Case Report

C1Q Nephropathy, An Unusual Occurrence in a Middle-Aged South Asian Woman

C1Q Nephropathy

Zohaib Ramzan[1], Shahid Anwar[1], Syed Ali Raza[2] and Zoha Majeed[3]

ABSTRACT

We present an interesting but rare occurrence of C1q nephropathy in a middle-aged South Asian woman with a history of edema and fatigue who responded well to steroids. C1q nephropathy is a glomerulopathy characterized by large amounts of C1q deposits in mesangium and is a diagnosis of exclusion after ruling out SLE, affecting a predominately pediatric population. Our case highlights the importance of lateral thinking while dealing with management and treatment outcomes in C1q nephropathy.

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BACKGROUND

C1q nephropathy was described by Jennette and Hipp in 1985. It is characterized by large amounts of mesangial Ig and complement deposition with the predominant appearance of C1q after the exclusion of systemic lupus erythematosus and mesangial-proliferative disease.[1-2] The pathogenesis is unclear. Incidence of C1q nephropathy varies in reports ranging from 0.2 to 16% with no gender differences and appears to be higher in children. Clinical presentation ranges from asymptomatic hematuria or proteinuria to frank nephrotic or nephritic syndrome in children and adults.[3] The disease pattern on biopsy may vary, but the core component of diagnosis remains C1q deposition with no features of SLE. Biopsies may range from no lesion in the kidney besides C1q deposition in the mesangium; those with features of FSGS may have associated mesangial proliferation, and mesangial hypercellularity may be seen with those presenting with proliferative glomerulonephritis.[4]

For the most part, though, it is considered steroid-resistant. Those with minimal change disease-like patterns may have greater remission rates, whereas those with FSGS patterns may be more prone to the development of end-stage renal disease.

[1.] Department of Nephrology / Medicine[2], Fatima Jinnah Medical University, Lahore.
[3.] Department of Medicine, Sir Ganga Ram Hospital, Lahore.

Correspondence: Dr. Zohaib Ramzan, Department of Nephrology, Fatima Jinnah Medical University, Lahore
Contact No: 03330160858
Email: zohaib321@live.com

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A large meta-analysis found that partial remission rates were 28% and complete was 49%. Some data shows complete and partial remission with steroids. However, cyclosporine and Cytoxan have also been used with steroids for remission. Relapses may also be common[5].

CASE PRESENTATION AND DISCUSSION

A 30-year-old female from Lahore came to the Nephrology clinic in May 2020, complaining of generalized body swelling for two weeks associated with fatigue, exertional dyspnea, and epigastric pain. Swelling is more pronounced in her lower limbs; her epigastric pain was mild, radiating, and not associated with nausea and vomiting. She was dyspneic about taking 10 to 20 steps but could carry out her daily activities without discomfort. All the symptoms were concordant in time. Her past medical and surgical history was unremarkable. Her family history and personal history are also unremarkable.

Her bp was 140/90 at the presentation, and the rest of the vitals were normal. A general physical examination showed periorbital puffiness and 2+ bilateral pitting edema up to the knees. On Respiratory examination, there was bilateral decreased air entry with normal vesicular sounds and a respiratory rate of 22 after minimal exertion.

The rest of her systemic examination was normal. Ultrasound of the abdomen showed splenomegaly with a spleen size of 12.0cm. The splenic index was 60.

ECG at presentation was normal with no acute changes, and chest x-ray showed bilateral basal infiltrates, most likely pulmonary edema. (Figure 1)

At this stage, our differential diagnoses included the following:

- Membranous glomerulopathy
- Lupus nephritis
- Ascending urinary tract infection

Symptomatic treatment was begun at this stage with further directed investigations.

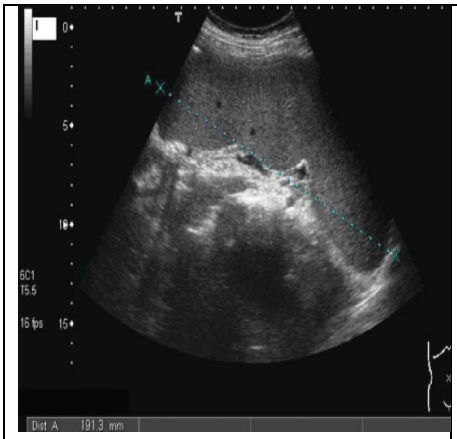
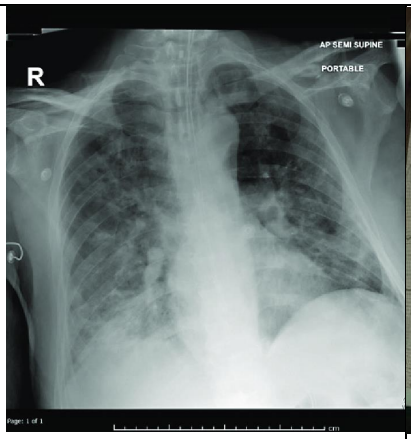
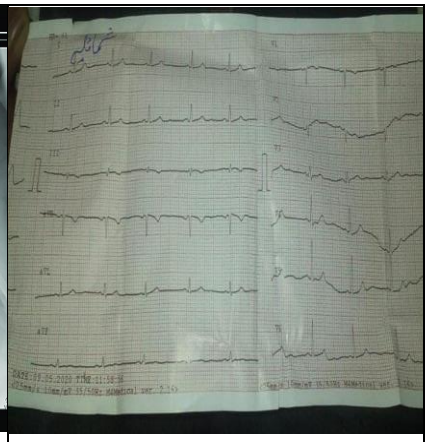


