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REVIEW ARTICLE

A Study on Nephrotic Case Series

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ABSTRACT
Nephrotic syndrome (NS) is one of the most common glomerular diseases in children. The frequently identified symptom of childhood Nephrotic syndrome is edema, which is caused by profound proteinuria and hypoalbuminemia. Although the goal of primary treatment is to maximize the proportion of patients in sustained remission, several patients (ranging from 1 to 20) experience relapses during childhood, which can result in significant morbidity. Bacterial infections and hyper coagulopathy are the most serious and potentially fatal medical complications associated with nephrotic syndrome. We present a case series of five cases of the pediatric nephrotic syndrome as the underlying disease. All the patients were admitted with common clinical presentations such as periorbital swelling, generalized edema, and decreased output. One of the five patients showed a moon-like face with a buffalo hump, and three of the five patients presented with facial puffiness and abdominal distension. Laboratory investigations showed protein in the urine, and reduced serum albumin in all the patients. Patients were mainly treated with albumin, prednisolone, furosemide, and antibiotics. In all the cases, the patients were advised to follow a high protein-salt-restricted diet. This study highlights the clinical presentations, history, and management of nephrotic syndrome in the pediatric department.
Keywords: *Nephrotic syndrome, edema, proteinuria, hypoalbuminemia.*

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INTRODUCTION

The clinical condition known as nephrotic syndrome (NS) is characterized by severe proteinuria that causes hypoalbuminemia and leads to hyperlipidemia, edema, and other consequences. It is caused by an aberration in glomerular permeability, which can be secondary to congenital infections, diabetes, systemic lupus erythematosus, neoplasia, intrinsic renal disease in the kidneys, or particular drug usage.[1][2] Nephrotic range proteinuria (urinary protein excretion above 50 mg/kg per day or 40 mg/m2 per hour), hypoalbuminemia (serum albumin concentration below 30 g/L), edema, and hyperlipidemia (the later two symptoms may not be present in all patients) are its four clinical hallmarks [3]. With 16 in every 100 000 children affected, it is one of the most prevalent kidney disorders in children.[4]

Etiology

Intrinsic kidney disorders such as membranous nephropathy, minimal-change nephropathy, and localized glomerulosclerosis are frequent primary causes of nephrotic syndrome. Systemic conditions like lupus erythematosus, diabetes, and amyloidosis can be secondary causes[5]. Genetic changes in podocyte proteins such podocin, nephrin, or the cation channel 6 protein may result in congenital or inherited localized glomerulosclerosis.[6] Nearly half of instances are caused by an episode of an infectious condition, particularly one of the upper respiratory tract, a third by an allergic reaction, and less frequently by an insect bite or a vaccination.[7] Heroin , gold, penicillamine, NSAIDS, lithium,cisplatin therapy etc are some of the drugs that can cause nephrotic syndrome.[8]

Symptoms

Your urine contains a lot of albumin (more than 3.5 grams) (albuminuria).

- Hyperlipidemia or high blood levels of fat and cholesterol.
- Edema, or swelling, typically in the legs, foot, or ankles.

- Facial or hand swelling.
- (hypoalbuminemia) Low quantities of albumin in the blood.
- Decrease in appetite.
- Feeling ill or uncomfortable.
- Pain in the abdomen, which can occur anywhere from the ribs to the pelvis.
- Foamy poop.

A loss of nutrients, such as calcium and vitamin D, that are crucial for your health and development is another sign of nephrotic syndrome. The growth of kids with nephrotic syndrome may be impacted by this.[9,10]

Pathophysiology

There is no clear explanation for how edema develops in NS. Increased glomerular permeability to albumin and other plasma proteins appears to be the main problem. Edema is brought on by increased extravasation of fluid from the intravascular space into the interstitial space as a result of primary renal sodium retention and decreased oncotic pressure from hypoalbuminemia.[11][12] Though not fully understood, the pathophysiology of thrombogenesis in NS appears to be multifaceted and involves both a loss of coagulation regulatory proteins and a shift in the hemostatic balance toward a prothrombotic milieu [13]. A patient's risk of thrombosis is substantially elevated if they also have prothrombotic genetic variants and NS.

Diagnosis

A crucial component of this is evaluating the patient's renal function; serum urea and creatinine levels should be evaluated, and an estimated glomerular filtration rate should be computed. It is crucial to check the urine with a dipstick for haematuria (which would indicate glomerulonephritis) and proteinuria (3-4+ protein suggests the nephrotic range). The protein:creatinine ratio or albumin:creatinine ratio should be performed on a spot urine sample, especially in the early morning, as these tests are less error-prone, produce results more quickly, and have been demonstrated in cross sectional longitudinal investigations to be as accurate as 24-hour urine collections.[14][15] Nephrotic range proteinuria is indicated by a protein :creatinine ratio value greater than 300-350 mg/mmol. Renal size and morphology are evaluated by renal ultrasonography.

