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CASE REPORT: STEROID-RESPONSIVE NEPHROTIC SYNDROME IN THIRD RELAPSE COMPLICATED BY PRE-RENAL FAILURE, LOWER RESPIRATORY TRACT INFECTION, THROMBOPHLEBITIS, HYPOPROTEINAEMIA, AND MICROCYTIC HYPOCHROMIC ANAEMIA

Lavanya M.[1], Ragul E.[2*], Pavithran G.[2], Varnish kumar M.[2] and Sivaramaswamy N.[2]

[1]Assistant Professor, Department of Paediatrics, Karpagam Hospital, Coimbatore, Tamil Nadu, India.

[2]Clinical Pharmacist Intern, Department of Clinical Pharmacy, Karpagam College of Pharmacy, Coimbatore, Tamil Nadu, India.

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***Corresponding Author**
Ragul E.
Clinical Pharmacist Intern, Department of Clinical Pharmacy, Karpagam College of Pharmacy, Coimbatore, Tamil Nadu, India.

ABSTRACT

Background: This case report describes a 4-year, 9-month-old female with steroid-responsive nephrotic syndrome (SRNS) experiencing her third relapse, complicated by pre-renal failure, anasarca, lower respiratory tract infection (LRTI), thrombophlebitis, hypoproteinaemia, and microcytic hypochromic anaemia. The patient presented with facial puffiness, abdominal pain, reduced urine output, and pedal edema. Laboratory findings revealed microcytic hypochromic anaemia, elevated WBC count, fluctuations in renal function tests, hypoproteinaemia, elevated CRP, and significant proteinuria. The patient's urine albumin levels remained elevated during the initial days of treatment, and her weight increased, indicating persistent fluid retention. **Methods:** The patient was managed with fluid restriction, diuretics, antibiotics, corticosteroids, and albumin infusion. **Conclusion:** The patient's condition improved with treatment, demonstrating the importance of a multidisciplinary approach in managing relapsing NS. This case report contributes to the understanding of the clinical course and management of complicated relapsing SRNS in children.

KEYWORDS: Steroid-responsive nephrotic syndrome, relapse, pre-renal failure, lower respiratory tract infection, thrombophlebitis, hypoproteinaemia, microcytic hypochromic anaemia.

1. INTRODUCTION

Nephrotic Syndrome (NS) is a kidney disorder characterized by significant proteinuria (>3.5 g/24 hours in adults or >40 mg/m²/hr in children), hypoalbuminemia (<3.0 g/dL), hyperlipidemia, and generalized edema.[1,2] It can be classified into primary (idiopathic) NS, which includes conditions such as Minimal Change Disease (MCD), Focal Segmental Glomerulosclerosis (FSGS), and Membranous Nephropathy, or secondary NS, which arises due to systemic diseases like systemic lupus erythematosus (SLE), infections, malignancies, or drug-induced causes.[3,4] Among the different types of NS, steroid-responsive nephrotic syndrome (SRNS) is the most common in pediatric populations and is characterized by a positive response to corticosteroid therapy.[2,5] However, some patients experience multiple relapses, leading to increased morbidity and complications.[5,6] Relapsing NS is defined by the recurrence of nephrotic-range proteinuria after achieving remission.

The exact cause of NS is unknown, but immune system dysregulation and genetic susceptibility play a significant role. Steroid-responsive nephrotic syndrome is commonly idiopathic but can be associated with minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), or mesangioproliferative glomerulonephritis.

The global incidence of nephrotic syndrome in children is approximately 1–3 per 100,000 population per year. It is more common in males, with a male-to-female ratio of about 2:1 in children. About 80–90% of children with idiopathic nephrotic syndrome respond to steroids, but nearly 50% experience frequent relapses.[7,9]

Nephrotic syndrome, particularly with frequent relapses, can lead to severe complications, including acute kidney injury (pre-renal failure), severe edema (anasarca), infections, thromboembolic events (thrombophlebitis), electrolyte imbalances and hypoproteinaemia, cardiovascular risks, growth retardation and bone health issues, and anaemia.[8,10]

2. CASE PRESENTATION

A 4-year, 9-month-old female presented with facial puffiness, abdominal pain, reduced urine output, intermittent loose stools, and pedal edema of several days' duration. She also reported a history of wet cough for 4 days, one episode of vomiting, and frothy urine.

