



Case report

A non-surgical approach: Ampicillin's success in *Listeria monocytogenes* endocarditis

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ABSTRACT

Background: *Listeria monocytogenes*, a Gram-positive bacillus, primarily affects immunocompromised individuals. Endocarditis is a rare but severe complication of *L. monocytogenes* bacteremia, irrespective of native or prosthetic valves. While there is no standardized treatment, the use of ampicillin proves effective in most cases. Surgical intervention is reserved for cases involving valve dehiscence, heart failure, or myocardial abscess.

Case presentation: A 54-year-old female, with mitral valve replacement, presented with fever, chest pain and dyspnea at rest. Patient was initially diagnosed with bacterial pneumonia; however, subsequent evaluation revealed *L. monocytogenes* bacteremia, resulting in endocarditis. Surgical management was contraindicated due to multiple prior valve replacement surgeries. Symptoms resolution, along with improvements in echocardiographic and clinical parameters, was achieved through extended antibiotic treatment only with no surgical intervention.

Conclusion - key takeaways: This case underscores the critical importance of individualized treatment approaches in endocarditis, particularly in patients with surgery approach contraindication, and emphasized the success achieved through ampicillin-based management.

Introduction

Listeria monocytogenes, a gram-positive bacillus primarily affecting immunocompromised individuals, is often associated with foodborne infections, ranking as the third leading cause of food-related mortality in the United States [1]. Invasive listeriosis exhibits varied risk factors, with neonates and those over 50–60 years old being commonly affected. Neonates, particularly with macrophage dysfunction, are vulnerable, while the elderly face increased susceptibility due to solid tumors, hematologic diseases, and immunosuppressive treatments. HIV-infected patients also demonstrate heightened risk.

Clinical manifestations range from self-limiting febrile gastroenteritis to life-threatening conditions like bacteremia, meningitis, and endocarditis, the latter occurring in less than 8% of cases with a considerable mortality rate [2]. Optimal antibiotic therapy for *Listeria monocytogenes* endocarditis lacks robust clinical studies. Common regimens involve ampicillin monotherapy or with aminoglycosides such as gentamycin. While antimicrobial therapy alone appears superior in NVE (Native valve endocarditis) cases, a combination of medical and surgical approaches confers a profound survival benefit for PVE (Prosthetic valve

endocarditis) [3]. Here, we present a case of successful prolonged ampicillin management in a patient with contraindications for surgical intervention, demonstrating favorable clinical and radiological outcomes.

Case presentation

A 54-year-old female with a medical history of hypertension, heart failure with a reduced ejection fraction of 48%, pulmonary hypertension, prior strokes without sequelae, protein S deficiency, cystic fibrosis, asthma, osteochondroplasty, eosinophilic granulomatosis, chronic atrial fibrillation with a rapid ventricular response, and multiple prior bioprosthetic mitral valve replacements (first one 15 years ago due to rheumatic valve disease) with the most recent surgery 6 months prior (due to valvular dysfunction). She received imipramine 25 mg daily, topiramate 25 mg every 12 h, prednisolone 25 mg daily, metoprolol succinate 25 mg every 12 h, furosemide 40 mg every 24 h, amiodarone 200 mg every 12 h, omeprazole every 24 h, and enoxaparin 50 mg every 12 h. The patient was a homemaker and denied any substance use or occupational exposure to animals, did not own any pets and reported no

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recent consumption of unusual or potentially contaminated food items. She was admitted due to four days of severe, stabbing chest pain radiating to the scapular region, dyspnea at rest, and overall poor general condition.

On admission, blood pressure was 103/68 mmHg, heart rate 54 bpm, respiratory rate 31 breaths per minute, oxygen saturation 96%, and temperature 38.7 °C. Arterial blood gases showed metabolic acidosis with lactate at 1.9 mmol/L, leucocyte count 12,470/μL, with 80.6% neutrophils and 14.6% lymphocytes and C-reactive protein was 20.3 mg/L (Table 1), with capillary refill time markedly prolonged, leading to increased respiratory distress, and intubation was initiated with subsequent milrinone infusion for inotropic support. Chest X-ray revealed right lower lobe consolidation (Fig. 1), raising suspicion of bacterial superinfection. Empirical antibiotic therapy was initiated. Transesophageal echocardiography showed a bioprosthetic mitral valve with no insufficiency, but a mobile mass (10 ×4 mm) was detected on the atrial aspect of the valve ring (Fig. 2). Pulmonary CT angiography ruled out pulmonary embolism but indicated multilobar pneumonia.

