CASE REPORT

UDC: 616.517-06:616.14-005.6/.7(043)
https://doi.org/10.2298/VSP170717077M

Psoriasis as a risk factor of pulmonary embolism – case report

Psorijaza kao faktor rizika od plućne embolije

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Abstract

Introduction. Deep vein thrombosis and pulmonary embolism, known as venous thromboembolism, constitute a major global burden of disease. Both entities share the same risk factors. Psoriasis is a common, chronic skin disease. It also presents multisystemic inflammation, mainly affecting skin and joints, but it is also associated with the significant cardiovascular and metabolic states and comorbidities, on the so-called "psoriatic march". **Case report.** We presented a 78-year-old female patient, with psoriasis associated with pulmonary embolism which is accidentally discovered. We did not find any other predisposing factor of this disease (primary or secondary thrombophilia), except hyperhomocysteinemia. The patient was treated with low molecular weight heparin (enoxaparin), followed by the administration of an oral vitamin K antagonist (warfarin sodium) in the weight adjusted regimens. Additionally, we recommended vitamin B complex, including folate. Supposed link between hyperhomocysteinemia and psoriasis was the decreased serum folate level as the result of increased vitamin utilization in the skin because of increased DNA synthesis. **Conclusion**. The reported case reflects existing literary knowledge about the increased risk of VTE and arterial thromboembolic events in the psoriatic patients. The highest risk appears in the patients with a severe disease and may be a consequence of systemic inflammation and hyperhomocysteinemia.

Key words:
venous thrombosis; pulmonary embolism; psoriasis; risk factors; comorbidity; homocysteine.

Apstrakt

Uvod. Duboka venska tromboza i plućna embolija, poznate kao venski tromboembolizam (VTE), predstavljaju veliko globalno opterećenje. Oba entiteta dele iste faktore rizika. Psorijaza je česta hronična bolest kože. Takođe, predstavlja multisistemsko inflamatorno oboljenje, dominantno zahvatajući kožu i zglobove koje je povezano sa značajnim kardiovaskularnim, metaboličkim stanjima i komorbiditetima, tzv. "psorijatični marš". **Prikaz bolesnika.** U radu prikazujemo 78-godišnju bolesnicu sa psorijazom udruženom sa plućnim embolizmom koji je slučajno otkriven. Nije utvrđen drugi predisponirajući faktor (primarna ili sekundarna trombofilija), izuzev hiperhomocisteinemije. Bolesnica je lečena niskomolekulskim heparinom (enoksafarin) i oralnim antagonistom vitamina K (varfarin natrijum), u dozama određenim prema telesnoj težini. Dodatno smo preporučili kompleks vitamina B i folate. Pretpostavljena veza između hiperhomocisteinemije i psorijaze predstavlja snižen nivo folata u serumu, kao posledica njegove povećane potrošnje u koži, zbog povećane sinteze DNK. **Zaključak.** Prikazani slučaj ilustruje podatke iz literature da su bolesnici sa psorijazom u povišenom riziku od venskog i arterijskog tromboembolizma. Rizik je viši kod bolesnika sa teškim oblikom bolesti, što može biti posledica sistemske inflamacije i hiperhomocisteinemije.

Ključne reči:
tromboza, venska; pluća, embolija; psorijaza; faktori rizika; komorbiditet; homocistein.

Introduction

Deep vein thrombosis (DVT) and pulmonary embolism (PE), collectively referred to as venous thromboembolism (VTE), constitute a major global burden of disease [1]. Both entities share the same risk factors. Clinical presentation ranges from asymptomatic, incidentally discovered emboli to massive embolism causing right ventricle failure and immediate death.

VTE may be "provoked" in the presence of a temporary or some reversible risk factor (such as surgery, trauma, immobilization, pregnancy, oral contraceptive use or hormone replacement therapy) within the last 6 weeks to 3 months be-

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fore diagnosis, and "unprovoked" in the absence thereof. PE may also occur in the absence of any known risk factor [2].

