

Antiphospholipid vasculopathy or Polyarteritis nodosa – case of „both“ or „either“

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Abstract

Background: Polyarteritis nodosa is a systemic necrotizing vasculitis affecting medium-sized arteries and, less commonly, small-caliber vessels. In the differential diagnostic context, one of the conditions that may present with a similar clinical picture is vasculopathy associated with antiphospholipid syndrome. Case presentation: We present the clinical case of a 62-year-old female patient whose symptoms began approximately three months prior to her first hospitalization in the Rheumatology Clinic. The initial manifestations included gradual appearance of a rash on the lower extremities in the form of livedo reticularis/purpura retiforme, progressing to ulcerations, accompanied by pain in the lower limbs. Following outpatient assessment, the patient was admitted to the Rheumatology Clinic. After completion of a stepwise diagnostic workup, a diagnosis of polyarteritis nodosa was established based on the ACR criteria. Immunological testing demonstrated a tenfold elevation of anticardiolipin antibodies. According to the 2023 EULAR classification criteria, the patient

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fulfilled the required criteria for antiphospholipid syndrome/antiphospholipid vasculopathy. Pulse therapy treatment was initiated consisting of methylprednisolone and cyclophosphamide, in combination with vasodilator and anticoagulant therapy. After four months, a favorable therapeutic response was observed. However, due to secondary infection of the ulcerations, surgical intervention became necessary, along with reduction of the immunosuppressive therapy. During the subsequent follow-up period corticosteroid therapy was successfully discontinued completely, and sustained remission without new relapses was achieved. Conclusion: An open question remains regarding the extent of overlap between the two nosological entities and whether the positive antiphospholipid antibodies may represent merely an immunological phenomenon occurring in the setting of active vasculitis.

Keywords: polyarteritis nodosa, antiphospholipid syndrome, vasculitis, livedo reticularis

1. Introduction

Polyarteritis nodosa is defined as a necrotizing systemic vasculitis predominantly affecting medium- and small-sized arteries [1]. It is typically not associated with antineutrophil cytoplasmic antibodies (ANCA). The disease is characterized by a complex pathogenesis and multisystem involvement. A localized cutaneous form of polyarteritis nodosa may also be observed as a subtype of the disease. The etiology of the condition remains insufficiently elucidated. Associations have been established between polyarteritis nodosa and hepatitis B and C viral infections, as well as certain oncohematological disorders [2,3]. Pathoanatomically, the disease is usually characterized by localized necrotizing arteritis accompanied by inflammatory infiltration within the vessel wall. The diagnosis is established on the basis of defined classification criteria [4]. Treatment includes immunosuppressive therapy and management of the underlying disease, when present. In the differential diagnostic approach, a number of conditions should be considered, including HIV infection, ANCA-associated vasculitides, and cryoglobulinemia. One of the conditions included in the differential diagnosis of polyarteritis nodosa is vasculopathy associated with antiphospholipid syndrome. The presented manuscript was prepared in accordance with the CARE (Case Report) guidelines.

2. Case Presentation

We present the clinical case of a 62-year-old female patient. The patient was referred to the Rheumatology Clinic following hospitalization in a Dermatology Department. The onset of symptoms occurred approximately three months earlier, in June 2024, initially presenting with a rash on the lower extremities consistent with livedo reticularis/purpura retiforme. The patient reported pain in the lower limbs, for which she had undergone multiple outpatient consultations with a general practitioner and a vascular surgeon. During hospitalization in the dermatology clinic, multiple ulcerations and skin defects of the lower extremities were identified. A punch biopsy was performed, demonstrating necrobiotic changes and occluded vascular lumina. During the same admission, the patient was evaluated by a neurologist because of the lower-limb pain syndrome; multiple mononeuritis and polyneuritis were excluded. A vascular surgery consultation was also conducted in view of CT angiographic findings demonstrating an abdominal aortic aneurysm; however, the vascular surgeon did not identify definitive evidence of vasculitic etiology for the abnormality. Subsequently, the patient was evaluated by a rheumatologist and admitted to the Rheumatology Clinic.

