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antibody test, Ismail and Wijayaratham found filarial antibodies in only 57% of their patients and concluded that the cause for TPE in antibody negative patients could be non-filarial (unpublished data). However, a comparison of the *W. bancrofti* mf excretory-secretory antigen (mfESAg) with *W. bancrofti* larval (L₃) excretory-secretory antigen (L₃ ES Ag) showed an antibody positivity rate of only 54% with mf ES Ag and a 96% positivity rate with L₃ ES Ag, suggesting that L₃ ES Ag was more specific in the diagnosis of TPE.²¹

In TPE and other occult filarial manifestations, specific antifilarial IgE antibody titres to mf antigens from *W. bancrofti*, *B. malayi* and *D. immitis* are increased. But in filarial TPE, IgE antibodies are more highly sensitized and respond more to mf antigens than the IgE antibodies of other filarial manifestations.³ Microfilariae, which are destroyed in the lungs through an IgG mediated response, provoke hypersensitivity and lead to an increase in IgE levels.^{22,23} This points to the existence of a type I reaction. The occurrence of an additional type III reaction is indicated by an increase in IgG, IgM and IgA²⁴ and the presence of immunoglobulins in the lungs.²⁵ Although TPE may occasionally present atypically, the diagnosis is seldom difficult. However, other occult filarial syndromes such as filarial arthritis are often not as easy to detect.

FILARIAL ARTHRITIS

This is a form of arthritis which usually affects the knee joints and is fairly common in endemic areas. Though it had been recognized as a possible manifestation of Bancroftian filariasis twenty years ago,²⁶⁻²⁸ no detailed investigations were done until 1973, when Ismail and Nagaratham⁶ using mf of *W. bancrofti* in a fluorescent antibody test found that 90% of their patients with filarial arthritis tested positive for filarial antibodies. Chaturvedi *et al.*²⁹ found that 80% of children with arthritis, where no other diagnosis could be made, had filarial antibodies. The need to differentiate filarial arthritis from other diseases, especially rheumatoid arthritis, is important as the treatment of both conditions is entirely different. Filarial arthritis may be caused by species other than *W. bancrofti*.³⁰⁻³²

It is usually monoarticular but two-joint involvement also occurs. Only large joints are affected and the occurrence of the symptoms in small joints rules out the diagnosis of filarial arthritis. The condition runs a short, benign course and the majority of patients do not have fever but a painless swelling of one or more joints (usually the knee). Sometimes the affected joint may be painful, warm and tender with restriction of movement.² The symptoms may recur, often in the same joint but occasionally in some other joint and may be mistaken for rheumatoid arthritis.^{6,28}

These patients show normal or moderately elevated eosinophil counts and erythrocyte sedimentation rates; X-rays of the involved joints show soft tissue swelling but no bony abnormalities. Microfilariae in night blood smears may be seen in some instances. The antistreptolysin O titre is generally normal.⁶

The pathogenesis of the disease is still obscure. Das

and Sen²⁹ in a study of chylous arthritis (which they believed to be of filarial origin) found lymphangiectasia, stasis and varicosities in the popliteal lymphatics with short blind channels leading to the joint suggesting lymphatic fistulization into the synovial sac. The condition responds well to DEC but poorly to salicylates.⁶

GLOMERULOPATHIES

Glomerulonephritis associated with lymphatic filariasis was reported by Chugh *et al.* in 1978.⁴ Chaturvedi *et al.*²⁹ also found that 2 of 5 children they had seen with filariasis and acute glomerulonephritis had filarial antibodies. Renal biopsies in these patients showed diffuse mesangial proliferative glomerulonephritis with C₃ deposition on the basement membrane. The condition responds well to DEC therapy.³³ The production of typical lesions of glomerulonephritis in cats infected with *Brugia pahangi*³⁴ is in keeping with this hypothesis. The demonstration of filarial antigens and specific filarial antibodies in the immune complexes deposited in the glomeruli would provide definitive evidence for a filarial aetiology.

ENDOMYOCARDIAL FIBROSIS

Endomyocardial fibrosis is a rare disease seen in the equatorial belts. The incrimination of filarial infection in its causation is based largely on circumstantial evidence.^{35,36} The geographic distribution of the disease in areas endemic for filariasis, the detection of antibodies to *Loa loa* in patients with EMF,³⁷ certain clinical features resembling filarial infection and the occurrence of eosinophilia and EMF with Loeffler's syndrome³⁸ have led to the hypothesis of EMF being filarial in origin. Further, Harinath in 1987³⁹ found filarial antibodies in 8 of the 10 patients with EMF, further supporting the theory that EMF may be of filarial origin.

FILARIAL GRANULOMAS IN THE BREAST

This manifestation is particularly prevalent in India and Sri Lanka where *W. bancrofti* is the predominant species. It has not been reported from areas endemic for Brugian filariasis. Filarial granulomas present as hard breast lumps attached to the overlying skin and are at times difficult to distinguish from malignant tumours.⁴⁰ A histological examination can confirm the diagnosis by the finding of an eosinophilic granulomatous reaction around the filarial parasites which are in varying stages of degeneration. Both adult worms and mf have been found in the granulomas.^{40,41} Filarial antibodies have been demonstrated in these patients and the condition responds to DEC therapy which, in many instances, can lead to complete disappearance of the lump.

Finally a variety of manifestations such as thrombophlebitis, tenosynovitis and nerve palsies found in endemic areas, sometimes coexisting with filariasis, have been suggested to be of filarial origin without much convincing evidence.²

SUMMARY

Classical filariasis presenting with lymphangitis, lymphoedema, chyluria or elephantiasis with microfilaraemia is

well documented. In occult filariasis, microfilariae are not found in the blood but may be seen in the tissues. Earlier, occult filariasis was synonymous with tropical pulmonary eosinophilia but other manifestations such as glomerulopathies, endomyocardial fibrosis, arthritis and filarial infections of the breast are now well recognized. The occult manifestations are generally microfilaraemic and the clinical manifestations are sometimes impossible to distinguish from well known clinical entities. The diagnosis of these occult manifestations can be confirmed by the ELISA test using specific antigens. Therefore, in endemic areas, a high index of suspicion is necessary to establish a diagnosis because specific therapy against microfilariae is effective and easily available.

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