Chyluria due to Lymphatic Filariasis: Case Report and Review

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Abstract
Chyluria involves excretion of chyle into the urine, and worldwide is most commonly caused by lymphatic filariasis. With filarial infection, irreversible lymphatic damage can occur, and chyluria is a late complication. We present a patient with chyluria from filariasis who underwent laparoscopic nephrolysis with short-term success. We also review the literature and discuss the pathogenesis, diagnosis, and management strategies available.

Introduction
Chyluria involves passage of chyle in the urinary system and results in a milky-appearance of the urine. The most common etiology worldwide is filarial infection from one of three filarial worms: Wuchereria bancrofti, Brugia malayi, or Brugia timori. Recent figures estimate that worldwide, greater than 120 million people are infected, and the majority are due to infections from W. bancrofti. W. bancrofti is endemic to Southeast Asia and India, many Pacific islands, sub-Saharan Africa, and certain parts of Latin America. In endemic areas, up to 10% of the population may be infected, and up to 10% of those individuals can develop chyluria.

Case Report
A 52 year-old man from American Samoa with a past medical history significant for diabetes mellitus and hyperlipidemia presented with complaints of milky-colored urine (Figure 1). He described a history of hematuria and milky-appearing urine with mucus clots that had worsened over the past 3-4 years. He denied any alcohol use or liver disease, and denied any scrotal edema, prior trauma, or constitutional complaints. His physical exam revealed bilateral lower extremity non-pitting edema. Urinalysis revealed proteinuria, hematuria, and glucosuria but no evidence of infection. A urine triglyceride level was 1092 mg/dL. PPD, urine culture and urine acid-fast bacillus testing were negative. A complete blood count demonstrated mild eosinophilia, and by serologic testing, was positive for filarial IgG antibody, but negative for filarial antigen. Peripheral blood smears were negative for microfilariae. Computed tomography of his abdomen and pelvis demonstrated only bilateral simple renal cysts, and nuclear lymphoscintigraphy revealed delayed lymph flow and dilated lymphatic channels surrounding the left kidney suggesting lymphatic obstruction. He underwent cystoscopy and bilateral retrograde pyelograms, and was found to have chyluria lateralizing to the left ureteral orifice and severe lymph fistula formation involving the left kidney. He underwent laparoscopic nephrolysis of multiple dilated lymph vessels and left ureteral stent placement. He also was treated with a short course of ivermectin and for a few months had temporary resolution of his chyluria.

Discussion
Other than filariasis, there are other infectious and non-infectious causes of chyluria that include tuberculosis, fungal infections, Hansen's disease, malignancy (genitourinary, gastrointestinal, thoracic duct or thyroid tumors), trauma, pregnancy, hydrocele, and inguinal hernia. There are case reports of chyluria being caused by a thoracic aortic aneurysm and following cardiac catheterization.

In filariasis, the filariae are transmitted through a mosquito bite, with multiple mosquito species serving as possible vectors for transmission. The mosquito transmits third stage larvae which are deposited into the skin. The larvae travel to the lymphatic system and develop into adult worms usually by nine months. The adult worms live in the lymphatics where they mate and produce microfilariae (first stage larvae) which are intermittently showered into the bloodstream. Through another mosquito bite, these microfilariae are uptaken, and over a period of 10-14 days they develop into second and then third stage larvae. The mosquito then bites another human and the life cycle is completed. The adult worms live an average of five years, and it is the dying worms rather than the microfilariae which are responsible for most symptoms, as they incite an inflammatory reaction which results in lymphatic damage and obstruction. Patients may have recurrent episodes of lymphadenitis with fever and malaise, and repeated attacks lead to chronic manifestations of hydrocele, lymphedema, elephantiasis, and chyluria. Due to the lymphatic obstruction, dilation of these vessels occurs, as well as backflow of chyle and fistula formation to the urinary tract. In severe cases, chyluria can cause hypoproteinemia,
nutritional deficiencies, iron deficiency anemia, weight loss, and abnormalities of the immune system.\textsuperscript{4,5,6}

The initial evaluation of chyluria involves urinalysis and urine culture to evaluate for possible infection.\textsuperscript{4} Naked eye examination of the urine after it stands for a few hours may reveal a film of fat.\textsuperscript{7} Further analysis includes Sudan stain to confirm the presence of fat droplets, lipid electrophoresis to evaluate for chylomicrons, or measurement of cholesterol and triglyceride levels in the urine.\textsuperscript{4,7} Ultrasound and lymphoscintigraphy are useful in demonstrating evidence of abnormal lymphatic drainage, and are less invasive and have less potential complications than lymphangiography.\textsuperscript{5,7}

If filariasis is suspected, eosinophilia is a nonspecific finding and peripheral blood smears should be obtained to evaluate for microfilariae. Antifilarial antibody tests are available, but cannot distinguish between active or prior infections, and also cannot differentiate between the type of filarial infections.\textsuperscript{8} Circulating filarial antigen tests are considered the gold standard to diagnose infections from \textit{W. bancrofti}.\textsuperscript{5}

Various strategies are available to manage chyluria. Conservative measures include bed rest, abdominal binders that increase intra-abdominal pressure to prevent further chyle leakage, and dietary modifications to include a high protein diet, and low fat diets supplemented with medium chain triglycerides.\textsuperscript{5} Medium chain triglycerides are transported from the gut directly to the liver through the portal system and bypass the lymphatics.\textsuperscript{5,7} Instillation of silver nitrate into the renal pelvis can induce chemical lymphangitis and fistula fibrosis initially in 50-80\% of patients, but relapses in 23-50\% of patients occurred within two years.\textsuperscript{7,9} Lymphangiovenous anastomoses also have a limited success rate, postoperative chyluria secondary to incomplete fistula closure may persist in 50-60\% of patients.\textsuperscript{7} The most effective and long-term treatment option involves nephrolysis, or surgical stripping of lymphatic connections to the kidney, which have been performed using open surgical or laparoscopic techniques.\textsuperscript{3,10} There is an overall success rate of 98\% with nephrolysis, but the relapse rate approached 25\% after two years of follow up due to new fistula formation or incomplete lysis.\textsuperscript{7} Including this case, nineteen cases of laparoscopic nephrolysis have been reported in the literature with recurrence of chyluria in three of the total patients.\textsuperscript{10,11} Nephrectomy and renal autotransplantation have also been described in patients who have failed the above approaches.\textsuperscript{7}

\textbf{Conclusion}

There are numerous etiologies of chyluria and also a variety of management strategies. In Hawaii, with the high likelihood of seeing patients from filarial endemic regions, it is important to have a basic understanding in how to evaluate and manage patients with similar presentations.

The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. government.

\textbf{References}