

Filariasis: diagnosis, treatment and prevention

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Abstract. Lymphatic filariasis caused by the mosquito-borne, lymphatic-dwelling nematodes *Wuchereria bancrofti* and *Brugia malayi* is still a common tropical parasitic disease and 120 million people are affected in the world, of which two-third in Asia. *W. bancrofti* is responsible for 90% of this disease, while *B. malayi* for the remaining 10%. Next to psychiatric illness, this is the leading cause for permanent and long-term disability. Some recent studies have evidenced new aspects in the diagnosis, management and in planning effective strategies for its global prevention. The aim of this up to date is to evidence clinical, diagnostic and therapeutic aspects of this very important infection. (www.actabiomedica.it)

Key words: Lymphatic filariasis, *Wuchereria bancrofti*, *Brugia malayi*, diagnosis, prevention, treatment

Clinical aspects

Patients affected by microfilaraemia may present an asymptomatic infection or acute and chronic manifestations. In the endemic areas the majority of affected subjects show a clinically asymptomatic infection and harbour microfilaria in their peripheral blood. It is important to know that even at this stage of the disease abnormalities of the lymphatic vessels such as dilatation appear to be irreversible even after treatment (1). Acute manifestations include Acute Adeno-Lymphangitis (ADL) and Acute Filarial Lymphangitis (AFL). ADL is the most common acute manifestation and is characterized by attacks of fever. These episodes may occur both in the early and late stages of the disease. The affected area is painful, tender, warm, red, and swollen. The lymph nodes in the groin and axilla are frequently inflamed. These acute ADL attacks recur many times a year in patients with filarial swelling and their incidence increases with the degree of lymphedema.

Secondary infections due to bacteria such as streptococci are responsible for these acute episodes (2). In the affected limbs, lesions which favour entry of these infecting agents may be frequently demon-

strated, either in the form of fungal infection in the webs of the toes, minor injuries, eczema, insect bites or infections. These ADL attacks are responsible for the persistence and progression of the swelling leading to elephantiasis not only of the limbs but also of the external genitalia and breasts (3). AFL are caused by adult worms and are usually rare. They generally subside without any treatment. They are observed when the adult worms are destroyed in the lymphatics either spontaneously or by drug administration such as diethylcarbamazine. Small tender nodules form at the location of adult worm death either in the scrotum or along the lymphatics. Lymph nodes may become tender. Inflamed large lymphatics may stand out as long tender cords underneath the skin, usually along the sides of the chest or upper arm and axilla associated with restriction in movement of the affected limb. Though transient oedema may sometimes occur, these episodes are not associated with fever, toxemia or evidence of secondary bacterial infections. They generally subside without any treatment. The chronic manifestations represent Lymphoedema and Elephantiasis and Genito-urinary lesions. The most common chronic manifestation of lymphatic filariasis is lymphoedema, which may progress to elephantiasis. Even

though lower limbs are commonly affected, upper limbs and male genitalia are frequently involved. In females, rarely the breasts and external genitalia may also become elephantoid. Repeated ADL episodes responsible for the progression of lymphoedema continue to occur with greater frequency in higher grades of oedema. This is due to the presence of moisture in the web spaces of the closely apposed swollen toes which promotes fungal infections that damage the skin, which in turn favour infecting organisms. For this reason the frequency of ADL episodes is shown to increase in the rainy season, when people have to wade through water in the lanes (4). Hydrocoele is a common chronic manifestation of bancroftian filariasis in males. Chylocoele, chyluria and chylous ascites rarely occur. Microscopic and rarely macroscopic haematuria is known to occur in people with asymptomatic microfilaraemia.

Tropical pulmonary eosinophilia associated with high eosinophil counts in the blood is an occult manifestation of both *W. bancrofti* and *B. malayi* filariasis.

New advances in diagnosis

The recent developments in the diagnosis of lymphatic filariasis are given below:

Membrane filtration method for microfilaria detection: Venous blood drawn at night and filtered through millipore membrane filters, enables an easy detection of microfilaria and quantifies the load of infection. They are usually observed in the early stages of the disease before clinical manifestations develop. Once lymphoedema develops microfilaria are generally absent in the peripheral-blood (5).

Ultrasonography: Recently, ultrasonography has helped to locate and visualise the movements of living adult filarial worms of *W. bancrofti* in the scrotal lymphatics of asymptomatic males with microfilaraemia. The constant thrashing movement of the adult worms in their 'nests' in the scrotal lymphatics is described as the 'filaria dance sign' (6). The lymphatic vessels lodging the parasite are dilated and this dilation is not seen to revert to normal even after the worms are killed by diethylcarbamazine administration. Ultrasonography is not useful in patients with filarial lymphoedema be-

cause living adult worms are generally not present at this stage of the disease. Similarly ultrasonography has not helped in locating the adult worms of *B. malayi* in the scrotal lymphatics since they do not involve the genitalia (7).

Lymphoscintigraphy: After injecting radiolabelled albumin or dextran in the web space of the toes, the structural changes are imaged using a gamma camera. Lymphatic dilatation, dermal back flow and obstruction can be directly demonstrated in the oedematous limbs by this method. Lymphoscintigraphy has shown that even in the early, clinically asymptomatic stage of the disease, lymphatic abnormalities in the affected limbs of people harboring microfilaria may occur (5).

