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Chyluria: a mimicker of nephrotic syndrome

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BACKGROUND AND OBJECTIVE: Chyluria can be confused with nephrotic syndrome when massive proteinuria is present on urine examination during evaluation of a milky/white urine. Our objective was to attempt to resolve diagnosis in the case of nephrotic range proteinuria when there is no clear evidence of a significant kidney lesion.

DESIGN AND SETTING: Retrospective review of the medical records of all patients referred the nephrology department at a single institution.

PATIENTS AND METHODS: We identified a subgroup of patients misdiagnosed with nephrotic syndrome and treated aggressively with immunosupression with no benefit and who were later diagnosed as having chyluria.

RESULTS: Twelve patients were identified (8 men, 4 women) with a median age of 34.5 years. Chyle was positive in the urine in eight while chyle was positive on oral ingestion of butterfat in another 4. Six had undergone kidney biopsy and were treated as having minimal change disease. Eight had massive proteinuria and a history of treatment with prednisone, but none of these patients had shown improvement in their clinical presentation. Two patients showed excellent results with diethylcarbamazine with angiotensin-converting enzyme inhibitors in while eight required betadine instillation in the fistulous connection with success in six. Surgical correction was successfully tried in two of these resistant cases.

CONCLUSION: In individuals with nephrotic range proteinuria with a normal or low lipid profile status along with normal serum albumin levels, urine color and nature, frequency, and checking the urine for chyle can help identify the large subgroup who unnecessarily have to undergo kidney biopsy and at times are treated with immunosuppression, which is not only life threatening but useless in these patients.

Chyluria is defined as the passage of chyle into the urine. Chyle is comprised of large quantities of dietary lipids, proteins and fat soluble vitamins. Chyluria occurs when there is an abnormal communication between the lymphatic and urinary systems. Chyluria can be confused with nephrotic syndrome when massive proteinuria is present on urine examination during evaluation of milky or white urine. At times it becomes more difficult when patients present with nephrotic range proteinuria and active sediments, but lack of edema, normal serum albumin and an abnormal or normal lipid profile may alert physicians to nephrotic syndrome and the need for kidney biopsy and aggressive treatment with potentially harmful immunosuppression, with no benefit. We report a series of such cases when chyluria was confused with nephrotic syndrome and the patients subjected to kidney biopsy and immunosuppression or both. The idea was to resolve situations where an individual presents with nephrotic range proteinuria without any clear evidence of a significant kidney lesion or other explanation of the massive amount of protein leak from the kidneys.

PATIENTS AND METHODS

We retrospectively identified the records of all patients referred to the Department of Nephrology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, for evaluation of nephrotic syndrome, which on further evaluation was determined to be chyluria.

RESULTS

Twelve patients were referred for evaluation of nephrotic syndrome and later diagnosed with chyluria. Eight were men with median age of 34.5 years (**Table 1**). Not all patients had a prominent history of passing "white

Table 1. Twelve patients referred for evaluation of nephrotic syndrome.

Median age (years)	34.5
Age range (years)	31-44
Sex (M:F)	8:4
Continuous turbidity of urine	4
Intermittent turbidity of urine	4
History of no turbidity of urine	4
History of filarial infection	2
History of renal colic or passing of clots	2
Positivity of urine for chyle (random)	8
Positivity of urine for chyle after fat ingestion	4
Urine test for acid-fast bacilli	Negative in all
24-hour proteinuria (3-10 g/d)	6
24-hour proteinuria (>10 g/d)	6
Patients subjected to kidney biopsy	6

Values are number of patients unless noted otherwise.

Table 2. Clinical profile including side effects due to immunosuppression in the 12 patients.

Variable	Number of patients
History of usage of steroids	6
History of usage of other immunosuppressive agents	2
Cushingoid facies	4
Infection	2
Hypertension	3
Diabetes mellitus	1
Response to therapy[a]	
Diethylcarbamazine + ACE inhibitors	6/6
Betadine instillation	6/8
Surgical correction	2/2

[a]Positive response/number treated.

urine", but they had no anasarca, normal lipid profiles and serum albumin, and the urine was either positive or normal for chyluria. Urine tests for acid-fast bacilli were negative in all patients. Chyle was positive in the urine in 8 while another 4 were positive for chyle on oral ingestion of butterfat. Six of these patients had undergone kidney biopsy before being referred to us and were treated as having minimal change disease based on normal light microscopy changes. Eight had massive proteinuria and a history of treatment with immunosuppression, and none had shown improvement in clinical presentation. The condition was responsible for serious infection in two patients and worsening of hypertension in 3 (**Table 2**). Retrograde pyelography demonstrated the fistulous connection and dilated lymphatics in four patients while lymphangiography was the diagnostic modality in another four. Six of the patients showed a response to diethylcarbamazine and angiotensin-converting enzyme (ACE) inhibitors. Betadine instillation was successful in six of eight patients who had not responded to conventional treatment, all of whom were in remission. Chyluria did not resolve in two patients after two instillations of betadine, and open surgical ligation and excision of the renal pedicle lymphatics was tried with significant success (**Table 2**).

