Chyluria: a scourge of our region

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SUMMARY
Chyluria is endemic in the Gangetic belt of India with an average of 90 cases treated annually at our institute. It is almost exclusively caused by Wuchereria bancrofti in tropical areas. Chylomicrons and triglycerides are lost in the urine from an abnormal lymphouriniry fistula due to obstructive lymphatic stasis, most commonly at the renal pelvis. It is a distressingly recurrent condition with multiple exacerbations and remissions over years. Severe weakness, weight loss and haematuria occur in some patients. Diagnosis can be made by visual examination of milky urine along with the ether test of urine for chylomicrons. Intravenous urography is used to locate the site of the fistula, although the detection rate is poor. Treatment starts with conservative measures such as a high-protein low-fat diet and diethylcarbamazine therapy. In cases where conservative measures fail, endoscopic sclerotherapy (renal pelvic instillation of silver nitrate, povidone iodine or others) and surgical therapy are used.

CASE PRESENTATION
A 33-year-old woman presented with chief complaints of milky white urine accompanied by haematuria for the past 2 months along with severe weakness and weight loss. On examination the patient was severely dehydrated and cachexic. Her past history was significant for several similar episodes over the past 5 years. Some of the attacks had required treatment by drugs and others had spontaneously resolved. The patient was a resident of a village in the Jamui district of Bihar, India and often spent the summer nights sleeping outdoors. She described her village as a ‘muddy pond’ and ‘having more mosquitoes than stars in the sky’. There was a history of similar disease in her community. The patient was admitted and fluids and parenteral nutrition were administered. An early morning urine sample was collected after administering a fatty meal. On the ether test, the urine turned transparent and microscopic examination revealed chylomicrons. The patient’s general condition improved. In view of her long history and the severity of the disease, she was treated with renal pelvic instillation of sclerosant (RPIS) using 5% povidone iodine and 50% dextrose. She was advised to abstain from dietary fats.

The patient was informed that the disease was spread by mosquito bites. The patient’s village was about 300 km from our hospital. Although she had gone to her local health facility for treatment, this was the first time she had been evaluated and diagnosed. The patient was advised to attend regular follow-up visits at 2-monthly intervals at our hospital and to avoid mosquito breeding at her home and at the community level. After 2 months the patient presented in a healthy state and told us that her family had started using mosquito nets and had removed water pools from around her home. She was instructed to contact the local authorities regarding various health schemes running in her area and to be a part of it.

GLOBAL HEALTH PROBLEM ANALYSIS
Introduction
Chyluria has been rampant in our country, especially in the Gangetic belt, since time immemorial. The great Indian sage Charak described it as ‘suklameha’ in 300 BC. It is endemic in south-east Asia, China, India, Taiwan and parts of Australia and Africa. In tropical countries more than 95% of it is caused by parasitic infestation with Wuchereria bancrofti. The parasite is spread by mosquitoes of the genera Anopheles, Culex and Aedes. Water-logged areas promote the growth of these mosquitoes. Chyluria occurs in 2% of filarial-infested patients. Besides W bancrofti, other parasitic causes include Eustrongylus gigas, Taenia echinococcus, Taenia nana and malarial parasites. Other non-parasitic causes include congenital obstruction, lymphangioma, trauma, radiation, malignancy and following surgery.

Aetiopathogenesis
Chyluria is the passage of intestinal lymph in the urine. The pathophysiology of chyluria involves obstruction or dilation of the retroperitoneal lymphatics. The retroperitoneal lymphatics include a number of lymphatic trunks draining the kidneys and intestinal lymphatics draining the intestine, pancreas and spleen. All these lymphatics drain into the cisterna chyli. The aetiopathogenesis is not well known. There are two theories:

▸ Obstructive theory: the parasitic infections lead to obliterative lymphangitis and lymphatic hypertension which leads to varicosities and collaterals leading to backflow of intestinal chyle.