The patient was initially diagnosed with nephrotic syndrome at age 3 and treated with oral steroids. She experienced her first relapse 8 months after discontinuing steroids and was treated with tablet steroids for 3 months. Six months later, she had a second relapse and was again started on steroids. After stopping steroids for 5 months, she developed a third relapse and presented to our hospital with the aforementioned complaints. Notably, there was poor compliance with alternate-day steroid therapy during the second relapse.

On examination, the patient presented with facial puffiness, pedal edema minimal vulval edema, periorbital edema, and abdominal pain. Frothy urine was observed along with decreased urine output. The patient was conscious, alert, dull-looking looking & afebrile. The patient's weight increased from 15.500 kg to 20.500 kg over the course of the illness.

The laboratory and radiology investigations revealed several abnormalities consistent with the patient's diagnosis of steroid-responsive nephrotic syndrome and its complications. A complete blood count showed **microcytic hypochromic anemia**, with **hemoglobin levels as low** as **10.0** g/dL (reference range: 11.5-15.5 g/dL) and **PCV as low** as 28% (reference range: 30-45%). The **white blood cell count was elevated**, reaching **33.83** (10^3/AQL) (reference range: 5.5-15.5 10^3/AQL), with a **high neutrophil percentage of 84.5**% (reference range: 23-45%), indicating a leucocytosis likely due to a **lower respiratory tract infection (LRTI)**. Renal function tests revealed **elevated urea levels** up to **104.9** mg/dL (reference range: 10-40 mg/dL) (Fig 1) and **elevated creatinine** levels up to **0.9** mg/dL (reference range: 0.3-1 mg/dL), suggesting pre-renal failure. Liver function tests demonstrated **hypoproteinaemia**, with total protein levels as **low as 3.7** g/dL (reference range: 6.5-8.5 g/dL), and **hypoalbuminemia**, with albumin levels as **low as 1.3** g/dL (reference range: 3.5-5.5 g/dL). Electrolyte levels showed some imbalances, including fluctuations in sodium and bicarbonate. **The urine protein-to-creatinine ratio (PCR)** was **elevated**, with values of **7.53** and **16.01** (reference range: >5.00 for nephrosis), confirming nephrotic-range **proteinuria** Fig 2. Urine analysis also showed the **presence of albumin (2+ to 3+).** Inflammatory markers were **elevated**, with a **C-reactive protein level reaching 7.7** mg/L (reference range: <5.0 mg/L) and an **ESR of 46, indicating inflammation**. The lipid profile **revealed**

hyperlipidaemias, with **elevated triglycerides** (**350** mg/dL, reference range: <200 mg/dL) and total cholesterol (**636** mg/dL, reference range: <200 mg/dL). Radiological findings included a **chest X-ray showing increased broncho vascular markings fig 3**, consistent with the **lower respiratory tract infection**, and an abdominal ultrasound indicating **mild to moderate ascites with minimal left pleural effusion.**

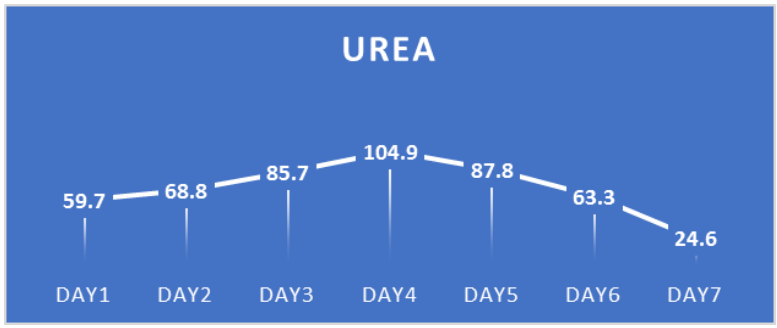

Fig.1: Elevated urea levels up to 104.9 mg/dL.

