Pathogenesis and Treatment of Chronic Symptoms with Emphasis on Chyluria and Elephantiasis

Isao Tada

1 Pathogenesis

1.1 Pathogenesis of elephantiasis, and historical controversy as to the role of bacterial infection

Elephantiasis occurs in the chronic stage of lymphatic filariasis due to the obstruction of lymphatic vessels by filariae. After invasion into lymph vessels, third stage larvae grow to maturity in the lymphatic system, mainly in and around the genitourinary system. Amaral et al. (1994) [1] observed actively moving adult worms in dilated and tortuous lymphatic vessels by ultrasonography. The subsequent blockage leads to lymphedema of the legs, arms, mammae, and other peripheral parts of the body. This situation causes hyperplasia of the connective tissues of the subcutis. The secondary and recurrent bacterial or fungal infections act to form the rough appearance of limbs and other parts of the body like elephant hide.

Historically, elephantiasis, or elephantiasis arabicum, was well known, but the etiology was enigmatic. Prior to the development of elephantiasis, lymphangitis, erysipelas-like skin changes and filarial fever occur. These early symptoms were called “kusafurui” or “baku” in Japan, “mumu” in Samoa and “wanganga” in Fiji. The acute symptoms led scientists to suspect various etiologies for elephantiasis. Matsushita et al. (1914) [2] mentioned in their review that Manson (1883) suggested filariasis as the cause of elephantiasis because of the similarity in the geographic distribution. They also introduced the work by Moncorvo (1886) who concluded streptococcal infection as the cause, and that by Innes (1886) who proposed the existence of two types of elephantiasis, one originating from filariasis and the other from erysipelas. In this way, no concrete causative mechanism was shown even in the early 1900s.

In Japan, Matsushita et al. (1911) [3] reported the result of their first survey performed in 1908 at Tanegashima Is., Kagoshima prefecture. They found streptococci from the skin and blood in 19 out of 26 elephantiasis cases. Later they examined some 4,500 patients and concluded that streptococci were responsible for the symptoms. The reason: they found very few microfilaremia in the elephantiasis cases but noted a rather high microfilaremia rate in the non-symptomatic persons. They even concluded that microfilariae were harmless to humans. Based on this hypothesis, they developed vaccine for elephantiasis and examined its protective activity. Matsushita and his colleagues reviewed all the results (1914) [2].

Mochizuki and his colleagues criticized Matsushita’s conclusion, which, based on the clinical and parasitological evidence, completely overruled the involvement of filariasis. From 1911, Mochizuki’s group adopted night blood surveys and examined inhabitants of endemic areas such as Amakusa in Kumamoto prefecture. Detailed clinical and epidemiological analyses were reported in their papers (1912, 1913a 1913b) [4-6]. At the 10th annual meeting of the Society of Internal Medicine, very interesting and heated discussions unfolded between the two groups, bacteriologists vs. clinicians, on the etiology of erysipelas-like fever/elephantiasis. It is now recognized that the basic cause of elephantiasis is filariasis and that bacterial and fungal infections are involved in the aggravation of the disease.

In the recent global elimination program of lymphatic filariasis conducted since 2000, as proposed by WHO, we are adopting morbidity control of lymphedema/elephantiasis using sterilizing techniques to suppress bacterial infections on the affected skin. This morbidity control program is reminiscent of the old but serious discussions on the etiology of filarial fever/elephantiasis.

Later, in order to clarify the causative mechanism in the erysipelas-like change, Bun (1921) [7] experimented by injecting Dirofilaria extract and streptococci into human and rabbit skin. He concluded that both parasite and bacterial components were necessary to cause the skin inflammation. Yamasaki (1953) [8] considered that proteinase-like components of filaria were responsible for the skin inflammation, based on his experiment using Dirofilaria extract.

1.2 Pathogenesis of chyluria

In the chronic stage of Wuchereria bancrofti infection,
chyluria or hemato-chyluria was commonly seen in endemic areas in Japan. Chyluria is essentially urine with the appearance of milk (chyle) due to the inclusion of fat, protein and coagulated fibrin. Hemato-chyluria is chyluria contaminated with blood. Clinically, chyluria is devastating for patients, because of the loss of protein and fat leading to fatigue, pain resulting from urethral obstruction with coagulated fibrin or protein, and mental suffering due to urine colored like milk.

Studies on this symptom have been conducted by various groups, particularly urologists. Hayashi (1921) [9] summarized the process of chyluria as follows based on pathological observations: First, congestion of lymphatic fluid and dilatation of vessels occur as a result of occlusion of the filarial parasite in a peripheral lymphatic vessel. Then the bacteria play a role to cause local inflammation and further promote congestion/dilatation of vessels (Fig 1). The fluid is gradually concentrated into a sticky state. Thus the ductus thoracicus is also affected showing dilatation and blockage of the lymphatic passage. Eventually, the fluid backflows into urine through renal fistulas formed by the structural deformity of lymphatics. Chyluria thus appears clinically.

Based on this hypothesis, Kume (1929) [10] experimentally ligated the ductus thoracicus of 25 dogs at the anastomotic portion of the ductus with the left subclavicular vein. This experiment successfully revealed chyluria in 6 dogs. However, the experiment done on rabbits was unsuccessful. Later, various urologists intensively investigated the radiological findings of chyluria cases using retrograde pyelography. By this technique, they revealed marked pyelo-lymphatic connections in chyluria patients (Fig. 2). The backflow of the lymph disappeared when chyluria was cured by the injection of sodium iodide into the renal pelvis. Actually, all these mechanisms of chyluria were investigated by researchers of Nagasaki University Hospital. As stated in the following section 7.2.2(2), a unique surgical technique was proposed by Prof. Katamine, Nagasaki Univ., in 1952.

2 Treatment

2.1 Treatment of scrotal and penile elephantiasis

As a result of the lymphatic occlusion by filarial parasites, elephantiasis occurs in genital organs such as the scrotum, penis, labium, and clitoris. In man in Japanese endemic areas, scrotal elephantiasis cases were not uncommon and the patients needed surgical treatment. In the early stage, swelling of the scrotum is mainly associated with hydrocele. This lesion can be rather easily treated by aspiration of liquid using a syringe fitted with a thick needle. Several hundred ml to (in rare cases) several liters of the liquid...
are seen in each hydrocele. However, in the chronic stage, elephantoid change occurs on the skin of the scrotum and penis, the latter becoming buried in the growth of elephantiasis of the scrotum. In the attempt to reconstruct surgically the affected scrotum or penis, various operations were reported historically. One of such early works is that of maturia since the age of 7 years. A pencil-sized lymph ves-

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