CASE REPORT

Filarial Chyluria as a Rare Cause of Urinary Retention

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Abstract

We herein describe a case of Wuchereria bancrofti infection in a previously healthy 37-year-old Nepalese man. The patient presented with a history of milky urine with subsequent acute urinary retention lasting for a few days. The presence of microfilariae was confirmed on both peripheral blood and urine smears obtained at midnight. He was conservatively treated with diethylcarbamazine combined with doxycycline. Filariasis was previously endemic in southern parts of Japan, although it has been eradicated. Clinicians should remember filariasis as a potential etiology of urinary retention, especially in cases that may be associated with imported infectious disease.

Key words: chyluria, diethylcarbamazine (DEC), filariasis, imported infectious disease, Wuchereria bancrofti


Introduction

Filariasis is caused by nematodes that primarily inhabit the lymphatic system. More than 120 million people worldwide are infected with filariasis, and approximately 40 million infected individuals are seriously incapacitated and/or disfigured due to lymphatic filariasis (1). In India, the most endemic region of filariasis, approximately one-third of children are infected with the disease before 5 years of age (2), and this infection has been reported to be a major cause of disfigurement and disability, with significant social and economic impact (3-5). The parasite is transmitted via mosquito vectors, including Culex, Anopheles, Aedes, Mansonia and Coquillettidia; thus, the disease can be transmitted in both rural and urban areas. The World Health Organization (WHO) regards lymphatic filariasis as the leading cause of physical disability worldwide, and a global eradication campaign to eliminate the disease was launched in 2000. However, various factors, such as population migration, make it difficult to control the infection (6).

Among the several etiologies of filariasis, Wuchereria bancrofti is the most common parasite, accounting for 70% of cases worldwide. Most cases of W. bancrofti infection occur in India. Conversely, 99% of filariasis cases in India are caused by W. bancrofti. In Japan, filariasis previously prevailed in southern regions, including Okinawa and Kyushu; however, it has been reported that microfilaria carriers have disappeared, likely in the early 1980’s (7). Imported cases of filariasis have been sporadically reported, although no newly infected patients have been confirmed domestically.

Common symptoms of filariasis include hydrocele and/or leg edema. Chyluria can occur as a result of lymphatic obstruction, although this symptom is relatively rare. We experienced a case of W. bancrofti infection that was diagnosed in a previously healthy Nepalese man who presented with milky urine and acute urinary retention, without hydrocele or leg edema. Although such cases are quite rare, we consider this case to be educational and worthy of being reported.

Case Report

A 37-year-old Nepalese man (height: 167 cm, weight: 76.7 kg, body mass index: 27.5) with a chief complaint of milky urine persisting for several days presented to our de-
The results of laboratory examinations were almost normal during the day but deteriorated at night with turbidity being most evident in the morning.

Upon arrival, the patient was afebrile and his vital signs were stable. He complained of difficulty in urinating, and his lower abdomen was apparently distended. The cause of urinary retention was unknown at that time; however, emergent urethral catheterization was performed. Approximately 1 liter of milky urine was obtained (Fig. 1). A urinalysis showed a urinary triglyceride level of 155 mg/dL against a serum level of 110 mg/dL, and a diagnosis of chyluria was made. The results of laboratory examinations were almost normal, with negative findings for an inflammatory state (white blood cell count: 6,480/μL and C-reactive protein level: 0.13 mg/dL). Serum eosinophils accounted for 2.6% of white blood cells, and the serum IgE level was within the normal range (9 IU/mL). The serum levels of lipids were as follows: total cholesterol: 212 mg/dL and LDL-cholesterol: 130 mg/dL. Considering the epidemiologic and microscopic features of this case, the worm was assumed to be *Wuchereria bancrofti*, and 450 mg per day (divided into three doses) of diethylcarbamazine (DEC) was administered. An antihistamine was combined with DEC to prevent allergic or inflammatory reactions. For close observation, the patient was managed under hospitalization for three days. He was subsequently discharged without any allergic reactions, and a total of two weeks of DEC treatment was completed. After the initial treatment, the continued presence of microfilariaemia was confirmed in the peripheral blood. Additional combination therapy consisting of DEC and doxycycline was given for four weeks, and complete remission of microfilariaemia was obtained.

