Gac Méd Caracas 2025;133(4):1211-1217
DOI: 10.47307/GMC.2025.133.4.20

Severe peripheral arterial compromise in polyarteritis nodosa: A case of acute limb ischemia

Compromiso arterial periférico severo en la poliarteritis nudosa: un caso de isquemia aguda de la extremidad

Mayang Rizki Anggraeni[1,2,a], Awalia[1,2,3,b]

SUMMARY

Polyarteritis nodosa (PAN) is a rare form of vasculitis that primarily affects medium-sized arteries, and it can occasionally present as acute limb ischemia (ALI). We report a case of a 31-year-old male with right foot ALI. Imaging revealed arterial occlusion, and the patient met four of the 1990 American College of Rheumatology (ACR) criteria for PAN. Initial therapy with azathioprine and low-dose glucocorticoids was ineffective, but clinical improvement occurred after switching to mycophenolate sodium and increasing steroid dosage. This case emphasizes the importance of considering PAN in ALI and highlights the role of early diagnosis and immunosuppressive treatment to prevent limb loss.

Keywords*: Polyarteritis nodosa, acute limb ischemia, peripheral vascular disease, medium vessel vasculitis*

RESUMEN

La poliarteritis nudosa (PAN) es una vasculitis poco frecuente que afecta a las arterias de mediano calibre y que ocasionalmente puede presentarse como isquemia aguda de extremidades (IAE). Presentamos el caso de un hombre de 31 años con IAE en el pie derecho. Las imágenes revelaron una oclusión arterial y el paciente cumplía con cuatro de los criterios del Colegio Americano de Reumatología (ACR) de 1990 para PAN. El tratamiento inicial con azatioprina y glucocorticoides en dosis baja fue ineficaz, pero se observó mejoría clínica tras el cambio a micofenolato sódico y el aumento de la dosis de esteroides. Este caso enfatiza la importancia de considerar la PAN en casos de IAE y destaca el papel del diagnóstico temprano y del tratamiento inmunosupresor para prevenir la pérdida de la extremidad.

Palabras clave*: Poliarteritis nudosa, isquemia aguda de extremidades, enfermedad vascular periférica, vasculitis de vasos medianos.*

DOI: https://doi.org/10.47307/GMC.2025.133.4.20

ORCID: https://orcid.org/0009-0002-4562-7686[a]
ORCID: https://orcid.org/0000-0002-4232-384X[b]

[1]Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.
[2]Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.
[3]Division of Rheumatology, Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

Recibido: 26 de agosto 2025
Aceptado: 16 de septiembre 2025

Corresponding author: Awalia, Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. E-mail: awalia@fk.unair.ac.id

INTRODUCTION

Acute limb ischemia (ALI) is a sudden reduction in arterial perfusion occurring within less than two weeks, posing a threat to limb viability (1). It presents with new or worsening ischemic symptoms and requires prompt recognition and intervention to prevent limb loss (2,3). The aetiologies of ALI are diverse and include embolism, thrombosis, arterial dissection, peripheral arterial aneurysm, and trauma (1,4). Several rare causes have also been identified, among which vasculitis is one (1). Polyarteritis nodosa (PAN) and Kawasaki disease are the two main subtypes of medium vessel vasculitis (5). Cases of ALI have been reported as clinical manifestations in patients with PAN (6,7).

PAN is considered a rare disease (8), with an annual incidence ranging from 0.9 to 8.0 cases per one million population in European countries (9). To date, there are no specific biomarkers for PAN. Therefore, diagnosis relies on clinical features, angiographic findings, and biopsy specimens, while laboratory tests are helpful for the evaluation and monitoring of organ involvement and damage (10). This report presents a case of a young adult who initially manifested with clinical features of acute limb ischemia, which was later identified as the presenting feature of PAN.

