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Risk of Venous Thromboembolism: The Prothrombin-G20210A Mutation and Combined Oral Contraceptives

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Risk of Venous Thromboembolism: The Prothrombin-G20210A Mutation and Combined Oral Contraceptives

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Abstract

The risk of venous thromboembolism in oral contraceptive pill users becomes dramatically increased in patients with inherited thrombophilias. The often undiscovered prothrombotic genetic conditions pose a potentially deadly threat to its generally young demographic. When thrombosis is discovered in oral contraceptive pill users with a strong family history of related events, it becomes essential to screen for prothrombotic genetic conditions and further mitigate any associated modifiable risk factors. Here we present a case of pulmonary embolism requiring cardiopulmonary resuscitation in 30-year-old female found to have a Prothrombin G20210A on oral contraceptive pills. The emergent management of the critical case, as well as the subsequent evaluation for prothrombotic conditions and the role of potential screening is discussed.

Keywords

Prothrombin mutation, Prothrombin G20210A, OCP, Combined oral contraceptives, venous thromboembolism

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Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

CASE REPORT

Risk of Venous Thromboembolism: The Prothrombin-G20210A Mutation and Combined Oral Contraceptives

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Abstract

The risk of venous thromboembolism in oral contraceptive pill users becomes dramatically increased in patients with inherited thrombophilias. The often undiscovered prothrombotic genetic conditions pose a potentially deadly threat to its generally young demographic. When thrombosis is discovered in oral contraceptive pill users with a strong family history of related events, it becomes essential to screen for prothrombotic genetic conditions and further mitigate any associated modifiable risk factors. Here we present a case of pulmonary embolism requiring cardiopulmonary resuscitation in 30-year-old female found to have a Prothrombin G20210A on oral contraceptive pills. The emergent management of the critical case, as well as the subsequent evaluation for prothrombotic conditions and the role of potential screening is discussed.

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1. Introduction

The three essential factors in the development of venous thrombosis are characterized by Virchow's triad-hypercoagulability, venous stasis, and venous damage. Risk factors for hypercoagulability include obesity, smoking, surgery, immobility, the use of oral contraceptive pills (OCPs), pregnancy and a personal or family history of inherited thrombophilias such as Factor V Leiden, Prothrombin G20210A, deficiencies of protein C, protein S, or antithrombin. Oral contraceptive pill (OCP) use is associated with an increased risk of venous thromboembolism (VTE), the incidence of which is exponentially pronounced in women with hereditary thrombophilias.¹ The Prothrombin G20210A mutation, present in anywhere from 0.7 to 8.0% of the healthy population, is a single missense mutation at the 20210 nucleotide position which

results in a 133% increase in blood levels prothrombin.² This case describes a young woman presenting with an unprovoked pulmonary embolism with workup for potential etiology revealing an inherited thrombophilia disorder, as well as OCP use as an additional contributing factor. The purpose of this report is to emphasize the importance of hypercoagulability workup when presented with an unprovoked thromboembolism and prevention strategies in patients with family history or current diagnosis of inherited thrombophilias.

2. Case presentation

A 30-year-old female with no significant past medical or surgical history, presented with two weeks of progressive shortness of breath. The only medication she took prior to admission were combined estrogen and progestin OCPs, started shortly

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after the natural birth of her daughter three years ago. She notably did have a known family history of multiple miscarriages in her mother and a cousin with a thrombotic stroke at the age of 23, with a normal BMI of 24.1 (weight 59.4 kg, height 157 cm), was a non-smoker, and did not recently have any trauma, surgery, or prolonged immobility of any kind. Upon arrival to the Emergency Department, her symptoms progressed rapidly, as the patient lost consciousness within 5 min and developed cardiac arrest due to severe right heart strain, necessitating cardiopulmonary resuscitation. Due to the rapid progression of her course, her first recorded vitals were post-intubation with a temperature of 36 °C, heart rate of 80, respiratory rate of 20, blood pressure of 111/51 mmHg, and pulse oxygen of 100% on 60% FiO₂. A CT pulmonary angiogram revealed pulmonary emboli causing complete occlusion of the lower lobe pulmonary arteries bilaterally (Fig. 1). Tissue plasminogen activator (tPA) was emergently administered followed by thrombectomy and thrombolysis of the pulmonary emboli (Fig. 2). After the patient was stabilized, investigation for hypercoagulable medical disorders revealed an underlying Prothrombin G20210A gene mutation, also known as Factor II mutation. Patient was negative for Factor V Leiden gene mutations, PTG gene mutations, and Cardiolipin antibodies.

Findings from the investigation suggest that the combination of an inherited thrombophilia disorder as well as OCP use was likely the contributing factors in her development of unprovoked VTE in the form of a pulmonary embolus, as patient lacked other risk factors or etiologies for her condition.

