Acta Dermatovenerol Croat 2025;33(3):129-132 CLINICAL ARTICLE

Livedoid Vasculopathy in a Female Patient With a History of COVID-19 Infection During Pregnancy: A Case Report

Iva Domić[1], Ilenia Romić[2], Majda Vrkic Kirhmajer[3], Joško Mitrović[1], Jadranka Morović-Vergles[4]

[1]Dubrava University Hospital, Zagreb, Croatia; [2]Dubrovnik General Hospital, Dubrovnik, Croatia; [3]University Hospital Centre Zagreb, Zagreb, Croatia; [4]Division of Clinical Immunology, Allergology and Rheumatology, Department of Internal Medicine, School of Medicine University of Zagreb, Dubrava University Hospital, Zagreb, Croatia

Corresponding author:
Iva Domić
Dubrava University Hospital
Avenija Gojka Šuška 6
Zagreb, Croatia
ivapdomic@gmail.com

ABSTRACT Livedoid vasculopathy is a rare, chronic thrombo-occlusive disease characterized by recurrent livedoid skin changes, atrophic white plaques, and ulceration. It most commonly affects the dermal vessels of the distal lower extremities, ankles, and feet, bilaterally. While it is commonly associated with hypercoagulable states, systemic autoimmune diseases, and malignancies, we report a case of a previously healthy 31-year-old female with a history of moderate COVID-19 infection during pregnancy, two years before the onset of livedoid skin changes.
The patient presented to a hematologist with a two-month history of erythematous to violaceous macules and patches on the dorsum of the feet, ankles, and lower extremities, along with mild ankle swelling. Multiple punch biopsies of the affected skin demonstrated thrombi, fibrinoid vascular changes, fibrosis, and hyalinization of the vessel walls – findings consistent with vasculopathy. Initial treatment included subcutaneous low-molecule weight heparin (dalteparin).
This case highlights the importance of early recognition, the performance of a skin biopsy with subsequent histopathologic diagnosis, and appropriate management of this rare, but potentially debilitating condition.

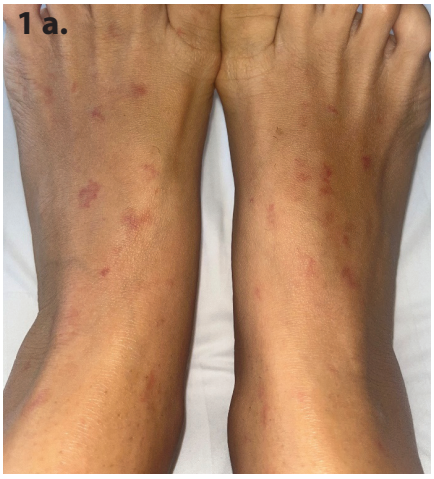
KEY WORDS: livedoid vasculopathy; pregnancy; COVID-19 infection; anticoagulation therapy.

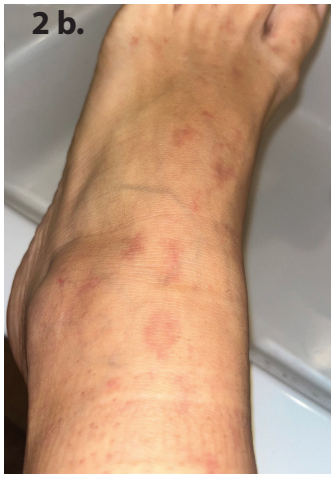
INTRODUCTION

Livedoid vasculopathy is a rare, chronic, thrombo-occlusive disease that primarily affects the dermal vessels of distal lower extremities, ankles, and dorsal feet bilaterally. It affects one person in 100,000 and is three times more common in young women than in men, the median age ranges from 35 to 53 years (1,2,3). This increased prevalence in women might be related to sex-specific physiological conditions, like pregnancy, which is itself a prothrombotic state (4).

Livedoid vasculopathy occurs independently or in association with different conditions that promote a hypercoagulable state, including acquired or inherited thrombophilia, systemic autoimmune diseases (e.g., primary antiphospholipid syndrome, systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis, connective tissue diseases), and malignancies (1,3,5). The underlying pathogenesis is believed to be caused by thrombus formation in the dermal capillaries due to increased thrombotic and

Acta Dermatovenerol Croat
2025;33(3):129-132





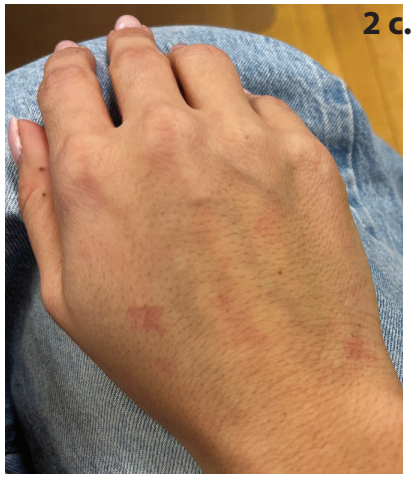


Figure 1 a. Livedoid patches on the feet; **Figure 1 b.** Livedoid patches on the left foot and ankle; **Figure 1 c.** Livedoid skin patches on right forearm

decreased fibrinolytic activity, along with endothelial damage (1,2,5,6).

