

# Polyarteritis nodosa

JAVIER ORLANDO BARÓN-BARÓN, CAROLINA MARCELA PÉREZ-CHONA,  
LEDMAR JOVANNY VARGAS-RODRÍGUEZ • TUNJA (COLOMBIA)

DOI: <https://doi.org/10.36104/amc.2020.1388>

## Abstract

Polyarteritis nodosa was first described in 1866 by Zarco. Histologically, it is characterized by necrosis of the medium-sized arteries.

**Clinical case:** A 63-year-old patient presented with myalgia, blurred vision, paresthesias and loss of muscle strength. On physical exam, he had hypesthesia in the left foot. Paraclinical studies ruled out small vessel vasculitis, and, in the end, the biopsy was compatible with polyarteritis nodosa.

**Discussion:** this is a low prevalence entity with widely variable clinical manifestations. Therefore, the American College of Rheumatology criteria must be used for diagnosis, keeping in mind that the gold standard is histopathology. It is treated with immunosuppressants and the patient's prognosis is determined through the assessment of four criteria. (*Acta Med Colomb 2020; 45*. DOI: <https://doi.org/10.36104/amc.2020.1388>).

**Key words:** *vasculitis; arteritis; polyarteritis nodosa (DeCS)*.

Dr. Javier Orlando Barón-Barón: Especialización en Medicina Interna Hospital San Rafael; Carolina Marcela Pérez-Chona: Estudiante XII Semestre de Medicina Universidad de Boyacá; Dr. Ledmar Jovanny Vargas-Rodríguez: Especialización en Epidemiología Universidad de Boyacá. Tunja (Colombia).

Correspondencia: Dr. Javier Orlando Barón-Barón. Tunja (Colombia).

E-mail: [javierbaronb@gmail.com](mailto:javierbaronb@gmail.com)

Received: 17/VI/2019 Accepted: 11/II/2020

## Introduction

Polyarteritis nodosa was first described in 1866 by Zarco (1). Histologically, it is characterized by necrosis of the medium-sized arteries, affecting the arterial bifurcations, with a predominance of neutrophils and mononuclear cells, necrotizing changes and thinning of the vessel wall, which facilitates the formation of aneurysms. It is also characterized by intimal proliferation causing stenosis and occlusion (2,3).

Due to its varied clinical manifestations, it is commonly confused with other vasculitides or other systemic diseases. Therefore, it is important to correctly identify the findings which allow the diagnosis to be confirmed, thus ruling out other autoimmune entities, including systemic vasculitides (2, 4).

The objective of this paper is to present the clinical case of a patient with polyarteritis nodosa.

## Clinical case

A male 63-year-old patient consulted due to a three-month history of generalized myalgia associated with nocturnal diaphoresis, weight loss of more than 4 kg, bilateral blurred vision, loss of scapular and pelvic muscle strength and paresthesias of the lower limbs, predominantly of the instep of the right foot.

He reported a medical history of hypertension and chronic gastritis, had been a smoker for 20 years and was a social

drinker. He was being treated with omeprazole 20 mg/day (on an empty stomach) and amlodipine 5 mg + valsartan 160 mg + hydrochlorothiazide 12.5 mg every 12 hours.

On physical exam, he had the following vital signs: heart rate 111 bpm, blood pressure 140/100 mmHg, respiratory rate 19 BPM, and SaO<sub>2</sub> 93% on 21% FiO<sub>2</sub>. He was hydrated, afebrile, and had symmetrical extremities without edema, which were painful on palpation, with hypoesthesia of the lateral left foot instep and right foot instep. The rest of the exam was strictly normal.