The proportion of patients with idiopathic or unprovoked PE was about 20% in the International Cooperative Pulmonary Embolism Registry (ICOPER) [3]. Thrombosis in the veins is triggered by venous stasis, hypercoagulability and the vessel wall inflammation or injury. These 3 underlying causes are known as the Virchow triad. All known clinical risk factors for DVT and PE have their basis in one or more elements of the triad. The most important clinically identifiable risk markers for DVT and PE are a prior history of DVT or PE, recent surgery or pregnancy, prolonged immobilization, or underlying malignancy.

Psoriasis is a common, chronic skin disease usually manifested as raised, well-demarcated, erythematous plaques with adherent silvery scales. It also presents multi-systemic inflammation, mainly affecting skin and joints, but also associated with significant cardiovascular and metabolic states and comorbidities, on the so-called "psoriatic march": insulin resistance, atherosclerosis, myocardial infarction, obesity and metabolic syndrome [4–7].

We present an old age female patient with severe psoriasis complicated with PE, which is accidentally discovered.

Case report

A female patient, 78 years old, was admitted to the Military Medical Academy, Clinic for Dermatology and Venereology because of generalized psoriasis. A diagnosis was established 31 years ago, since when she had been treated with topical corticosteroids and PUVA (psoralen + UVA treatment) phototherapy with temporary and partially improvement of psoriasis. A classic systemic oral therapy and biologics were never used. She denied any respiratory symptoms, except fatigue when she walked about 50 meters, during last two months. Her past medical history included stabile angina pectoris, chronic atrial fibrillation and arterial hypertension. She denied any other diseases, allergies, smoking, or alcohol consumption. A physical examination on admission revealed generalized dark red, sharply demarcated skin plaques covered with silvery scale on the trunk and extremities (Figure 1).