Bronchoalveolar lavage fluid cultures grew *Haemophilus influenzae* and *Streptococcus pneumoniae* (both at 10⁷ CFU/mL). Respiratory panel (BIOFIRE® FILMARRAY® Pneumonia Panel, bioMérieux, France) also identified *Moraxella catarrhalis* and further confirmation of *Haemophilus influenzae* and *Streptococcus pneumoniae* on day 2. No resistance genes were found, so therapy was adjusted to intravenous ceftaroline 600 mg every 8 h. On day 4, blood cultures (2/2) grew *Listeria monocytogenes*, leading to the addition of ampicillin at 12 g per day via continuous intravenous infusion. Given the suspicion of central nervous system involvement leading to altered consciousness and subsequent aspiration pneumonia, a cerebrospinal fluid analysis was conducted, which returned normal. An infectious workup and brain MRI were unremarkable.

Follow-up blood cultures at day 5 were negative, and a follow-up echocardiogram suggested potential prosthetic valve thickening with

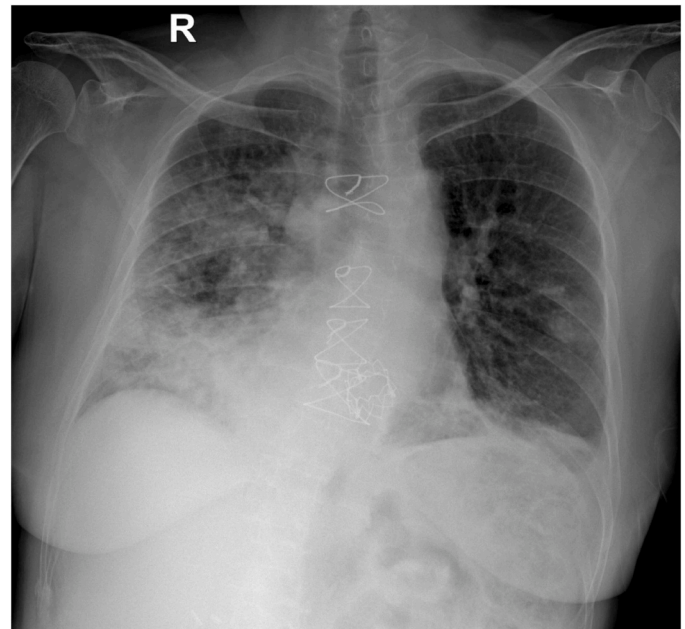


Fig. 1. Chest X-ray at admission. Patched alveolar occupation infiltrates in the lower two-thirds of the right lung and a nodular opacity at the left lung base with soft tissue density measuring 17 mm, and flat left basal atelectasis. Mediastinal widening with an increase in pulmonary artery caliber. Global cardiomegaly with an endoprosthesis and sternal cerclage. Left thoracic scoliosis.

apparent improvement compared to the prior evaluation. Ceftaroline was discontinued after 10 days, with ampicillin continued. Considering the patient’s extensive surgical history, the cardiothoracic surgery team deemed her unsuitable for further surgical intervention. High suspicion of infective endocarditis led to a PET-CT scan, which revealed hypermetabolic activity at the mitral valve prosthesis, suggestive of an infecto-inflammatory process. Additionally, a hypermetabolic focus was observed at the T6 vertebral body (Fig. 3), raising concerns of an associated infectious process. Subsequent PET-CT findings prompted the continuation of ampicillin therapy and the addition of trimethoprim/sulfamethoxazole 800/160 mg every 12 h orally for 10 days.

An MRI of the spine showed nearly complete collapse of the T6 vertebral body with reduced spinal canal width, along with mild loss of T5 vertebral body height and apparent marrow edema. The patient underwent spine surgery, after blood cultures returned negative, and the procedure was carried out without complications. Despite the presence of hypermetabolic foci on PET scan and suggestive MRI findings, no definitive signs of osteomyelitis or spondylodiscitis was found upon direct visualization during the surgical intervention; the observed abnormalities were attributed to poor bone quality. Intraoperative cultures were not obtained. Remarkably, the patient experienced significant pain relief following the surgery.

