

Grand Rounds

Anasarca and Acute Kidney Injury in an Adolescent Girl

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A B S T R A C T

A 17-year-old adolescent female presented with complaints of generalised swelling and pain in the abdomen since 15 days and fever since 10 days. Initial investigations were suggestive of Nephrotic Syndrome with Acute Kidney Injury (AKI). Considering the age and gender of the patient, a workup for secondary causes of Nephrotic Syndrome was sent. After admission, her AKI worsened as she developed oliguria and progressively rising serum creatinine levels. Simultaneously, she developed various complications associated with AKI. Considering multiple indications, she was started on renal replacement therapy; initially on peritoneal dialysis and later shifted to haemodialysis. Once the diagnosis was established, she was started on treatment for the same. When AKI improved following renal replacement therapy, she was discharged on oral medications and planned to be followed up on an outpatient basis.

Keywords: AKI, Lupus nephritis, Haemodialysis

Case History

Dr Suchismita Saha, 2nd Year Postgraduate Medical Student

A 17-year-old girl presented to our Emergency Department (ED) with complaints of generalised swelling and pain in the abdomen since 15 days, along with fever since 10 days. The swelling was insidious in onset and predominantly presented during early morning hours. Initially, it was localised to bilateral feet and later progressed gradually to involve the abdomen and face. The pain in abdomen was generalised, dull aching, mild to moderate in intensity, not radiating to any other site, not related to food intake and had no specific aggravating or relieving factors. Fever was documented up to 101 °F, not associated with chills or rigour; relieved temporarily by medication. She denied any history of yellowish discolouration of skin, vomiting, cola or red coloured urine, frothy urine, burning or pain

during micturition, reduced urine output, or any similar illness in the past. There was no history of rashes, joint pain, photosensitivity, progressive pallor, palpitation, and difficulty in breathing.

She was the first-born child of a non-consanguineous marriage and a known case of epilepsy with intellectual disability. On day 10 of life, she was admitted in view of yellowish discolouration of the skin and abnormal body movements. She continued to have seizures, for which she was managed with antiepileptic drugs for about a decade and has remained seizure-free since then. Subsequently, she had delayed milestones and was diagnosed with intellectual disability. Presently, she is able to do the activities of daily life under the guidance of her parents. There was no history of similar illness in other family members.

In the ED, her PR was 108 bpm, RR was 20/min, BP was 110/64 mmHg (between 50th to 90th centile) in right

arm-supine position, and the temperature was 100 °F. Her weight was documented as 40 kg (with oedema), height 141 cm (-3.7 standard deviation score). The examination was suggestive of pallor, anasarca, abdominal distension with guarding and generalised tenderness, and fluid thrill was appreciable. Rest of the examination was unremarkable. Laboratory investigations were notable for anaemia, neutrophilic leucocytosis and high C-reactive protein (Table 1). Serum creatinine was elevated with an eGFR of 58 ml/min/1.73 m² accompanied by low serum albumin and dyslipidaemia. Urine routine microscopy showed 6 RBCs/HPF and protein of 4+. Urine protein creatinine ratio was 2.1. Ascitic tap cytology reported 500 leucocytes/ μ L with 70% neutrophils. She was admitted to the general paediatrics ward and parenteral antibiotics were started.

Table 1. Laboratory Investigations

Baseline Investigations	Values
Haemoglobin (g/dL)	8.5
Total leukocyte count (per microlitre)	12000
Platelet count (per microlitre)	2,90,000
Urea (mg/dL)	37
Creatinine (mg/dL)	1.06
Sodium (mmol/L)	132
Potassium (mmol/L)	4.5
Aspartate Amino Transferase (IU/L)	35
Alanine Amino Transferase (IU/L)	40
Alkaline Phosphatase (IU/L)	216
Total protein (g/dL)	5.2
Albumin (g/dL)	1.56
Total cholesterol (mg/dL)	300
Triglycerides (mg/dL)	540
Amylase (U/L)	34
Lipase (U/L)	28
Human Immunodeficiency Virus (HIV) 1 and 2	Non-reactive

Dr Suchismita Saha

Dr Aditi Das, what did the initial assessment in the ED suggest?