▸ Regurgitative theory: regurgitation of chyle from the cisterna chyli or large intestinal trunks into the renal lymphatics leads to rupture of these lymphatics into the renal calyces or pelvis.
**Grading**
Chyluria is graded according to the mode of presentation: grade 1 is milky white urine; grade 2 is white clots or episodes of clot retention; and grade 3 is haematochyluria.³

**Diagnosis**
**Urination examination**
Chyluria can be diagnosed by examining a freshly voided sample of morning urine. A fatty meal should be taken before voiding. On visual examination, chylous urine is milky in appearance and may contain fibrin and blood clots. The urine becomes clear on adding ether and bright red with ingestion of Sudan III mixed butter. Analysis of urine reveals chylomicrons and triglycerides. Estimation of urinary chylomicrons is the most specific and sensitive test for chyluria.⁴

**Haematological examination**
A haemogram typically shows eosinophilia.

**Imaging**
Intravenous urography, retrograde pyelography and lymphangiography are used to locate the lymphourinary fistulas. Recently, magnetic resonance pyelography and lymphoscintigraphy have also been used.⁶ If available, lymphangiography is an excellent diagnostic modality. It can demonstrate the site, caliber and number of fistulous communications. Findings include lymphourinary fistula at the level of the kidneys, ureters or bladder. The presence of lymphangiectasias may be noted. In 40% of cases contrast enters the pelvicalyceal system. Lymphangiography is rarely used nowadays as it is an invasive, time-consuming and technically demanding procedure. Lymphoscintigraphy is a non-invasive technique which uses Tc-99m diethylenetriamine pentaacetic acid (DTPA) radionucleotides for patients not responding to conservative therapy, RPIS is used. It is based on the observation that the lymphourinary fistula is most commonly located at the renal pelvis. Injection of sclerosant here causes it to pass to the lymphatic channels and induce a chemical lymphatic reaction. The resultant oedema leads to blockade of the lymphatics and immediate relief to the patient. Permanent relief of chyluria occurs when the lymphatics heal by fibrosis. The procedure is performed under local anaesthesia or sedation. A fatty meal in the morning or previous night facilitates identification of the affected ureteric orifice. If the chyluria is intermittent, the orifice needs to be observed for 15 min or longer for diagnosis. Pressing the kidney through the abdominal wall also sometimes helps. A ureteric catheter is passed to the renal pelvis under radiological control and an amount of sclerosant equal to the renal pelvic capacity (7–10 mL) is injected. The instillation is done in the head-down position and continues until the patient experiences pain.¹⁰
The commonly used sclerosants include silver nitrate (0.1–1%), povidone iodine (0.2–5%), potassium bromide (15–25%), sodium iodide (10–25%), 50% dextrose, hypertonic saline (3%) or a combination of these. For instillation, an 8-hourly instillation for 3 days has been found to be superior to a weekly instillation for 6 weeks.¹²

**Silver nitrate**
The most extensively studied agent in the past was silver nitrate (0.1–1%); 2 g of silver nitrate is dissolved in 200 mL water and kept in a dark bottle to protect it from sunlight as silver nitrate becomes unstable on exposure to sunlight. Freshly prepared solution is needed every time, so it must be procured 8–24 h before the procedure and autoclaved. It can precipitate with normal saline to form insoluble silver chloride salt which can lead to ureteric obstruction. It is a water insoluble compound. These problems have led to a decrease in its use.¹² One death after bilateral instillation has been reported.¹³

**Povidone iodine**
Povidone iodine is believed to be the most commonly used agent at present. It is stable at room temperature, water soluble and easily available. Chemically it is polyvinyl pyrrolidone and releases iodine slowly. It also has antibacterial, antifungal and antiseptic properties. It has been used in a concentration of 0.2–3%.¹⁴ We have been using a mixture of 5% povidone iodine and 50% dextrose¹⁵ for 5 years with good results and have not observed any strictures, deaths or other untoward incidents. Our cure rate at 6 months exceeds 90% (table 1). Patients who fail one course of sclerotherapy should be treated with a second course. Singh and Srivastava¹¹ have shown that the time to

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**References**


BMJ Case Reports: first published as 10.1136/bcr-2014-209188 on 6 July 2015. Downloaded from http://casereports.bmj.com/ on 7 March 2024 by guest. Protected by copyright.
failure has a prognostic significance, with immediate failure being associated with a lower chance of final success.