The patient exhibited remarkable clinical improvement without recurrent fever, systemic inflammatory response, or positive blood cultures. After a three-month hospitalization, she was discharged with a 4-week prescription of ampicillin-sulbactam (3 g every 8 h) for home care, followed by oral amoxicillin (1 g every 12 h) indefinitely. At the 15-day follow-up, a transesophageal echocardiogram revealed no valve abnormalities (Fig. 4). At 3 months follow-up, paraclinical tests indicated normal results. There was no clinical evidence of relapse, and the patient continued to tolerate amoxicillin treatment well. The patient was readmitted 4 months later due to decompensation of her atrial fibrillation. It’s important to note that during this readmission, there was no systemic inflammatory response or fever observed. Imaging studies, including cardiac CT, revealed severe left atrial dilation with no

Table 1 Laboratory tests results at hospital admission.

Laboratory Tests	Values
Hematologic	
Hemoglobin	12.1 g/dL
Leukocyte count	12.470 /uL
Neutrophils	80.6%
Lymphocytes	14.6%
Eosinophils	1%
Basophils	0.2%
Platelet count	197.000 /uL
Arterial Blood Gases	
pH	7.29
pCO2	43 mmHg
pO2	76 mmHg
sO2	93.3%
BE	-5.7 mmol/L
HCO3	20.7 mmol/L
FiO2	55%
Lactate	1.9
Other serum tests	
Creatinine	0.8 mg/dL
BUN	20.3 mg/dL
Sodium	138.6 mmol/L
Potassium	4 mmol/L
NT-proBNP	905 pg/mL
Glucose	150 mg/dL
Immunoglobulin (IgG)	9.4 g/L
Immunoglobulin (IgM)	1.32 g/L
Infectious profile	
C reactive protein	20.3 mg/dL

Abbreviations: BE: base excess, BUN: blood urea nitrogen, FiO2: fraction of inspired oxygen, HCO3: arterial bicarbonate, NT-proBNP: N-terminal pro-brain natriuretic peptide, pCO2: arterial carbon dioxide pressure, pO2: arterial oxygen pressure, sO2: arterial oxygen saturation.

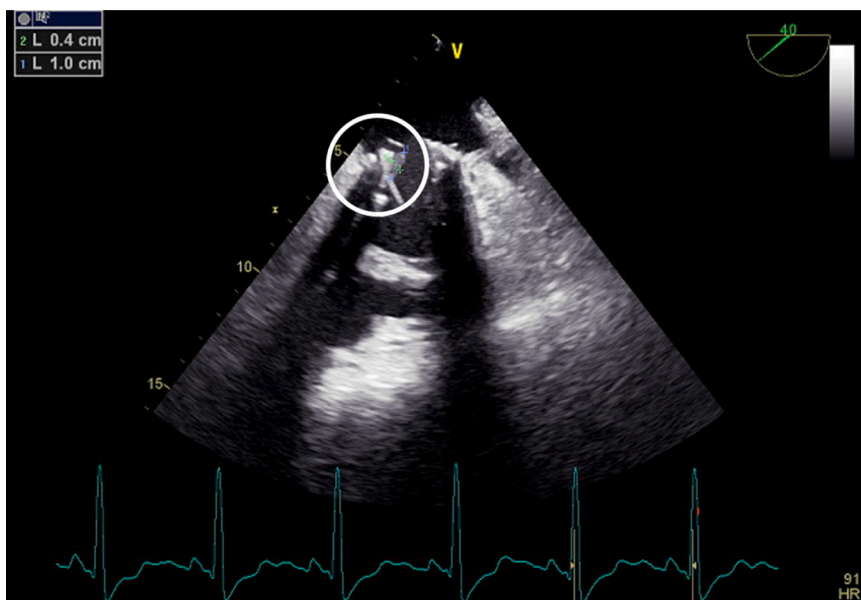


Fig. 2. Transesophageal echocardiogram at admission. Mitral valve Bioprosthesis with normal opening and closing movements, without insufficiency or paravalvular leaks, peak velocity 2 m/s, mean gradient 9 mmHg. A mobile, soft mass, located in the atrial aspect of the prosthetic ring, measuring 10 × 4 mm (White circle).