Management

Children who have idiopathic nephrotic syndrome are typically treated with corticosteroids. Children with frequently relapsing or steroid-dependent nephrotic syndrome frequently require other immunosuppressive medications. These medicines include levamisole, cyclophosphamide, mycophenolate mofetil (MMF), and calcineurin inhibitors. First-line options for treating steroid-resistant nephrotic syndrome include calcineurin inhibitors; if they don't work, other options include MMF or extended and/or intravenous pulse corticosteroids.[16][17][18] Rituximab, an anti-B cell antibody, has shown promise as a steroid-sparing treatment in children. However, in children who are dependent on both calcineurin inhibitors and steroids, rituximab may not be able to bring about drug-free remission. In children with a condition that is resistant to steroids, rituximab may potentially be useful. [19] Rituximab has been shown to be effective in treating children with complex steroid-resistant nephrotic syndrome, and Okutsu et al. found that continuing rituximab treatment during B cell recovery may prolong the duration of remission. [20]

CASE DETAILS

We collected and analyzed 5 patients suffering from Nephrotic Syndrome. All the five patients had previous multiple relapses. The following are the brief details of the 5 cases.

Case-1: A 12 year old male patient weighing 38 kilograms, presented with a dry cough and a recent decrease in urine output, passing only small quantities despite the administration of diuretics. He also complained of high-grade fever for the past day and increased weight gain along with ongoing body pain. The swelling started insidiously in the abdomen and gradually progressed to involve the entire body, including the legs and limbs. On examination, Bhanu exhibited a moon-like face and a buffalo hump, characteristic features of steroid toxicity.

The patient's vital signs were as follows: pulse rate of 104 beats per minute, respiratory rate of 21 breaths per minute, and blood pressure of 110/70 mmHg. Cardiac auscultation revealed normal heart sounds (S1S1+) and clear bilateral breath sounds. His abdomen was soft, and there were no focal neurological deficits. Laboratory investigations revealed proteinuria of +3 on dipstick examination. The abdominal girth measurement was 97 centimeters. A color Doppler study indicated mild hydronephrosis in the left kidney. Based on previous renal biopsies, his nephrotic syndrome was attributed to minimal change disease. The patient's treatment regimen included oral Wysolone (5mg once daily), which was initiated

due to his 10th relapse of nephrotic syndrome. He had been diagnosed with nephrotic syndrome at the age of 8 and had experienced multiple relapses since then. In addition to Wysolone, he was prescribed with Tacrolimus (0.5mg once daily), Enalapril (0.3mg once daily), and other supportive medications. He was advised to follow a salt-restricted diet and consume a high-protein diet. Intravenous fluids (DNS) were administered, and albumin infusions (1gm daily) were given to manage his edema. Medications such as Atorvastatin (10mg), Pantoprazole (20mg once daily), Calcium (500mg once daily), and Folic acid (1mg once daily) were also included in the treatment plan. Additionally, he received antibiotic therapy with Piptaz (50mg per dose) and Cefotaxime (100mg once daily). He was prescribed Nifedipine (24.8mg) for blood pressure control and a protein powder supplement.

Case-2: A 3 year old female patient weighing 11 kilograms, presented with a history of a cold for one week, which was followed by the subsidence of fever. She had been coughing for the past four days and developed facial puffiness, which progressively involved her entire body. Sweety also exhibited pedal edema and abdominal distension. On examination, her vital signs were as follows: pulse rate of 97 beats per minute, respiratory rate of 25 breaths per minute, and blood pressure of 120/70 mmHg. Cardiac auscultation revealed normal heart sounds (S1S1+) and clear bilateral breath sounds. She had distension in her abdomen, but no abnormalities were found in her central nervous system. Laboratory investigations showed a protein-to-creatinine ratio of 0.6. Abdominal ultrasonography revealed mild ascites and bilateral pleural effusion, with the right side being more affected. She had a urine output of 10 milliliters with a dipstick showing protein ++++. Her medical history indicated that she had previously been admitted at 18 months of age with similar complaints. At that time, she started on Wysolone (a steroid) daily for three weeks, followed by alternate-day steroid treatment for three months. During a subsequent check-up, she developed macular lesions on her mouth, foot, and hand, which were diagnosed as hand-foot-mouth disease. Steroids were discontinued, and symptomatic management was provided. Regarding her immunization status, she had received immunizations up to 9 months, but the MR2 vaccine at 18 months was not administered. The treatment plan for her current relapse included an oral salt-restricted diet with high protein intake. Medications such as amoxicillin/clavulanate potassium(50 mg/kg once daily), Paracetamol (15 mg/kg once daily), Nifedipine (0.2mg/kg once daily), Chlorpheniramine(2.5ml twice daily orally), Pantoprazole (20mg intravenous once daily), Ambroxol (3 ml twice daily orally), and Ceftriaxone (550mg intravenous twice daily) were prescribed. She also received albumin infusions (1g daily) to manage her condition effectively.