Surgical therapy
Patients who do not respond to two or three courses of RPIS are labelled as ‘refractory chyluria’ and are considered for surgical therapy. Other indications for surgery include extensive weight loss, hypoproteinaemia, anasarca, recurrent clot retention, haematochyluria, recurrent urinary tract infections secondary to chyluria, altered immune status and psychological disturbances. Hemal et al classified chyluria into the following three grades based on involvement of the calyces on retrograde pyelography (RGP):

- Mild chyluria: involvement of a single calyx on RGP (figure 1A).
- Moderate chyluria: involvement of two or more calyces on RGP (figure 1B).
- Severe chyluria: involvement of most calyces with/without involvement of the ureter on RGP (figure 1C).

They advocated surgery in failed cases of mild to moderate grade and in those with severe grade of chyluria.

The operations described for chyluria include chylolymphatic disconnection, lymphovenous anastomosis, retroperitoneal lymphovenous anastomosis, transinguinal spermatic lymphovenous anastomosis, inguinal lymph node–saphenous venous anastomosis and autotransplantation or nephrectomy.

Chylolymphatic disconnection
Chylolymphatic disconnection is the most commonly performed procedure. It was first described by Ketamine in 1952. This operation can be done by a flank incision or laparoscopically through either the transperitoneal or retroperitoneal route. Before surgery patients are put on high-fat diet for 24–36 h to facilitate intraoperative identification of the lymphatics. Methylene blue dye is also used for the same purpose. Five procedures can be used:

1. Nephrolympholysis: the kidney is dissected free from its surrounding perirenal fascia.
2. Hilar stripping: this includes skeletonisation of the renal vessels and ligating the perihilar lymphatics.
3. Ureterolympholysis: this includes stripping of the ureteral lymphatics downward to the common iliac vessels.
4. Fasciectomy: this includes removal of perirenal tissues and fat.
5. Nephropexy: the kidney is fixed to the psoas muscle at its upper, middle and lower poles to restrict its hypermobility.

After dividing the renal fascia, the lymphatics around the renal hilum and upper ureter are routinely stripped and ligated in most cases.

Patna operation
The original ‘Patna operation’ described the concept of ‘ureter in a lymphatic tunnel’ and utilised lymphatic disconnection of the abdominal ureter up to the bladder. However, disconnection up to the bladder is not used nowadays as most of the leak is localised to the renal pelvis. In case of recurrence or if radiological studies demonstrate lymph leak from the ureter, complete stripping is performed.

Lymphovenous anastomosis
Lymphovenous anastomosis is a more physiological way of treating chyluria as it diverts the lymph flow into the venous system and decreases intralymphatic pressure. The thin calibre of lymph vessels makes the procedure technically demanding and requires microsurgical expertise. The anastomosis can be done retroperitoneally, at the inguinal area or anastomosis of the inguinal lymph node with the saphenous veins. These anastomoses are more superficial and hence are preferred in older and weaker patients who would not tolerate lymphatic ligation. In women, the vessel calibre is thinner and hence the anastomosis is done at the level of the dorsum of the foot, leg or thigh while, in men, the inguinal region is preferred. Patency of the anastomosis is essential for a successful operation, and it may take up to 6 months to show results. It is advisable to do at least 6 months before deciding the success or failure of the anastomosis.

Table 1 Results of patients with chyluria treated at our institute by sclerotherapy with 5% povidone iodine and 50% dextrose over a 1-year period (January to December 2013)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients</td>
<td>97</td>
</tr>
<tr>
<td>Age distribution (years)</td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>24</td>
</tr>
<tr>
<td>21–39</td>
<td>45</td>
</tr>
<tr>
<td>40–60</td>
<td>28</td>
</tr>
<tr>
<td>Male/female</td>
<td>61/36</td>
</tr>
<tr>
<td>Mean follow-up (months)</td>
<td>6 (range 3–11)</td>
</tr>
<tr>
<td>Success rate</td>
<td>92.7%</td>
</tr>
<tr>
<td>Major complications</td>
<td></td>
</tr>
<tr>
<td>Flank pain</td>
<td>27</td>
</tr>
<tr>
<td>Haematuria</td>
<td>18</td>
</tr>
<tr>
<td>Chyluria persisting</td>
<td>7</td>
</tr>
</tbody>
</table>

