Is Swine-origin Influenza a Predisposing Factor for Deep Vein Thrombosis?

Domuz Gribi Derin Ven Trombozu için Predispozan bir Faktör müdür?

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Abstract

Herein we report a sixteen-year-old female that developed deep vein thrombosis (DVT) while undergoing treatment for H1N1 pneumonia. To the best of our knowledge this is the first report of H1N1/09 infection complicated by DVT in an adolescent patient with no detected risk factors other than immobilization. Healthcare providers should be aware of the possibility of thrombosis in patients with swine-origin influenza, especially in those with additional risk factors.

Key Words: Children, Deep venous thrombosis, Swine-origin (pandemic) influenza

Özet

Burada H1N1 enfeksiyonu için tedavi alırken, derin ven trombozu gelişiren bir olguyu sunmaktayız. Mevcut bilgilerimize göre; H1N1 enfeksiyonu sırasında - immobilizasyon dışında başka hiçbir risk faktörü olmayan - bir adolesanda tromboz gelişimi ilk defa bildirilmektedir. Domuz gribi pandemilerinde özellikle eşlik eden risk faktörleri olanlarda tromboz gelişebileceğini akılda tutulmalıdır.

Anahtar Sözcükler: Çocukluk çağı, Derin ven trombozu, Domuz gribi, H1N1 pandemi

Introduction

Venous thromboembolism (VTE) is a multifactorial entity that arises due to variable interactions between genetic and environmental components, with an incidence among children of 0.07-0.14/10,000 [1]. The incidence of VTE in hospitalized children has been reported to be as high as 58 cases per 10,000 hospital admissions [2]. The majority of children with VTE have comorbid medical conditions. Infection, dehydration, trauma, cancer, central venous catheterization, and chemotherapy are the most common predisposing factors for the development of thrombosis in children [3]. We reported earlier that thrombosis was associated with infection in 68% of hospitalized children with thrombosis [4]. Since April 2009, H1N1 infection has been a major concern, as it has spread rapidly worldwide. Herein, we report a sixteen-year-old female that developed thrombosis in the deep femoral vein while undergoing treatment for H1N1 pneumonia.

Case

A sixteen-year-old female was admitted to the hospital due to fever (41 °C), difficulty breathing, and perioral cyanosis. She had been prescribed oseltamivir phosphate (Tamiflu) for pandemic influenza A. She has cerebral palsy due to periventricular leukomalacia as a complication of premature birth, and had undergone surgery for developmental dysplasia of the left hip without thrombotic com-
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In addition to coagulation cascade activation, inflammatory response plays a role in thrombus formation via production of microparticles (MPs) that carry cell-specific molecules—proteins such as galectins [6]. Stimulation of monocytes, especially by galectin-1, leads to cell activation and tissue factor expression that triggers the coagulation pathway. Furthermore, oxygen free radicals produced during inflammation are known to induce thrombosis in microvessels via activation of platelet aggregation [7]. Infectious agents, including bacteria, viruses, and parasites, may initiate this process. A 13-year-old male that developed deep vein thrombosis (DVT) and pulmonary embolism following pneumonia caused by *Mycoplasma pneumoniae* was reported; however, protein S deficiency and transient lupus anticoagulant were underlying risk factors [8]. It is also known that varicella zoster infection can cause thrombosis in patients with protein S and C deficiency [9]. An 8-year-old boy that developed middle cerebral artery thrombosis as a result of *Streptococcus oralis* infection was reported [10].

Since being identified in Mexico City in April 2009, pandemic influenza A (H1N1) has become a significant cause of morbidity and mortality worldwide. Till 6 December 2009, 208 countries have reported laboratory-confirmed cases of pandemic influenza H1N1 to the World Health Organization (WHO) [11]. Although hospitalized children with swine-origin influenza infection are more likely to have underlying medical conditions, healthy individuals are also at risk from H1N1 infection and infection-related death. Unusual clinical presentations of H1N1 infection reported to date have included parotitis, conjunctivitis, and extensive bowel involvement with mesenteric thrombosis and hemophagocytic syndrome [12,13].

The presented case developed DVT while undergoing treatment for H1N1 pneumonia. The patient did not
have any coagulation abnormality or prothrombotic risk factor other than immobilization. The patient’s history of thrombotic episodes was negative despite having cerebral palsy and having undergone surgery for hip dysplasia. The patient’s family history of thrombosis was also negative. Detailed thrombotic risk factor analysis was performed to clarify the association between swine flu and DVT. H1N1 infection in the presented case might have triggered the formation of thrombosis because of endothelial injury in the left deep femoral vein due to previous surgery. D-dimer elevation indicated acute thrombosis. Harms et al. performed autopsy on 8 patients with H1N1 infection and reported that 5 had peripheral pulmonary vascular thrombosis and all 8 had cytophagocytosis [14]. An in vitro study reported that monocytes and endothelial cells that were incubated with influenza were able to activate coagulation via endothelial dysfunction and elevated tissue factor levels [15,16]. It is known that seasonal flu vaccine reduces the risk of cardiovascular events in patients with coronary heart disease. A novel study reported that influenza vaccination is associated with a reduced risk of VTE, whereas influenza infection itself may predispose individuals to thrombus formation, especially DVT [17].

In conclusion, thrombotic events should be considered among the possible complications of H1N1 infection, and low molecular weight heparin prophylaxis might be considered in immobilized patients with H1N1 infection.

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Conflict of Interest Statement
The authors of this paper have no conflicts of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

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