Upon admission to the Rheumatology Department, the patient presented with pronounced cutaneous lesions on the lower extremities in the form of purpura retiforme, accompanied by multiple ulcerations, some extending through the dermis and hypodermis with involvement of the underlying fascia and tendons. Past medical history revealed concomitant hypertensive heart disease and insulin resistance. Physical examination demonstrated no evidence of involvement of other organs or systems. Borderline elevated arterial blood pressure values were recorded.

Initial laboratory investigations revealed mild anemia (hemoglobin 118 g/L), leukocytosis with neutrophilia (WBC $19.9 \times 10^9/L$, segmented neutrophils 84%), and preserved platelet count ($443 \times 10^9/L$). Biochemical analysis showed no abnormalities in transaminases or creatine kinase, normal electrolyte balance, no complement abnormalities, immunoglobulin fractions within normal limits, and non-elevated inflammatory markers (ESR and CRP). Coagulation profile and D-dimer values were within the reference range. Chest radiography showed no significant abnormalities; subsequent chest CT also demonstrated no relevant pathological findings. Abdominal ultrasonography revealed hepatic steatosis. Microbiological examination of urine and throat swab cultures showed no pathogenic bacterial flora.

Of note was the elevation of residual nitrogenous compounds: serum creatinine 123 µmol/L, uric acid 463 µmol/L, and urea 15.9 mmol/L. Review of previous medical records demonstrated that elevated creatinine levels had been present chronically. Twenty-four-hour proteinuria and Hamburger sediment analysis were within reference limits.

Specific immunological testing was subsequently performed, demonstrating ANA titer 1:160 (negative), rheumatoid factor 31.4 RU/mL, and negative results for cryoglobulins, anti-dsDNA, anti-Sm antibodies, anti-Jo1, anti-RNP antibodies, anti-Scl-70 antibodies, as well as negative pANCA and cANCA testing. HIV, HBsAg, and anti-HCV testing were all negative.

A remarkable finding was the significant, approximately tenfold elevation of IgG and IgM anticardiolipin antibodies, while anti-β2-glycoprotein antibodies and lupus anticoagulant were negative.

Based on the clinical presentation patient was assessed according to the 1990 ACR criteria for polyarteritis nodosa.

Table 1. 1990 ACR classification criteria for polyarteritis nodosa

1990 ACR classification criteria for polyarteritis nodosa (PAN)
1. Unexplained weight loss >4 kg
2. Livedo reticularis
3. Testicular pain or tenderness
4. Myalgias, muscle weakness, or leg tenderness
5. Neuropathy
6. Diastolic hypertension
7. Elevated renal function tests
8. Hepatitis B infection
9. Arteriographic abnormality
10. Arterial biopsy

Based on the fulfillment of the second, fourth, and ninth criteria, a probable diagnosis of polyarteritis nodosa was considered. However, given the markedly elevated anticardiolipin antibody levels, antiphospholipid vasculopathy was prioritized in the differential diagnosis. Despite the

absence of prior thromboembolic events or obstetric pathology in the patient's history, antiphospholipid syndrome (APS) could not be excluded.

According to the 2023 EULAR classification criteria for APS, the patient fulfilled the entry criteria, namely livedoid vasculopathy and positive antiphospholipid serology. Furthermore, she accumulated the required number of points across the clinical and laboratory domains to establish the diagnosis of antiphospholipid syndrome.

Within the differential diagnostic framework, a number of conditions were excluded. Based on the absence of a pulmonary–renal syndrome and the negative ANCA serology, ANCA-associated vasculitides were considered unlikely and subsequently ruled out. The patient did not exhibit clinical features fulfilling the diagnostic criteria for Takayasu arteritis. In view of the cutaneous involvement and its clinical presentation, hypersensitivity vasculitis was also excluded. Furthermore, there was no evidence to support a diagnosis of secondary vasculitis associated with systemic lupus erythematosus (SLE) or any other systemic autoimmune disease.



Figure 1. Ulcers affecting both legs of the patient with secondary inflammation due to local infection.