Figure 1: Ultrasound abdomen



chest x-ray



ECG

The following results of investigations done in the first week of June 2020 were found:

Investigation	Result	Normal Range
Complete Urine Examination a) Color b) Specific gravity c) pH d) glucose e) Ketones f) Proteins g) Hemoglobin h) Bilirubin i) Nitrite j) Leucocyte esterase k) Pus cells l) RBCs m) Epithelial cells n) Casts o) Organisms p) Yeast	 Yellow 1.030 5.0 nil nil ++ +++ nil negative nil 8-10 25-30 12-15 nil nil nil	
Spot urinary to creatinine ratio Spot Urinary Protein Spot urinary creatinine	3.18 mg/mg 99.7 mg/dL 31.4 mg/dL	<0.20 mg/mg <14.0 mg/dL
Serum urea	22mg/dL	10-50mg/dL
Serum Creatinine	1.2mg/dL	0.6-1.4mg/dL
Serum Sodium	129 mmol/dL	135-150mmol/dL
Serum Potassium	3.2 mmol/dL	3.5-4.5mmol/dL
Serum uric acid	4.4 mg/dL	2.6-6.0mg/dL
Lipid profile Cholesterol Triglycerides	 157 mg/dL 93mg/dL	 <200mg/dL <150mg/dL
ESR	23mm	<20mm
Hepatitis B Screening	Negative	
Hepatitis C screening	Negative	
Autoimmune profile a) ANA b) Pattern c) Estimated endpoint titer	 Positive Fine cytoplasmic Speckled 1/160	 Pattern: Fine cytoplasmic speckled appearance associated with Anti synthetase syndrome,

d) ASMA	Negative	polymyositis,
e) AMA	Negative	dermatomyositis, limited
f) dsDNA	5.6 IU/ml	systemic sclerosis
g) RA Factor	Negative	DsDNA (<20.0 IU/ml)
Serum C3 Levels	0.4 g/L	0.8-1.6 g/L
Serum C4 Levels	0.24 g/L	0.1-0.4 g/L

Ultrasound KUB: Right and left kidney size normal. The bladder is normal. Bilateral pleural effusion, right-sided 40ml, left-sided 20ml.

Based on these investigations and her clinical picture, lupus nephritis was suspected. A renal biopsy was planned. A renal biopsy was scheduled for the 15th of June 2020.

In the interval week till the biopsy, she developed a generalized morbilliform rash associated with itching, initially thought to be perhaps a drug eruption. She was prescribed Kestine 10mg HS, and the rash settled in two days. No inciting factors were recognized. A CBC done showed platelets of 93x10. However, the rash was not purpuric or petechial; thus, urticaria was suspected due to the sudden nature and prompt response to antihistamines.

A renal biopsy was done, and the histopathology report is as follows:

Sections revealed the core of renal tissue consisting of cortical regions containing up to 10 glomeruli in a serial section. The glomeruli show increased cellularity with mild mesangial proliferation. Occasional segments show increased endothelial cells with few polymorphs. The glomerular capillary wall appears unremarkable. Few tubules show focal mild tubular atrophy. Occasionally, they have amorphous casts in lumina. Interstitium reveals a patchy sprinkling of mononuclear cells and eosinophils. Blood vessels appear unremarkable.

Her next follow-up was a month later. Clinically, her pedal edema and hypertension had resolved. Her dyspnea had improved, as had her fatigue. Based on her lab investigations, she had responded to the steroid therapy, and her lab parameters and clinical parameters had normalized to a great extent. The leucocytosis was secondary to the steroid therapy, and she had no signs or symptoms of any ongoing infection. A repeat chest x-ray done at this time also showed no pulmonary edema, and her furosemide was stopped.

Her next follow-up was in August 2020, during which she was clinically doing well with no complaints. Her lab parameters that were routinely done came back within the normal range, including her protein-to-creatinine ratio, which had further decreased significantly from 0.21 mg/mg to 0.11 mg/mg, which was now well within the normal range. She has received steroids now for 6 weeks, and it was tapered by 10mg per week. And she will be maintained on 10mg prednisolone daily once tapering is complete over 4 months. Urinary protein to creatinine ratio monitoring will continue. As we saw, though the most common presentation in the series published from Pakistan was minimal change disease, our patient, though presenting with nephrotic syndrome, had a pattern of proliferative glomerulonephritis. Beyond patterns, patterns of age groups affected by the disease in the South Asian population may be different and more centered around adults, and possibly responsiveness to therapy might also be different. In conclusion, larger reviews and studies from the communities' native countries would prove extremely beneficial in piecing together the jigsaw.

Author's Contribution:

Concept & Design of Study:	Zohaib Ramzan
Drafting:	Shahid Anwar
Data Analysis:	Syed Ali Raza, Zoha Majeed
Revisiting Critically:	Zohaib Ramzan, Shahid Anwar
Final Approval of version:	Zohaib Ramzan

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