Livedoid vasculopathy often presents initially with erythematous or purpuric macules or papules with a linear or angular shape. These lesions may progress to ulceration, healing slowly over a period of three to four months, and eventually forming residual white atrophic plaques (called atrophie blanche) surrounded by hyperpigmentation and telangiectasias (3,5,7).

The diagnosis of livedoid vasculopathy is confirmed by skin biopsy in a patient with suggestive physical findings (e.g., livedoid changes, atrophie blanche, ulceration) on the lower extremities (1,2,3). The biopsy should include the full thickness of the dermis and subcutaneous fat. Optimal sites for punch biopsy are new purpuric macules or patches, and the edges of new ulceration. Histopathologic features consistent with livedoid vasculopathy include intraluminal fibrinous thrombi, endothelial proliferation, and subintimal hyaline degeneration within the dermal blood vessels (6,7,8).

The most common disorders in the differential diagnosis of livedoid vasculopathy are chronic venous disease of the lower extremities, peripheral artery disease, and vasculitis (1,2,3). After the diagnosis is confirmed histopathologically, patients should be evaluated for underlying thrombotic or systemic autoimmune disorders. This evaluation should begin with a detailed history, review of systems, and physical examination to assess for findings suggestive of thrombophilia or a systemic autoimmune disease.

Recommended laboratory assessments include a complete blood count, comprehensive metabolic panel, urinalysis, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), rheumatoid factor (RF) and antibodies to cyclic citrullinated peptides (anti-CCP), serum complement levels, antinuclear antibody (ANA) titer, antineutrophil cytoplasmic antibodies (ANCA), serum cryoglobulins, serum protein electrophoresis and immunofixation, tests for acquired and inherited thrombophilia (1,2,3).

Treatment of livedoid vasculopathy usually involves a combination of therapies, but antiplatelet drugs and anticoagulants are preferred as first-line treatments, along with general supportive measures such as wound care, compression therapy, and pain management (9,10,11). Among pharmacologic options, anticoagulants are the most commonly used monotherapy (12,13,14). Livedoid vasculopathy frequently recurs upon discontinuation of therapy, so long-term therapy with an effective and well-tolerated regimen is usually required.

CASE REPORT

We report the case of a 31-year-old female with a history of moderate COVID-19 infection during the second trimester of pregnancy, occurring two years before the onset of livedoid skin changes. The patient presented to a hematologist with a two-month history of livedoid patches on the feet, ankles, and distal lower legs. On physical examination, erythematous to violaceous macules and patches were observed on the dorsum of the feet, ankles, distal lower legs, and forearms, along with discrete ankle swelling (Figure 1 a, b, c). The clinical presentation resembled purpura pigmentosa and lichen aureus.

The patient had no systemic symptoms. Aside from elevated D-dimer levels, routine laboratory tests were unremarkable. She was initially prescribed acetylsalicylic acid. Multiple punch biopsies were performed on lesions located on the forearm, distal lower legs, ankles, and feet. Histopathological examination revealed intraluminal thrombi, fibrinoid change of blood vessels, fibrosis, and hyalinization of the vessel wall, find-

Acta Dermatovenerol Croat
2025;33(3):129-132

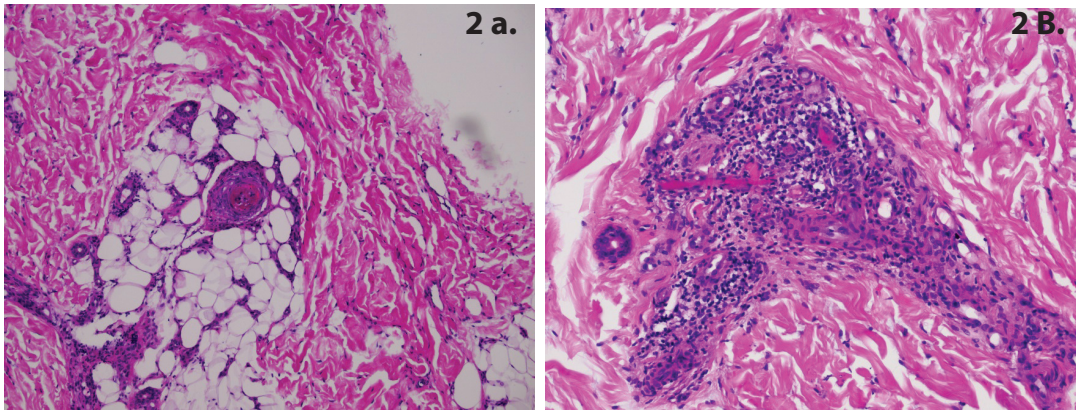


Figure 2 a. Intraluminal thrombus in the artery of subcutaneous fat tissue (hematoxylin and eosin, original magnification x100)

Figure 2 b. Obliterated blood vessel in the deep reticular dermis (hematoxylin and eosin, original magnification x200)

ings consistent with a diagnosis of vasculopathy, without evidence of vasculitis (Figure 2 a, b).