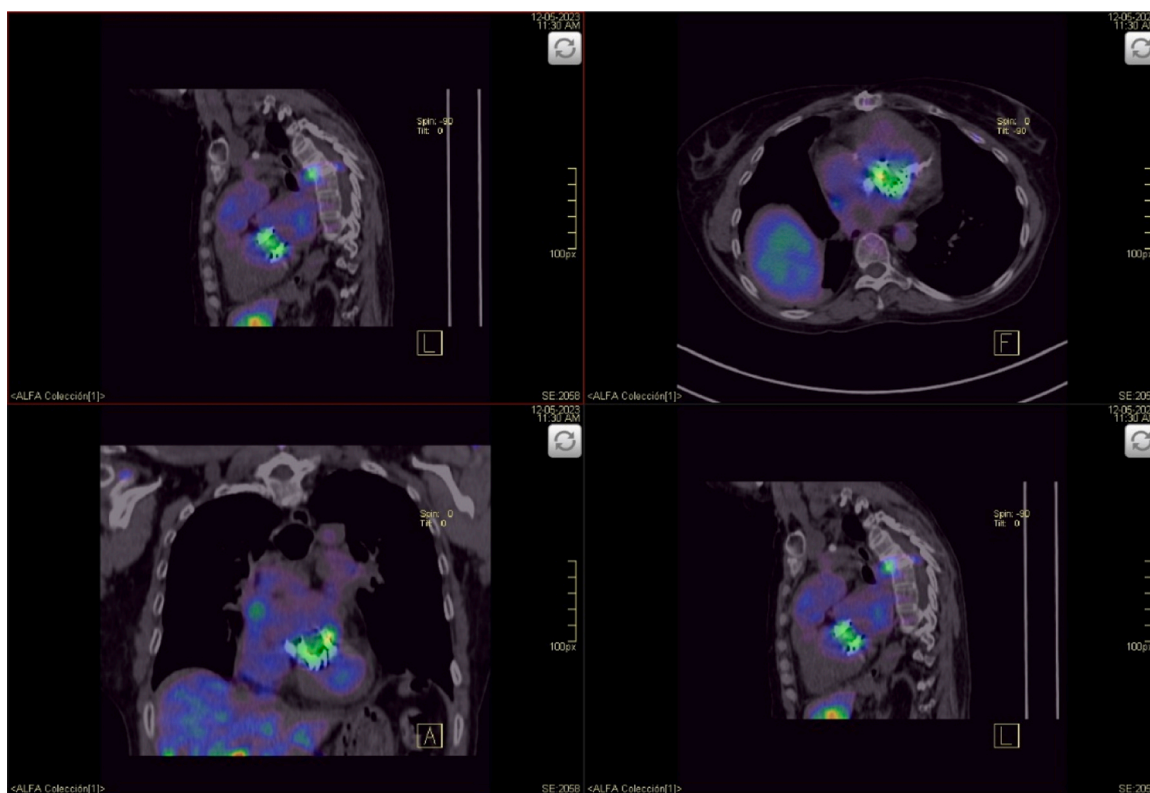


Fig. 3. PET-CT (Positron Emission Tomography-Computed Tomography). Hypermetabolic focus on mitral valve prosthesis, persisting on unattenuated images, suggestive of infecto-inflammatory process, along with hypermetabolic wedging of T6 vertebral body, raising doubt regarding an infectious process.

evidence of masses, suggesting a distinct clinical concern unrelated to the previous endocarditis. Anticoagulant therapy was initiated with no further complications. No additional symptoms or signs indicative of endocarditis recurrence were noted.

Discussion

A patient with a history of multiple mitral valve replacements,

prolonged immunosuppression, and numerous comorbidities. Presented with bacteremia and a high suspicion of *Listeria monocytogenes* endocarditis, complicated by contraindications for surgical intervention due to prior multiple procedures. The management strategy employed a prolonged course of ampicillin, followed by amoxicillin, resulting in a satisfactory resolution of the clinical and radiological presentation.