In light of the clinical picture, laboratory tests were conducted showing leukocytosis and elevated C-reactive protein; with urinalysis, electrolyte panel, HIV, antiHbC, anti-HCV, creatine phosphokinase, aldolase, antiJo, cryoglobulins, ANAs, ENAs, ANCA-P, and ANCA-C reported as normal. Thus, ANCA-negative vasculitides, such as granulomatosis with polyangiitis (Wegener) and eosinophilic granulomatosis with polyangiitis (Churg Strauss), were ruled out. An electrocardiogram showed anterolateral subendocardial injury waves, and the echocardiogram evidenced mitral and aortic valve sclerosis with aortic regurgitation, concentric hypertrophy with diastolic dysfunction and slight dilation of the left atrium.

A computerized tomography (CT) of the abdomen showed hepatomegaly associated with steatosis, simple cysts on the left kidney, diverticular disease of the colon, lumbar disc herniation and umbilical hernia. Electromyography (EMG) was also performed, with conduction velocity in the

four extremities suggestive of chronic bilateral L4 and L5 radiculopathy, with no signs of active denervation or loss of functional motor units.

Given the clinical characteristics, his age group and the results of the paraclinical exams, an ophthalmology consult was requested. This consult proposed left eye neuropathy, and polymyositis was ruled out as the cause since the Bohan and Peter criteria were not met (there were no skin lesions, there was clinical improvement with the use of steroids, there were normal muscle enzymes and there was no myopathic pattern on the EMG), suggesting small fiber neuropathy. Thus, additional treatment was begun with pregabalin and vascular and muscular biopsies were performed (Figures 1 and 2) which confirmed the diagnosis of polyarteritis nodosa (PAN) with the finding of mixed inflammatory infiltrate (predominantly polymorphonuclear cells, lymphocytes and histiocytes), and meeting five of the 10 ACR criteria for PAN. With these results, treatment was begun with cyclophosphamide (six cycles of 1 gr diluted in 250 cc of NS), oral prednisone 1 mg/kg/day, oral azathioprine (50 mg every 12 hours), and folic acid (1 mg/day). A favorable progression was seen with this regimen, the treatment objectives were met, and the patient was discharged with an order to return once a month for the cyclophosphamide cycles.

The patient was seen as an outpatient one month later, at which time he reported improved symptoms with persistent paresthesias in his right big toe. His follow up paraclinical exams had no alterations. He completed six cycles of cyclophosphamide and continued treatment with prednisone po 5 mg q12h, azathioprine 50 mg q12h, and vitamin D + calcium 600 mg q12h.

## Discussion

Polyarteritis nodosa is a necrotizing vasculitis of the medium or small arteries which is not associated with antineutrophil cytoplasmic antibodies (ANCA) (4). Its incidence ranges from 0.3-8 cases per million people in Colombia (19). The low national and international prevalence of this

disease is associated with limited literature on the subject, which led to the writing of this paper.

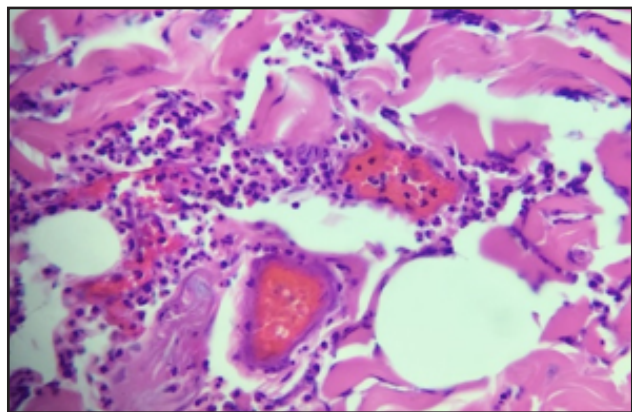
The symptoms are very heterogeneous since the arterial inflammation may affect a single organ or even, in more severe cases, lead to fulminant multiorgan failure, thus involving several systems and creating a wide constellation of clinical manifestations, which will depend mainly on the number and location of the affected arteries. The frequency of the clinical manifestations of polyarteritis nodosa is described in Table 1 (5, 6).