A therapeutic decision was made to initiate monthly pulse therapy consisting of intravenous methylprednisolone 1000 mg daily for three consecutive days and cyclophosphamide 1000 mg intravenously. Adjunctive treatment included low-molecular-weight heparin (enoxaparine 0.6 mL subcutaneously), amlodipine 5 mg daily, and pentoxifylline 400 mg orally. Between pulse therapy cycles, the patient received oral methylprednisolone at a dose of 24 mg daily.

In January 2025, following four pulse therapy cycles, the patient presented with complete resolution of the livedoid rash on the lower extremities, reduction in serum creatinine levels, and remission of lower-limb myalgias. Nevertheless, anticardiolipin antibody levels remained markedly elevated. Secondary infection of the ulcerative lesions developed, characterized by purulent and necrotic inflammation. Some lesions extended deeply to involve underlying musculature and tendons. The patient was referred for septic surgery management and underwent surgical treatment, including necrectomy and partial excision of the right Achilles tendon. Hospital treatment in a hyperbaric chamber was conducted in combination with twice-daily prostavasin infusions over a 60-day period. During surgical management, wound sanitation and initial epithelialization were achieved.

During subsequent follow-up in the Rheumatology Clinic, discontinuation of pulse therapy was decided because of reduced clinical activity. Gradual tapering of corticosteroid therapy was initiated, leading to complete discontinuation by December 2025. Throughout follow-up, no new lesions or disease exacerbations were observed. The majority of lower-extremity lesions healed by secondary intention; by March 2026, only one lesion on the right leg had not yet fully closed. Serum creatinine levels remained stable at the upper limit of normal (100–115 $\mu\text{mol/L}$).

Follow-up CT angiography of the abdominal aorta and its branches, performed in March 2026, demonstrated no progression compared with previous imaging. Anticardiolipin antibody levels remained persistently and significantly elevated.

The patient continues maintenance therapy with an oral anticoagulant, calcium-channel blocker, and vasodilator, and remains under rheumatological follow-up every three months.

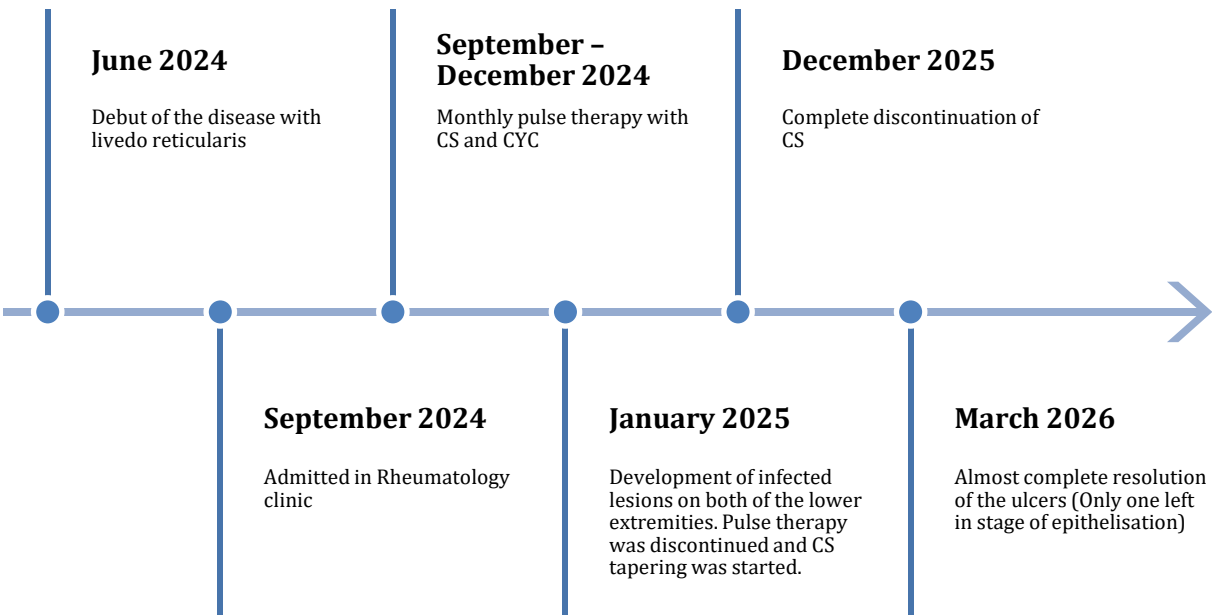


Figure 2. Timeline of patient history.