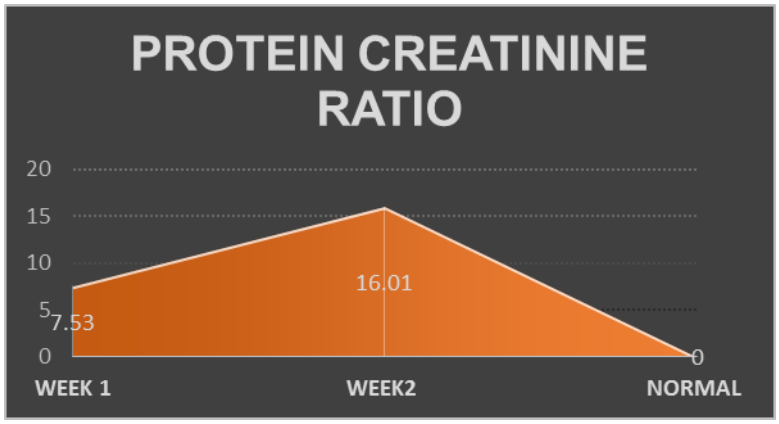

Fig. 2: Urine Protein-To-Creatinine Ratio (PCR)- Proteinuria.

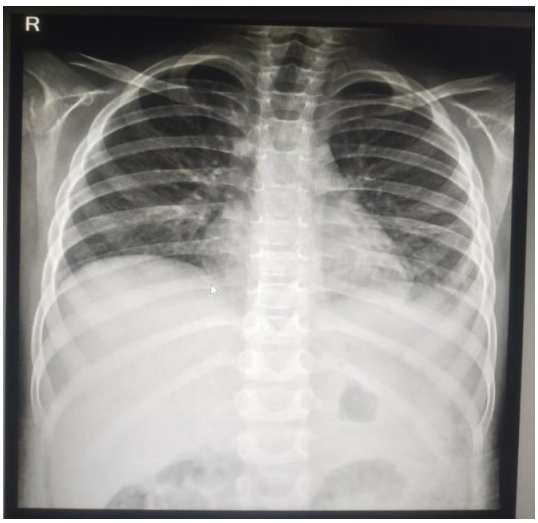

Fig. 3: Chest X-ray.

3. THERAPEUTIC INTERVENTIONS

The patient was managed with fluid restriction (700-800 mL/day orally), a salt-restricted 2g/kg per day, high-protein diet and she received **Nebulization** with Asthalin, 1.5 ml, and 3% NaCl, 4 ml as needed every 8 hours, and later every 12 hours. **Antibiotics** (Cefotaxime, Piperacillin-Tazobactam)Initially, Injections of Cefotaxime, 500 mg, were administered intravenously every 8 hours; later, switched to Piperacillin-Tazobactam injections, 1.5 g, were given intravenously every 8 hours. Then, they were increased to Piperacillin-Tazobactam injections, 2 g in 20 ml normal saline, and were given intravenously three times daily, at a dosage of 100 mg/kg/day. Enalapril tablets, 2.5 mg, were given orally twice daily and stopped after two doses were administered. Nifedipine tablets, 10 mg, were given orally at a dose of one-half tablet once daily. **A proton pump inhibitor (Pantoprazole)** was initially started. Oral Pantoprazole, 20 mg, was given daily. later switched to injections of Pantoprazole, 20 mg, which were administered intravenously, and later switched to Omeprazole capsules, 20 mg, which were given orally once daily before food. **Steroid** Prednisolone tablets were administered at 30 mg daily, and then increased to 40 mg daily, (2 mg /kg /day) and later switched to Methylprednisolone injections, 290 mg in 90 ml normal saline, at the dosage of 15 mg/kg/day, were administered intravenously once a day for 3 days for alternative days**. Diuretics** furosemide 15 mg was administered intravenously in one dose and then increased to 20 mg once a day for alternative days, Metolazone tablets, 2.5 mg, were given orally at a dose of one-third of a tablet once daily and later switched to Aldactone tablets, 25 mg, were given orally at a dose of one-half tablet once daily for 3 days. Tablets of calcium 500 mg and vitamin D3 250 IU were given orally at a half tablet dose twice daily. Sachets of vitamin D3 60000 IU were given orally at a dose once a week. Albumin infusion of 100 ml (10 ml over 10 hours) was administered intravenously in 2 doses on alternate days with furosemide.