Figure 1 Drawing showing amount of calyx involvement marked by dotted red line. (A) Involvement of single calyx. (B) Involvement two calyces. (C) Involvement of most of the calyx plus the ureter.
two anastomoses to enhance lymphatic flow. If the diameter of the lymphatics is <0.1 mm, a vein of corresponding diameter is anastomosed to a bunch of lymphatics.\textsuperscript{16}

\textbf{Retroperitoneal lymph node anastomosis}

This technique was originally described by Cockett and Goodwin.\textsuperscript{20} Operating in the retroperitoneum can be associated with problems of a deep-seated operative field, risk of renal pedicle injury, risk of renal artery stenosis and renovascular injury.

\textbf{Transinguinal spermatic lymphovenous anastomosis}

This procedure is performed via an inguinal incision. Methylene blue is injected to stain the lymphatics and they are anastomosed to spermatic veins of similar calibre using 10-0 nylon.\textsuperscript{21}

\textbf{Inguinal lymph node–saphenous vein anastomosis}

The inguinal lymph node is anastomosed to the saphenous vein. The procedure provides a wide anastomosis for free passage of lymph into the venous system and avoids damage to the efferent and afferent lymphatic vessels.\textsuperscript{22}

\textbf{Autotransplantation and nephrectomy}

Autotransplantation and even nephrectomies have been described for severe unremitting chyluria.\textsuperscript{23} We have no experience with these procedures and have never had a requirement for them.

Stepwise approach to the management of patients with chyluria

Suspected chyluria (white urine, haematuria)

\downarrow

Urinary triglycerides, urinary chylomicrons present

\downarrow

Dietary therapy, medium-chain triglycerides, DEC

\downarrow

Recurrence

\downarrow

Intravenous urography, CT scan, MRI

\downarrow

RPIS: betadine, silver nitrate (up to two courses)

\downarrow

Chylolymphatic disconnection (open or laparoscopic)

\downarrow

Recurrence

\downarrow

Lymphovenous, lymph node–venous anastomosis

\downarrow

Nephrectomy, autotransplantation

Mass chemoprophylaxis

An important strategy in the control of tropical lymphatic diseases such as filariasis includes mass chemoprophylaxis in endemic areas. Globally, the preferred regime is DEC 6 mg/kg along with albendazole 400 mg. In India a single dose of DEC is used. It is estimated that chemoprophylaxis has to reach 90% of the population for elimination of filariasis.\textsuperscript{24}

Environmental measures

Filaria is transmitted by mosquito bite of the genera \textit{Aedes}, \textit{Anopheles} and \textit{Culex}. These mosquitoes thrive around sources of stagnant water. Community and government participation to clean up the surroundings is essential to control the disease. The government carries out periodic spraying of dichlorodiphenyltrichloroethane (DDT) and other disinfectants in endemic areas. Other personal measures to combat mosquitoes include use of mosquito nets and repellents.

\textbf{CONCLUSION}

Chyluria caused by lymphatic filariasis is a public health problem in our region. It is essentially a benign disease which can be effectively controlled by public awareness, drugs and dietary restrictions. A small proportion of patients have severe and unremitting disease which requires surgical intervention. Filariasis as an endemic tropical disease requires medical treatment as well as community participation for control.

\textbf{Learning points}

- Chyluria is caused in most cases by mosquito-borne \textit{Wuchereria bancrofti}.
- It can be diagnosed by urine examination for chyle and chylomicrons.
- Most cases can be controlled by diet and drug therapy.
- A small proportion have severe, unremitting and refractory disease which requires surgery or sclerotherapy.
- Prevention of mosquito bites is essential to prevent the spread of this disease.

\textbf{Contributors} RKS: manuscript design, preparation, editing. NR: manuscript design, preparation, editing. KA: final editing.

\textbf{Patient consent} Obtained.

\textbf{Provenance and peer review} Not commissioned; externally peer reviewed.