DISCUSSION

The clinical suspicion of chyluria was raised in these 12 patients who initially presented as having nephrotic syndrome (all had proteinuria >3 g in 24 hours) and a history of continuous or intermittent turbid urine, but with no stigmata of the clinical syndrome. After testing for chyle in urine, eight patients were positive while another four tested positive on challenge with dietary fat. A kidney biopsy was attempted in six patients, which was later reported as normal with some suggestion of minimal change disease. Eight of these 12 patients were treated with immunosupression, which resulted in serious infections in two patients. Treatment options tried were diethylcarbamazine with ACE inhibitors in two with excellent results, while eight required betadine instillation in the fistulous connection with success in six. Surgical correction was successfully tried in two of these resistant cases.

Chyluria may be associated with dysuria or hematuria due to rupture of small blood vessels adjacent to the fistulous communication.[1-5] Individuals can at times present with anemia, hypoproteinemia due to loss of protein, and fat in the urine subsequent to weight loss and malnutrition.[6,7] However, usually these individuals are clinically asymptomatic as was evident in our study population where, despite documented proteinuria >3 g/24 hours with active urinary sediments, none of these individuals showed any evidence of gross anascarca, hypoproteinemia or lipid abnormalities that clinically aroused a suspicion of a nonglomerular pathology for this massive proteinuria. Chylous clots may cause renal colic and obstruction, which is significant when the stigmata of classical nephrotic syndrome are not present and after ruling out other systemic causes. On repeated questioning, two patients admitted a history of turbid urine, hematuria and at times clots, which are never present in patients with classical nephrotic syndrome.

Clots rule out nephrotic syndrome.

Once a clinical diagnosis of a nonglomerular cause for proteinuria and hematuria is made, the investigations necessary for chyluria are intravenous pyelography, cystoscopy, retrograde pyelography and lymphangiography. Retrograde pyelography can demonstrate the fistulous connection and dilated lymphatics,[8] which was used to diagnose the fistulous communication in four of our patients. Lymphangiography, which can clearly demonstrate the lymphopelvic fistulous communication[9] was used to diagnose chyluria in another four patients. Genitourinary tuberculosis should be considered in the differential diagnosis and a urine test for acid-fast bacilli is necessary to rule out tuberculosis in a country like India. All our patients had a negative urinary acid-fast bacilli report.

The natural history of chyluria is still not clear. Spontaneous remission can be observed in 50% of cases so not all require treatment. When chyluria presents with proteinuria, a favorable outcome has been reported following treatment with ACE inhibitors.[10] Six patients in our study group showed a response to diethylcarbamazine and ACE inhibitors, but this could also be because of spontaneous remission. Sahoo et al in their study were able to show similar results as proteinuria resolved after treatment with diethylcarbamazine and ACE inhibitors. Surgical management is indicated in refractory severe chyluria with recurrent clot colic and urinary retention.The available surgical techniques are endoscopic sclerotherapy, surgical lymphatic disconnection and microsurgeries. Instillation of AgNO3 or even betadine[11] has been used and is considered to be a safe effective and a minimally invasive procedure with an initial success rate of about 70% to 80% and a long-term recurrence rate of 50%. However, in eight of our patients betadine instillation showed significant success with remission in six. Another two underwent open surgical ligation and excision of renal pedicle lymphatics with significant success following repeated betadine instillation.

Sahoo et al screened 282 cases of Bancroftian filariasis over a period of 7 years and found 42 cases with proteinuria over 150 mg/24 h.[12] Light microscopic examination of renal biopsy tissue from 27 patients revealed predominantly mesangioproliferative changes in 18 cases and endocapillary proliferation in 9 cases. Basement membrane thickening and tubular degeneration were observed in six cases each. Immunofluorescence showed mesangial deposits of IgG alone, or in combination with C3 in 12 patients, and granular deposits of IgG and C3 along capillary wall in three patients, suggesting immune-mediated glomerulopathy/filiarial nephropathy. However, in our kidney biopsy specimens we were able to appreciate only focal and mild effacement of visceral epithelial cell foot processes without electron dense deposits, thus suggesting a glomerular and nonglomerular association with filiarial infection.

In conclusion, in nephrotic-range proteinuria with a normal or low lipid profile status along with normal serum albumin levels, a careful history is mandatory to determine the color of the urine, its nature and frequency of urination. Checking the urine for chyle can help reduce a large subgroup of these patient who unnecessarily undergo kidney biopsy and at times are treated with immunosuppression, which is not only life threatening but useless in chyluria.The degree of proteinuria and its association with chyluria is still under evaluation. Th is question needs to be answered in future large-scale studies.

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