Dear editor,

Nephrotic syndrome is defined by the presence of peripheral edema, heavy proteinuria (greater than 3.5 g/24h), and hypoalbuminemia (less than 3 g/dL). Nephrotic syndrome is relatively rare, with an incidence of 3 new patients per 100,000 per year in adults. Despite being a known cause for new onset edema in patients at any age, nephrotic syndrome is often neglected in considering differential diagnoses for this presentation in primary care settings, and initial workups often focus on ruling out cardiac and hepatic causes of edema. In this case report, we describe a 25-year-old male patient who presented to the emergency department (ED) complaining of a 10-day history of anasarca. He was later diagnosed with nephrotic syndrome secondary to minimal change disease. This case served as a reminder to include the differential diagnosis of nephrotic syndrome early in the workup of an adult with peripheral edema presenting to the ED.

CASE

A previously healthy 25-year-old male presented to the ED with periorbital edema, as well as edema in his abdomen and lower extremities. He had been prescribed an oral dose of furosemide 60 mg daily for his anasarca by a family physician at a clinic five days prior. Laboratory investigations were not performed. He felt that his symptoms have since been worsening. He denied any recent shortness of breath or loss of consciousness. He reported an allergy to kiwi with no known recent exposure and had not regularly taken medications before the recently initiated diuretic.

On exam, he was not in any acute distress. His blood pressure was 120/90 mmHg, his heart rate was 88 beats per minute, his respiratory rate was 18 per minute, and his temperature was 37.3 °C. On auscultation, he had normal S1 and S2 heart sounds, no S3 or S4, no murmurs, and his lungs were clear bilaterally. His abdomen was soft and non-tender to palpation. His legs had pitting edema up to his knees bilaterally.

Workup in the ED included chest radiographs and routine blood work. Chest radiographs showed small bilateral pleural effusions. Routine blood work showed a total protein of 45 g/L (normal range 64–83), serum albumin of 9 g/L (normal range 35–50), platelet count of 420×10^9/L (normal range 150–350), and slightly elevated neutrophils at 71.0% (normal range 45.0–70.0). A midstream urine culture is negative.

A urine dip was positive for significant proteinuria: the urine contains greater than 10 g/L of protein (normal range, negative or trace). It was straw colour, cloudy, contained 244 epithelial cells per low power field (LPF) (normal range 0–100), had more than 100 hyaline casts per LPF (normal range, 0–1), and contained 8 white blood cells per high power field (HPF) (normal range 0–5). The urine microscopy showed 10 RBCs per HPF (normal range 0–5). Finely granular and coarsely granular casts were also visible, with 50–100 finely granular casts counted per LPF and 0–2 coarsely granular casts counted per LPF.

After admission to the nephrology service, bloodwork was done with the following results: an ANA screening panel was negative for dsDNA, chromatin, ribosomal P, SS-A/Ro, SS-B/La, centromere B, SM, SmRNP, Scl-70, and Jo-1 antinuclear antibodies. Hepatitis B and C, HIV, and syphilis serology screens were negative.

No monoclonal protein was detected by immunofixation electrophoresis. C3 and C4 complement were both in the
normal range. A protein loss pattern on serum protein electrophoresis showing low albumin, beta-1, and gamma globulin, with highly elevated alpha-2 globulins suggested the patient’s edema was caused by nephrotic syndrome or gastrointestinal enteropathy.

The patient met criteria for diagnosis of nephrotic syndrome, with peripheral edema, heavy proteinuria, hypoalbuminemia, a protein loss pattern suggestive of a nephrotic syndrome, and no other identifiable cause for his edema. He initially was treated with diuresis in hospital with an oral dose of furosemide 60 mg twice daily. After two days of diuresis, his facial edema had resolved, but there was still some bilateral pitting edema of the lower extremities. He was discharged home on his second day in hospital with a prescription for a 7-day course of furosemide 40 mg to be taken daily and instructions for a low salt diet. He was initiated on a daily oral course of prednisone 60 mg at a nephrology follow-up appointment 3 weeks post-discharge. The diagnosis of minimal change nephropathy as a primary cause of the nephrotic syndrome was confirmed via ultrasound guided kidney needle biopsy the following week. At his 5-week follow-up visit, he no longer had any sign of edema and a plan was made to taper his prednisone dose over 2 months, for a total of 4 months of prednisone treatment. He had a relapse of his nephrotic syndrome within days after finishing his initial 4-month course of prednisone and restarts a 12-week course of prednisone which led to remittance with no further known relapses.

**DISCUSSION**

The differential diagnosis for this patient initially included congestive heart failure, hepatic disease, and protein losing enteropathy. Nephrotic syndrome was much lower on the differential and was not initially considered due to its rarity. Initial investigation of this patient in the ED by the attending emergency room physician consisted of a CBC, serum total protein and albumin, and a chest radiograph. A urine dip was also later completed, followed by urinalysis after a finding of proteinuria.

Although nephrotic syndrome is a well-known presentation, it is rare. Focus on cardiac and renal causes of edema is known to be a common barrier to the identification of nephrotic syndrome in primary care settings, with initial investigations tending to be focused on ruling out cardiac and hepatic causes.

The absence of any pulmonary edema or vascular redistribution on the chest radiograph made the diagnosis of congestive heart failure less likely, although it is possible the patient’s bilateral pleural effusions acted as a red herring in this case, further biasing the initial differential diagnosis toward cardiac causes. The later finding of proteinuria on urine dip suggested kidney disease. Urinalysis confirmed a nephrotic-range proteinuria with a bland urine sediment consistent with nephrotic syndrome and serum albumin was low. Further tests were ordered, and included an ANA screening panel, serology tests for hepatitis B and C, syphilis, and HIV, serum protein electrophoresis, and C3/C4 complement levels. Hepatitis B and C, HIV, syphilis, amyloidosis, and lupus nephritis were ruled out as causes of the nephrotic syndrome with negative serologic screens and normal serum complement levels. Normal complement levels made hypocomplementemia-related causes of nephrotic syndrome unlikely. A needle biopsy post-admission later identified the cause of the nephrotic syndrome to be a primary cause, minimal change disease (MCD) felt to be idiopathic in nature.

The pathogenesis of minimal change disease is poorly understood but evidence is mounting that T cell dysfunction leads to altered glomerular capillary wall permeability. In most cases, MCD is idiopathic. Secondary causes of MCD leading to nephrotic syndrome include drugs, neoplasms, infections, and allergies. Allergy may have been a trigger in this patient, with no history of malignancy, infection, or reported drug use. Reported allergies associated with MCD include pollens, fungi, house dust, and bee stings. There is some evidence that food allergies can trigger relapsing MCD.

Management in the ED was supportive and no further treatment was initiated until the patient was admitted under the nephrology team. There are no guidelines for the diagnostic workup or acute management of nephrotic syndrome in adults. If treatment of nephrotic syndrome is delayed, possible sequelae include infection caused by loss of immunoglobulins, thromboembolism caused by loss of clotting factors, and more rarely, acute renal failure. The approach taken here was effective in diagnosing the patient’s nephrotic syndrome and allowed initiation of timely management with steroids and continued diuretics.

**CONCLUSION**

We detailed an approach to diagnosis and management of a case of nephrotic syndrome presenting as progressive anasarca. Nephrotic syndrome is often initially neglected as an etiology for new onset edema in primary care.
settings. It is important to include renal disorders such as nephrotic syndrome on the differential for management of such patients in the ED to avoid diagnostic delays and development of potentially serious complications such as thromboembolism, infection, and kidney injury.

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