CASE PRESENTATION

A 31-year-old Indonesian male presented with black discoloration, coldness, and pain of the right hallux (Figure 1), accompanied by paraesthesia in the remaining toes of both feet. One week prior, he noted a painful subcutaneous nodule at the same site, previously diagnosed as a clavus and surgically excised. He denied fever, myalgia, or arthralgia, but reported a 2-kg unintentional weight loss over the past two months. The patient had no personal or family history of autoimmune disease, did not smoke or consume alcohol, and worked as a heavy equipment mechanic without chemical exposure. There was no history of COVID-19 infection. CT angiography and Doppler ultrasonography demonstrated arterial occlusion in both lower extremities. The patient subsequently underwent debridement and necrotomy of the right hallux and was referred to our center for further evaluation to exclude an underlying autoimmune aetiology.

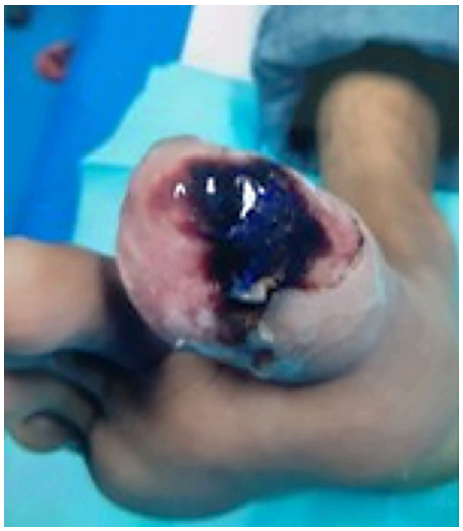

Figure 1. Ischemic necrosis of the right toe was documented before necrotomy and debridement.

On examination, the patient had diastolic hypertension in the right arm and a post-necrotomy wound on the right hallux with healthy granulation. Oxygen saturation in all right toes was <95 %, while the left foot was normal. The right dorsalis pedis pulse was absent, and the left was diminished. Laboratory results showed haemoglobin 16.3 g/dL, platelets 126 000/μL, normal renal and liver function, D-dimer 390 ng/mL, and HbA1c 5.2 %. Viral serologies for HBV, HCV, and HIV were negative. Lipid profile was unremarkable. Erythrocyte Sedimentation Rate (ESR) was elevated (35 mm/hour). Autoimmune work-up showed normal antinuclear antibody (ANA) titer, complement levels, negative C-reactive Protein (CRP), and negative antineutrophil cytoplasmic antibody (ANCA).

Pre-necrotomy Doppler of the right foot showed weak anterior and posterior tibial pulses with reduced lumen and oxygen saturation of 89 %. The left foot had a weak anterior but intact posterior tibial pulse, with toe saturation of 78 %. Computed tomography (CT) angiography

(Figure 2) revealed complete occlusion of the right lower limb at the ankle level. Similar distal non-visualization on the left foot was likely due to poor contrast flow. No vascular abnormalities were noted in the cervical, thoracic, or abdominal regions. Skin biopsy from the right hallux, performed three months post-necrotomy and one month after immunosuppressive therapy, showed no definitive signs of vasculitis. Arterial wall biopsy was not performed to avoid invasive intervention.

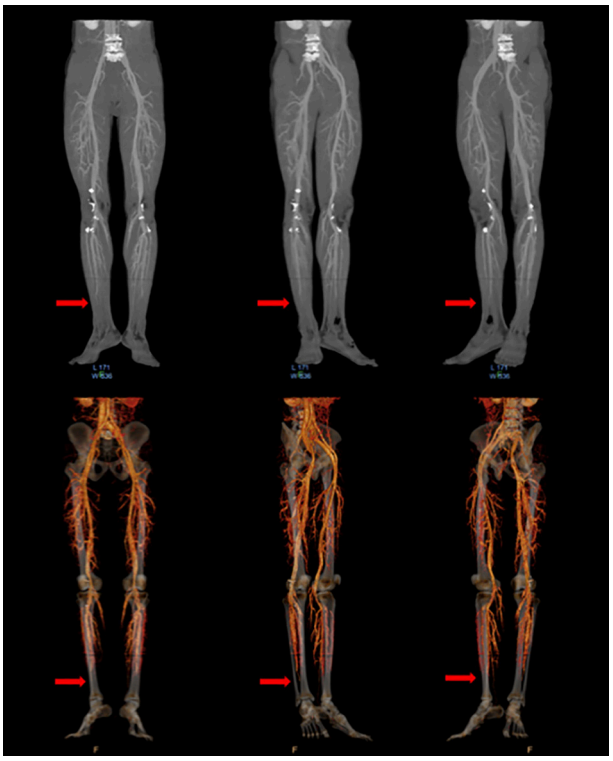

Figure 2. CT angiography of the lower limbs showing filling defects. The red arrow indicates the level of arterial occlusion.