Case-3: A 10 year old male patient presented with a two-day history of abdominal pain in the left iliac region, along with a four-day history of a cold. He developed edema, starting from the periorbital region and progressing to the cheeks, hands, abdomen, and legs over a three-day period. Additionally, he had decreased urine output for two days and had been experiencing a high-grade fever for four days, indicating a relapse of nephrotic syndrome. On examination, his vital signs were as follows: pulse rate of 84 beats per minute, respiratory rate of 26 breaths per minute, and blood pressure of 100/60 mmHg. His cardiovascular and respiratory examinations were within normal limits. He had a soft, distended abdomen, and no abnormalities were detected in his central nervous system. Laboratory investigations revealed a urine output of 1.7 milliliters per hour. The abdominal girth measured 54 centimeters, and a dipstick test showed proteinuria with a score of 4+. Abdominal ultrasound showed mild ascites and free fluid in the peritoneal cavity. The protein-to-creatinine ratio was 5.2. His medical history indicated previous episodes of LRTI. Notably, he experienced a relapse of nephrotic syndrome in 2018, which coincided with an episode of LRTI. The specific details of his other relapses were not provided. The treatment plan for his current relapse included an oral salt-restricted diet with high protein intake. He was prescribed amoxicillin/clavulanate potassium(50 mg/kg once daily), Prednisolone (2 mg/kg once daily), Nifedipine (0.2mg/kg once daily), Chlorpheniramine (2.5ml at bedtime orally), Pantoprazole (20mg intravenous once daily), Ambroxol (8 ml three times daily orally), Calcium (40 mg once daily), and daily albumin infusions (1g).

Case-4: A year old female presented with a five-day history of periorbital swelling, which developed insidiously. She also had abdominal distension for three days, accompanied by a one-day history of fever. She experienced two episodes of vomiting the previous day and exhibited facial puffiness. Additionally, she had decreased urine output since the morning of the presentation. On examination, her vital signs were as follows: pulse rate of 103 beats per minute, respiratory rate of 28 breaths per minute, and blood pressure of 110/60 mmHg. Her cardiovascular and respiratory examinations did not reveal any abnormalities. The abdomen was soft and nontender, and no abnormalities were noted in the central nervous system. Laboratory investigations revealed a urine output of 3 milliliters per day. The abdominal girth measured 61.5 centimeters, and a dipstick test showed proteinuria with a score of 3+. Abdominal ultrasound indicated mild ascites and mild fluid in the peritoneal cavity. The protein-to-creatinine ratio

was elevated at 5.2. A subsequent ultrasound revealed mild to moderate ascites and free fluid in the peritoneal cavity.

Her medical history indicated a total of seven relapses of nephrotic syndrome. The first relapse occurred at three and a half years of age in 2019, which was confirmed to be Minimal Change Disease (MCD) on biopsy. Treatment involved prednisolone for six weeks. Subsequent relapses occurred in 2019, January 2020, May 2020, November 2020, April 2021, and January 2022. Medications such as prednisolone and enalapril were prescribed during these relapses, but poor drug compliance was noted. The treatment plan for her current relapse included an oral salt-restricted diet with high protein intake. She was prescribed Elanapril (0.1mg/kg once daily), daily albumin infusions (1g), intravenous ceftriaxone (550 mg twice daily), Paracetamol (250mg once daily as needed), Lasix (0.5ml per dose), prednisolone (2 mg/kg once daily), and calcium tablets (1 tablet twice daily). Additionally, he received isoniazid (10mg) and pyridoxine (10mg) as prophylaxis.