Dr Aditi Das, Senior Resident (Paediatric Nephrology Services)

The causes of generalised swelling or anasarca could be due to a number of underlying aetiologies. The clinical findings suggested the presence of bacterial peritonitis and the cause of anasarca could be an underlying renal disorder. Given the fact, she did not have any complaints of progressive pallor, palpitation, difficulty in breathing and absence of murmur

on chest auscultation, a cardiovascular cause could be ruled out. Hepatic possibilities were less likely as there was no organomegaly and liver function tests were reported as normal. The absence of any history of chronic diarrhoea made protein-losing enteropathy an unlikely diagnosis. The initial laboratory investigations of hypoalbuminemia, nephrotic range proteinuria, and hypercholesterolemia favoured a possibility of glomerulopathy (Table 1). The findings of anasarca in association with hypoalbuminemia and nephrotic range proteinuria suggested the diagnosis of nephrotic syndrome. The absence of hypertension, and oliguria at presentation helped to rule out acute nephritic syndrome. Given the age and gender of the patient, the association of connective tissue disorder with renal disease was also considered as a differential diagnosis.

Nephrotic syndrome could either be primary or secondary. Idiopathic or primary nephrotic syndrome usually presents at a younger age. Thus, in our patient, secondary nephrotic syndrome was more likely. The initial investigations did not reveal any infective causes of secondary nephrotic syndrome. History, examination findings, and laboratory investigations did not point towards underlying haematological malignancy. The patient being an adolescent female, associated connective tissue disorder leading to nephrotic syndrome and associated acute kidney injury (AKI) in the form of raised serum creatinine was possible. Thus, a provisional diagnosis of Systemic Lupus Erythematosus (SLE) was kept. The absence of gross haematuria and rash helped to rule out renal vasculitis.

Dr Suchismita Saha

Dr Abhijeet Saha, what was the final diagnosis and how did the case progress?

Dr Abhijeet Saha, Consultant (Paediatric Nephrology Services)

Given the history of generalized oedema along with hypoalbuminemia and nephrotic range proteinuria, in the absence of any cardiovascular or hepatic manifestations, nephrotic syndrome was kept as a provisional diagnosis. Investigations for secondary causes of nephrotic syndrome showed high ANA titre (1:640; large, coarse, speckled pattern), positive anti-ds-DNA antibody, low C3 (30 mg/dL) and low C4 (4 mg/dL). She was diagnosed as a case of SLE with renal involvement, as per EULAR 2019 criteria.¹ Entry criteria were satisfied by ANA titres (by immunofluorescence method) of more than 1:80. Among the clinical domains, she had a constitutional symptom of fever, ultrasound chest was suggestive of bilateral pleural effusion and 24 hours urine protein was more than 0.5 g/day. Under immunological domains, levels of serum C3 and C4 levels were low and anti-ds-DNA antibody was positive. Once diagnosed, pulse methylprednisolone was started.

The patient, on presentation, had AKI stage 1 in accordance with KDIGO criteria as serum creatinine was raised to more than 1.5 times the upper normal limit for age and gender.² Soon after admission, urine output reduced (< 0.5 ml/kg per hour for > 6 hours) while creatinine continued to rise steadily and by day 7 of admission, AKI had progressed to stage 3 in accordance with the KDIGO criteria (serum creatinine 4.2 mg/dL).² Simultaneously, she developed complications of AKI such as metabolic acidosis, hyperkalaemia, and hyperphosphatemia for which appropriate medical management was done. Her clinical condition worsened with progressive oliguria, development of altered sensorium (abnormal behaviour) and signs of fluid overload in the form of respiratory distress. At that point, it could not be decided if the neuropsychiatric symptoms were caused as a complication of uraemia or as a part of central nervous system lupus. Peritoneal dialysis was started. In view of the progressively worsening sensorium, endotracheal intubation was performed and mechanical ventilation was started on day 12 of admission.

Dr Suchismita Saha

Dr Abhijeet Saha, our patient had complaints of pain in abdomen from the time of admission. The intensity worsened with time. How should we approach pain in abdomen in this patient?