The diagnosis is based on the criteria established in 1990 by the Chapel Hill Consensus and the American College of Rheumatology (ACR), which have only been validated in adults (Table 2) (7). The presence of three or more criteria has a sensitivity of 82.2% and a specificity of 86.6% (7-9).

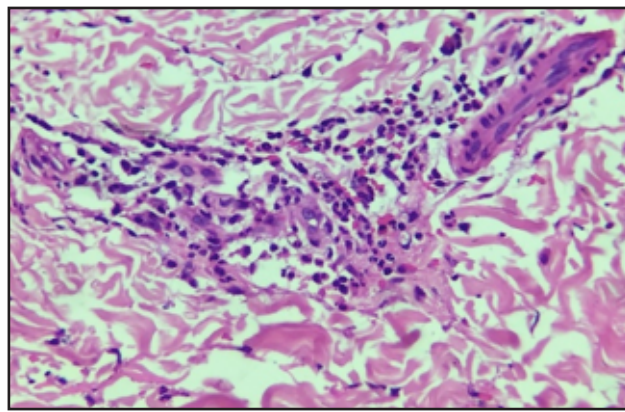
A less aggressive approach is preferred for biopsies (skin or muscle biopsies), since taking a sample from organs such as the kidney or liver poses a risk of bleeding (10). Usually, lymphocyte, macrophage, and neutrophil infiltrates are found, along with a variable number of eosinophils, and, in active lesions, fibrinoid necrosis. In more advanced stages, the formation of new vessels becomes apparent. In advanced lesions, vascular remodeling leads to hyperplasia of the tunica intima and diffuse fibrotic changes in the vessel wall. Severe wall injury may result in the formation of microaneurysms, and thrombosis may also contribute to vascular occlusion (11-13).

This case's diagnosis was suspected due to the patient's clinical presentation. In addition, elevated acute phase reactants are constant findings and the immunological studies ruling out other vasculitides ultimately led us to perform the histopathological study considered to be the gold standard, which confirmed PAN (12-14).

The treatment guidelines for this vasculitis recommend the use of glucocorticoids and cyclophosphamide to induce remission in patients with systemic illness; low dose glucocorticoids and azathioprine or methotrexate for remission maintenance; and referral of patients to a higher level of



**Figure 1.** Blood vessel biopsy. Medium-sized epimysial arteries showing predominantly lymphoid severe perivascular inflammation and karyorrhexis, associated with hemosiderophages and segmental fibrinoid necrosis of the wall. Biopsia vascular.



**Figure 2.** Muscle biopsy. Stroma with thin-walled arteries, with mixed inflammatory infiltrate, predominantly polymorphonuclear cells, lymphocytes and histiocytes.

complexity if they do not achieve remission with standard treatment (13-15).

For now, the current therapeutic approach for patients with mild forms of primary PAN (an FFS score of zero) is steroid monotherapy. Typically, prednisone or prednisolone is used at doses of 1 mg/kg/day, with subsequent titration. When symptom remission is achieved, a dose reduction is considered, and complete withdrawal of the medication should be avoided to prevent future relapses (16). In cases with systemic or multiorgan involvement, or involvement of vital organs, methylprednisolone pulses of 15 mg/kg over 60 minutes every 24 hours for 1-3 days may be used (17), adding cyclophosphamide at 2 mg/kg/day orally, or pulses of 600 mg/m<sup>2</sup> intravenously at 2-4 week intervals (18). In regard to the presented case, it was treated as mentioned; initially, treatment was begun with cyclophosphamide cycles and glucocorticoids together with azathioprine. Later, once disease remission was achieved (demonstrated by decreased erythrocyte sedimentation and CRP as the inflammatory response decreased), the patient continued on low dose glucocorticoids and azathioprine.

