CASE REPORT

A Case of Occlusive Myocardial Infarction Caused by Nephrotic Syndrome in a 26-Year-Old Type 1 Diabetic

Kyle Admire, DO¹, Charlotta Jornlid, DO¹, Chelsea Ryan, MD¹, Rebecca Pauly, MD, FACP¹

ABSTRACT

Nephrotic syndrome is a rare condition distinguished by proteinuria exceeding 3g per day. Other associated characteristics include hematuria, hypoalbuminemia, edema, and hyperlipidemia. There are an array of complications of this syndrome, primarily due to the profound losses of protein in the urine. One such complication is thromboembolism, with most documented cases in the form of venous thromboembolism of the extremities, partly due to urinary loss of antithrombin III and increased synthesis of prothrombotic factors. There is limited available data regarding arterial thrombi and especially few reports about coronary thromboses, which can be life-threatening. In this report, we present the case of a 26-year-old patient with known nephrotic syndrome who developed an occlusive myocardial infarction from coronary artery thrombosis after a delay in care. We discuss the need for prompt diagnosis and treatment of nephrotic syndrome. Additionally, we review the differences between primary and secondary etiologies and their management.

KEYWORDS
nephrotic syndrome, myocardial infarction, thrombosis

INTRODUCTION

Nephrotic syndrome is a rare condition with an incidence of 3 cases per 100,000 people. It is distinguished by proteinuria exceeding 3g per day, leading to hypoalbuminemia with resultant edema and hyperlipidemia. Nephrotic syndrome can either be caused by an external process affecting the kidneys or, more frequently, intrinsic glomerular disease. Common primary etiologies of nephrotic syndrome include focal glomerulosclerosis, membranous nephropathy, and minimal change nephropathy, with membranous nephropathy being the most common cause in white patients and focal segmental glomerulosclerosis seen more frequently in black patients. Secondary causes of nephrotic syndrome include medications, infections, and congenital etiologies as well as systemic diseases such as amyloidosis, diabetes mellitus, lupus, multiple myeloma, and lymphoma. In the United States, diabetes is the most common cause of secondary nephrotic syndrome, reflecting its increasing prevalence.

Guidelines on evaluating nephrotic syndrome are based primarily on expert opinion, as its heterogeneity and rarity limit the opportunity for large, high-quality clinical trials. Diagnosis can be made solely with clinical features and proteinuria exceeding 3g daily. Suggested investigations include serum creatinine, serum albumin, and serum lipids to assess for the presence of concomitant renal failure, hypoalbuminemia, and hyperlipidemia. As there are many potential causes of nephrotic syndrome with limited specific therapies, further diagnostic evaluation should be based on clinical suspicion for specific causes. Even the role of renal biopsy is debated as a recent clinical trial only showed biopsy findings altered treatment in 42% percent of patients, primarily by adding corticosteroids.

It is important to initiate appropriate diagnostic
testing and treatment early in nephrotic syndrome as there are many potential complications. One of the well-described complications is thromboembolism, which can occur in either arterial or venous sites. However, thrombosis of coronary arteries is an uncommon, life-threatening occurrence for those with nephrotic syndrome, with a 1-year absolute risk of 1.5%.5 We explore the case of a 26-year-old man with nephrotic syndrome due to diabetic nephropathy who presented with an occlusive myocardial infarction.

CASE PRESENTATION

Our patient is a 26-year-old man with a past medical history of uncontrolled type 1 diabetes (hemoglobin a1c of 12.1%), hypertension, and hyperlipidemia. He initially presented to his primary care clinic with lower extremity edema and normal renal function, at which time oral furosemide, an echocardiogram, and a cardiology referral were ordered. The echocardiogram revealed an ejection fraction (EF) of 60-65% and no wall motion abnormalities. Despite taking oral diuretics, the patient continued to have worsening lower extremity edema and gained approximately 65 pounds over 6 months. Ultimately, he became non-ambulatory due to the severe diffuse edema. Further urine studies revealed a urine protein over 3g, and he was diagnosed with nephrotic syndrome. The patient underwent a renal biopsy, which was non-diagnostic. His primary care physician and nephrologist attempted to manage his condition with a low-sodium diet, diuretics, and an angiotensin-converting enzyme inhibitor (ACEi). However, they were met with resistance from the patient, leading to ineffective treatment.

Five months later, the patient presented to the emergency department with new-onset, sharp, substernal, non-exertional chest pain, which improved with aspirin and nitroglycerin. A physical exam revealed diffuse anasarca, an S3 gallop, and poor air movement with coarse rhonchi. Initial laboratory evaluation revealed a mild leukocytosis, elevation in both troponin and pro-BNP, and acute kidney injury. Urine studies showed glucose, blood, undetectably high protein, and granular casts. An electrocardiogram (ECG) exhibited anteroseptal infarct with Q-waves not seen on ECG 15 days prior (Figure 1). The patient underwent computed tomographic angiography of the chest, which

![Figure 1](https://mds.marshall.edu/mjm/images/figure1.png)

