

[CASE REPORT]

Idiopathic Chyluria with Nephrotic-range Proteinuria and Hypothyroidism

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Abstract:

The patient was a 75-year-old man who was admitted to our hospital because of fatigue, leg edema and heavy proteinuria. Due to his cloudy urine and elevated triglyceride level in his urine, he was diagnosed with chyluria. Tests for infectious disease were negative, and lymphoscintigraphy showed no blockage in the lymphatic system. He was therefore diagnosed with idiopathic chyluria. Hypothyroidism was also found and his cloudy urine and heavy proteinuria disappeared without dietary modifications after starting levothyroxine treatment for hypothyroidism. The patient is currently being followed up in an outpatient clinic and is doing well, with no recurrence of chyluria.

Key words: chyluria, non-parasitic, hypothyroidism

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Introduction

Chyluria is milky, clouded urine that is caused by lymph leaking into the urinary tract. It is classified into parasitic and nonparasitic forms. In Japan, while parasitic forms are almost exclusively responsible for detected cases, nonparasitic forms have also been reported (1). The most common causes of nonparasitic chyluria are traumatic factors, infectious disease, and tumors. Nonparasitic chyluria without any history of significant trauma (including surgical therapy) is very rare (2). In addition, the natural history and pathophysiology of nonparasitic chyluria are not well known. We herein report the case of an elderly without a parasitic infection or significant trauma who presented with chyluria and nephrotic-range proteinuria and whose abnormalities disappeared without dietary modifications after starting treatment for hypothyroidism.

Case Report

A 75-year-old retired man was admitted to our hospital because of fatigue, leg edema and heavy proteinuria. He was born and lived in Okinawa, the southernmost prefecture of Japan, until 15 years of age and then moved to Osaka. He

performed office work until 65 years of age. He had a history of cerebral infarction and had been treated with antihypertensive drugs and antiplatelet therapy. Three months before this admission, he noted cloudy urine, and his primary-care doctor referred him to our hospital. At his first visit to our office, the physical examination findings were unremarkable, although a urine analysis revealed heavy proteinuria and hematuria. His serum total protein was 6.2 g/dL. On admission, a physical examination revealed that his blood pressure was 162/84 mmHg and bilateral pitting edema was observed on his lower legs.

Laboratory examinations showed the following results: total protein, 4.8 g/dL; serum albumin, 2.9 g/dL; total cholesterol, 226 mg/dL; triglycerides, 133 mg/dL; serum creatinine, 1.14 mg/dL; blood urea nitrogen, 14 mg/dL; hemoglobin, 15.1 g/dL; white blood cell count, 5,200/ μ L (eosinophils 1.9%); and platelet count, 201,000/ μ L. Serological tests revealed C-reactive protein, 0.03 mg/dL and antinuclear antibody \times 40. Serological tests for parasites, including filariae, were negative.

His urine was cloudy, and a urinalysis showed nephrotic-range proteinuria (protein-creatinine ratio of 13 g/gCr) with hematuria and 10-19 lymphocytes per high-power field. Neither oval fatty bodies nor fatty casts were found in his urine. When ethanol and ether were added to his cloudy urine, the

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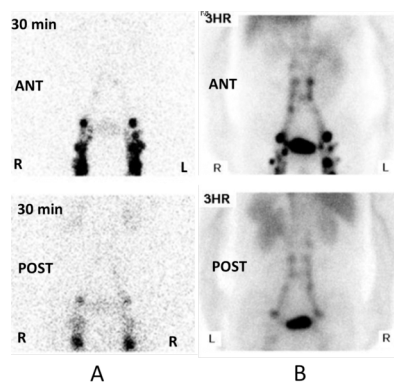


Figure. Technetium-99m-human serum albumin lymphoscintigraphy shows small amounts of radioactive materials in the urinary bladder in the early phase (30 minutes after administration) (A). The presence of communication between the lymphatic system and urinary tract was not observed, even in the late phase (3 hours after administration) (B).

opacity completely cleared. In addition, the triglyceride level in his morning urine was 134 mg/dL. These findings indicated that the cause of his cloudy urine was chyluria. To determine the cause of the edema, we also checked his thyroid-stimulating hormone (TSH) level on admission. His serum TSH level was elevated (46 μ IU/mL), and his serum levels of free thyroxine (fT4) and free triiodothyronine (fT3) were decreased (0.62 ng/mL and 2.03 pg/mL, respectively). His thyroid was not swollen and thyroid peroxidase and thyroglobulin antibodies were not detected. He also had no history of using drugs affecting the thyroid function. Thus, he was diagnosed with idiopathic hypothyroidism. The chest X-ray findings were normal. Abdominal echography and computed tomography revealed no abnormal findings. Technetium-99m-human serum albumin lymphoscintigraphy (RI-lymphography) showed early enhancement of the urinary bladder (Figure A) but no evidence of communication between the lymphatic system and kidneys or ureters, even in the late phase. No obstruction of the lymphatic system was found (Figure B).