A molecular analysis of the pathogenic parasite was performed according to a previously reported method (8). A QIAamp® DNA mini kit (QIAGEN, Hilden, Germany) was used for DNA extraction from whole blood samples. We performed direct polymerase chain reaction using the primers UNI-1R (5′-CGC AGC TAG CTG CGT TCT TCT CG-3′), FIL-1F (5′-GGT GAA CCT GCG GAA GGA TC-3′), FIL-2F (5′-GGT GAA CCT GCG GAA GGA TC-3′) and FIL-2R (5′-TGC TTA TTA AGT CTT AA -3′). DNA sequencing was performed using a BigDye® cycle sequencing kit (Applied Biosystems, Foster City, USA) and an automated DNA sequencer (3130xl Genetic Analyzer; Applied Biosystems). The sequence data were analyzed using the BLAST sequence homology search program at GenBank, and the organism was confirmed to have 99.6% homology (264/265 bps) with the published sequence of the *Wuchereria bancrofti* strain (GenBank Accession No. EU272178).

**Discussion**

The clinical characteristics of filariasis include adenolymphangitis, hydrocele, elephantiasis and pulmonary eosinophilia. The laboratory features include peripheral blood eosinophilia and elevated serum IgE levels. However, the disease is often subclinical, making the diagnosis difficult, especially in developed countries, including Japan. Patients with characteristic symptoms and/or findings may be diagnosed as having filariasis earlier in the clinical course; however, our patient did not present with any of these findings. Only his nationality and the presence of chyluria were the keys to the diagnosis in this case.

The definitive diagnosis of the infected organism is usually based on the detection of microfilariae in the peripheral blood or urine. *W. bancrofti* exhibits nocturnal periodicity,
and a blood smear should be examined around midnight (between 10 p.m. and 4 a.m.). In fact, we found no microfilariae during the day, although the presence of microfilariae was easily confirmed in both blood and urine samples obtained at midnight. Circulating filarial antigen assays, which detect antigens released by adult filarial worms, have been recently developed. This test has better sensitivity and specificity than that of microscopic examinations (9, 10). The antigen levels remain stable, even during the day and in microfilaremic individuals (11); however, the test can only be used for *W. bancrofti*. Other methods for diagnosis include the detection of filarial DNA in the blood or adult worms in the lymphatic system.

Genetically, we identified the nematode worm to be *W. bancrofti*. Based on the epidemiological and microscopic aspects of this case, the filaria was assumed to be *W. bancrofti*. Globally, more than 90% of cases of filariasis are caused by *W. bancrofti*. In India, the presence of *W. bancrofti* and *Brugia malayi*, but not *Onchocerca* or *Loa*, has been reported (12). Identifying the exact species of filaria is essential for treatment since DEC, the first choice for *W. Bancrofti* infection, can induce an intense allergic reaction in patients infected with *Onchocerca* or *Loa*. In non-endemic countries, such as Japan, there can be various pathogenic organisms, since the disease is an imported infectious disease.

Our patient was complicated with chyluria, “milky” urine, and consequent urinary retention. Chyluria is generally associated with an abnormal retrograde or collateral flow through the lymphourinary fistula; lymph from the intestinal lymphatics is discharged into the urinary system. The differential diagnosis of chyluria includes pathological conditions that occlude lymphatic or thoracic ducts, such as those involving parasites (filariasis, echinococcosis, bilharziasis, schistosomiasis, ascariasis), tuberculosis, malignancies and a postoperative state. In patients with filariasis, the adult worms cause lymphatic obstruction and hypertension, then finally pass into the urinary system through the fistula. The symptoms of lymphatic obstruction generally appear one or two years after infection. It has been reported that chyluria has occurred in two (1.7%) of 119 filarial patients (13), two (2.5%) of 80 filarial patients (14) and up to 10% of filarial patients (15, 16). Therefore, the complication of chyluria is a relatively rare condition in patients with filariasis.

