LYMPHATIC FILARIASIS IN CHILDREN: ADENOPATHY AND ITS EVOLUTION IN TWO YOUNG GIRLS

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Abstract.   Lymphatic filariasis is a widespread infectious disease of children in endemic areas, but little is known about the early lymphatic damage in children and its evolution, either with or without treatment. Two girls (ages 6 and 12 years) from a *Wuchereria bancrofti* endemic region of Brazil presented with chronic inguinal adenopathy. Neither had microfilaremia. By ultrasound both were shown to have living adult worms in their enlarged inguinal nodes and had occult local lymphatic damage (lymphangiectasis). One girl spontaneously developed acute adenitis in the affected node prior to any intervention; this adenitis resolved within 10 days and was associated with the progressive disappearance over 45–90 days of all local abnormalities detectable by ultrasound. In the other child, after treatment with a single dose of diethylcarbamazine (DEC), the same clinical picture of transient adenitis and resolving abnormalities (detectable by ultrasound) occurred. These findings demonstrated filariasis as the cause of adenopathy in children, and also both spontaneous and treatment-induced worm-death, with subsequent reversal of lymphatic abnormalities.

INTRODUCTION

The importance of lymphatic filariasis (LF) in children has been remarkably overlooked and understudied. The development of techniques to diagnose infection much more sensitively than in the past by detecting antigen in the blood[1] and to identify subclinical lymphatic disease by ultrasonography[2–4] has led to the recognition that LF is a common infectious disease of children in endemic areas.[5]

Disease associated with LF infection in children, however, is poorly understood. Although case reports attest to the occurrence in some children of the same LF manifestations commonly recognized in adults (e.g., elephantiasis,[6] hydrocele,[7] tropical pulmonary eosinophilia[8]), these manifestations are not as frequent in children as they are in adults. Other non-pathognomonic syndromes have also been suggested as clinical presentations for LF in children (including adenopathy, fever, arthropathy), but specific techniques to establish the etiology of these presentations have been lacking.

In our earlier, retrospective histopathological study[9] of patients presenting with unexplained chronic adenopathy who had lymph nodes removed or biopsied to establish a diagnosis, adult filarial worms were identified in 58 specimens examined, and two-thirds of these filaria-positive patients were children (0–19 years old). Such findings demonstrate that unexplained, chronic adenopathy can be an important clinical presentation of LF in children.

Subsequently, the development and application of ultrasonography to identify living *Wuchereria bancrofti* adult worms presented the opportunity to localize these worms non-invasively in infected patients. Though such studies have focused on adult-age populations,[3,4,10–12] we recently described the use of ultrasound to identify filarial worms in the lymphatics of children.[5] In that study of 11 parasite-positive children, most parasites were seen in pubertal or post-pubertal boys and were localized to the intrascrotal lymphatics, similar to that characteristically found in adult men.

The present report extends these earlier observations by describing the clinical presentation and the clinical course of definitively diagnosed filarial adenopathy in 2 girls whose ultrasonographic studies revealed specific LF and lymphatic abnormality. The changes in their clinical and ultrasonographic findings over time (with and without specific treatment) provide insight into the evolution of lymphatic filarial infection and disease in children (Table 1).

CASE REPORTS

Patient #1. A 12-year-old pre-pubertal girl was seen at the filariasis outpatient clinic of Hospital das Clínicas in Recife, Brazil, with a 4-month history of enlarged painless right inguinal lymphadenophathy. There was no present or recent past history of limb abnormality or bacterial infection. On physical examination, 3 discrete, mobile painless lymph nodes were palpable (the largest being 3.5×3.0 cm) with a rubbery consistency. The overlying skin was normal, and there was no limb or vulvar lymphedema. The rest of the physical exam was unremarkable.

Ultrasound examination of the right inguinal area revealed multiple lymph nodes, the largest showing a heterogenous echogenic pattern with a tubular anechoic structure measuring 2.5 mm and presenting the filaria dance sign (FDS) that suggests living *W. bancrofti* adult worms (Figure 1).[2] Examination for circulating microfilariae was negative in 11 ml of blood filtered through a 3 μm polycarbonate membrane.[13] The Og4C3 and immunochromatographic (ICT) card tests for circulating filarial antigen[1,14] were also negative.

