CASE REPORT

Filarial chyluria with nephrotic-range proteinuria and associated hypoalbuminaemia and hypogammaglobulinaemia secondary to bilateral lymphorenal fistulae

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SUMMARY

A 55-year-old man of Indian descent, presented to the emergency department with a 2-year history of passing 'milky' white urine, associated with dysuria, urinary retention, bilateral flank pain and 15 kg weight loss. He had migrated to Australia from India at the age of 16, with no overseas travel since, and denied having any fevers, rigours or chills. He was found to have chyluria and nephrotic-range proteinuria with marked hypoalbuminaemia and hypogammaglobulinaemia. Due to his ethnic origin and by diagnostic exclusion, a presumptive diagnosis of filariasis was made. With bilateral lymphorenal disconnection, as definitive management, the patient's chyluria and proteinuria resolved with restoration of normal plasma protein and immunoglobulin levels.

BACKGROUND

Presentations of filarial chyluria with chylous clots are exceedingly rare in developed countries, such as Australia,^{1,2} and as such, can be mistaken for a urinary tract infection. We describe a case of filarial chyluria with nephrotic-range proteinuria and associated hypoalbuminaemia and hypogammaglobulinaemia who presented with 'milky' white urine, associated with dysuria, urinary retention, bilateral flank pain and weight loss. With bilateral lymphorenal disconnection, as definitive management, the patient's chyluria resolved with restoration of normal immunoglobulin (Ig) levels.

CASE PRESENTATION

A 55-year-old homeless man of Indian descent, presented to the emergency department of Royal Perth Hospital with a 2-year history of passing 'milky' white urine, associated with dysuria, urinary retention, bilateral flank pain and 15 kg weight loss. He had migrated to Australia from India at the age of 16, with no overseas travel since, and denied having any fevers, rigours or chills.

On examination, the patient weight was 65 kg, 1.73 m in height, with a body mass index of 21.71 kg/m². A cardiorespiratory examination was normal, with no evidence of peripheral oedema. His abdomen was soft, with no distention, palpable masses or organomegaly; however, he was tender

in both flanks and over the suprapubic region. Penile and scrotal exam were unremarkable with no inguinal lymphadenopathy. His prostate was moderately enlarged, but otherwise smooth and non-tender.

INVESTIGATIONS

Macroscopically, his urine was 'milky' white in appearance, with no gross haematuria. A urine dipstick was positive for leucocytes, blood, protein and glucose, with a pH of 7.0. Urinary electrophoresis was negative for Bence-Jones protein. He had marked hypoalbuminaemia, nephrotic-range proteinuria, with a protein/creatinine ratio of 3800 mg/mmol (<13) and urine triglyceride concentration of 31.4 mmol/L (<0.1), confirming the presence of chyluria. A standardised oral fat tolerance test was performed, given in the form of a fatty 'milkshake' (1305 kcal; 87% from fat, 7% from carbohydrates, and 6% from protein) to quantitatively assess the magnitude of chyluria (figures 1 and 2). Immunological testing showed the presence of hypogammaglobulinaemia, with a serum IgG of 3.1 g/L (5.8–13.7), primarily due to reductions in IgG subclasses 1–3, but not 4 (table 1).

Investigations were undertaken to establish the cause of chyluria. Microfilariae were not detected in blood or urine and filarial serology was negative. Acid-fast bacilli were not detected in urine. No secondary or coinfection was identified. A percutaneous renal biopsy was not performed, but biopsies of perirenal tissue were obtained with only non-specific findings. Contrast pedal lymphangiography was unsuccessful. Although lymphoscintigraphy showed tracer activity in both inguinal lymph nodes, no lymphatic channels were visualised in the lower limbs nor was there evidence of transit of activity in the abdomen and pelvis at 2 hour. MRI of the abdomen demonstrated retroperitoneal T2 high signal intensity tubular structures without contrast enhancement below the level of the renal vessels, suggestive of dilated lymphatics leading to the left kidney (figure 3). Based on the above findings, a presumptive diagnosis of filarial chyluria was made.

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Figure 1 Preoperative urine samples taken before (0 hour) and after (2, 4, 6, 8 and 10 hours) an oral fat load. C indicates a normal control urine sample.