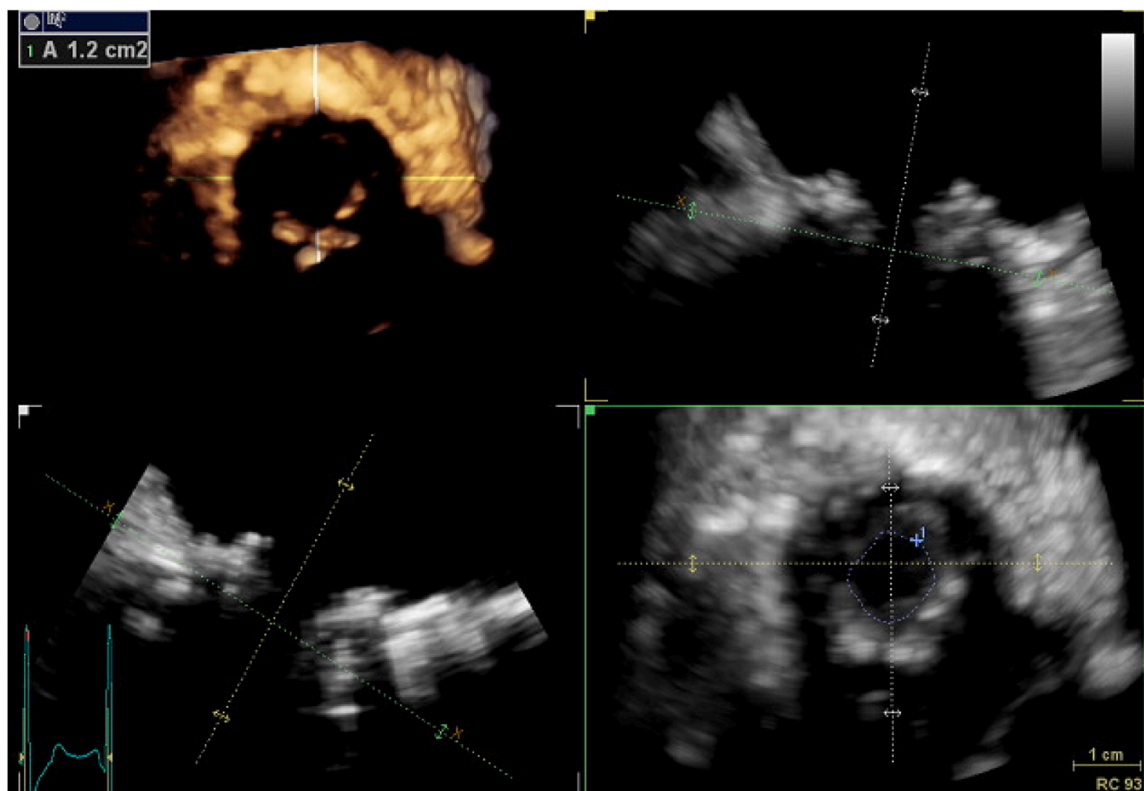


Fig. 4. Follow-up transesophageal echocardiogram. Proper valve opening and closing are observed without thickening, and there are no images suggestive of thrombi or vegetations adhered to the valve leaflets of the prosthesis.

Epidemiology

Listeriosis poses an increased risk influenced by multiple factors, including pregnancy, hematologic malignancies, especially leukemia, patients with cellular immunity alterations (chronic steroid use or HIV), autoimmune diseases, and chronic conditions such as cirrhosis, alcoholism, and diabetes mellitus [4]. While community-acquired infections are commonly associated with foodborne contamination, recent hospitalization has emerged as an additional risk factor, challenging traditional perspectives [5]. Although traditionally more prevalent in women, cases of *Listeria*-induced infectious endocarditis, particularly in the context of prosthetic valve involvement, are observed more frequently in males.

Although the patient did not report occupational risk factors or a history of consuming contaminated food associated with listeriosis, it is important to note that she did have other clinically relevant factors, including multiple comorbidities, recurrent interventions on a prosthetic mitral valve, recent hospitalizations, and prolonged immunosuppression with steroids, stands as an exemplar. The latter is acknowledged to compromise cellular immunity, directly heightening susceptibility to infections caused by intracellular microorganisms such as *Listeria monocytogenes* (LM). Identifying and considering these additional factors can provide a more comprehensive perspective for understanding the clinical presentation and management of the case.