The lifespan of adult worms is approximately four to five years; however, chyluria can be observed after more than 10 years. Possible reasons for this phenomenon include: (1) ir-
reversible damage to the lymphatic duct, (2) the longer survival of adult worms and (3) a non-filarial etiology. Fat intake, pregnancy and exercise are considered to be aggravating factors of chyluria, and these conditions should be avoided, especially in patients with recurrent or prolonged chyluria (16). In the present case, moderate to severe fatty liver was confirmed, which may have directly induced the patient’s chyluria. The patient remained free from more common symptoms related to filariasis, such as lymphangitis, cellulitis, lymphedema, elephantiasis and hydrocele. However, the severity of chyluria was graded as a moderate to severe based on the patient’s intermittent milky urine with chylous coagulum and urinary retention (17). The detection of microfilariae in the chylous urine of otherwise asymptomatic filarial patients, as observed in the present case, has rarely been reported (18-20).

The administration of DEC (6 mg/day) for two weeks is generally recommended for the treatment of *W. bancrofti* infection. Although its mechanism of action is unclear, DEC has microfilaricidal and macrofilaricidal activities against *W. bancrofti*, *B. malayi* and *B. timori* (21). DEC kills approximately half of adult worms and potentially decreases the microfilarial burden (22). Side effects are generally mild (dizziness, nausea, fever, headache, muscle pain and/or arthralgia), although they depend on the number of microfilariae in the blood. Allergic or inflammatory responses can be serious in patients with severe microfilaremia, and we therefore combined an antihistamine with the above treatment in the present case. In some cases, repeated courses may be required to eliminate adult worms. Doxycycline, ivermectin and albendazole are considered alternatives. Importantly, the presence of only lymphedema or elephantiasis is not an indication for DEC therapy, since these conditions are not caused by acute filarial infection, but rather due to chronic obstructive states.

Before starting treatment, obtaining a definitive diagnosis of filariasis is essential. In cases of onchocerciasis or loiasis, the administration of DEC is considered to be a contraindication since the drug may provoke serious adverse reactions, such as encephalopathy and even death. In our patient, a diagnosis of *W. bancrofti* infection was made based on the results of morphological and genetic investigations.

Conservative treatment of lymphatic filariasis includes bed rest and a fat-restricted diet. As a result of prolonged chyluria, large amounts of fat and protein can be lost in the urine, leading to nutritional deficiencies. In addition, lymphocytopenia may occur since recirculating lymphocytes in the chyle are lost in urine (23). Therefore, providing nutritional

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**Figure 3.** Microscopic appearance of microfilaria on a peripheral blood smear. Direct smear (A) and Hematoxylin and Eosin staining (B, C) results are shown. Sweep curved, sheathed microfilariae exhibiting a uniformly tapering delicate end with no terminal nuclei were found (B, C).
education is essential. Generally, a high-protein diet without fat-containing foods is recommended. Fat should be avoided as much as possible; however, medium-chain triglycerides are permissible since they enter the circulation through the portal system, not the intestinal lymphatic ducts. Coconut oil is an example of such foods. Our patient had fatty liver and therefore received instructions regarding nutrition.

Surgical intervention is helpful in cases of recurrent chyluria (16). According to Tandon et al., the cure rate of conservative therapy is approximately 60% (16). In Japan, Ohyama et al. reported a cure rate of 61% (13), while Okamoto et al. reported a cure in 15% and an improvement in 23% of conservatively treated patients (24). Invasive therapy includes retrograde instillation of sclerosing agents (primarily silver nitrate, povidone iodine solution and 50% dextrose), lymphovenous anastomosis, renal hilar lymphatic disconnection and autotransplantation. These surgical therapies were not administered in our patient since the chyluria was intermittent and he was not undernourished.

In summary, we herein presented a case of W. bancrofti infection that caused milky urine and consequent urinary retention. Although the disease is considered to have been eradicated in Japan, filariasis should be considered as a potential etiology of urinary retention, especially in cases that may be associated with imported infectious disease.

The authors state that they have no Conflict of Interest (COI).

References


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