[Editorial]

Pulmonary Thromboembolism: a rare but life-threatening complication of nephrotic syndrome

Running title: Plumonary thromboembolism in nephrotic syndrome

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Pulmonary thromboembolism (PTE) is often diagnosed in children with underlying medical disorders, and the prevalence of PTE in patients with nephrotic syndrome was reported to be 7.93% by meta-analysis.\(^1\) Patients with nephrotic syndrome have a hypercoagulable state caused by several factors, such as abnormalities in platelet activation (increased number and aggregation) and an imbalance between anticoagulation/antithrombosis (decreased levels of antithrombin III) and procoagulant/prothrombotic mechanisms (increased levels of factors V, VII, fibrinogen), and there’s at increased risk for deep venous and arterial thrombosis, renal vein thrombosis and PTE.\(^2,3\)\(^\) The thromboembolic complications tend to have more severe presentations, which may be associated with the severe hypoalbuminemia in children with nephrotic syndrome.\(^4\) Additionally, the thromboembolic risk is higher in adolescent patients with nephrotic syndrome compared with children. In a report by You et al., the patient was an adolescent with persistent proteinuria and hypoalbuminemia in spite of steroid therapy, and was supposed to be under the risk of thromboembolism.\(^5\) However, prophylactic anticoagulation are not usually recommended because of lacking of large randomized trials and guidelines.\(^2\)\(^\)\(^\) The symptom of PTE consist of pleuritic chest pain, shortness of breath and hemoptysis, and the diagnosis of PTE can be missed or delayed in children because of nonspecific symptom, and difficulty to assess pain in young children.\(^6\) Thus, the physician’s suspicion is highly necessary to diagnose PTE.\(^6\) In patients with nephrotic syndrome, high level of plasma D-dimer was associated with the occurrence of PTE.\(^7\) For the aspect of underlying etiologic factors, there is a possibility that children with nephrotic syndrome and PTE might have the other thrombophilia states such as anticardiolipin antibody, antithrombin deficiency, and deficiencies of protein C, S, and sometimes it is necessary to evaluate the presence of risk factors in addition to nephrotic syndrome.\(^8\)
The management guidelines in children are extrapolated from the adult data, and treatment includes thrombolysis or thrombectomy, and pharmacologic anticoagulation.\textsuperscript{8)\textcircled*} Anticoagulation should be initiated with a rapid-acting agent, either unfractionated heparin or low-molecular-weight heparin, followed by continued anticoagulation with low-molecular-weight heparin or vitamin K antagonist.\textsuperscript{9,10)\textcircled*} Recently, the low-molecular-weight heparin has been widely used in children. There is no consensus regarding duration of therapy, with American College of Chest Physicians (ACCP) guidelines recommending anticoagulation for 3 months or until resolution of the precipitating risk factor for secondary PTE, and longer anticoagulation of 6 to 12 months for idiopathic PTE.\textsuperscript{9)\textcircled*}

You et al. reported a case that extracorporeal membrane oxygenation (ECMO) with anticoagulation could be helpful in a life-threatening condition caused by massive PTE in children with nephrotic syndrome.\textsuperscript{5)\textcircled*} Massive PTE cause hemodynamic instability, right ventricular failure, and circulatory collapse.\textsuperscript{8)\textcircled*} According to the 2016 ACCP Antithrombotic Guidelines, therapy for massive PTE should include systemic thrombolytic therapy combined with anticoagulation and supportive care.\textsuperscript{9)\textcircled*} Systemic thrombolysis generally requires tissue plasminogen activator infusion of 50–100 mg intravenously over 1–2 hours and carries a 20% risk of major bleeding and a 2%–5% risk of hemorrhagic stroke.\textsuperscript{11)\textcircled*} However, in patients with a contraindication to systemic thrombolitics, ECMO and/or surgical embolectomy may be used to improve oxygenation, achieve hemodynamic stability, and successfully treat massive PTE.\textsuperscript{8)\textcircled*} The European Society of Cardiology 2014 guidelines state that ECMO can be used for massive PTE as a method for hemodynamic support and as an adjunct to surgical embolectomy.\textsuperscript{12)\textcircled*} Additionally, the ECMO can be applied in the setting of massive PTE and hemodynamic instability, when the invasive diagnostic studies are not feasible and urgent intervention is warranted.\textsuperscript{7)\textcircled*}
In conclusion, PTE is increasing in children, and the physician’s suspicion is important for the prompt diagnosis, especially if there is an underlying disease such as nephrotic syndrome that may cause it. Rapid initiation of anticoagulation is important for the favorable outcomes, and ECMO may be helpful when the patient is hemodynamically unstable.

Conflict of interest

No potential conflict of interest relevant to this article was reported.
References