The person's prognosis in these cases is assessed using four associated factors, each of which is assigned one point: age >65 years, cardiac symptoms, gastrointestinal involve-

ment and kidney failure (serum creatinine > 1.7 mg/dL) (18). Five-year mortality for patients with a score of zero was 12%, for those with a score of one it was 26%, and when the FFS was equal to or greater than two, mortality was 46%. Seven-year survival for PAN is 79% (3). In our case, the patient should have a good prognosis (FFS of zero), with a 12% probability of mortality at five years.

### Conclusion

Polyarteritis nodosa is a rare systemic necrotizing vasculitis of small and medium arteries, which limits the individual's day to day activities. Several factors must be considered for its diagnosis: age, associated diseases and the symptoms motivating the consult. To establish a reliable diagnosis, complementary exams must be ordered such as a biopsy (muscular or of the most affected areas), ANAs and ENAs, among others. Treatment should be personalized, taking into account the pertinent considerations for disease remission, always monitoring the inflammatory response and clinical progression of the patient at each timely follow up.

### Referencias

1. Morgan, A. J. and Schwartz, R. A. Cutaneous polyarteritis nodosa: a comprehensive review. *Int. J. Dermatol.* 2010; **49**: 750-756.
2. J. C. Jennette, R. J. Falk, P. A. Bacon, N. Basu, M. C. Cid, F. Ferrario, et al. 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthrit Rheumat.* 2013; **65** (1): 1-11.
3. De virgilio A, Greco A, Magliulo G, Gallo A, Ruoppolo G, Conte M. *Poly-*

**Table 1.** Principal clinical manifestations of patients with polyarteritis nodosa.

Systemic symptoms	%
Fever	31-69
Weight loss	16-69
Myalgias	30-59
Arthralgias	44-58
<b>Skin involvement</b>	<b>28-58</b>
Nodules	17
Livedo reticularis	16
<b>Neurological manifestations</b>	<b>40-79</b>
Mononeuritis multiplex	39-72
Peripheral neuropathy	74
CNS	2-28
Cranial nerve paralysis	< 2
<b>Gastrointestinal tract involvement</b>	<b>4 - 90</b>
Abdominal pain	14-44
Nausea / vomiting	36-97
Diarrrhea	32
Hematochezia / melena	16
Hematemesis	3-5
Esophageal ulcers	13
Gastroduodenal ulcers	32
Colorectal ulcers	5
Acute abdomen / peritonitis	14-32
<b>Urological and renal involvement</b>	<b>2 - 70</b>
Hypertension (recent onset)	8-66
Hematuria	10-63
Proteinuria	15
Hematuria	22
Orchitis / epididymitis	2-18
Ophthalmological manifestations	3-44
Heart disease	4-30
Pleuritis	5

**Table 2.** American College of Rheumatology classification criteria for diagnosing polyarteritis nodosa..

Weight loss > 4 kg	Not due to dieting or other factors
Livedo reticularis	A reticular pattern on the skin of the extremities and trunk
Testicular pain and hypersensitivity	Not secondary to infection, trauma or other causes
Myalgia, weakness or leg pain	Diffuse myalgias (excluding the pectoral and pelvic girdles) or weakness or hypersensitivity
Mononeuropathy or polyneuropathy	Mononeuropathy, mononeuritis multiplex or polyneuropathy
Arterial hypertension	Diastolic arterial hypertension > 90 mmHg
Elevated urea nitrogen or creatinine levels	BUN >40 mg/dL or creatinine >1.5 mg/dL, not secondary to dehydration or obstruction
Hepatitis B virus	Presence of hepatitis B surface antigen or antibody
Arteriographic abnormalities	Aneurysms or occlusions of the visceral arteries not secondary to atherosclerosis, fibromuscular dysplasia or other noninflammatory causes
Biopsy of small or medium-sized arteries containing polymorphonuclear cells	Presence of neutrophils or mononuclear leucocytes in the arterial wall

