CASE REPORT

Fatal Pulmonary Embolism in a 10-Year Old With Nephrotic Syndrome

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ABSTRACT:

We present a case report of a 10-year-old male with nephrotic syndrome who presented with a complaint of shortness of breath. The patient had been recently hospitalized for an exacerbation of nephrotic syndrome and had received steroid and diuretic therapy. Initial vital signs showed tachycardia and mild tachypnea. After being observed for more than four hours without deterioration he was discharged home for close follow up. The patient returned 4 hours later with worsening symptoms and went into cardiac arrest in the ED. Autopsy revealed bilateral large pulmonary emboli. Pulmonary embolism is a known complication of nephrotic syndrome. Hyperviscosity occurs due to a variety of mechanisms. Nearly all reported incidents are associated with the use of steroids and diuretics. It is essential to maintain a heightened suspicion of pulmonary embolism (PE) when children with nephrotic syndrome present with pulmonary complaints, particularly when they have been treated with steroids and diuretics.

KEYWORDS: pulmonary embolism, nephrotic syndrome, hyperviscosity, respiratory distress, tachypnea.

INTRODUCTION

Nephrotic syndrome carries with it an increased risk of thromboembolism secondary to a hypercoagulable state.[1,2] The etiology of this hypercoaguability is due to a number of factors which include loss of antithrombin III (ATIII) in the urine, increased production of clotting factors, increased platelet aggregation, hemoconcentration due to diuresis and effects of corticosteroids. There also seems to be a strong association of PE with concurrent steroid and diuretic therapy.[3,4] Pulmonary embolism has been reported to occur among pediatric nephrotic patients on numerous occasions.[4-9] In one retrospective study 11 of 204 nephrotic children had thrombotic complications, including two pulmonary embolisms.[6] Another study reports the incidence of thromboembolic complications in patients with severe nephrosis to be as high in children as it is for adults.[5]

CASE REPORT

A ten year old Hispanic male with a five year history of minimal change type nephrotic syndrome presented to the emergency department with six hours of dyspnea on exertion and three episodes of emesis. He had recently been hospitalized for two days for increasing proteinuria, edema, shortness of breath and abdominal pain. He had received corticosteroids, albumin, and furosemide. Serum albumin was noted to be 0.6 mg/dl during the hospitalization. The patient was discharged from the hospital with continued and unexplained tachypnea and tachycardia. Current medications included prednisone, cyclosporin, procardia, and carbamazepine. Past medical history was significant for minimal change nephrotic syndrome with multiple relapses. The patient also suffered from generalized seizures secondary to a previous venous sinus thrombosis. Physical examination was significant for tachycardia with a heart rate of 145 beats per minute, blood pressure of 110/72, respiratory rate of 28 breaths per minute, temperature of 97.2 F, and an oxygen saturation of 95%. Lung sounds were clear, extremities showed minimal edema. Chest x-ray revealed normal cardiac silhouette, no infiltrates or ef-

fusions, and mild bilateral atelectasis. A pediatric consultation was obtained due to the abnormal vital signs, but the patient was felt to be stable and at "baseline". The patient was observed for more than 4 hours without a change in vitals. He was discharged home with close follow-up. The patient returned to the ED four hours later by ambulance with respiratory distress. Upon this second presentation he had an oxygen saturation of 88%, a heart rate of 168 beats per minute, a respiratory rate of 45 breaths per minute, and a temperature of 100°F. Arterial blood gas (ABG) on room air was pH 7.21, pCO2 = 57mmHg, pO2 74mmHg. While in the ED the patient's vital signs deteriorated rapidly and was endotracheally intubated. Despite aggressive resuscitation, the patient went into asystole and was later declared dead. Autopsy revealed multiple pulmonary emboli. No source of the emboli was found.

DISCUSSION

Pulmonary embolism is rare in the pediatric population, and delayed diagnosis can lead to devastating consequences. Nephrotic syndrome imparts an increased risk for thrombosis through a hypecoaguable state. Thrombotic events have been reported to occur in 3-5% of nephrotic children. Most cases occur while the patients are receiving steroid and diuretic therapy.[10]

The hypercoaguable state of nephrotic syndrome is multifactorial.[11] There is still debate over the relative importance of various mechanisms. Recent onset or relapse of nephrosis leads to increased risk for thrombosis.[10] Mechanisms of hypercoagulability that have been identified include urinary loss of ATIII, thrombocytosis and increased platelet aggregation, hemoconcentration due to diuresis, increased clotting factors due to corticosteroid therapy, and increased hepatic synthesis of clotting factors.[2] Antithrombin III serum levels are strongly correlated with serum albumin levels. Antithrombin III and albumin have nearly identical molecular weights and renal clearance rates. Serum albumin levels of less than 2 mg/dl are especially worrisome.[12, 13] Studies have also shown increased levels of high molecular weight proclotting factors such as factor VIII and fibrinogen, which may increase the risk for thrombosis.