Immediately after clinical and parasitological investigation, and before antifilarial treatment, the patient spontaneously developed acute right inguinal lymphadenitis with mild pain. Distal lymphedema, retrograde lymphangitis, and systemic signs or symptoms were not present. The lymph nodes were not fluctuant. Ultrasound examination showed that the previously anechoic tubular structure was filled with material of mixed echogenicity. The ultrasound failed to detect the FDS at 2, 7, 15, 30, 45, and 60 days after the acute

	Patient #1	Patient #2
Gender	F	F
Age	12 yr	6 yr
Family history of LF	Mother (28 yr), ICT positive	Mother (34 yr), no evidence of infection
	Father (32 yr), post-treatment for circulating microfilaria	Father (36 yr) hydrocele; ICT positive; Sister (3 yr), history of adenitis; no other evidence of infection
	Brother (4 yr), no evidence of infection	Sister (7 yr), no evidence of infection
		Brother (13 yr), no evidence of infection
		Brother (14 yr), FDS in right intrascrotal lymphatic
Clinical presentation		
Painless adenopathy	Right inguinal nodes	Left inguinal node
	4 months	5 months
Duration	none	none
Other		
Diagnostic findings		
Ultrasound	FDS	FDS
	Dilated lymphatic in lymph node	Dilated lymphatic in lymph node
Microfilaremia	Negative (11 ml)	Negative (11 ml)
Circulating antigen	Negative	Positive ICT
Treatment	None	DEC (6 mg/kg once)
Changes	Spontaneous	Post-treatment
Adentis (duration)	Acute (10 days)	Acute (7 days)
Adenopathy	Normalized (60 days)	Normalized (45 days)
Ultrasound	FDS negative (by 2 days)	FDS negative (by 2 days)
	Lymphatic not visible (by day 60)	Lymphatic not visible (by day 45)

ICT = immunochromatographic card test for circulating filarial antigen; DEC = diethylcarbamazine; FDS = the filaria dance sign.
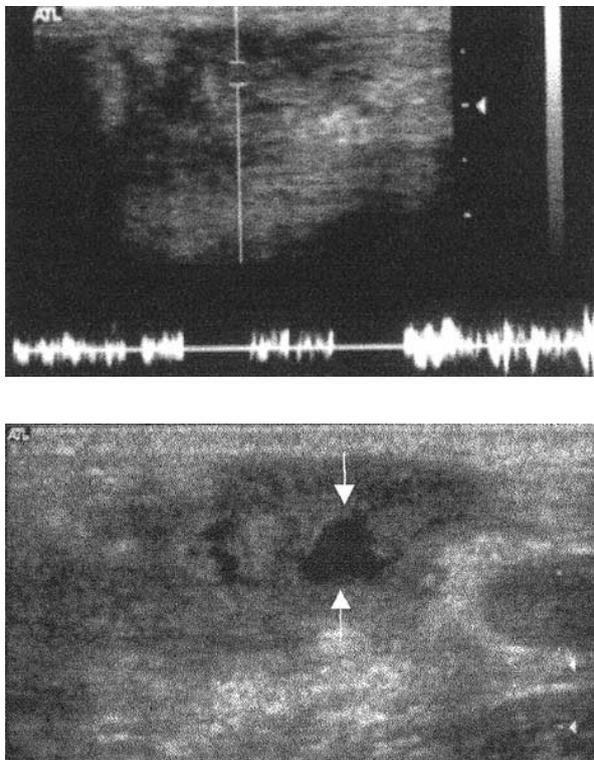

FIGURE 1. Ultrasonography of the largest lymph node from patient #1. **A.** An ultrasonography B-mode image showing a segment of intranodal dilated lymphatic vessel—represented by an anechoic area with 2.5 mm diameter (arrow). **B.** Pulsed doppler of the same lymph node and the same anechoic area displaying the characteristic aleatory pattern of the adult *Wuchereria bancrofti* worm called the filaria dance sign.

episode. The acute and subacute phases disappeared within 10 days. Thereafter, a progressive reduction of the size of the lymph nodes was observed, and the lymph nodes were no longer palpable at 60 days after the acute episode. The patient never developed ipsilateral lymphedema. Only cold compresses were used for treatment at the local site of the lymphadenitis during the first 3 days. The child was seen again 9 months after the acute episode, when both the physical examination and laboratory tests for filarial infection were normal.

