Inquilino Improvável: Um Caso Clínico de Endocardite da Válvula Pulmonar

An Unlikely Guest: A Case Report of Pulmonary Valve Endocarditis

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Resumo:

A endocardite infeciosa é uma patologia grave e potencialmente fatal. O envolvimento do coração direito é menos frequente, afetando preferencialmente a válvula tricúspide, associado à toxicodependência endovenosa e à presença de dispositivos intracardíacos. A endocardite infeciosa da válvula pulmonar é, por isso, uma raridade (1,5%-2% dos casos), sendo o seu envolvimento único ainda mais raro, com poucos casos descritos na literatura. Relatamos um caso de endocardite infeciosa de válvula pulmonar nativa, numa mulher sem fatores de risco, com quadro febril e aparecimento de sopro holossistólico, após 48 horas de internamento. O ecocardiograma transtorácico demonstrou vegetação única na válvula pulmonar, que associado a bacteriemia a *Staphylococcus aureus*, confirmou o diagnóstico. A evolução foi favorável, com resolução do quadro após 6 semanas de antibioterapia dirigida. Este caso destaca a importância major da suspeita clínica e do exame objetivo nesta patologia, mesmo na ausência de fatores de risco típicos, que constitui um desafio diagnóstico.

Palavras-chave: Doenças das Válvulas Cardíacas; Ecocardiografia; Endocardite Bacteriana; Infecções Estafilocócicas; Válvula Pulmonar.

Abstract:

Infective endocarditis is a serious and potentially fatal condition. Right heart involvement is less frequent, preferentially affecting the tricuspid valve, associated with intravenous drug use and with the presence of intracardiac devices. Infective endocarditis of the pulmonary valve is, therefore, very rare (1.5%-2% of cases) and its occurrence as a standalone event is even rarer, with few cases described in the literature. We report a case of native pulmonary valve endocarditis, in a woman without risk factors, with fever and onset of a holosystolic murmur, after 48 hours of hospitalization. The transthoracic echocardiogram showed unique vegetation in the pulmonary valve, which, combined with Staphylococcus aureus bacteremia, confirmed the diagnosis. Evolution was favorable, with resolution after 6 weeks of targeted antibiotic therapy. This case highlights the importance of clinical suspicion and objective examination to identify this pathology, including in the absence of typical risk factors, when diagnosis is especially challenging.

Keywords: *Echocardiography; Endocarditis, Bacterial; Heart Valve Diseases; Pulmonary Valve; Staphylococcal Infections.*

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Introduction

Infective endocarditis (IE) is a potentially fatal disease with high morbidity and mortality (20%-30%).[1-3] There are 3 main high-risk patients for IE: prosthetic valves carriers, those with previous episodes of IE and those with congenital heart disease (CHD).[1]

Despite improvements in the approaches to IE diagnosis and treatment options, its overall incidence is increasing, with higher prevalence in older patients and it remains a growing health concern.[1,3] There has been an increase in the rates of health-care associated IE (30% of all IE), of IE related to intracardiac/prosthetic devices and in the incidence of *Staphylococcus aureus*.[1,2]

IE affects the left-side of the heart (LSIE) in 90% of cases. Right-sided IE (RSIE) is rarer, accounting for 5%-10% of cases.[1,3,5-8] It is more frequent in intravenous drug users (IVDUs) (90% of cases)[1,3,5,7,8] and most frequently affects the tricuspid valve.[7] The most relevant risk factors are IVDU, intracardiac devices, central venous catheters, health-care infections, hemodialysis and immunosuppression.[1,3,5,7] RSIE has a better prognosis, better outcomes and lower mortality rates than LSIE.[1,3,7]

Pulmonary valve (PV) IE is rare, accounting for 1.5%-2% of cases.[6,8,10-13] The unique involvement of native and structurally normal PVs is an even rarer event.[4,8,12] Risk factors are the same as for RSIE, with IVUD, intracardiac devices, sepsis and CHD being the most common.[2,4-6,8] Yet, 28% of the cases had no predisposing factor.[12,13] *Staphylococcus aureus* is, as for RSIE, the main responsible agent.[8,10-12]

The most commonly associated findings are fever, bacteremia and respiratory symptoms[1,4,7] which are often misinterpreted as pneumonia, resulting in 76% of patients receiving empirical antibiotics before diagnosis.[7] Pulmonary

embolization is frequent and can cause atelectasis, abscess and pleural effusion.[1,3,7] Physical examination in PVIE is relatively nonspecific, lacking vascular and immunological phenomena typical of IE. Regurgitant pulmonary murmur is often a late finding.[4,11]

Diagnosis and treatment include clinical evaluation, blood cultures, echocardiography[5,7] and targeted antibiotic therapy.[3] Echocardiography is the gold standard for identification of vegetations and of emergence of complications.[5] If empirical therapy is necessary, it should cover *Staphylococcus* spp.[1] and consider local resistance profiles. Modified Duke criteria should be applied to all patients with suspected IE,[6] although their sensitivity may be reduced in RSIE.[5]

The diagnosis is often hampered by the absence of classic clinical signs, which can lead to delays in diagnosis and intervention, especially in patients without traditional risk factors. Nevertheless, PVIE is usually medically managed with good outcomes.[2,8]

Case Report

We present the case of an 87-year-old woman with severe disability, living in a nursing home, with medical history of dementia and Parkinson's disease, admitted to the emergency department due to a five-days long fever and hematuria. She was normotensive, with tympanic temperature of 39ºC and tachypneic with peripheral oximetry 88% (room air). She had a skin wound in the proximal phalanx of the first finger of the left hand. The remaining physical exam was unnoteworthy.