Based on clinical, laboratory, and imaging findings, the patient was diagnosed with PAN presenting as acute limb ischemia. Initial treatment with azathioprine (50 mg twice daily) and low-dose methylprednisolone (4 mg daily) led to partial improvement. Due to persistent absence of distal pulses, therapy was switched to mycophenolate sodium (360 mg twice daily), and methylprednisolone was increased to 24 mg daily. At 6-month follow-up, the patient showed complete resolution of symptoms with restoration of palpable pulses.

DISCUSSION

This case highlights a rare clinical manifestation of PAN in the form of ALI, which required prompt treatment to prevent further damage to the lower extremity. Peripheral vascular disease is one of the recognized manifestations of PAN. Vascular involvement of the lower limbs in PAN may present with a broad spectrum of symptoms, including claudication (6), Raynaud's phenomenon (11), peripheral gangrene (12-14), and ALI (6,7,13,15). Vasculitis contributes to the development of ALI through inflammatory processes affecting the blood vessels (1). Vessel wall thickening and intimal proliferation resulting from inflammation can significantly narrow the lumen, predisposing the vessel to thrombosis (15). Similar to other types of vasculitis, impaired endothelial function may indicate direct activation and injury of endothelial cells caused by primary inflammatory processes or by proinflammatory cytokines or antibodies. This activation can contribute to the establishment of an inflammatory milieu through the production of cytokines and adhesion molecules (10,16,17). $CD4^+$ and $CD8^+$ T lymphocytes play a key role in vascular inflammation. $CD4^+$ T cells secrete cytokines that mediate the activation and recruitment of macrophages. Cytotoxic T cells and macrophages constitute the major cellular components of vessel wall inflammation in muscle and nerve biopsies from PAN patients (18). Elevated serum levels of interleukin (IL)-8, IL-2, tumor necrosis factor-α (TNF-α), and IL-1β have been reported in PAN (18–20).

Clinically, patients with PAN often present with nonspecific constitutional symptoms such as malaise, weight loss, fever, arthralgia, and myalgia, which occur in more than 90 % of cases (21). The peripheral nervous system and skin are among the most frequently involved organ systems. Neurologically, mononeuritis multiplex is the most prevalent presentation, followed by symmetrical polyneuropathy (22,23).

Dermatologic findings may include livedo reticularis, subcutaneous nodules, necrosis, and ulcers (24). In this case, before the onset of significant ischemic symptoms, the patient initially presented with a painful nodule on the right great toe, which was initially diagnosed as a clavus. However, we suspect that this lesion may have represented a cutaneous manifestation of PAN—specifically, a painful subcutaneous nodule, as commonly reported in patients with this form of vasculitis. An overview of PAN clinical features is provided in Table 1.

Table 1. Clinical features of systemic PAN as reported in several studies.

	Reeves and Bresnihan (25)	Bae et al. (26)	Rohmer et al. (23)	Karadag et al. (24)
Patients (n)	9	27	196	282
Mean age (years)	53	47.4	53.62	41.5
Male/female ratio	1.25	1.7	1.6	1.25
Constitutional signs				78.8
Fever		52	54.3	45.2
Weight loss		44	49.2	50.6
Musculoskeletal manifestation				71
Myalgia	67	70	34.5	51.7
Joint manifestation	33	30	46.7	53.2
Neurologic manifestation	100	63	58.9	61.2
Mononeuritis multiplex	89		40.6	
Polyneuropathy	100		6.6	
Central nervous system manifestation	22		9.1	16.8
Cutaneous manifestation	56		58.4	62.5
Livedo reticularis	33	11	17.3	25
Subcutaneous nodules		11		19.1
Purpura	56		13.2	
Peripheral ischemia, Raynaud's phenomenon		11		10.5
Gangrene, necrosis	11		40.6	16.6
Renal impairment	67	30	19.8	48.2
Hypertension		30	15.7	36.3
Gastrointestinal manifestation	67	33	27.4	52.2
Cardiac manifestation	67		9.1	8.5
Orchitis, testicular tenderness		24	15.7	12.6