- arteritis nodosa: A contemporary overview. Elsevier - Autoimmunity Reviews. 2016; 27: 564-570*
4. **Jennette J, Falk R, Bacon P, et al.** 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum.* 2013; **65**: 1-11.
  5. **Nunokawa T, Yokogawa N, Shimada K, Enatsu K, Sugii S.** The use of muscle biopsy in the diagnosis of systemic vasculitis affecting small to medium-sized vessels: a prospective evaluation in Japan. *Scand J Rheumatol.* 2016; **45(3)**: 210-4.
  6. **Jennette JC.** Implications for pathogenesis of patterns of injury in small- and medium-sized-vessel vasculitis. *Cleve Clin J Med.* 2002; **69**: 33-8.
  7. **Lightfoot RW, Michel BA, Bloch DA, Hunder GG, Zvaifler NJ, Mchane DJ, et al.** The American College of Rheumatology 1990 criteria for the classification of polyarteritis nodosa. *Arthritis Rheum.* 1990; **33**: 1088-1093.
  8. **Guillevin L, Lhote F.** Treatment of polyarteritis nodosa and microscopic polyangiitis. *Arthritis Rheum.* 2007; **41(12)**: 2100-5.
  9. **Soto O, Conn DL.** Polyarteritis nodosa and microscopic polyangiitis. In: Hochberg MC, Silman AJ, Smolen JS, Weimblatt ME, Weisman MH, editors. *Rheumatology. Edingurgh: Mosby. 2003; p. 1611-21.*
  10. **Hernández RJ, Alba MA, Prieto GS, Cid MC.** Diagnosis and classification of polyarteritis nodosa. *J Autoimmun.* 2014; **48-49**: 84-89.
  11. **Ishiguro N, Kawashima M.** Cutaneous polyarteritis nodosa: A report of 16 cases with clinical and histopathological analysis and a review of the published work. *J Dermatol.* 2010; **37**:85-93.
  12. **Ragab, G., & Hussein, M. A.** Vasculitic syndromes in hepatitis C virus: A review. *Journal of Advanced Research.* 2017; **8(2)**: 99-111.
  13. **Ozen S.** The changing face of polyarteritis nodosa and necrotizing vasculitis. *Nature Reviews Rheumatology.* 2017; **13**: 381-386.
  14. **Balwani, M. R., Kute, V. B., Shah, P. R., Shah, M., Shinde, S. G., Shah, J., & Trivedi, H. L.** Hepatitis B viremia manifesting as polyarteritis nodosa and secondary membranous nephropathy. *Journal of Nephroarmac.* 2016; **5(2)**: 119-121.
  15. **Mukhtyar, C. et al.** EULAR recommendations for the management of primary small and medium vessel vasculitis. *Ann. Rheum. Dis.* 2009; **68**:310-317.
  16. **Ribi C, Cohen P, Pagnoux C, Mahr A, Arène JP, Puéchal X, et al.** French Vasculitis Study Group. Treatment of polyarteritis nodosa and microscopic polyangiitis without poor-prognosis factors: a prospective randomized study of one hundred twenty-four patients. *Arthritis Rheum.* 2010; **62**:1186-97.
  17. **Chan M, Luqmani R.** Pharmacotherapy of vasculitis. *Expert Opin Pharmacother.* 2009; **10**:1273-1289.
  18. **Ribi C, Cohen P, Pagnoux C, Mahr A, Arène JP, Puéchal X, et al.** French Vasculitis Study Group. Treatment of polyarteritis nodosa and microscopic polyangiitis without poor-prognosis factors: a prospective randomized study of one hundred twenty-four patients. *Arthritis Rheum;* 2010; **62**:1186-97.
  19. **Ochoa Carlos D, Ramírez Fabián, Quintana Gerardo, Toro Carlos, Cañas Carlos, Osio Luis Fernando et al.** Epidemiología de las vasculitis primarias en Colombia y su relación con lo informado para Latinoamérica. *Rev. Colomb. Reumatol.* 2009; **16 (3)**: 248-263.