**FIGURE 1.** Panel A demonstrates evolving anteroseptal infarct with Q waves and ST segment depressions compared to EKG in panel B 15 days prior.
demonstrated large bilateral pleural effusions with compression atelectasis, splenic infarction, and anasarca. No pulmonary embolism was seen. An echocardiogram was obtained, which showed his EF reduced to 20% with severely decreased left ventricular systolic function and new akinesis in the region of the left anterior descending artery. The patient received aggressive diuresis with continuous bumetanide infusion and acetazolamide for augmentation with appropriate urinary response and a subsequent weight loss of 90 pounds. He then underwent renal biopsy, which revealed advanced diabetic glomerulosclerosis, marked arteriosclerosis, and acute tubular injury with prominent cytoplasmic vacuoles, which were immunofluorescent negative (Figure 2). This was consistent with diabetic nephropathy. After completing diuresis, he underwent cardiac catheterization, which showed diffuse 80% concentric atherosclerosis of mid to distal left anterior descending (LAD) artery with 95% diffusely diseased diagonal branches, 90% tubular eccentric smooth lesion in obtuse marginal-1 (OM-1) artery, 80% tubular concentric lesion in proximal left circumflex (LCx), mild non-obstructive atherosclerosis of medium caliber right coronary artery with moderate to severe diffuse disease in the distal small caliber right posterior descending artery, and left ventricular end-diastolic pressure of 31mmHg.

These lesions were determined to be high risk for percutaneous coronary intervention (PCI). Cardiothoracic surgery was consulted for coronary artery bypass graft consideration. After he was deemed a poor surgical candidate, cardiac magnetic resonance imaging was performed, revealing the LAD territory’s viability. He eventually went for PCI of the LAD with drug-eluting stent placement. The procedure was complicated by plaque shifting following stent deployment, which compromised the diagonal arteries, requiring classic balloon angioplasty to re-establish flow.

The patient was discharged with close cardiology follow-up and later required PCI with a drug-eluting stent (DES) placed in the OM-1, Proximal LCx, and OM branch of the LCx. Subsequent echocardiogram showed improved EF to 40% with only mild left ventricular wall motion abnormalities. He has since been re-admitted for further episodes of chest pain; however, his cardiac evaluation did not reveal further evidence of ischemia.

**DISCUSSION**

Nephrotic syndrome is an uncommon syndrome that not only causes proteinuria, edema, and hematuria but also carries with it many complications, which include acute renal failure (ARF), cardiovascular compromise, hypovolemia, and thromboembolism.\(^1,2\)

In our case, the patient developed thromboembolism. Thrombosis is thought to be due to the urinary loss of antithrombin III and increased
synthesis of prothrombotic factors in combination with activation of the coagulation cascade and stasis from volume depletion and hemoconcentration. Venous thromboembolism (VTE) is significantly more common than arterial thrombi, with the most common site being deep vein thromboses in the upper and lower extremities. Studies have shown that the incidence of renal vein thrombosis ranges from 5 to 62% in patients with nephrotic syndrome, making nephrotic syndrome the most significant risk factor for renal vein thrombosis. Available data are primarily in the form of case reports; therefore, the true incidence of arterial thrombosis is difficult to ascertain. Some sources point toward the absolute risk of arterial thromboembolism in adults with nephrotic syndrome being approximately 8 times that of the general population. However, this risk also seems to correlate with known risk factors for atherosclerotic disease.

Another unique aspect of this case is the degree of coronary artery disease found on the patient’s left heart catheterization. This is atypical for someone of his age, even with risk factors of type 1 diabetes mellitus (T1DM), hypertension, and hyperlipidemia. One cohort study showed that in people under the age of 35, the absolute risk of cardiovascular disease in type 1 diabetics versus people without diabetes was 11.3 per 1,000-person years. Additionally, type 1 diabetes also increases one’s risk of developing nephrotic syndrome. It has been shown that 25% of patients with type 1 diabetes developed nephrotic range proteinuria; however, for most patients, it took more than 15 years to develop. Similarly, the patient in our case had been diagnosed with diabetes 16 years prior to his diagnosis of nephrotic syndrome. Unfortunately, we do suspect that the length of time it took for the patient to be tested for nephrotic syndrome contributed to his atherosclerotic burden and accelerated his coronary artery disease due to the dysregulation of lipid metabolism associated with nephrotic syndrome. All these factors combined likely led to his eventual occlusive myocardial infarction.

Similar to the evaluation of nephrotic syndrome, there is a paucity of evidence for the management. As such, treatment recommendations are based on expert opinion and case series. Presently, the agreed-upon pillars for treatment are nutrition, diuretics, and ACEi therapy. In our patient, in addition to the above, better control of the patient’s underlying diabetes likely would have led to either prevention of the development of secondary nephrotic syndrome or prevention of severe complications from the condition.

CONCLUSION
Nephrotic syndrome has many associated complications, including ARF, infection, dyslipidemia, malnutrition, and thromboembolism. We describe a patient who developed many of these, including the uncommon complication of coronary artery thrombosis. The complications of nephrotic syndrome are diverse but, generally, are the result of profound protein losses in the urine. Providers should know that although VTE is more common, arterial thrombosis can also occur. This is particularly severe, especially when thrombosis occurs in the coronary arteries. Thromboembolism can be life-threatening and should be treated promptly in all patients, but especially those with nephrotic syndrome.

AUTHOR AFFILIATIONS
1. Virginia Tech - Carilion, Internal Medicine Department, Roanoke, Virginia

REFERENCES
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