

Hyperprolactinemia: An Unfamiliar Acquired Cause of Pulmonary Embolism

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Abstract

Despite our knowledge of congenital and acquired hypercoagulable states, many unprovoked venous thromboemboli remain idiopathic. High prolactin levels may add diagnostic differential to these unexplained thrombi. We report a case of prolactinemia as a potential cause of a pulmonary embolus (PE) and review the literature to elucidate the connection between high prolactin levels and thrombosis. A 68-year-old female presented with dyspnea and frontal headaches. Exam showed tachycardia, tachypnea, and hypoxemia with an oxygen saturation of 91% on room air. Labs were positive for an elevated troponin. Imaging with a computed tomography (CT) angiogram of the chest and an echocardiogram confirmed a diagnosis of sub-massive PE. A CT of the head showed a mass lesion in the pituitary fossa. A hypercoagulable workup was negative and pituitary hormone levels were within normal limits aside from a high prolactin of 270.9 ng/mL. In our patient, high prolactin secondary to a prolactinoma remained the main culprit in her venous thromboembolism given a thorough negative history and workup for other etiologies. Literature investigating prolactin's effect on adenosine diphosphate-mediated platelet aggregation along with clinical scenarios in which elevated prolactin is the only sound explanation for a venous thrombosis may make it a risk factor which should be checked following a patient history indicative of a prolactin derangement.

Keywords: Prolactin; Prolactinoma; Thrombosis; Platelet activation

Introduction

Despite our knowledge of congenital and acquired hypercoagulable states, many unprovoked venous thromboemboli remain of unknown etiology. High prolactin levels, secondary

to a number of iatrogenic and medical conditions, may explain the cause for some of these idiopathic thrombi. In this paper, we report a case of hyperprolactinemia as a potential cause of pulmonary embolism (PE) and review the literature to elucidate the connection between high prolactin levels and increased thrombotic risk.

Case Report

A 68-year-old female presented with sudden onset of dyspnea on exertion and frontal headaches, mainly in the mornings. On physical examination, she was found to be tachycardic and tachypneic with an oxygen saturation of 91% on room air. Routine labs were positive for an elevated troponin. Imaging studies with an echocardiogram and computed tomography (CT) angiogram of the chest showed right heart strain and confirmed a diagnosis of sub-massive PE. She was then admitted to the hospital for initiation of anticoagulation and observation. A CT scan of the head performed for morning headaches showed a mass lesion on the right side of the pituitary fossa. Given imaging findings of a PE and a pituitary mass, additional laboratory studies were obtained. A hypercoagulable workup including levels of protein S, protein C, homocysteine, anti-phospholipid antibodies (e.g. lupus anticoagulant, anti-cardiolipin antibodies, and anti-beta 2-glycoprotein antibodies), prothrombin G20210A mutation, and factor V Leiden mutation was negative. Pituitary hormone levels obtained in existence of the pituitary mass were within normal levels, with exception to a markedly elevated prolactin of 270.9 ng/mL (4.8 - 23.3 ng/mL).

Discussion

Prolactin is commonly known for its effects on human milk production, but it also plays a key role in a number of other cellular processes. Prolactin acts in a cytokine-like manner to regulate cell cycle related functions such as growth, differentiation and apoptosis. These cytokine-mediated functions influence hematopoiesis and angiogenesis and are involved in the regulation of blood clotting through several pathways [1]. High prolactin levels caused by pituitary tumors, prescription drugs, paraneoplastic processes, hypothyroidism, and substances like marijuana may explain the cause for some cases of

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idiopathic thrombosis.

Although the data are somewhat limited, results have indicated that elevated prolactin levels may be associated with an increased risk of venous thromboembolism (VTE). Wallaschofski et al demonstrated higher prolactin levels in patients with thrombosis without an identified congenital or acquired hypercoagulable state compared to patients with a thrombus explained by a congenital and acquired hypercoagulable state and in healthy subjects. Based on this research, platelets express a prolactin receptor which plays a role in adenosine diphosphate (ADP)-induced platelet aggregation. As evidenced by platelet aggregation studies, no clotting took place with prolactin alone and modest platelet aggregation was seen with ADP alone. However, when platelets were incubated with prolactin in combination with ADP, a cumulative effect was seen on platelet aggregation which was more pronounced than with each agent alone. In addition, more robust platelet aggregation was seen with increasing concentrations of prolactin. Furthermore, epinephrine co-stimulation of platelets exposed to prolactin and ADP induced marked platelet aggregation suggesting prolactin's effect on the Gi-protein-coupled pathway associated with the P2Y₁₂ ADP receptor [2].

In 2012, Stuijver et al reported results of a case-control study evaluating prolactin in relation to coagulation factors as a risk of VTE. This study demonstrated that patients with prolactin levels > 150 µg/L had a concomitant increase in factor VIII and von Willebrand factor. Patients with prolactin levels in the 99th - 100th percentile (> 42.6 µg/L) had an increased risk of developing a VTE (odds ratio 1.4), compared to subjects with a prolactin level in the 0 - 1st percentile (< 3.4 µg/L) (odds ratio 0.8). These patients were more prone to developing pulmonary emboli rather than deep venous thrombosis with odds ratios of 1.8 versus 1.2, respectively [3].

In our patient, elevated prolactin secondary to a prolactinoma remained the most likely etiology of VTE given a negative history and workup for other causes. Literature investigating prolactin's effect on ADP-mediated platelet aggregation along with clinical scenarios in which elevated prolactin is the only sound explanation for a venous thrombosis may make it a novel risk factor which should be evaluated following a patient history indicative of a prolactin derangement.

Author Contributions

B. Walczyszyn wrote the first draft, and participated in subsequent drafting, revisions, and submission. G. Zacharia participated in manuscript drafting and revisions. O. Ilyas participated in reference search and discussion revision. D. Shani participated in the final revision.

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