Following diagnosis, an extensive workup was conducted to evaluate for underlying coagulopathies. Immunology laboratory findings were negative for lupus anticoagulant, beta-2 glycoprotein I antibodies, anti-cardiolipin IgM and IgG antibodies, antinuclear antibodies, antineutrophil cytoplasmic antibodies, rheumatoid factor, antibodies to cyclic citrullinated peptides, and cryoglobulins were normal. Serum complements levels, uric acid, immunofixation and immunoelectrophoresis were in normal range. Tests for hepatitis B and C were in normal range. Other laboratory tests to evaluate thrombophilia (activity of protein C and S, antithrombin, factor V Leiden, factor II prothrombin, methylenetetrahydrofolate reductase C677T, homocysteine) were negative.

Anticoagulation therapy with subcutaneous low-molecule weight heparin (dalteparin) was initiated, and the patient reported gradual fading of the livedoid skin lesions within several weeks of therapy. Diagnostic studies – including echocardiography, color Doppler ultrasonography of the lower limb veins, and Ankle-Brachial Index measurement – were all within reference values. Plethysmographic waveforms on the upper and lower extremities showed no deviation, and transcutaneous oximetry was normal.

Due to the higher prevalence of thrombophilic conditions in patients with livedo vasculopathy, therapy with a direct oral anticoagulant (DOAC) was recommended. Based on current studies, rivaroxaban 10 mg twice daily was proposed, with a plan to consider treatment de-escalation depending on clinical progress.

However, the patient declined recommended anticoagulant therapy due to plans for pregnancy and chose to discontinue anticoagulation, accepting the associated risks. Skin lesions continue to recur intermittently, although her most recent laboratory results showed normalized D-dimer levels.

DISCUSSION

Livedoid vasculopathy is a rare, chronic thrombo-occlusive cutaneous vasculopathy characterized by livedoid skin changes, atrophic white plaques, and ulceration, predominantly affecting the lower extremities. Its pathogenesis involves thrombotic occlusion mainly of dermal blood vessels, leading to tissue ischemia and subsequent skin ulceration (15). In our previously healthy patient, livedoid vasculopathy was preceded by pregnancy and COVID-19 infection during pregnancy a year and a half ago.

Pregnancy itself is a prothrombic state, characterized by increased levels of clotting factors and decreased fibrinolytic activity. This hypercoagulable state is further exacerbated by COVID-19 infection, which has been shown to induce endothelial dysfunction and a hypercoagulable state through mechanisms such as direct viral effects on endothelial cells and activation of the complement system (16,17,18). These factors may contribute to the development of livedoid vasculopathy in susceptible individuals.

In our case, the patient's development of livedoid vasculopathy following a moderate COVID-19 infection during pregnancy suggests that COVID-19 may act as a triggering factor for livedoid vasculopathy in susceptible patients. The negative thrombophilia screening and immunology laboratory findings, combined with the temporal association with COVID-19 infection, can support this hypothesis. Although the skin changes that prompted our patient to seek medical help appeared a year and a half after giving birth, it remains unclear whether earlier, less noticeable skin changes had occurred that the patient may have overlooked and deemed unimportant.

Management of livedoid vasculopathy typically involves anticoagulation therapy to address the underlying hypercoagulable state (10,11,12,13). In our patient, low-molecular weight heparin was initiated, which is

considered also safe during pregnancy. Wound care measures, including topical antiseptics and dressings, were employed to promote healing of the skin ulcerations. In our patient, lifelong anticoagulant therapy (direct oral anticoagulants – DOACs) was recommended based on the chronic, relapsing nature of the disease, the frequent recurrence of symptoms upon discontinuation of therapy, and to help prevent further microvascular thrombosis, ulceration, and pain (10,11,12,13).