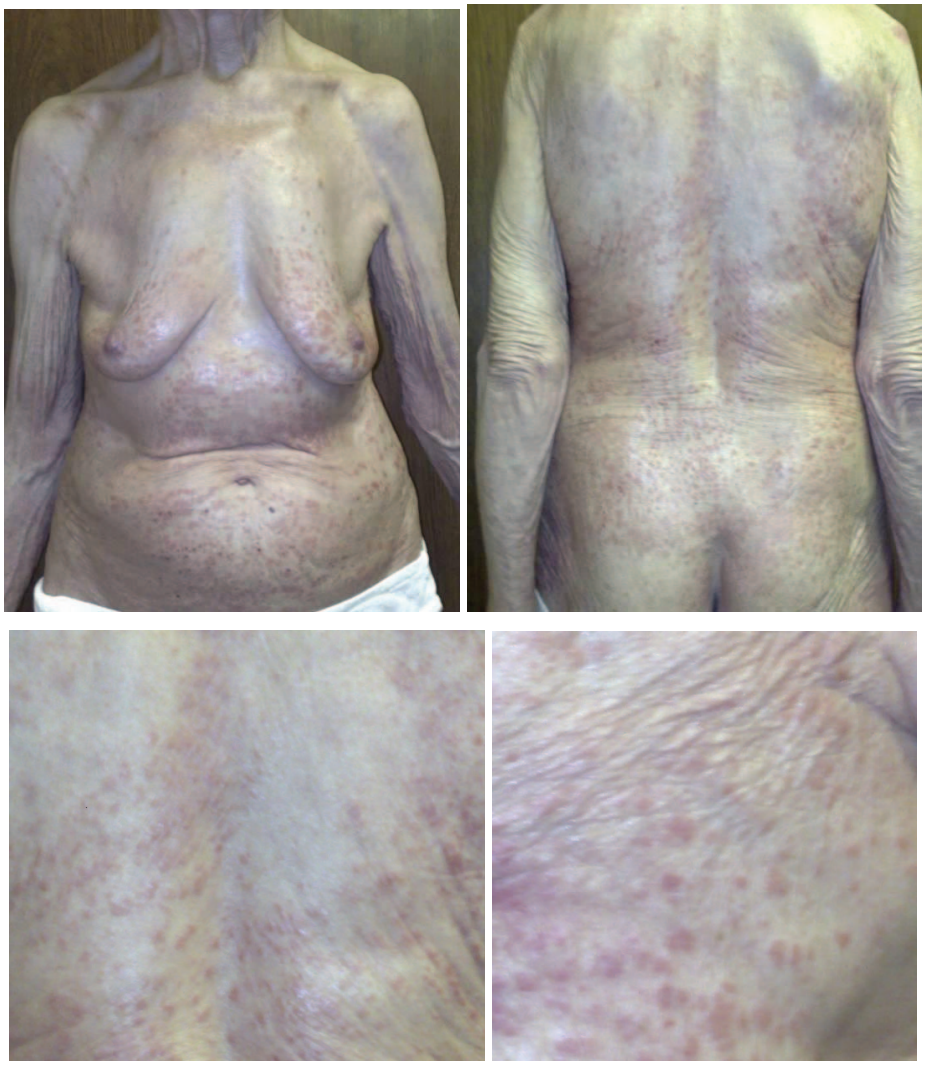

Fig. 1 – Psoriatic skin changes: scaly erythematous plaques on trunk and extremities.

PASI (Psoriasis Area and Severity Index) was 44. The physical finding on the respiratory system and heart was normal, except absolute arrhythmia. Also, varicose veins of lower legs were noted. Chest radiography (CXR) showed elevated right hemidiaphragm and bilateral diffuse linear and reticular pattern, predominantly in the lower lung fields. The heart's shadow was enlarged (Figure 2). Chest multidetector computed tomography (MDCT) revealed moderate fibrous changes in the lung parenchyma and bilateral embolus in the lobar and segmental branches of pulmonary artery (Figure 3).

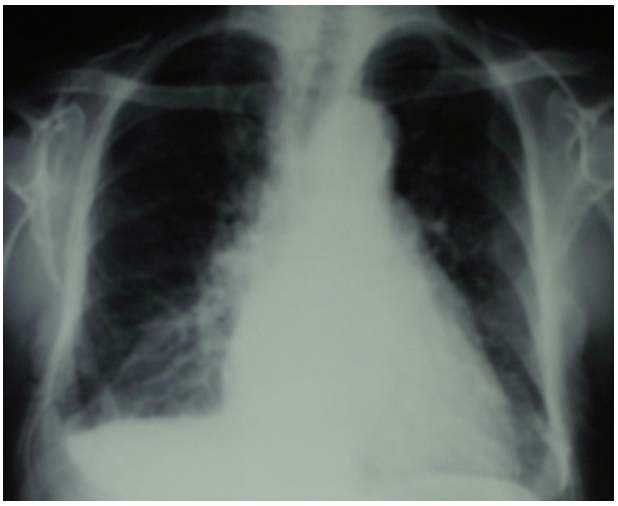

Fig. 2 – Chest radiography of the patient.

The patient was moved to the Clinic for Pulomonology because of additional examination and treating. Initial laboratory tests revealed an erythrocyte sedimentation rate (ESR) of 39 mm/h (normal range 0–12), elevated C-reactive protein (CRP) – 11.39 mg/L (normal range 0–3 mg/L), normal platelets, white and red blood cells counts, decreased hemoglobin level – 94 g/L (normal range 115–165 g/L), decreased hematocrit – 0.31 (normal 0.37–0.47). The differential blood count was normal. The routine biochemical analyses (electrolytes, glucose, urea, creatinine, bilirubin, transaminases, lactate dehydrogenase, gama-glutamyl-transpeptidase, triglycerides, low density lipoprotein (LDL) cholesterol and high density lipoprotein (HDL) cholesterol and tumor markers (CEA, CA 15-3, CA 125, CA 19.9, CA 72.4, NSE, Cyfra 21.1) were normal. The homocystein level was elevated – 23 μmol/L (normal range 4.9–15 μmol/L), the folate level was decreased – 4.22 nmol/L (normal 7–46 μmol/L), vitamin B12 – 249 pmol/L (normal 156–672 pmol/L). Autoantibodies (antinuclear, antibodies for extractable nuclear antigens, anticardiolipin, anti-CCP (cyclic citrullinated peptide), anti-neutrophil cytoplasmic and lupus anticoagulant) were normal. Protein C, protein S and antitrombin III were in the range of predicted values. Screening for mutations of Factor V Leiden, prothrombin variant 20210A and MTHFR (methylenetetrahydrofolate reductase) showed wild type of genes.