Several studies have reported peripheral ischemic manifestations in patients with PAN. It has been described that cases of PAN presenting with claudication are a clinical manifestation (6,27). Rohmer et al. (23) documented a relatively high incidence of necrotic skin lesions at 40.6 %, while Karadag et al. (24) reported a lower frequency of 16.6 %. Other studies have noted gangrene as a less common manifestation, occurring in approximately 11 % of cases (25). Shukla et al. (6) reported a case of PAN initially presenting with claudication, which progressed to acute-on-chronic limb ischemia. The patient achieved remission following initial treatment with intravenous methylprednisolone at a dose of 1 gram per day for three days, followed by tapering, in combination with azathioprine.

Currently, there are no specific biomarkers available for the diagnosis of PAN. Therefore, diagnosis relies on a combination of clinical features, angiographic findings, and histopathological evaluation (10,20). Laboratory investigations help evaluate the degree of organ

involvement. Acute phase reactants, including erythrocyte sedimentation rate and C-reactive protein, are frequently elevated (8,20). Other key tests include serum creatinine, liver function tests, muscle enzyme levels, hepatitis B and C serologies, and urinalysis. Additional laboratory evaluations—such as ANCA (antineutrophil cytoplasmic antibody) and ANA (antinuclear antibody), complement levels (C3 and C4), and cryoglobulins—help differentiate PAN from other forms of vasculitides (8).

CT or Magnetic Resonance (MR) angiography is commonly used to detect both aneurysmal and stenotic changes in medium-sized vessels (27). Biopsies should be obtained from symptomatic sites, and when multiple organ systems are involved, less invasive sites such as the skin, muscle, or sural nerve are preferred (28). In our case, histopathological examination of the skin biopsy obtained post-necrotomy did not demonstrate definitive features of vasculitis. This may be attributed to the timing of the biopsy, which was performed approximately three months after symptom onset and one month after the initiation of immunosuppressive therapy.

Based on the 1990 ACR classification criteria, as outlined in Table 2, a diagnosis of PAN was established (29). In this case, our patient exhibited myalgia and leg pain, polyneuropathy, diastolic blood pressure >90 mmHg, and abnormalities on CT angiography—fulfilling 4 out of the 10 classification criteria of the 1990 ACR for PAN, thus classifying the vasculitis as PAN with sensitivity and specificity >80 %

Table 2. 1990 ACR criteria for classification of PAN and the provisional seven-item criteria.

1990 ACR criteria for classification of PAN (29)	The provisional seven-item criteria (30)
1. Weight loss ≥4 kg	1. Mononeuropathy multiplex
2. Livedo reticularis	2. Gastrointestinal involvement
3. Testicular pain or tenderness	3. Absence of MPO-ANCA
4. Myalgias, weakness, or leg tenderness	4. Urine protein <2+
5. Mononeuropathy or polyneuropathy	5. Fever for 1 week or weight loss of ≥4 kg
6. Diastolic blood pressure ≥90 mmHg	6. Angiographic abnormality
7. Elevated BUN or creatinine	7. Histologic evidence on biopsy
8. Hepatitis B virus	
9. Arteriographic abnormality	
10. Biopsy of a small or medium-sized artery containing PMN	

In Japan, the diagnostic criteria for PAN established by the Ministry of Health, Labour and Welfare (MHLW) were revised in 2006. Yamamoto and Oiwa (30) conducted a study to evaluate the sensitivity and specificity of both the ACR and MHLW criteria. Based on this cohort study of patients with suspected PAN in a real-world clinical setting, they proposed a new diagnostic framework known as the provisional seven-item criteria, which demonstrated high sensitivity and specificity—92.3 % and 91.7 %, respectively—using a cutoff score of ≥4 points. While promising, this new set of criteria requires further validation in larger and more diverse patient populations. The provisional seven-item criteria are summarized in Table 2.