Case-5: A two and half year old female patient presented with generalized edema, initially manifesting as periorbital swelling for four days, followed by the progression of pedal edema, abdominal distension, and lower limb edema over the same duration. She also had a one-day history of decreased urine output. Physical examination revealed a pulse rate of 99 beats per minute, respiratory rate of 18 breaths per minute, blood pressure of 100/80 mmHg, and a soft and distended abdomen. She had a puffy face, and diagnostic findings indicated an albumin level of 1.5, an abdominal girth of 61 centimeters, proteinuria of 4+ on the dipstick, anasarca, and pleural effusion with mild ascites. Her medical history included her first relapse in April 2022, which was managed with Wysolone (10mg twice daily) for six weeks, followed by Tacrolimus (0.5mg twice daily), and later shifted to Wysolone (5mg every alternate day) for two months. Additionally, she was diagnosed with hypothyroidism and prescribed Thyroxine (50 mcg once daily). She also had primary coenzyme Q10 deficiency and was receiving Coenzyme Q10 supplements (100mg once daily). It was noted that she had used herbal medication four months ago. The treatment plan for her current relapse consisted of an oral salt-restricted diet with high protein intake. Medications included Coenzyme Q10 supplements (100mg once daily), KCL syrup (10ml in 100ml water daily), intravenous albumin infusions (1g daily), intravenous cefotaxime (500mg twice daily), intravenous Lasix (6.6mg three times daily), prednisolone (5mg every alternate day), calcium tablets (500mg once daily), Tacrolimus (0.5mg twice daily), Nifedipine (1mg three times daily), enalapril (0.5mg per kilogram per day), Thyroxine (50 mcg once daily), and B complex tablets (once daily).

DISCUSSION AND CONCLUSION

Cases of Nephrotic syndrome(NS) have been emerging recently. In order to increase the understanding of NS we reviewed the articles currently available on this topic. It is already known that patients with NS are at a higher risk for infections than the general population. Clinical triad of nephrotic syndrome arises from the large urinary losses of protein, comprises of Hypoalbuminemia (s2.5 g/dL), Oedema (due to fall in plasma oncotic pressure) Hyperlipidemia, (cholesterol>200 mg/dL).among the cases we reviewed almost all of the patients are with oedema. Have a disease that affects the kidneys such as FSGS, lupus or diabetes. And some drugs also cause NS like anti inflammatory drugs(NSAIDS) or antibiotics. Children of all ages can develop NS but the condition most often affects 2 to 7 years. Our case reports consist of 3 female and 2 male patients suffering with NS. NS is common in both males and females(children). Most of them are experiencing swelling in the different body parts, and weight gain due to fluid retention. Fever is the most common symptom in all the cases, And more frequently observed symptoms in all cases are decrease in urine output(foamy urine) a result of excess protein in the urine, facial fluffiness and abdominal distention. Loss of the proteins from your blood allows fluid to leak out of the blood vessels into the nearby tissues causing swelling and leads to fluid retention causing abdominal distention. NS is diagnosed by the urine test with important parameters like heavy proteinuria (dipstick 3–4+ or urine protein/creatinine ratio >0.2 g/mmol = >200 mg/mmol) and Hypoalbuminemia(<25 g/L). Among all the case reports proteinuria observed is 3+ in case 1&4 and in 2,3,5 cases 4+ proteinuria is observed through dipstick. In case 5 albumin tests revealed Hypoalbuminemia (1.5g/L). Corticosteroids, or steroids, are the medicines most often used to treat children with primary nephrotic syndrome. These medicines suppress the immune system, reduce the amount of protein passed into the urine, and decrease swelling. ACEs and ARBs can help reduce protein loss and also lower blood pressure, which is often high in people with nephrotic syndrome. A diuretic (water pill), which reduces swelling by helping the kidneys remove fluid from the blood. Prednisolone and Wysolone are the most commonly prescribed in patients with multiple relapses in our case series. Wysolone tablet helps relieve symptoms of eye infections such as redness, swelling, itching and watering of eyes. The common treatment given in all cases include salt restricted diet, calcium supplements, diet with high protein intake and nifedipine, cefotaxime, enalapril, ceftriaxone,

prednisolone and intravenous albumin infusions. Tacrolimus is prescribed only for cases 1 & 5. In comparing these cases, it is evident that nephrotic syndrome in pediatric patients can present with diverse clinical features, including edema, abdominal symptoms, fever, and decreased urine output. Laboratory investigations consistently showed proteinuria as a hallmark finding. Treatment approaches varied depending on the underlying cause and response to previous therapies. Common interventions included dietary modifications, corticosteroids, immunosuppressants (such as tacrolimus), diuretics, albumin infusion, and supportive medications. All the patients had a history of multiple relapses with 10 being the highest number of relapses in our case series. A patient had poor drug compliance to prednisolone in his previous relapse. Further investigation can help in reducing the number of relapses of nephrotic syndrome in pediatrics.

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