The pulmonary function tests showed normal spirometry, carbon monoxide diffusion capacity and the respiratory arterial blood gases at rest.

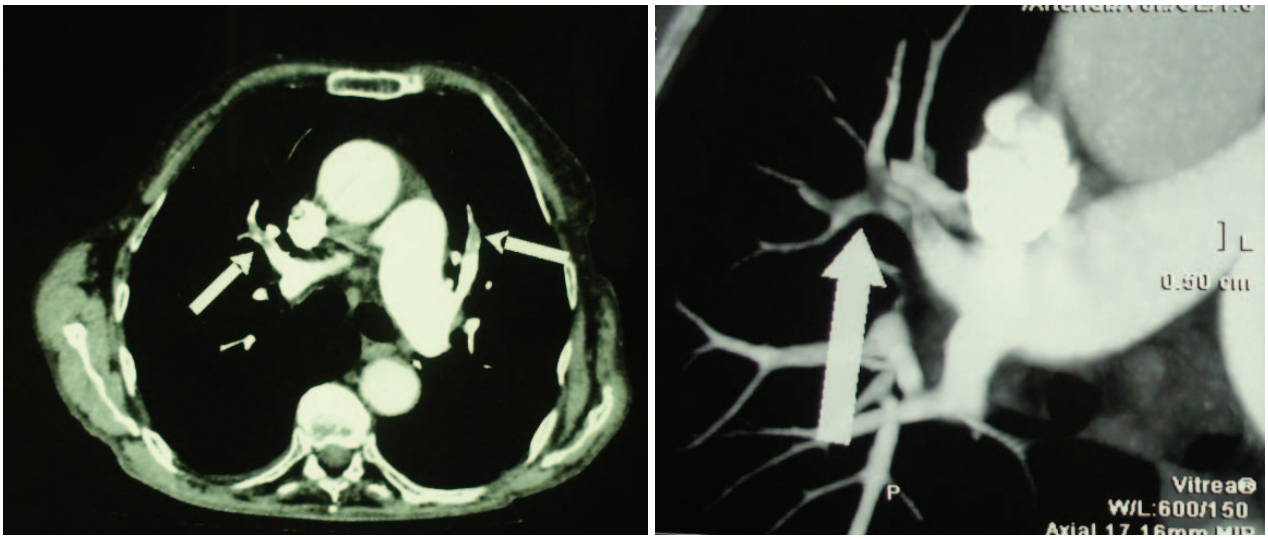

Fig. 3 – Multidetector computed tomography (MDCT) of the same patient (emboli are marked with a white arrow).

Electrocardiography revealed atrial fibrillation with ventricular rate 64/minute, negative T wave in D2, D3, aVF and V3-V6 precordial leads.

Doppler ultrasound of legs blood vessels showed the moderate atherosclerotic plaques in the arteries with luminal stenosis to 50% and no evidence of DVT.

Due to the fibrotic changes on the MDCT, bronchoscopy was performed. The bronchoscopic finding was normal. The bronchoalveolare lavage (BAL) fluid analysis did not show the bacterial, fungal agents, or acid fast bacilli. The BAL cytology cell profile showed macrophages 45%, lymphocytes 15% and neutrophils 40%.

The patient was treated with low molecular weight heparin (enoxaparin), followed by the administration of an oral vitamin K antagonist (warfarin sodium) in the weight adjusted regimens. Additionally, we recommended vitamin B complex, including folate.

