Case Report

Psoriatic Inflammation-Induced Atypically Located Venous Thromboembolism: A Case of Immuno-Thrombosis

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Abstract

The immune and hemostatic systems share a common evolutionary origin, both defend against threats to organisms, and inflammation can cause venous thromboembolism. We would like to report a patient with a history of psoriasis, a chronic inflammatory disease, who has been admitted to our clinic with a swollen right arm and collateral veins visible throughout the right upper arm and right pectoral region, which have been present for almost 2 years. Investigations revealed a thrombus extending from the proximal basilic vein into the axillary and subclavian veins but sparing the superior vena cava. Further investigation was performed to reveal any likely cause other than psoriasis, including malignancy, rheumatological disease, or genetic thrombophilia, but none were revealed. This report illustrates that psoriasis-related inflammation can cause atypically located venous thromboembolic events.

Keywords: *Hemostasis, immunity, inflammation, psoriasis, thromboembolism*

Introduction

Venous thromboembolism (VTE), as defined by Rudolf Virchow, is the abnormal clotting of blood inside the vessels due to hypercoagulability, hemodynamic changes, and endothelial injury or dysfunction. VTE, consisting of deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common disorder with a high morbidity and mortality burden. Although differences are observed between races, their incidence ranges from 104 to 183 per 100,000 person-years among people of European ancestry.[1] VTE is one of the leading causes of cardiovascular mortality and the first preventable cause of death among hospitalized patients.[2] Alongside its mortality, VTE is associated with substantial morbidity (e.g., a post-thrombophlebitis syndrome in DVT, chronic thromboembolic pulmonary hypertension in PE), extended hospitalization periods, and higher costs.[3-5] Several risk factors for VTE have been defined, including aging, obesity, prolonged immobility, recent surgery or trauma, ongoing malignancy, genetic conditions altering the functions of coagulation factors, heart failure, and acute or chronic inflammation.[6] It has been shown that systemic inflammation has various effects on clot formation by triggering platelet aggregation, activating the coagulation cascade, stimulating the procoagulant activity of monocytes, changing the properties of blood flow, and damaging the endothelium.[7] Proinflammatory cytokines alter the properties of the endothelium to a state where thrombus formation is facilitated and fibrinolysis is halted.[8] Studies also indicate a correlation between elevated serum inflammation markers and a higher incidence of VTE.[9] This correlation can be explained by the existence of a shared evolutionary origin for coagulation and innate immune systems.[10]

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The interactions between the immune and coagulation systems have a clear reflection in the clinical context, where increased VTE is observed among patients with chronic inflammatory and autoimmune diseases.[10,11] Psoriasis is a chronic inflammatory disease in which Th1 and Th17 inflammatory pathways are activated, resulting in increased IL-6, TNF-alpha, and C-reactive protein (CRP) levels.[11] Studies indicate that IL-6 increases levels of several prothrombotic factors, namely intravascular tissue factor, fibrinogen, factor VIII, and von Willebrand factor. Furthermore, IL-6 lowers levels of anti-coagulant factors such as antithrombin, protein S, and thrombomodulin.[12] Recent studies indicate a 40 to 50% increased VTE risk among patients with psoriasis.[13,14] We would like to describe a psoriatic patient who is in remission but has mild CRP elevations, indicating ongoing mild inflammation. She has been admitted to our clinic with long-standing arm swelling and visible collateral veins and diagnosed with an atypically located VTE. Thorough investigations revealed no other culprit other than psoriasis-related inflammation.

Case

A 59-year-old woman was admitted to the outpatient cardiology clinic with complaints of right upper extremity edema and right chest wall venous dilatation. Her medical history showed that she was diagnosed with psoriasis five years ago and treated with psoralen and ultraviolet A (PUVA) light. She had no visible skin lesions, and she was under treatment with topical agents. Her physical examination was non-revealing except for the venous collaterals at the right side of the chest wall, and right upper extremity edema [Figure 1]. Her complete blood count, kidney, and liver function tests were all within normal reference ranges. The D-dimer level was mildly increased (1.13 mg/L; reference: 0–0.55 mg/L), and Doppler ultrasonography of the right extremity veins revealed a thrombus partially obstructing the lumen at the proximal part of the basilic vein.