Patient #2. A 6-year-old girl was seen at the filariasis outpatient clinic of Hospital das Clínicas in Recife, Brazil. Her mother described a painless lump in the left inguinal area of approximately 5 months duration. In addition, a history was elicited of two episodes of past adenitis in the axillary area, 3 months apart and occurring 12 and 15 months earlier, without evidence of antecedent trauma or infection in the hand or arm. The acute episodes were not associated with distal lymphedema. On physical examination, a painless, movable, rubbery lymph node (approximately 2.5 × 1.5 cm), was palpable in the left inguinal area. The overlying skin was normal, and no limb or vulvar lymphedema was observed. The rest of the physical exam was unremarkable.

Ultrasound examination of the left inguinal region showed a single lymph node with mixed echogenicity and a tubular anechoic structure (1.7 mm in diameter) exhibiting the FDS.[2] Examination for circulating microfilariae was negative in 11 ml of blood filtered through a 3 μm polycarbonate membrane. The ICT card test for filarial antigenemia was positive.

Diethylcarbamazine treatment was given as a single dose (6 mg/kg body weight). Twenty-four hours later the patient developed acute left inguinal lymphadenitis with mild pain, but without distal lymphedema, retrograde lymphangitis, or systemic signs or symptoms. Ultrasound examination failed

to show the FDS 2, 7, 15, 30, and 45 days after the acute episode. The acute and subacute phases subsided within 7 days. Subsequently, progressive involution of the lymph node developed, culminating with a lymph node of less than 0.5 cm diameter by palpation that was painless at 45 and 90 days after the acute episode. The patient did not develop ipsilateral lymphedema. Cold compresses were used for treatment at the site of the lymphadenitis during the first 2 days. At 45 and 90 days the ICT card test for circulating filarial antigen was still positive.

DISCUSSION

These 2 cases are instructive in several important ways. First, they reaffirm that lymphatic filariasis may present as painless adenopathy in children. The differential diagnosis of adenopathy in children is extensive,[15] but it is clear that in areas endemic for bancroftian filariasis, LF could be an important cause of otherwise-undiagnosed adenopathy.

Second, these cases provide direct evidence of previously-unrecognized occult lymphatic damage (lymphangiectasis) associated with painless adenopathy of LF. The implications of this lymphatic damage, however, still need to be defined; although no clinically manifest functional compromise was seen, only extended follow-up of such children will allow one to appreciate the long-term consequences of this lymphatic damage. It is also possible that lymphoscintigraphy can provide another means helpful for defining such lymphatic damage in children and its evolution post-treatment.[16] What is needed, however, is agreement on the clinical significance of such findings.[17]

Third, insight is gained concerning the natural history of LF-induced adenopathy and lymphatic lesions in children—both related to and in the absence of chemotherapy. Patient #1 received no anti-filarial treatment; patient #2 received DEC. In both cases, however, the patients showed essentially the same clinical and ultrasonographic evolution. This observation suggests that regardless of what kills the adult worm, the host inflammatory response and the progressive resolution of local changes are similar. Indeed, it is possible that the previous episodes of adenitis in the left axilla 12 and 15 months before the current presentation of patient #2 might have been a manifestation of 'spontaneous' adult-worm death at that time, but in the absence of specific diagnostic techniques, such as ultrasonography, the etiology of such episodes will remain uncertain.

Fourth, the apparent resolution of the local lymphatic changes both naturally and post-treatment offers distinct hope for the reversibility of occult lymphatic damage in children if their infections can be treated effectively in programs seeking to eliminate lymphatic filariasis through mass treatment of at-risk populations in endemic areas.[18] Only long-term follow-up of such individuals will determine whether filaria-induced lymphatic damage in children is reversible.

Finally, these cases show that no single diagnostic test can identify every case of lymphatic filariasis.[19] While antigen detection has greatly extended our diagnostic capabilities (particularly in children[20]), it could not diagnose patient #1, although ultrasonography could. Most likely the discordance results from a small number of adult worms in this girl. It is also possible that the antigen detection tests have different performance characteristics in pediatric populations. Alternatively, there could be an association of antigen negativity and the impending spontaneous destruction of the parasite. All of these possibilities merit further assessment. Localizing adult worms by ultrasonography is more labor- and technique-intensive than detecting circulating antigen or microfilariae in the blood, but to evaluate an individual patient thoroughly when the diagnosis of lymphatic filariasis is being considered may require all three of these diagnostic approaches. It is clear from the first case and from similar experiences that ultrasonography will be useful in the diagnosis of lymphatic filariasis, not only in Brazil[3,4,10–12] but elsewhere as well.[21–25]

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