INTERNAL MEDICINE

□ CASE REPORT □

Pigmented Purpuric Dermatosis Associated with Primary Antiphospholipid Syndrome

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Abstract

Pigmented purpuric dermatosis (PPD) is a group of chronic disorders characterized by the extravasation of erythrocytes and marked hemosiderin deposits in the dermis. Schamberg disease is a subtype of pigmented purpuric dermatosis in which nonpalpable purpura is prominent on the lower extremities. No cases of primary antiphospholipid syndrome and pigmented purpuric dermatosis have so far been reported in the literature. We herein report a case of pigmented purpuric dermatosis associated with primary antiphospholipid syndrome.

Key words: antiphospholipid antibody, capillaritis, dermatosis, purpura

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Introduction

Pigmented purpuric dermatosis (PPD) is a group of chronic disorders characterized by the extravasation of erythrocytes in the dermis with marked hemosiderin deposition. PPD is divided into five distinct clinical entities. Schamberg disease or purpura (SD) is a subtype of PPD in which nonpalpable purpura is prominent on the lower extremities. This condition is usually seen in childhood, although it can occur during any period of life (1). SD was first described in an 11-year-old boy in 1901. Antiphospholipid antibody syndrome (APS) is an autoimmune clinical pathology characterized by the production of antiphospholipid antibodies, recurrent fetal loss, arterial or venous thrombosis and the presence of lupus anticoagulant (2). There is a wide variety of cutanous findings of APS. We herein present the case of a patient who presented with a rare association of APS and PPD.

Case Report

A 37-year-old woman was admitted to another hospital with a complaint of leg swelling. Five months previously, she was diagnosed with deep venous thrombosis in her legs, and anticoagulant therapy (warfarin) was therefore initiated at that time. She had received warfarin treatment for three months before it was discontinued. Subsequently, the swelling became advanced and pain developed. One month previously, a nonpruritic rash appeared on both legs. The patient was referred to our hospital for an evaluation. Her medical history included a fetal loss at the 10th week of pregnancy. On a physical examination, red-brown plaques surrounded by pethechial and purpuric papules were observed (Fig. 1). Other findings of the physical examination were normal. A lower extremity venous doppler ultrasonographic examination revealed recanalized thrombi in the right and left femoral veins, a nonrecanalized thrombus in the left popliteal vein and venous insufficiency. The diagnosis was deep venous thrombosis. Arterial color doppler ultrasonography was normal. Disorders associated with a tendency toward hypercoagulability and thrombosis were investigated. The findings of a hemogram, acute phase reactants, a urinalysis and routine blood biochemistry tests were all normal. Tests for rheumatoid factor (RF), antinuclear antibodies (ANA), anti-dsDNA, antineutrophil cytoplasmic anti-

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Figure 1. **Red-brown plaques and purpuric papules on the legs.**

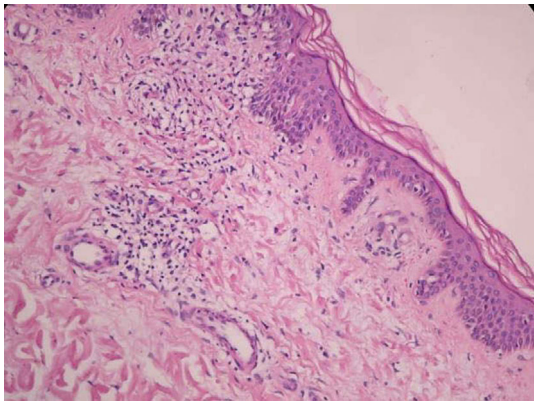


Figure 2. **Typical histopathological findings of PPD on a skin biopsy.**

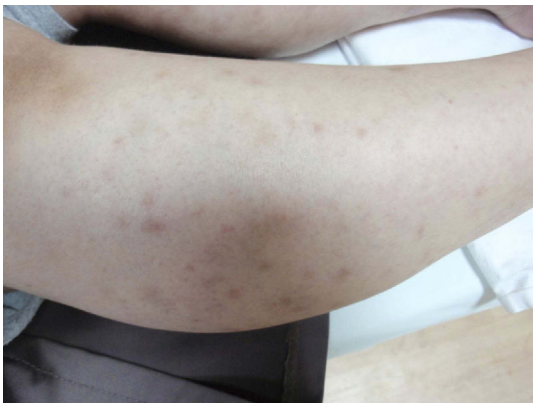


Figure 3. **After one month of therapy.**

bodies (ANCA), cryoglobulin and cryofibrinogen were negative. The levels of complements (C3) and (C4) and the activated partial thromboplastin time (aPTT) were normal. Lupus anticoagulant was positive. The level of anticardiolipin antibody (ACA) IgM was 22 IU/mL (N: 0-7), indicating positivity, whereas IgG was negative. Tests for hepatitis B and C and HIV were negative. The levels of antithrombin-3 and Protein C and S were in the normal ranges. Tests for factor-V-Leiden and MTHFR mutations were normal. A skin biopsy was obtained from the purpuric lesion on the front side of the tibia, which revealed an orthokeratinized epidermis, spongiosis, edema in the upper dermis, perivascular lymphocyte-rich cellular infiltration, capillary vessel proliferation, thickening of the vessel wall, swelling of the endothelium and marked erythrocyte extravasation. There was no evidence of microthrombi (Fig. 2). The histopathological findings were congruent with a diagnosis of PPD, which was diagnosed based on the typical appearance and site of the lesions. Findings suggestive of systemic lupus erythematosus were absent. According to the Sydney 2006 Sapporo revision criteria, primary antiphospholipid syndrome was diagnosed concommittantly based on the clinical and laboratory findings of deep venous thrombosis, the medical history of fetal loss, the positive lupus anticoagulant results and the positive anticardiolipin antibody findings. Topical corticosteroid therapy was initiated to treat the purpuric lesions. In addition, the patient was administered warfarin and an antimalarial drug, 'hydroxychloroquine,' to treat APS and DVT. After one month of therapy, the purpuric lesions improved (Fig. 3).