The therapeutic interventions were directly correlated with the patient's laboratory findings and complications.

4. FOLLOW-UP AND OUTCOMES

Initial Challenges in Fluid Management: During the early phase of treatment, the patient exhibited persistent signs of nephrotic syndrome activity, specifically elevated urine albumin (3+) and increased weight. This indicated ongoing fluid retention and a suboptimal response to the initial treatment regimen.

Therapeutic Adjustments and Monitoring: In response to the persistent fluid overload, the treatment strategy was adjusted. This involved increasing the steroid dosage, a key intervention for managing nephrotic syndrome, and adding metolazone, a more potent diuretic, to enhance fluid removal. This highlights the importance of close monitoring of clinical and laboratory parameters to guide treatment modifications.

Positive Response to Intervention: The patient's condition improved following these therapeutic adjustments. This suggests that the increased steroid dosage and the addition of a more potent diuretic were effective in addressing the fluid overload and improving the overall clinical status.

Emphasis on Dynamic Management: The follow-up demonstrates the dynamic nature of managing relapsing nephrotic syndrome. It underscores the need for frequent assessment and a willingness to modify the treatment plan based on the patient's response.

5. DISCUSSION

Multifaceted Complications and the Need for a Multidisciplinary Approach: The case highlights the occurrence of pre-renal failure, lower respiratory tract infection, thrombophlebitis, hypoproteinaemia, and microcytic hypochromic anemia in a child with relapsing nephrotic syndrome. This underscores the importance of a multidisciplinary approach involving nephrologists, infectious disease specialists, hematologists, and other relevant specialists for effective management.

Importance of Prompt and Aggressive Management: The successful outcome in this case was attributed to close monitoring and aggressive management. This emphasizes the need for timely intervention and proactive treatment strategies to prevent life-threatening complications in relapsing nephrotic syndrome.

Fluid Management and Diuretic Use: The case report details the challenges in managing fluid overload, with the patient initially showing persistent fluid retention. The subsequent improvement after adjusting diuretic therapy highlights the importance of careful fluid management and individualized diuretic regimens in patients with nephrotic syndrome.

Infection Risk and Antibiotic Therapy: The patient developed a lower respiratory tract infection, necessitating antibiotic treatment. This underscores the increased risk of infections in nephrotic syndrome and the need for prompt diagnosis and appropriate antibiotic therapy.

Anemia Management: The patient presented with microcytic hypochromic anemia, requiring appropriate management. This highlights the need to monitor and address hematological complications in patients with relapsing nephrotic syndrome.

Role of Albumin Infusion: Albumin infusion was used to correct hypoalbuminemia and reduce edema. The discussion should emphasize the role of albumin replacement therapy in managing severe hypoalbuminemia and its associated complications.

Variations in Steroid Responsiveness and the Need for Tailored Therapy: The patient's treatment course involved adjustments in steroid dosage and the addition of other immunosuppressive agents. This highlights the variability in steroid responsiveness and the need for tailored therapeutic strategies based on individual patient needs and response.

6. CONCLUSION

In conclusion, this case report highlights the significant challenges in managing a 4-year, 9-month-old female with steroid-responsive nephrotic syndrome experiencing a third relapse complicated by a constellation of serious conditions, including pre-renal failure, lower respiratory tract infection, thrombophlebitis, hypoproteinaemia, and microcytic hypochromic anemia. The patient's clinical presentation, laboratory findings, and treatment course underscore the critical importance of prompt recognition, meticulous monitoring, and aggressive multidisciplinary management to achieve favourable outcomes in such complex cases. The successful resolution of the patient's immediate complications following treatment adjustments emphasizes the need for individualized therapeutic strategies and close clinical observation. To optimize care for children with relapsing nephrotic syndrome, future efforts should focus on enhancing medication adherence, promoting early detection of relapses, preventing and proactively managing complications, and establishing comprehensive long-term follow-up plans, with a strong emphasis on minimizing treatment-related toxicity. Further research is warranted to identify predictive factors for complicated relapses and to develop evidence-based guidelines for preventing and mitigating these severe manifestations of nephrotic syndrome, while also prioritizing strategies to reduce the adverse effects of prolonged and intensive therapies.

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