3. Discussion

While the risk of thrombosis with OCP is well researched and established, it must further be emphasized that OCP users who are also carriers of prothrombin gene mutation G20210A have a 16-fold increased risk of VTE in comparison to non-OCP users without prothrombotic genetic mutations.³ It stands to reason that any possible triggers of this often-quiet disease must be avoided, demonstrating the importance of a hypercoagulability workup when presented with a VTE in an otherwise healthy young female, as seen in our case. Current WHO recommendations advise against the use of hormone based OCPs in women with inherited thrombophilias as they pose an unacceptable health risk.⁴ Primary prevention by identifying these disorders with targeted questions prior to initiating OCPs, including inquiry into personal and family history of stroke and pulmonary embolism, in conjunction with a thorough history, can be lifesaving and avoid unanticipated VTEs. Recognition of known extrinsic risk factors such as OCP use and smoking history should also be performed. Screening for common genetic mutations seen in inherited thrombophilias such as Prothrombin gene mutations, Factor V Leiden and Antithrombin mutations should be done if suspicion is high based on history intake. However, the WHO advises against routine screening for thrombophilia prior to initiating OCPs due to high screening cost as well as low prevalence of the disorders, so appropriate assessment of personal and family history is vital.⁵ In those with prothrombotic genetic conditions, the need for long term anticoagulation should be assessed. Secondary prevention by educating patients using OCPs should be encouraged, especially if patient has a known prothrombotic genetic mutation. It becomes

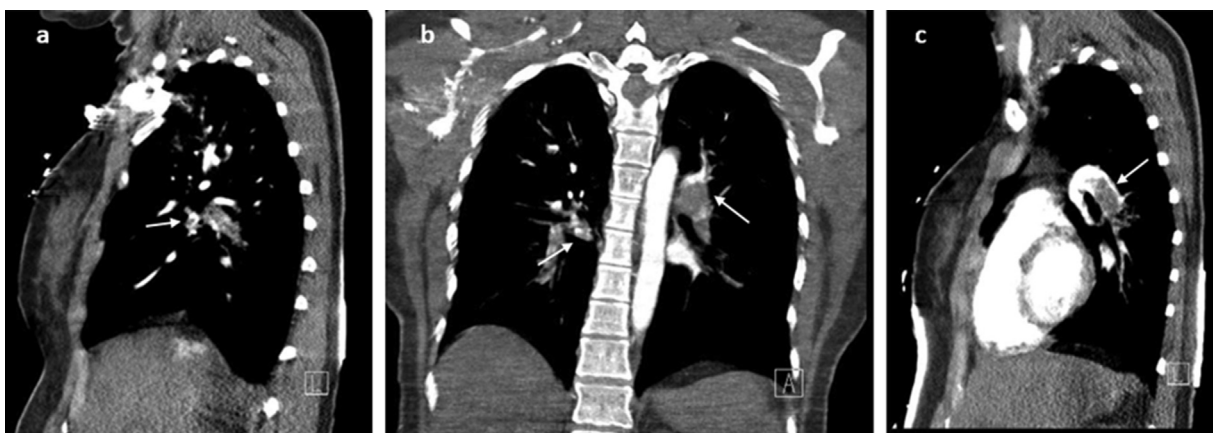


Fig. 1. CTA Chest in multiple planes demonstrating bilateral pulmonary embolisms. Sagittal image of the right lung with a filling defect in the right middle lobe branch (a). A coronal image of the chest with bilateral pulmonary emboli involving the left main pulmonary artery and the right anterior segmental artery (b). Sagittal image of the left lung with a filling defect in the left main pulmonary artery (c).

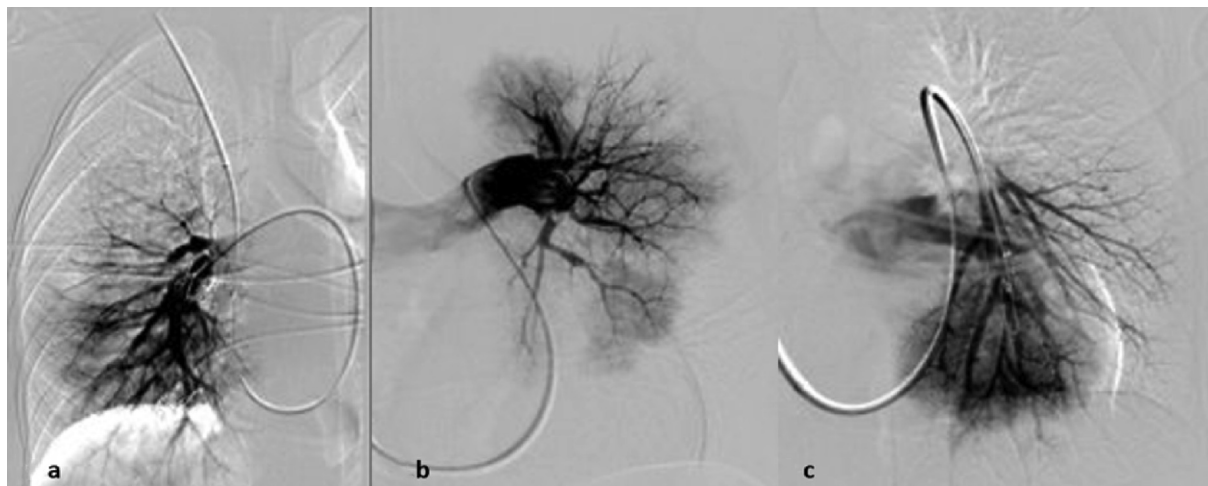


Fig. 2. Digital subtraction angiography of right and left lungs. A single coronal DSA frame of the right lung with near total opacification of the right pulmonary segmental branches (a). DSA coronal image of the left pulmonary artery with incomplete opacification of the basilar segments (b). Single coronal DSA image following catheter directed thrombolysis demonstrating complete opacification of the left basilar segmental arteries is appreciated (c).

paramount for physicians to counsel such patients to avoid additional risk factors that could contribute to the development of a VTE, such as obesity, smoking, hormone replacement therapy, and prolonged immobility.

Conflict of interest

The authors have no conflicts of interest to disclose.

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