Discussion

The skin findings of antiphospholipid syndrome include livedo reticularis, ulcers, necrosis, thrombophlebitis, purpuric and cyanotic macules and acral erythematous lesions that develop as a result of microthrombi. More rarely, distal ischemia and gangrene are also seen as a result of arterial occlusion of the hands and feet. The skin findings of APS generally result from vascular abnormalities or ACA positivity. Such vascular abnormalities include capillaritis, livedo reticularis, acrocyanosis, Raynaud's phenomenon and thrombophlebitis. Although purpuric dermatosis usually occurs before preadolescence, PPD can develop in any decade of life. The typical presentation of the disease involves a rash on the lower extremities described as 'cayenne pepper' that is seen in nearly half of patients (3). The major pathological finding of PPD is capillaritis. Capillaritis is also seen in patients with APS (1-3). Various medications (NSAIDs, steroids, sildenafil, glipizide, bezafibrate), food additives, external contact agents and infections have been suggested to play roles in the etiology of PPD (4-6). PPD also manifests as skin involvement in some hematological, oncological, immunological and infectious diseases, such as hepatitis C (7, 8). In the present case, we ruled out the presence of hematological, oncological, immunological and infectious diseases in addition to primary and secondary vasculitic syndromes and coagulopathies. In addition, our patient was not receiving any medications that could account for the etiopathogenesis of PPD. Increased venous pressure, exercise and gravity are also important cofactors for the development of purpuric dermatosis (2). In our case, PPD may be clinically speculated to have been caused by APS based on the presence of capillaritis.

Although the histopathological findings in this case were

not strong enough to clarify the APS-PPD association, the clinical findings support this association. The patient had been on warfarin therapy for three months before the medication was subsequently discontinued. There are reports in the literature of cases of warfarin-induced necrotic purpura (9). However, in our case, the purpura developed after the cessation of warfarin therapy. Furthermore, no worsening of the lesions was obseved after the warfarin treatment was reintroduced. These data suggest that the purpuric lesions did not result from the warfarin therapy. There is no currently established therapy for PPD. Topical steroids used to treat purpuric lesions, pentoxifylline, griseofulvin, PUVA and antiallergic medications are of limited efficacy (1). In this case, topical steroids were used for local treatment of PPD. Warfarin was administered to treat the DVT. Hydroxychloroquine was also inititated, being a drug that is suggested to reduce the risk of thrombosis via decreasing the ACA titer (10).

Capillary vessel proliferation, thickening of the vessel wall, swelling of the endothelium and erythrocyte extravasation are the pathological findings of capillaritis seen in patients with PPD and may be attributable to APS and/or DVT. To our knowledge, there is currently no evidence in the literature regarding the occurrence of PPD with secondary APS or SLE.

Conclusion

We suggest that PPD should be considered in the etiopathogenesis of purpuric lesions in patients with primary APS. In our case, the clinical and histopathological findings corroborated the association between PPD and APS. However, further studies are needed to prove the existence of this association.

The authors state that they have no Conflict of Interest (COI).

References

1. Iagăru N., Monica Dărmănescu, Irina Mărgăritescu, Chirița D. Pigmented pupuric dermatitis. Therapeutics, Pharmacology and Clinical Toxicology **15**: 160-163, 2011.
2. Naldi L, Locati F, Marchesi L, et al. Cutaneous manifestations associated with antiphospholipid antibodies in patients with suspected primary antiphospholipid syndrome: a case-control study. Ann Rheum Dis **52**: 219-222, 1993.
3. Darius Mehregan, Jennifer Michelle Hey. Pigmented Purpuric Dermatitis, Dermatology Online J Updated: Jan 19, 2010.
4. Yung A, Goulden V. Pigmented purpuric dermatosis (capillaritis) induced by bezafibrate. J Am Acad Dermatol **53**: 168-169, 2005.
5. Adams BB, Gadenne AS. Glipizide-induced pigmented purpuric dermatosis. J Am Acad Dermatol **41**: 827-829, 1999.
6. Koçak AY, Akay BN, Okçu Heper A. Sildenafil-induced pigmented purpuric dermatosis. Cutan Ocul Toxicol **32**: 91-92, 2013.
7. Sawamura D, Ohata Y, Shibaki A, Shimizu H. Pigmented purpuric dermatosis in mixed cryoglobulinaemia associated with rheumatoid arthritis and hepatitis C infection. Acta Derm Venereol **85**: 460-461, 2005.
8. Wakusawa C, Fujimura T, Haga T, Aiba S. Granulomatous pigmented purpuric dermatitis associated with primary Sjögren's syndrome. Acta Derm Venereol **93**: 95-96, 2013.
9. Meierhofer S, Colucci G, Steiner S. Coumarin-induced necrotic purpura of the skin: case report and review of the literature. Praxis (Bern 1994) **101**: 609-613, 2012.
10. Rand JH, Wu XX, Quinn AS, Chen PP, Hathcock JJ, Taatjes DJ. Hydroxychloroquine directly reduces the binding of antiphospholipid antibody-β2-glycoprotein I complexes to phospholipid bilayers. Blood **112**: 1687-1695, 2008.

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