Although our patient had a normal platelet count, thrombocytosis has been noted and is believed to be another risk factor for PE.[2, 6, 10] Increased availability of arachidonic acid occurs when serum albumin falls due to decreased protein binding. This leads to increased synthesis of aggregatory prostaglandins, with resultant enhanced platelet aggregation.[14] Increased platelet turnover in nephrosis is also believed to play a role in increased platelet aggregation.[5]

Most cases of PE in nephrotic children are associated with the use of steroids and diuretics. Thromboembolism in nephrosis was rare prior to the use of steroids. The use of diuretics can lead to hemoconcentration with resultant increased viscosity, with increased risk for thrombosis.[15] Steroids have been noted to raise the concentration of various clotting factors, most notably factor VIII. Our patient had just completed a two day course of intravenous furosemide and was currently receiving oral prednisone. The exact role played by steroids and diuretics in thrombotic events has not been defined. Due to the serious morbidity and potential mortality associated with PE, it is imperative for emergency physicians to maintain a high degree of suspicion when evaluating dyspnea in a child with nephrotic syndrome.

REFERENCES

1. Urch C, Pusey C. Sagittal sinus thrombosis in adult minimal change nephrotic syndrome. Clin Nephrol. 1996 Feb; 45(2):131-2.

2. Ahmed K, Saeed E. Nephrotic syndrome and pulmonary artery thrombosis. Am J Nephrol. 1995; 15(3): 274-6.

3. Beaufils F, Schlegel N, Loirat C, Marotte R, Pillion G, Mathieu H. Urokinase treatment of pulmonary artery thrombosis complicating the pediatric nephrotic syndrome. Crit Care Med.1985 Feb; 13(2):132-4.

4. Jones CL, Hebert D. Pulmonary thrombo-embolism in the nephrotic syndrome. Pediatr Nephrol. 1991 Jan; 5(1):56-8.

5. Hoyer PF, Gonda S, Barthels M, Krohn H, Brodehl J. Thromboembolic complications in children with nephrotic syndrome. Risk and incidence. Acta Paediatr Scand. 1986 Sep; 75(5):804-10.

6. Mehls O, Andrassy K, Koderisch J, Herzog U, Ritz E. Hemostasis and thromboembolism in children with nephrotic syndrome: differences from adults. J Pediatr.. 1987 Jun; 110(6):862-7.

7. Zimmerman RL, Novek S, Chen J, Roggli V. Pulmonary thrombosis in a 10-year-old child with minimal change disease and nephrotic syndrome. A clinical, radiologic, and pathologic correlation with literature review. Am J Clin Pathol. 1994 Feb; 101(2):230-6.

8. Garbrecht F, Gardner S, Johnson V, Grabowski E. Deep venous thrombosis in a child with nephrotic syndrome associated with a circulating anticoagulant and acquired protein S deficiency. Am J Pediatr Hematol Oncol. 1991 Fall; 13(3):330-3.

9. Goldsby RE, Augusta J, Helton J. Pediatric pulmonary artery thromboembolism: An illustrative case. Pediatrc Em Care. 1996; 12(2):105-7.

10. Lieberman E, Heuser E, Gilchrist GS, Donnell GN, Landing BH. Thrombosis, nephrosis, and corticosteroid therapy. J Pediatr. 1968 Sep; 73(3): 320-8.

11. Igarashi M, Roy S, Stapleton F. Cerebrovascular complications in children with nephrotic syndrome. Pediatr Neurol. 1988; 4:362-5.

12. De Luca M, Dugo M, Arduini R, Liessi G. Acute venous thrombosis of spleno-mesenteric portal axis: an unusual localization of thromboembolism in the nephrotic syndrome. Am J Nephrol. 1991; 11(3):260-3.

13. Sullivan MJ, Hough D, Agodoa L. Peripheral arterial thrombosis due to the nephrotic syndrome: the clinical spectrum. Southern Med J. 1983 Aug; 76(8):1011-16.

14. Cameron JS. Coagulation and thromboembolic complications in the nephrotic syndrome. Adv Nephrol Necker Hosp. 1984; 13:75-114.

15. Shimamatsu K, Onoyama K, Maeda T, Ohryoji F, Fujimi S, Omae T. Massive pulmonary embolism occurring with corticosteroid and diuretics therapy in a minimal-change nephrotic patient. Nephron. 1982; 32(1):78-79.

16. Hoyer PF, Gonda S, Barthels M, Krohn H, Brodehl J. Thromboembolic complications in children with nephrotic syndrome: differences from adults. J Pediatr. 1987 Jun; 110(6): 862-7.