3. Discussion

In the presented case, our patient fulfilled the classification criteria for the diagnosis of polyarteritis nodosa. From a differential diagnostic perspective, several conditions were considered, including antiphospholipid vasculopathy. Upon review of the patient’s history, particular attention was drawn to the consultation with a vascular surgeon, whose opinion did not support the diagnosis. Owing to the lack of previous imaging studies, it was not possible to determine with certainty whether the observed abdominal aortic aneurysm represented a new finding associated with polyarteritis nodosa or a pre-existing condition. The patient declined a repeat biopsy, which further complicated the diagnostic process. Moreover, the histopathological findings described in the previously performed skin biopsy were not supportive of polyarteritis nodosa.

In the presented case, our medical team identified several limitations in the diagnostic and therapeutic approach. The lack of sufficiently comprehensive prior medical documentation significantly constrained our diagnostic assessment. Consequently, it was not possible to determine the duration of the renal dysfunction, as evidenced by the elevated serum creatinine levels. The same limitation applied to the observed abdominal aortic aneurysm, for which the duration and progression could not be

established. Furthermore, the patient's refusal to undergo an arterial biopsy restricted the diagnostic workup and limited the ability to achieve a definitive diagnosis.

A review of the medical literature on the subject reveals a number of reported cases of patients presenting with concomitant polyarteritis nodosa and antiphospholipid syndrome [5,6,7]. In the majority of these cases, however, antiphospholipid syndrome manifested predominantly with thromboembolic events, which were not observed in our patient. D-dimer levels were repeatedly assessed as a marker for thrombotic events and remained persistently low throughout the observation period. It usually stays unclear as to what the exact association is between the APS and the PAN [8]. Another aspect that is unclear is the chronological association between the two entities [9]. Which one is the primary and which the secondary. As of today no pathophysiological understanding has been established.

In a study on the subject [10], involving 144 patients with primary systemic vasculitis and concomitant antiphospholipid antibodies, the prevalence of anticardiolipin antibodies or lupus anticoagulant was reported in 17% of participants. Another big cohort study aimed at assessing the prevalence of antiphospholipid antibodies and their clinical significance in elderly patients compared to younger patients failed to reach any significant conclusions [11]. The interpretation of the presence of the antibodies is difficult. Particularly noteworthy are the results of a cohort study conducted in Egypt, which included nearly 60 patients with primary and secondary antiphospholipid syndrome [12]. The findings demonstrated that approximately 98% of patients with secondary antiphospholipid syndrome were positive for antinuclear antibodies (ANA), while 94% tested positive for anti-double-stranded DNA (anti-dsDNA) antibodies. In contrast, both of these autoantibodies were negative in our patient, a finding that merits attention.

The therapeutic approach and the expected complications differ between the two disease entities. We consider the significant clinical improvement observed following the initiation of immunosuppressive therapy in the presented patient to be supportive of the adopted diagnosis of polyarteritis nodosa.

4. Conclusions

Polyarteritis nodosa is a rare entity. It should be present in the differential diagnosis list whenever there is a patient suspicious for systemic vasculitis. Antiphospholipid vasculopathy has been reported in a number of cases to be co-existing along with PAN, so the question is open as to whether it is only an immunological phenomenon or there are two distinct diseases at the same time. Thorough laboratory, imaging and immunological evaluation should be undertaken before the patients are treated accordingly.

Declarations

Author Contributions

Conceptualization: I.Y.; Methodology: I.Y., M.G; Formal analysis: S.P; Investigation: V.H, I.S; Writing—original draft: K.K, M.G., S.DZ.; Writing—review & editing: all authors.

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Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

The data presented in this study are available on reasonable request from the corresponding author.

Conflicts of Interest

The authors declare no conflict of interest.

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