Immunochromatographic test (ICT): Highly sensitive and specific filarial antigen detection assays, both as card test and in ELISA based format are now available for the diagnosis of *W. bancrofti* infection. This test is positive in early stages of the disease when the adult worms are alive and becomes negative once they are dead (8).

DNA probes using Polymerase Chain Reaction (PCR): These tests are of high specificity and sensitivity, and are able to detect parasite DNA in humans as well as vectors in both bancroftian and brugian filariasis (5).

Treatment

Diethylcarbamazine (DEC): This drug is effective against both microfilaria and adult worms. DEC markedly lowers the blood microfilaria levels even in single annual doses of 6 mg/kg, and this effect is sustained even after one year. Even though DEC kills the adult worms, this effect is only observed in 50% of patients. By ultrasonography it is shown that even single doses of DEC kill the adult worms when they are sensitive to the drug. When they are not sensitive even repeated doses do not show any effect on the adult parasite. This drug does not act directly on the parasite but its action is mediated through the immune system of the host. The earlier recommended dose of this drug was 6 mg/kg given daily for 12 days. Recent studies have shown that a single dose of DEC 6 mg/kg is as effective as the above standard dose given

for 12 days. The sustained destruction of microfilaria by this drug even in annual single doses makes it a good tool to prevent the transmission of this disease. The adverse effects produced by the drug are mostly observed in patients who have microfilaria in their blood and are due to their rapid destruction which is characterized by fever, headache, myalgia, sore throat or cough lasting for 24 to 48 hours (10). They are usually mild and self-limiting requiring only symptomatic treatment. Direct adverse effects related to the drug are very rare. Recent trials have clearly shown that DEC has no action either in the treatment or prevention of the acute ADL attacks occurring in lymphoedema (2-4). DEC is the drug of choice in the treatment of Tropical Eosinophilia syndrome in which it should be given for longer periods of 3 to 4 weeks.

Ivermectin: This drug acts directly on the microfilaria and in single doses of 200 to 400 $\mu\text{g}/\text{kg}$ keeps the blood microfilaria counts at very low levels even after one year, such as DEC. The adverse effects noticed in microfilaraemic patients are similar to those produced by DEC but are milder due to the slower clearance of the parasitaemia. Ivermectin has no proven action against the adult parasite or in tropical eosinophilia (11). Ivermectin is the drug of choice for the treatment of onchocerciasis because of its safety and efficacy, when compared to DEC. It is also the drug of choice for the prevention of filariasis in African countries endemic for *Onchocerca* and *Loa loa*, where DEC cannot be used due to possible severe adverse reactions. Ivermectin is also effective against human ectoparasites such as head and body lice, scabies var hominis and many intestinal helminths. This drug is not licensed for human use in India.

Albendazole: This antihelminthic drug is shown to destroy the adult filarial worms when given in doses of 400 mg twice a day for two weeks. The death of the adult worm induces severe scrotal reactions in bancroftian filariasis since this is the common site where they are lodged (12). Albendazole has no direct action against the microfilaria and does not immediately lower the microfilaria counts. When given in single dose of 400 mg in association with DEC or ivermectin, the destruction of microfilaria by these drugs becomes more pronounced. Albendazole combined with DEC or ivermectin is recommended in the

global filariasis elimination programme. The strategy that appears most suitable for the elimination of filariasis in India is the administration of a single annual dose of albendazole 400 mg along with DEC 6 mg/kg of body weight. This not only prevents transmission of filariasis in the community by reducing the microfilaria levels, but also has the added benefit of clearing the intestinal helminths (13).

Prevention of ADL

Some recent studies have shown that with proper 'local care' of the affected limb these ADL attacks can be prevented even in case of severe lymphoedema. This 'foot-care programme' involves the following steps: washing of the affected area, especially the webs of the toes and deep folds of skin, with soap and water twice a day or at least once before going to bed and wiping dry with a clean cloth to avoid moisture; clipping the nails at intervals and keeping them clean; preventing or promptly treating any local injuries or infections using antibiotic ointments; applying antifungal ointment such as Whitfield's (being the cheapest) to the webs of the toes and sides of the feet daily. 5. Regular use of properly fitting foot wear; raising the affected limb at night in order to reduce the swelling; to prevent repeated ADLs in such patients, administration of long term antibiotic therapy with oral penicillin or long acting parenteral benzathine penicillin.

Prevention of chronic manifestations

Once lymphoedema is established there is no cure and the following treatment offers relief and may prevent further progression of the swelling: using elasto-crepe bandage or tailor made stockings while ambulant; keeping the limb elevated at night or while resting, after removing the bandage; regular exercise of the affected limb; regular light massage of the limb to stimulate the lymphatics and to promote flow of lymph towards larger patent vessels; intermittent pneumatic compression of the affected limb using single or multicell jackets; heat therapy either using wet heat or hot oven; surgical procedures such as lymph

nodo-venous shunts, omentoplasty, excisional surgery, skin grafting; prolonged treatment with oral or topical coumarin or flavonoids is considered to be effective in reducing the lymphoedema.

Conclusions

The recent availability of drugs for the prevention of transmission of the disease and of simple, low cost treatments which offer relief to persons with evident disease, herald a brighter future in tackling this potentially eradicable disease. Mass administration of a single annual doses of albendazole 400 mg along with DEC 6 mg/kg of body weight is the recommended strategy to prevent the transmission of filariasis.

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