DIFFERENTIAL DIAGNOSIS

Causes of chyluria are usually divided into parasitic and non-parasitic. The most common cause for chyluria is filariasis and chyluria should be considered filarial unless proven otherwise. Various parasitic agents include *Wuchereria bancrofti*, *Echinococcus*, *Cysticercus cellulosae*, *Ascaris lumbricoides* and malaria can induce renal lymphatic obstruction, resulting in chyluria.³

Non-parasitic causes for chyluria include congenital lymphatic malformation, lymphorenal fistulas and lymphatic obstruction secondary to trauma, abscesses, neoplasms, pernicious anaemia and tuberculosis. C.⁴ Chyluria has been reported in nephrotic syndrome with focal segmental glomerulosclerosis and nephrotic syndrome due to retroperitoneal lymphangioma.^{4,5}

Milky coloured urine is also produced by urates, which clear on heating or phosphates and on adding 10% acetic acid.⁶

TREATMENT

The patient was initially treated with a povidine-iodine sclerosing agent and the antifilarial medications, ivermectin and albendazole, and then underwent a left surgical lymphorenal disconnection with partial improvement of his chyluria (figure 2). A subsequent bilateral retrograde pyelogram revealed an abnormality of the right renal tract with marked ureteropelvic junction dilatation and he was treated with retrograde instillation

Figure 2 Preoral and postoral fat load urinary triglyceride concentrations taken before and after unilateral and bilateral surgical lymphorenal disconnection.

Table 1 Laboratory results

Analyte	Presentation	Postsurgery	Unit	Reference interval/limit
Immunology				
IgG	2.8	9.6	g/L	5.8–13.7
IgG1	2.15		g/L	4.9–11.4
IgG2	0.97		g/L	1.5–6.4
IgG3	0.14		g/L	0.2–1.1
IgG4	0.37		g/L	0.08–1.4
IgA	0.7		g/L	0.6–3.4
IgM	0.3		g/L	0.3–1.7
Complement 1	1.25		g/L	0.78–1.5
Complement 2	0.28		g/L	0.16–0.52
Complement 3	1.83		g/L	0.88–1.98
Complement 4	0.36		g/L	0.16–0.52
Biochemistry				
Total protein	42	73	g/L	60.80
Albumin	19	41	g/L	35–50
Bilirubin	10	7	μmol/L	<20
Cholesterol	4.6	4.2	mmol/L	<5.5
Triglyceride	1.1	1.4	mmol/L	<1.8
Urine total protein	9.78	0.43	g/day	0.02–0.15
Urine triglyceride	43.24	<0.1	mmol/L	<0.1
Haematology				
Haemoglobin	154	141	g/L	130–170
Platelets	435	243	×10 ⁹ /L	150–400
Leucocytes	11.5	8.59	×10 ⁹ /L	4.0–10.0
Lymphocytes	0.52	0.58	×10 ⁹ /L	1.50–4.00
INR	1.1			<1.3
APTT	30.7		s	25–35

APTT, activated partial thromboplastin time; INR, international normalised ratio.

of lymphatic sclerosant povidine-iodine. However, 3 months postoperatively, he represented with chyluria, urinary retention and fevers and underwent right lymphatic disconnection with resolution of the chyluria (figure 2).

OUTCOME AND FOLLOW-UP

On outpatient review, 6 months after his second surgical intervention, there was no evidence of chyluria as documented by an undetectable urinary triglyceride concentration and complete resolution of his hypoalbuminaemia and hypogammaglobulinaemia (table 1).

DISCUSSION

We report a patient presenting with chyluria and chylous clot urinary retention, nephrotic-range proteinuria with associated hypoalbuminaemia and hypogammaglobulinaemia. Due to his ethnic origin and by diagnostic exclusion, a presumptive diagnosis of filariasis was made. With bilateral lymphorenal disconnection, as definitive management, the patient's chyluria resolved with restoration of normal albumin and Ig levels.

Chyluria, defined as the presence of chyle in urine, which comprises lipids, fat-soluble vitamins and proteins, has been recognised since antiquity. Its aetiology can be classified as parasitic and non-parasitic.⁷ Most common cause of the parasitic form is filariasis, first described by Joseph Bancroft in the mid-nineteenth century, due to *W. bancrofti*, which is endemic in subcontinent and southern Asia, particularly India and Sri Lanka, and should be excluded before considering non-parasitic

Figure 3 MRI of abdomen showing intestinal lymphatic dilatation (A) and high-intensity tubular structures below the level of the renal vessels, highly suggestive of dilated lymphatics leading to the left kidney (B).

causes.^{8,9} Chyluria represents a relatively rare, chronic complication of filarial infection that occurs on average 5–10 years after the primary infestation.¹⁰

Chyluria although alarming in appearance to the patient, may be asymptomatic and can continue intermittently for many years without compromising the health of the patient. The ‘clearing’ of chyluria during the day and on a low-fat diet is well described.⁹ However, chyluria may be complicated by dysuria, colic, loin pain, haematuria, anaemia, loss of protein and fat causing hypoproteinaemia, weight loss, malabsorption and cachexia.¹¹ Chyluria has been shown to result in depletion of lymphocytes, IgA and C3.¹² However, to our knowledge, chyluria has not previously been associated with hypogammaglobulinaemia.

