

Intracardiac Thromboembolic Complications in Nephrotic Syndrome

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Abstract

Children with nephrotic syndrome are prone to hypercoagulation disorders and thromboembolism. Of these patients, intracardiac thrombus is the most serious and life-threatening complication, which is detectable by echocardiography and can be successfully treated with plasminogen activator. This review deals with the very rare occurrence of intracardiac thrombi in children with nephrotic syndrome.

Keywords: Thrombosis, Embolism, Nephrotic Syndrome

1. Introduction

Nephrotic syndrome (NS) in children is characterized by proteinuria with resulting hypoalbuminemia, consequent edema, and hypercholesterolemia (1). Furthermore, in some patients, hypercoagulation disorders occur, resulting in thromboembolism, which is the most serious and rare complication of NS (2-5). This review deals with the very rare occurrence of intracardiac thrombi in children with NS.

1.1. Pathophysiology and Incidence of Thrombosis in Nephrotic Syndrome

The hypercoagulation status in NS occurs as a result of Antithrombin III (ATIII) deficiency, increased fibrinogen level, decreased protein C and S activity, increase in platelet number, and increased platelet aggregation. There are several risk factors of thromboembolic complications in patients with NS: hypovolemia, infection, diuretic treatment, immobilization, trauma, glucocorticoid therapy, hypoalbuminemia (< 20 g/L), and proteinuria (> 10 g/L) (2-5). All these factors contribute to the increased risk of thromboembolic complications in NS.

The incidence of thromboembolism in NS differs between children and adults. While reported as relatively high in adults, where the incidence varies between 9% and 70%, it is much lower in pediatric patients ($\leq 5.3\%$). However, the incidence of clinical vascular thromboembolic events may be higher (up to 66%), regarding specific complications (2). Furthermore, pediatric patients with secondary forms of NS have a higher incidence of thrombotic events than those with minimal change disease (2). Thrombi form mostly in deep leg veins, inferior

vena cava, rarely in superior vena cava, renal veins, axillary, subclavian, femoral, coronary and mesenteric arteries, and hepatic veins (2-5). Large retrospective studies from Bulgaria included 447 children with NS and the incidence of thromboembolic complications was 2% (9/447), while 16 clinically inapparent thromboembolic complications were recorded in 9 children. The reported incidence of thromboembolic events was 1.5% among patients with steroid-sensitive NS and 3.8% among those with steroid resistant NS (4). In a Turkish study, 16 children (median age of 2.2 years) with various primary diagnoses and confirmed intracardiac thrombus were analyzed. Six patients were newborns and two were infants. The localization was right atrium in 7, right ventricle in 5, left ventricle in 1, pulmonary artery in 1, and superior vena cava in 2 patients. The primary diagnoses were prematurity in 5, cyanotic congenital heart disease in 1, blood culture positivity in 3, malignancy in 4, nephrotic syndrome in 1, indwelling catheters in 10, and acquired or genetic thrombophilia in 6 patients (6).

Intracardiac location of thrombus in NS patients is extremely rare (3-18). To date, intracardiac thrombi have been reported in 15 patients (3, 6-18); in 5 adults (7-11) and 10 children (3, 6, 12-18).

1.2. Clinical Manifestations

Clinical manifestations of intracardiac thrombus include chest pain, shortness of breath, cardiac arrhythmias, heart failure, and acute coronary syndrome with myocardial infarction (14, 16). Such clinical manifestations may be even absent and the patients might be asymptomatic or with a subclinical course (13, 17, 18).

1.3. Diagnosis

Diagnostic tools include imaging procedures and laboratory assessment of several indices of coagulation status.

Echocardiography is the most reliable diagnostic tool in detecting intracardiac thrombus (7-18).

The diagnostic workup should also include complete blood count and laboratory assessment of fibrinogen, antithrombin III, protein C, protein S, International Normalized Ratio (INR) index, Activated Partial Thromboplastin Time (APTT) index, and serum level of homocysteine. The mutational analysis of coagulation factors V, II and Methylene-Tetra-Hydro-Folate-Reductase (MTFHR) is also helpful. Lung perfusion scan can be performed in patients with thrombus or thrombi in the right ventricle and anticipated lung perfusion defect (14).

1.4. Treatment

Treatment of intracardiac thrombus in NS is a medical emergency. Heparin and low-molecular heparin have been employed (16, 17), however, thrombolysis with alteplase, which is a tissue-type plasminogen activator is the most effective therapy, leading to thrombus dissolution within several hours after application (14). Surgical removal of thrombus has also been reported (12, 17). Prophylaxis with low-molecular heparin and consequently with warfarin should follow for several months (14).

Undoubtedly, adequate treatment of NS (corticosteroids, cyclophosphamide, cyclosporine A, levamisole, mycophenolate mofetil, and atorvastatin) is also necessary.

2. Conclusions

Pediatric nephrologists should be aware of thromboembolic complications in patients with NS. Intracardiac location of thrombus is a life-threatening complication of NS and physicians must be aware of this possibility.

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