Clinical presentation

Infective endocarditis on prosthetic valves, particularly affecting the mitral and aortic valves, is an uncommon yet severe complication of listeriosis. Structural factors, including hypertrophic cardiomyopathy, rheumatic valve disease, mitral valve prolapse, or ischemic cardiomyopathy, elevate the risk of infection. Most common manifestations of listeriosis encompass meningitis or rhomboencephalitis. Subacute onset,

characterized by fever, constitutional symptoms, and signs of heart failure, akin to our patient's presentation, often precedes embolic complications occurring in approximately two-thirds of cases [6].

Diagnosis

Diagnosing *Listeria*-induced infective endocarditis mandates the presence of vegetations on the valve and LM bacteremia. In cases involving native valves, antecedent streptococcal endocarditis episodes or other cardiac diseases are common precursors [7]. According to the Task Force for the Management of Infective Endocarditis of the European Society of Cardiology, echocardiographic findings, positive blood cultures, and clinical manifestations are pivotal diagnostic elements. In instances where the diagnosis persists as "probable," repeating blood cultures and echocardiograms is recommended, and in specific cases, such as ours, additional tests like PET-CT scans are warranted [8]. Our patient met modified Duke criteria with echocardiographic findings suggestive of mobile mass indicative of vegetation, accompanied by two blood cultures positive for LM with over 12 h of separation. Additionally, the PET scan exhibited findings consistent with infectious endocarditis, enhancing the sensitivity of Duke criteria upon patient admission to 97% [9].

Medical treatment

Due to the limited number of cases and a lack of controlled clinical trials, standardizing treatment remains elusive. Nevertheless, commonly employed treatment regimens involve penicillin or ampicillin (AMP), either as monotherapy or in conjunction with an aminoglycoside such as gentamicin (GENT). *In vitro* studies have demonstrated a synergistic bactericidal effect with combination therapy (AMP + GENT). However, retrospective studies have not conclusively demonstrated *in vivo* superiority of combination therapy over ampicillin monotherapy [10].

LM possesses five penicillin-binding proteins (PBP 1–5), with PBP 3 being identical across all species. Inhibition of PBP 3 is the primary objective of beta-lactams used in treatment. Third-generation cephalosporins exhibit weak activity against LM due to low affinity for PBP 3 [11]. Treatment for prosthetic valve cases is recommended to last a minimum of 6 to 8 weeks [12].

Surgical management

While antibiotic therapy alone has shown efficacy in native valve endocarditis, surgery confers profound benefits in prosthetic valve cases [13]. Despite our patient meeting clear surgical indications (signs of heart failure and a mobile and large vegetation > 10 mm) but being deemed high surgical risk, the decision was made to proceed with antibiotic therapy and symptomatic management due to the cumulative risks outweighing potential benefits. Follow-up echocardiography demonstrated resolution of findings and preserved valve function, accompanied by symptom resolution. Despite adequate treatment, LM-induced endocarditis carries a mortality rate of up to 20–30%, compared to 14% in other types of endocarditis [14].

This case presents a clinically favorable outcome with medical management alone. Although a specific source of contagion was not identified, multiple risk factors for LM-induced infective endocarditis were evident.

Conclusions

Our patient's complex medical history highlights the vulnerability of certain populations. The diagnostic approach, incorporating echocardiography, blood cultures, and PET-CT scans, underscores the need for precision. Treatment dilemmas reflect the absence of standardized protocols, emphasizing the importance of tailored interventions. Despite surgical indications, our patient's favorable response to medical management showcases the complexity of decision-making. This case contributes valuable insights into the nuanced management of *Listeria*-induced infective endocarditis, addressing diagnostic challenges and individualized treatment modalities.

Ethics approval and consent to participate

This study has been approved by the Institutional Ethical Board review of Fundación Valle del Lili.

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CRedit authorship contribution statement

Pablo Andrés Moncada-Vallejo: Supervision, Formal analysis, Conceptualization. **Natalia Ramos Ospina:** Writing – review & editing, Writing – original draft, Resources, Investigation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors contributions

Natalia Ramos-Ospina was responsible for the acquisition of consent by the patient, the collection and analysis of clinical information, and the initial version of the manuscript. Pablo A. Moncada-Vallejo participated in the critical review of the intellectual content. All authors read and approved the final and the revised version of the manuscript.

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report. A copy of the written consent is available for review by the editor of this journal.

Authors' contributions

All authors contributed, read and approved the submitted version of the manuscript.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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