It is recognised that in filarial chyluria and in chronic filariasis, microfilariae may be absent owing to the natural death of the adult worm and/or the development of suppressive immunological processes that destroy the microfilariae or block their production.¹³ Microfilariae were not detected in blood or urine and filarial serology was negative in our patient. The filarial antigen test was specific for *Wuchereria* and did not cross-react with other species, whereas, the enzyme immunoassay cross-reacted with the other Onchocercidae.

Contrast pedal lymphangiography, the imaging procedure of choice to assess the size, number and distribution of the

lymphatic vessels and location of fistulae, was unsuccessful in our patient. Lymphoscintigraphy,¹⁴ which allows functional assessment of lymphatic transport and depiction of regional lymph nodes, showed tracer activity in both inguinal lymph nodes, with no lymphatic channels observed in the lower limbs or evidence of transit of activity in the abdomen and pelvis. MRI of the abdomen demonstrated dilated lymphatics leading to the left kidney, as well as suspicion of intestinal lymphangiectasia, later confirmed with endoscopic studies. Despite MRI evidence of unilateral pathology, bilateral retrograde pyelography showed more dilation at the right ureteropelvic junction when compared with the left, raising the possibility of bilateral lymphorenal fistulae.

To determine whether the urine triglyceride concentration and/or pH were responsible for clot formation in chyluria, we varied the triglyceride concentration of normal urine (between 2.26 and 40 mmol/L) by adding intralipid, as well as adjusting the pH (between 3.5 and 10), but found no evidence of flocculation or proteinaceous gel formation, even after standing overnight. Similarly, chylous drain fluid (up to a triglyceride concentration of ~20 mmol/L) when added to normal urine also failed to induce chylous clot formation.

Medical therapies such as diethyl carbamazine, ivermectin and albendazole have been shown to rapidly eliminate microfilariae from the blood and directly injure adult worms.¹⁵ Our patient underwent empirical medical therapy despite having negative serology for filariasis. This decision was based on a high clinical suspicion for filarial chyluria given his acute presentation with chyluria, the patient’s subcontinent background and failure of medical therapies for non-filarial causes of chyluria. Although spontaneous remissions of chyluria have been reported, the treatment options for persistent chyluria include: dietary fat restriction or a medium chain triglyceride diet, sclerosing therapy with 1% silver nitrate and 0.5% povidine-iodine, surgical disruption and renal decapsulation.¹¹ Surgical lymphorenal disconnection represents a simple, permanent cure for chyluria with minimal complications.⁸

Nutritional support plays a major role in the treatment of chyluria, both to prevent malnutrition and to minimise chyle production and its flow.¹⁶ Our patient failed dietary modification, antifilarial treatment with ivermectin and albendazole, as well as sclerosing therapy. Left laparoscopic lymphorenal disconnection was performed, based on pathological findings on MRI, was initially deemed successful. However, he presented 3 months later with recurrence of chyluria (although to a lesser degree than before surgery) and IgG deficiency. Subsequent right renal lymphorenal disconnection was performed with complete resolution of the chyluria and restoration of normal circulating Ig levels.

IgG play a crucial role in the immune response by recognising foreign antigens and mediating effector mechanisms and physiological responses to eliminate invading organisms bearing that antigen. IgG is quantitatively the most functional and abundant class of Igs found in the circulation. IgG subclass deficiencies are observed in a wide range of illnesses encompassing primary immunodeficiency syndromes, atopic disorders, malignant and viral conditions.¹⁷ However, to our knowledge IgG deficiency has not been reported in association with chyluria.

In summary, we report a case of filarial chyluria and chylous clot retention, in an individual living in Australia where such presentations are exceedingly rare, with nephrotic-range proteinuria and associated hypoalbuminaemia and hypogammaglobulinaemia secondary to bilateral lympho-renal fistulae.

Learning points

- Presentations of filarial chyluria are exceedingly rare in developed countries; however, it should be considered in migrant patients from endemic areas presenting with infective urinary symptoms and 'milky' urine.
- Filarial chyluria can be associated with Ig deficiency.
- Urinary triglyceride concentration and urinary pH were not responsible for chylous clot formation.

Contributors JF was involved in drafting the manuscript. JRB and DP were involved in the conception of the case report. JM, JRB and DP were involved in the critical revision of the manuscript for important intellectual content. All the authors were involved in the final approval of the version to be published and were also involved in the agreement to be accountable for all aspects of the work.

Competing interests None declared.

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