Management strategies for active PAN depend on disease severity (31). Initially, our patient exhibited features consistent with severe PAN, which led to a necrotomy being performed at the referring hospital. However, upon presentation to our center, the patient no longer showed signs or symptoms indicative of organ-threatening features. For patients with newly diagnosed active, non-severe PAN, current guidelines conditionally recommend treatment with a combination of a non-glucocorticoid immunosuppressive agent and glucocorticoids over glucocorticoid monotherapy. The recommended non-glucocorticoid agents include methotrexate or azathioprine (31). In this case, the patient initially received treatment

with azathioprine in combination with low-dose glucocorticoids. Due to suboptimal clinical response, azathioprine was subsequently replaced with mycophenolate sodium. Following this adjustment, the patient's symptoms and clinical condition gradually improved, allowing for tapering of immunosuppressive therapy.

Ethics And Consent

Written informed consent was obtained from the patient during admission to unveil the case details, including the examination results and other accompanying images, for publication and educational purposes. There was no institutional approval required for publication.

Disclosure Statement

The authors stated that this work has no conflicts of interest.

Acknowledgement

We want to thank Dr. Soetomo General Academic Hospital for providing the essential data, access to the patient, and facilities required for this study. We are especially thankful to the patient for granting permission to publish this case. We are deeply grateful to all those who have supported us throughout the writing.

REFERENCES

1. Björck M, Earnshaw JJ, Acosta S, Gonçalves FB, Cochennec F, Debus SE, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2020 Clinical Practice Guidelines on the Management of Acute Limb Ischaemia. Eur J Vasc Endovasc Surg. 2020;59(2):173-218.
2. Arnold J, Koyfman A, Long B. High risk and low prevalence diseases: Acute limb ischemia. Am J Emerg Med. 2023;74:152-158.
3. Kulezic A, Acosta S. Epidemiology and prognostic factors in acute lower limb ischaemia: A population based study. Eur J Vasc Endovasc Surg. 2022;63(2):296-303.
4. Costa D, Ielapi N, Perri P, Minici R, Faga T, Michael A, et al. Molecular insight into acute limb ischemia. Biomolecules. 2024;14(7).
5. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum. 2013;65(1):1-11.
6. Shukla A, Aggarwal A. Polyarteritis nodosa presenting as peripheral vascular disease and acute limb ischemia. J Postgrad Med. 2017;63(1):47-49.
7. Héron E, Fiessinger JN, Guillevin L. Polyarteritis nodosa presenting as acute leg ischemia. J Rheumatol. 2003;30(6):1344-1346.
8. Hernández-Rodríguez J, Alba MA, Prieto-González S, Cid MC. Diagnosis and classification of polyarteritis nodosa. J Autoimmun. 2014;48-49:84-89.
9. Watts RA, Hatemi G, Burns JC, Mohammad AJ. Global epidemiology of vasculitis. Nat Rev Rheumatol. 2022;18(1):22-34.
10. Ralli M, Campo F, Diletta A, Minni A, Artico M, Greco A, et al. Pathophysiology and therapy of systemic vasculitides. EXCLI J. 2020;19:817-854.
11. Andreu-Sanchez JL, Martin-Santos JM, Isasi-Zaragoza C, Trujillo-Castellanos A, Cuende-Quintana E, Mulero J. Raynaud's phenomenon as initial manifestation of cutaneous polyarteritis nodosa. Ann Rheum Dis. 1991;50(1):48-50.
12. Ninomiya T, Sugimoto T, Tanaka Y, Aoyama M, Sakaguchi M, Uzu T, et al. Symmetric peripheral gangrene as an emerging manifestation of polyarteritis nodosa. J Rheumatol. 2007;34(2):440-441.
13. Fred HL, Serna JH, McDonald GA, Ahmed SS. Polyarteritis Nodosa Inducing Symmetric Peripheral Gangrene. Circulation. 2003;107(22):2870-2870.
14. Zahoor S, Siddique S, Mahboob HM. An unusual presentation of polyarteritis nodosa: A case report. Reumatol Clin. 2022;18(2):124-126.
15. Aw DKL, Vijaykumar K, Cheng SC, Tang TY, Tay JS, Choke ETC. A case of severe polyarteritis nodosa with critical limb-threatening ischemia—promising treatment with sirolimus drug-coated angioplasty. J Vasc Surg Cases, Innovat Techn. 2023;9(4):101266.
16. De Virgilio A, Greco A, Magliulo G, Gallo A, Ruoppolo G, Conte M, et al. Polyarteritis nodosa: A contemporary overview. Autoimmun Rev. 2016;15(6):564-570.
17. Filer AD, Gardner-Medwin JM, Thambyrajah J, Raza K, Carruthers DM, Stevens RJ, et al. Diffuse endothelial dysfunction is common to ANCA-associated systemic vasculitis and polyarteritis nodosa. Ann Rheum Dis. 2003;62(2):162-167.
18. Hughes LB, Bridges SL. Polyarteritis nodosa and microscopic polyangiitis: Etiologic and diagnostic considerations. Curr Rheumatol Rep. 2002;4(1):75-82.