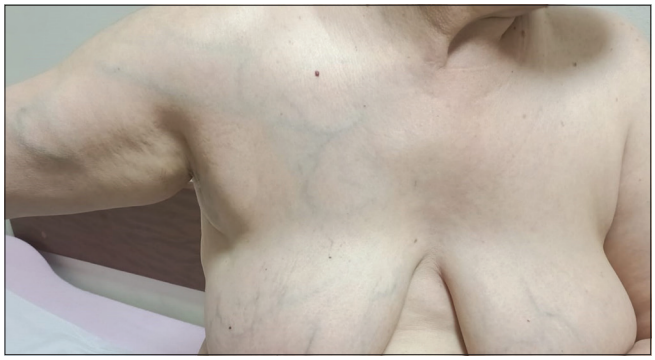

Figure 1: Venous collaterals at the right side of the chest wall

A computed tomography (CT) venography and thorax CT were performed to detect the presence of pulmonary embolism and reveal the extent of the thrombus. The thrombus was extending from the proximal basilic vein into the axillary and subclavian veins. Innominate veins and the vena cava superior were patents, and pulmonary thromboembolism was excluded. She was questioned for signs and symptoms of rheumatological diseases, including Behçet's disease, which is a highly prevalent disease in Turkey and creates a prothrombotic milieu, but it was non-revealing. All rheumatologic markers available, including anti-phospholipid antibodies, were negative. The homocysteine level was in the normal range, and the genetic thrombophilia panel revealed only a heterozygous mutation in the plasminogen activator inhibitor (PAI) gene. Additional screening for malignancy was performed via abdominal ultrasound, fecal occult blood test, and serum tumor markers, but none were revealed. CRP was slightly elevated (1.1 mg/dL; reference: 0–0.8 mg/dL). Apixaban 5 mg bid was started, arm elevation was recommended, and she was referred to the dermatology department for the reassessment of psoriasis treatment. The decision was to anti-coagulate the patient indefinitely, and no adverse events occurred since then. Informed consent was obtained before reporting of the case and acquisition of the image.

Discussion

Inflammation is a well-defined trigger for thrombosis. It has been shown that the immune system is linked to the hemostatic system; hence, the term "immune thrombosis" is defined.[8] While inflammatory signals produce signals for thrombus formation, growing clots recruit innate immune cells, creating a vicious cycle.[15] The clinical findings that thromboembolic events are more frequent among patients with chronic inflammatory and autoimmune disorders support these molecular observations. Psoriasis, a chronic inflammatory disease, is not an exemption either. Studies indicate a 50% higher VTE risk among patients affected by psoriasis.[13] The case we have presented is that of a lady with a history of psoriasis for 5 years who has received PUVA and topical agents but has not received any systemic therapies. Although she had non-visible skin lesions, a mild CRP elevation indicates that underlying chronic inflammation still persists. Unilateral upper extremity swelling with accompanying collateral veins aroused suspicion for VTE; hence, a CT was ordered. CT revealed thrombus extending from the proximal basilic vein into the axillary and subclavian veins. Newly diagnosed unprovoked VTE incited us to investigate for any potential triggers. The physical examination, history, and

signs or symptoms were unrevealing. Since malignancy is a well-known precipitator of VTE, age-appropriate malignancy screening was conducted, but it was not revealing. The duration of the signs, which lasted almost 2 years, also rendered malignancy an unlikely cause for VTE. She was examined with a physical examination and laboratory tests for any underlying rheumatological disorder, including psoriatic arthritis, systemic lupus erythematosus, and Behçet's disease, which is highly frequent in Turkey and characterized by a tendency to thrombosis, but they were also non-revealing. A genetic thrombophilia panel revealed only heterozygous mutations in the plasminogen activator inhibitor (PAI) gene, which are characterized by either no risk or a small risk of venous thromboembolism.[16,17] Although it may not be possible to determine whether underlying psoriasis or the PAI heterozygosity was the exact and sole cause of the long-standing, atypically located VTE seen in our case, it is likely that psoriasis-related inflammation is the foundation for the vicious immune-thrombosis cycle. Clinicians must be aware of the fact that even clinically silent chronic inflammatory diseases may trigger venous thrombosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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