Discussion

Several studies have demonstrated that cardiovascular diseases and their associated risk factors are more common in the patients with psoriasis than in the general population [4–7]. The cause of this increased risk is only particularly clear. Some authors suggested that there may be some intrinsic associated risk: elevated lipids were documented in the psoriasis patients at the time of their initial diagnosis when compared to the non-psoriasis controls who were matched for the body mass index (BMI) status as well as other demographic, clinical, and lifestyle characteristics [8]. Others suggested that psoriasis was an immune inflammatory disease characterized by T helper – Th1 and Th17-driven inflammation with a striking overlap of inflammatory markers and mediators with atherosclerosis [9–11]. Also, hyperhomocysteinemia, which may be associated with atherothrombosis and VTE [11], was reported in the psoriatic patients [12–14]. The relationship between chronic inflammatory diseases (psoriasis, psoriatic arthritis and rheumatoid arthritis) was evaluated in a cohort study which was conducted in a primary care medical record database in the UK with the data from 1994–2014. The patients with mild psoriasis had the significantly elevated risks of VTE (HR 1.35, 1.29, and 1.07, respectively) after adjusting for the traditional risk factors. Severe psoriasis and psoriatic arthritis threated with disease modifying anti-rheumatic drugs, had an elevated but not a statistically significant risk for VTE. The findings were similar for DVT. The age-and-sex-adjusted risk of PE was elevated in the rheumatoid arthritis, severe psoriasis **?**and psoritac arthritis patients prescribed a disease modifying anti-rheumatic drugs [15].**?** Likewise, a Danish Nationwide Cohort Study indicated that the patients with psoriasis were at increased risk of VTE. The highest risk was found to be in the young patients with severe psoriasis [16]. In a systematic review and meta-analysis Ungprasert et al. [17] demonstrated a significant association between psoriasis and VTE with an overall 1.46-folds (95% CI 1.29–1.66) increased risk compared with the non-psoriasis participants. The risk ratios were fairly consistent across the studies, ranging from 1.35 to 1.66 [17].

In our patient, with earlier diagnosed severe psoriasis, we established PE and generalized atherosclerosis (angina pectoris and arteries in the legs). We did not find any other causes of these diseases (primary, or secondary thrombophilia), except hyperhomocysteinemia (the serum level of the homocystein was 1.5-fold elevated). Hyperhomocysteinaemia is a known risk factor for atherosclerosis and thrombosis, and may interfere with the coagulation system, causing a direct endothelial injury followed by facilitated thrombosis and causing oxidative damage to the endothelium [13]. A supposed link between hyperhomocysteinemia and psoriasis was the decreased serum folate level as the result of increased vitamin utilization in the skin because of increased DNA synthesis. Homocysteine is metabolized by either being converted into methionine or cysteine. These processes require folic acid and vitamin B12. Also, the markers of systemic inflammation (ESR, CRP) were elevated in our patient, which is in correlation with the immune-inflammatory hypothesis [9, 10].

Clinical probability of PE in our patient was low (revised Geneva score 1), so the mild fibrotic changes seen at CXR were a reason to do MDCT. Pulmonary fibrosis (PF) in the psoriatic patients usually presents a complication of systemic therapy (methotrexate, tumor necrosis factor-α inhibitors like infliximab, etanercept and adalimumab) [18, 19]. PF as an extra-cutaneous manifestation of psoriasis is uncommon [20] and usually linked to psoriatic arthritis. Anyway, we established neutrophilic alveolitis in our patient, but we did not perform the lung biopsy because of increased risk (age, comorbidities). She did not receive systemic treatment, so we did not establish etiology of PF, therefore we cannot claim that PF in our patient is a consequence of psoriasis. Several studies showed a relationship between idiopathic pulmonary fibrosis and an increased risk of vascular diseases [21, 22]. However, in our case, there was mild pulmonary fibrosis, with no radiological criteria for diffuse parenchymal (interstitial) lung diseases.

Conclusion

The reported case reflects existing literary knowledge about an increased risk of VTE and arterial thromboembolic events in the psoriatic patients. The highest risk is in the patients with severe disease, and may be an effect of systemic inflammation and hyperhomocysteinemia.

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Received on July 17, 2017.
Revised on june 10, 2019.
Accepted July 18, 2019.
Online First September, 2019.