Dr Abhijeet Saha, Consultant (Paediatric Nephrology Services)

Since we admitted her with the provisional diagnosis of nephrotic syndrome, the initial cause of pain in abdomen was thought to be mesenteric ischaemia, being the commonest cause of pain in abdomen in nephrotic syndrome. Considering the risk of spontaneous bacterial peritonitis, ascitic tap was done. It was suggestive of peritonitis as per the ISPD (International Society for Peritoneal Dialysis) guidelines³ and appropriate antibiotics were started. However, the pain worsened over time. Paediatric surgery and gynaecology consultations were taken and conservative management was advised. Ultrasonography showed cholelithiasis, with bulky pancreas and peripancreatic fluid collection. Serum amylase and lipase were also found to be significantly raised. PD fluid examination continued to be suggestive of peritonitis. It could not be concluded if pancreatitis and lupus were co-related or just a coincidence in this patient. Approximately 0.85% to 4% of patients with SLE have shown a rare complication of acute pancreatitis which can develop within days to weeks of initiating medium-to-high dose corticosteroid therapy.⁴ A gastroenterology opinion was taken and she was advised to continue conservative management with IV antibiotics for 6 weeks to be followed by MRCP.

Dr Suchismita Saha

Dr Menka Yadav, our patient required renal replacement

therapy (RRT) for AKI. How did we decide on the need to start renal replacement therapy? She was initially started on peritoneal dialysis and later shifted to haemodialysis. How did we decide regarding the mode of renal replacement therapy?

Dr Menka Yadav, Consultant (Paediatric Nephrology Services)

The serum creatinine, on admission, was high, which steadily increased, accompanied by progressive oliguria. Nephrotic range proteinuria persisted and urine showed active sediments, and simultaneously the patient developed rapidly progressive glomerulonephritis (RPGN). There were multiple indications at that time for starting renal replacement therapy for this patient. She had developed hyperkalaemia, hyperphosphatemia and metabolic acidosis, which was refractory to medical management along with signs of uremic encephalopathy in the form of behavioural abnormalities and progressively worsening sensorium. Tenckhoff peritoneal dialysis catheter was inserted using the Seldinger technique and peritoneal dialysis (PD) was initiated. After a few cycles of PD, serum creatinine level decreased, and urine output and dyselectrolytemia improved. However, once PD fluid cytology was suggestive of peritonitis, the treating team in PICU (Paediatric Intensive Care Unit) decided to hold PD temporarily. As soon as RRT was withheld, the complications of AKI again worsened. There was an urgent need to continue RRT through some other modality. Table 2 shows the differences in the two most frequently used modes of renal replacement - PD and haemodialysis. As for our patient, initially, we started peritoneal dialysis; once it was stopped, her clinical condition deteriorated. Owing to the worsening uraemia with refractory electrolyte imbalance, haemodialysis was thus warranted. Vascular access was secured by inserting 12.5 Fr. haemodialysis catheter in the right femoral vein. After the first two sessions of haemodialysis, she showed significant improvement. However, before the 3rd dialysis session, swelling was noted in the right thigh. Ultrasound doppler revealed deep vein thrombosis (DVT) involving the pericatheter area of the right common femoral vein extending up to the right external iliac vein. Her parents did not give consent for new vascular access to continue further sessions of haemodialysis. Oliguria improved significantly and renal functions normalised over the next seven days. She was managed with low molecular weight heparin for DVT.

The induction phase treatment for lupus nephritis was started. At the time of discharge, she was on hydroxychloroquine, mycophenolate mofetil, and steroids. We had planned for a renal biopsy on the follow-up visit to stage the lupus nephritis and assess activity and chronicity index.

Dr Suchismita Saha

Dr Prajal Agarwal, our patient developed deep vein thrombosis in the pericatheter area for which her vascular access for haemodialysis needed to be replaced. Considering the diagnosis of lupus and the in situ haemodialysis catheter in great vessel was prophylactic anticoagulant therapy warranted?