On hospital day 5, the patient started taking levothyroxine (25 μ g/day) for hypothyroidism; his cloudy urine disappeared within two weeks of starting the treatment. During hospitalization, his medications, other than levothyroxine, were not changed and his blood pressure was 134-146/66-82 mmHg, while his fasting triglyceride levels were 124-148 mg/dL. The patient's urinary protein-creatinine ratio decreased drastically to <0.2 g/gCr and his hematuria also disappeared. At that time, his serum TSH level was 18 μ IU/mL, and his serum levels of fT4 and fT3 had normalized (0.84 ng/mL and 2.25 ng/mL, respectively). In addition, the edema in the lower extremities disappeared.

The patient is currently being followed up in an outpatient clinic with levothyroxine (50 μ g, daily) treatment, with no recurrence of chyluria, proteinuria, or hypoproteinemia at one year after discharge.

Discussion

Most patients with chyluria have infectious diseases, such as filariasis and granuloma (2, 3). Non-infectious cases are rare and have mainly been described in case reports. The etiologies of such cases include aortic aneurysms (4), neoplasms (5, 6), pregnancy (7), malformation lymphatic systems (8) and trauma (9). No apparent cause was found in some cases (10, 11). Although our patient was born on the tropical island of Okinawa, he moved to a non-tropical part of Japan (Osaka) 60 years previously and had not visited a tropical area since the move. His serum cholesterol level was not elevated and he was not taking statins. Furthermore, he had no signs or symptoms of damage to the lymphatic system, other than chyluria. In addition, in the present case, we found no lymphatic obstruction and could not determine the origin of the chyluria aside from a small lymphatic drainage route in the left renal pelvis. Thus, we diagnosed the patient with idiopathic chyluria.

Chyluria can mimic nephrotic syndrome, leading to a misdiagnosis and a potentially unnecessary renal biopsy. Patients with chyluria usually show non-pitting edema, flank pain and renal colic. In the present case, the patient developed hypoalbuminemia and heavy proteinuria with pitting edema. However, the remission of proteinuria was achieved, and pitting edema disappeared as the patient's cloudy urine disappeared. Cheng et al. reported a case in which a patient presented chyluria, heavy proteinuria and pitting edema with normal renal biopsy findings (12). In addition, because no lymphatic obstruction was observed in the present case, the patient might have had no flank pain or renal colic.

In cases with heavy proteinuria, the diagnosis of chyluria is confirmed by a urine examination. The presence of urinary triglyceride is 100% sensitive and specific for a diagnosis chyluria (2, 13). The gross examination of urine (milky urine) and the absence of fatty cast cells and/or lipid-laden oval bodies differentiate chyluria from nephrotic syndrome (12). It is important to obtain a detailed medical history, including the color and nature of the urine, especially in patients with positive tests for urinary protein.

In this case, the patient's milky urine disappeared and his serum protein levels normalized after treatment for hypothyroidism. However, to our knowledge, the relationship between chyluria and hypothyroidism has not been reported, and the mechanisms underlying the effects of levothyroxine, which can help resolve chyluria, are not well known. Chyle is triacylglycerol (TG) fluid that is formed in the small intestine. Free fatty acid is taken up from the intestinal lumen into the enterocytes and is used for biosynthesis of TG. It has been proposed that FAT/CD36, which is highly expressed in the small intestine (14), plays a key role in the uptake of free fatty acid (15). The expression of FAT/CD36 was reported to be downregulated by the presence of thyroid hormone (16). In addition, thyroid hormone enhances the somatostatinergic system, which inhibits nutrient absorp-

tion (17), by increasing the number of somatostatin receptors (18). Bed rest, abdominal binders and dietary modification have been reported to reduce the symptoms of chyluria. Nutrition interventions that remove long-chain triglycerides have been reported to play a major role in the conservative treatment of chyle leakage, and the spontaneous resolution of chyluria reportedly occurs in 50-70% of patients after dietary modification (19). However, in the present case, the chyluria disappeared without nutrition management. In addition, no recurrence of chyluria was noted for more than one year after discharge on the patient's usual diet.

In conclusion, we reported a rare case of idiopathic chyluria. In the present case, the patient's chyluria disappeared after starting levothyroxine treatment for hypothyroidism; however, the relationship between the chyluria and thyroid hormone is unclear. To the best of our knowledge, this is the first case report on the relationship between chyluria and thyroid hormones; thus, the accumulation of further cases is required to understand the relationship between chyluria and thyroid hormones in detail.

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

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