19. Freire A de L, Bertolo MB, de Pinho AJ, Samara AM, Fernandes SRM. Increased serum levels of interleukin-8 in polyarteritis nodosa and Behçet's disease. Clin Rheumatol. 2004;23(3):203-205.
20. Puéchal X. Polyarteritis Nodosa: State of the art. Joint Bone Spine. 2022;89(4):105320.
21. Rhee RL, Merkel PA. Classification and epidemiology of systemic vasculitis. In: Firestein GS, editor. Firestein & Kelley's Textbook of Rheumatology, Twelfth Edition. 12th edition. Philadelphia: Elsevier; 2025.p.1579-1587.
22. Hočevar A, Tomšič M, Perdan Pirkmajer K. Clinical approach to diagnosis and therapy of polyarteritis nodosa. Curr Rheumatol Rep. 2021;23(3):14.
23. Rohmer J, Nguyen Y, Trefond L, Agard C, Allain JS, Berezne A, et al. Clinical features and long-term outcomes of patients with systemic polyarteritis nodosa diagnosed since 2005: Data from 196 patients. J Autoimmun. 2023;139:103093.
24. Karadag O, Bolek EC, Ayan G, Mohammad AJ, Grayson PC, Pagnoux C, et al. Clinical characteristics and outcomes of polyarteritis nodosa: An International Study. Arthr Rheumatol. 2024;76(7):1120-1129.
25. Reeves A, Bresnihan B. Clinical features, treatment and outcome of polyarteritis nodosa. Ir J Med Sci. 1987;156(3):90-92.
26. Bae YD, Choi HJ, Lee JC, Park JJ, Lee YJ, Lee EB, et al. Clinical features of polyarteritis nodosa in Korea. J Korean Med Sci. 2006;21(4):591.
27. Fonseka CL, Galappaththi SR, Abeyaratne D, Tissera N, Wijayaratne L. A Case of polyarteritis nodosa presenting as rapidly progressing intermittent claudication of right leg. Case Rep Med. 2017;2017:4219718.
28. Pagnoux C, Seror R, Henegar C, Mahr A, Cohen P, Le Guern V, et al. Clinical features and outcomes in 348 patients with polyarteritis nodosa: A systematic retrospective study of patients diagnosed between 1963 and 2005 and entered into the French vasculitis study group database. Arthritis Rheum. 2010;62(2):616-626.
29. Lightfoot RW, Michel BA, Bloch DA, Hunder GG, Zvaifler NJ, McShane DJ, et al. The American college of rheumatology 1990 criteria for the classification of polyarteritis nodosa. Arthritis Rheum. 1990;33(8):1088-1093.
30. Yamamoto S, Oiwa H. Provisional seven-item criteria for the diagnosis of polyarteritis nodosa. Rheumatol Int. 2020;40(8):1223-1227.
31. Chung SA, Gorelik M, Langford CA, Maz M, Abril A, Guyatt G, et al. 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Polyarteritis Nodosa. Arthrit Rheumatol. 2021;73(8):1384-1393.