Table 2. Common Dialysis Modalities in LMICs (Low and Middle Income Country)

Variables	Peritoneal Dialysis	Haemodialysis
Continuous therapy	Yes	No
Haemodynamic stability	Yes	No
Easy to perform	Yes	No
Cost	Low/ moderate	Moderate/ high
Anticoagulation	Not required	Required
Vascular access required	No	Yes
Recent abdominal surgery	Contraindication	Not a contraindication
PD catheter leakage	Yes	No
Rapid toxin removal	No	Yes
Severe volume overload requiring rapid ultrafiltration, refractory hyperkalemia	Not optimal	Optimal

Dr Prajal Agrawal, Consultant (Paediatric Nephrology Services)

SLE patients experience an increased frequency of thrombotic events and generally have poor outcomes. The presence of antiphospholipid antibodies (APLA), along with the predisposing factors for thrombosis, like disease activity, ethnicity, nephritis, disease duration, and hypertension have been reported in patients with SLE. The blood report for APLA was negative for our patient. However, other risk factors like hypertension and nephritis were present. The procedure of haemodialysis itself is also a risk factor for inducing a prothrombotic state. However, there is no given guideline to prophylactically start anticoagulant therapy in SLE patients undergoing haemodialysis.

Antiphospholipid antibodies (APLA) are autoantibodies directed against phospholipid-binding proteins and include anti-beta-2-glycoprotein-I antibody, lupus anticoagulant, and anticardiolipin antibody. Antiphospholipid syndrome (APLS) is a multisystem autoimmune disorder with the presence of

APLA in the setting of thrombosis and/ or pregnancy loss. It can be primary or secondary to autoimmune conditions like SLE (in 40% cases).⁵ Thus all patients of SLE should be tested for these antibodies and those with positive APLA should be started on aspirin (1-5 mg/kg/day, maximum 100 mg/day). Studies reveal that prophylactic anticoagulant therapy in SLE patients, even with negative APLA, reduces the risk of arterial and venous thrombotic manifestations; but there are no recommendations for the same. Thrombotic events should be treated using low molecular weight heparin or warfarin as anticoagulants with a target INR (International Normalized Ratio) of 2-3 in case of venous events and 3-4 in case of arterial and recurrent venous events.⁶ Recurrence, presence of APLA and other precipitating factors, and site of thrombosis can influence the duration of treatment (usually 3-6 months).

Dr Suchismita Saha

Dr Prajal Agarwal, what findings would we expect when we perform a renal biopsy for this patient?

Dr Prajal Agarwal, Consultant (Paediatric Nephrology Services)

Our patient has been diagnosed with lupus nephritis and investigations show nephrotic range proteinuria with microscopic haematuria along with evidence of AKI. In view of the above, we expect her to show features of class IV or class V lupus nephritis on renal biopsy. Lupus nephritis has been classified into six stages⁷ with minimal mesangial proliferation in class I and class VI showing diffuse glomerular sclerosis involving more than 90% glomeruli. Class IV lupus nephritis is characterised by diffuse glomerular involvement (more than 50% of total glomeruli) that is marked by severe proteinuria along with microscopic haematuria as seen in our patient. On light microscopy of renal tissue, more than 50% of glomeruli may have glomerular endocapillary hypercellularity, cellular crescents, interstitial inflammation, and glomerular fibrinoid necrosis. On immunofluorescence, full house pattern is observed with positive IgG, IgM, C3, C1q, kappa and lambda deposits in glomeruli as well as mesangium. Electron microscopy shows subendothelial deposits (wire loop lesions). Class V lupus nephritis is clinically characterised by nephrotic syndrome, microscopic haematuria with normal or raised serum creatinine as seen in our patient. Light microscopy shows the thickening of glomerular basement membrane. Diffuse effacement of podocyte foot processes is generally seen on electron microscopy with global (involving more than 50% of one glomerulus) or segmental (involving less than 50% of one glomerulus) subepithelial and/ or mesangial deposits.

Authors' Contributions

All the authors contributed in the collection of data, management of patients, and correction of the manuscript.

Prof Abhijeet performed conceptualisation and design of the study, coordination and supervision of data collection, and critical review of the manuscript for significant intellectual content. The submitted manuscript has been approved by all the authors and they agree to be held accountable for all aspects of the work.

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