CONCLUSION

Our case report emphasizes the importance of considering livedoid vasculopathy in the differential diagnosis of livedoid skin lesions and ulceration of the distal lower extremities. On average, the diagnosis of livedoid vasculopathy is made between 5 and 8 years after symptom onset. In our patient, however, it was established within two months of initial medical consultation. This highlights the importance of performing a skin biopsy followed by histopathological diagnosis, which is essential for confirming the diagnosis and initiating appropriate treatment. Early recognition and appropriate management are essential to prevent complications and improve outcomes. Further research is needed to better understand the pathophysiology and to establish optimal management strategies for livedoid vasculopathy in this patient population.

Acknowledgements: We would like to express sincere gratitude to our colleagues, Assistant Professor Mirna Bradamante, MD, PhD (Department of Dermatology and Venerology, University Hospital Centre Zagreb, Zagreb, Croatia), and Assistant Professor Danko Müller, MD, PhD (Department of Pathology, Dubrava University Hospital, Zagreb, Croatia), for their valuable assistance with histopathology, which significantly contributed to the quality and completeness of this case report.

Conflict of interest and funding: The authors declare no conflict of interest and no funding.

References:

1. Burg MR, Mitschang C, Goerge T, Schneider SW. Livedoid vasculopathy – a diagnostic and therapeutic challenge. Front Med. 2022;9:1012178.
2. Seguí M, Llamas-Velasco M. A comprehensive review on pathogenesis, associations, clinical findings, and treatment of livedoid vasculopathy. Front Med. 2022;9:993515.
3. Weishaupt C, Strölin A, Kahle B, Kreuter A, Schneider SW, Gerss J *et al.* Characteristics, risk factors and treatment reality in livedoid vasculopathy – a multicentre analysis. J Eur Acad Dermatol Venereol. 2019;33(9):1784-91.
4. Bilgic A, Ozcobanoglu S, Bozca BC, Alpsoy E. Livedoid vaculopathy: a multidisciplinary clinical approach to diagnosis and management. Int J Wom Dermatol. 2021;7(5A):588-99.
5. Gao Y, Jin H. Livedoid vasculopathy and its association with genetic variants: a systematic review. Int Wound J. 2021;18(5): 616-25.
6. Eswaran H, Googe P, Vedak P, Marston WA, Moll S. Livedoid vasculopathy: a review with focus on terminology and pathogenesis. Vasc Med. 2022;27(6): 593-603.
7. Qi F, Gao Y, Jin H. Identification of challenging diagnostic factors in livedoid vasculopathy: a retrospective study. Clin Cosm Invest Dermatol. 2024;17:1747-56.
8. Nuttawong S, Chularojanamontri L, Trakanwittayarak S, Pinkaew S, Chanchaemsri N, Rujitharanawong C. Direct immunofluorescence findings in livedoid vasculopathy: a 10-year study and literature review. Clin Exp Dermatol. 2021;46(3):525-31.
9. Vasudevan B, Neema S, Verma R. Livedoid vasculopathy: a review of pathogenesis and principles of management. Ind J Dermatol Venereol Leprol. 2016;82(5):478-88.
10. Weishaupt C, Strölin A, Kahle B, Kreuter A, Schneider SW, Gerss J *et al.* Anticoagulation with rivaroxaban for livedoid vasculopathy (RILIVA): a multicentre, single-arm, open-label, phase 2a, proof-of-concept trial. Lancet Haematol. 2016;3(2):e72-9.
11. Micieli R, Alavi A. Treatment for Livedoid Vasculopathy: a systematic review. JAMA Dermatol. 2018;154(2):193-202.
12. Evans JM, Jensen JD, Sami N. Successful treatment of livedoid vasculopathy with rivaroxaban. J Am Acad Dermatol Case Reports. 2015;1(6):340-1.
13. Gao Y, Jin H. Rivaroxaban for treatment of livedoid vasculopathy: a systematic review. Dermatol Therapy. 2021;34(5):e15051.
14. Thao C, Qu M, Cheng X, Li S, Feng S. Associations between coagulation factors and livedoid vasculopathy and the efficacy and safety of rivaroxaban in patients with livedoid vasculopathy: a retrospective study. Clin Exp Dermatol. 2024;49(8):817-24.
15. Leeolou MC, Rieger KE, Yeh JE. Livedoid vasculopathy. Dermatology Online J. 2023;29(5).
16. Carballido Vázquez AM, Vega López TL; Manchado López P, Martinez Garcia G, Mateos Mayo A. Secondary livedoid vasculopathy following SARS-CoV-2 infection. J Eur Acad Dermatol Venereol. 2024;38(5):e368-70.
17. Valentim FO, Tsutsui GM, Miot HA. Recrudescence of livedoid vasculopathy induced by COVID-19. Int J Dermatol. 2021;60(5):e185-7.
18. Kawabe R, Tonomura K, Kotobuki Y, Ueda-Hayakawa I, Murota H, Fujimoto M. Exacerbation of livedoid vasculopathy after coronavirus disease 2019. Eur J Dermatol. 2022;32(1):129-31.