Blood tests revealed macrocytic anemia (hemoglobin 9.9 g/dL, mean cell volume 96.8%), neutrophilia (9100x10^9/L) and increased C-reactive protein of 239.9 mg/dL. Urinalysis excluded hematuria and urine culture was negative. Arterial blood gases showed hypoxemia (59.8 mmHg), which resolved after fever resolution. Chest X-ray was normal. A thoracoabdominopelvic computed tomography (CT) was requested (Fig. 1), showing pericardial and bilateral pleural effusion and excluding infectious processes.

Assuming fever of unknow origin, blood cultures were collected, urinalysis and urine culture were repeated and the following tests were performed: thyroid function tests, antinuclear antibodies, anti-doubled stranded DNA and serology tests (human immunodeficiency virus, hepatitis C and B virus, cytomegalovirus, Epstein-Barr virus). Methicilin-resistent *Staphylococcus aureus* (MRSA) screening was not performed. The start of antibiotic therapy was postponed and the patient was admitted for etiological study.

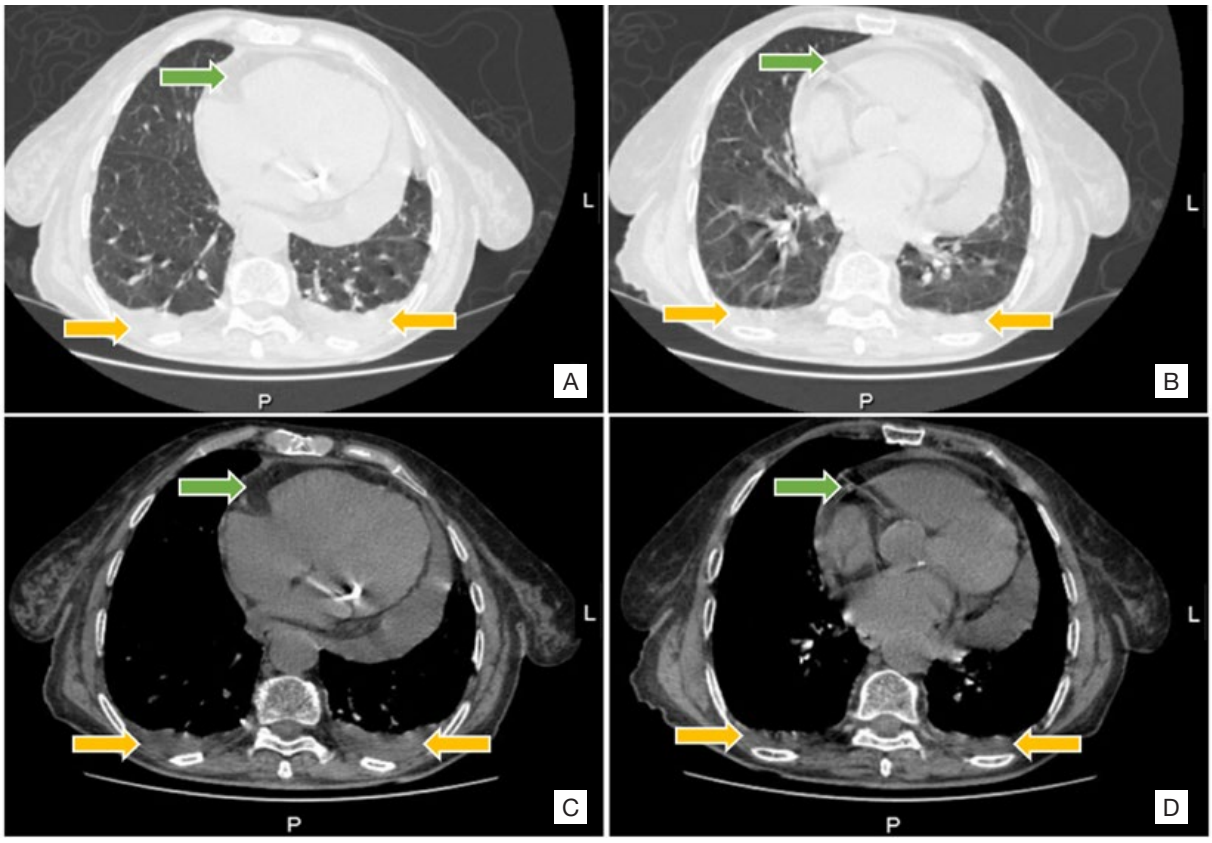

Figure 1 - (**A**) and (**B**) Computed tomography in two different plans using pulmonary window and showing circumferential pericardial effusion (green arrows) and bilateral pleural effusion (yellow arrows). (**C**) and (**D**): same computed tomography now using a mediastinal view reveals the same findings. Pleural effusion is best identified in the pulmonary view; the pericardial effusion, in the mediastinal view (L – Left, P – Posterior).

Table 1: Modified Duke Criteria – Major and minor criteria. The criteria presented by the patient are in bold and italic.

Major criteria		Minor criteria	
1	***Blood cultures positive for infectious endocarditis***	1	Predisposition such heart condition or injection drug use
a)	***Typical microorganisms from 2 separate blood cultures: Staphylococcus aureus***	***2***	***Fever: temperature > 38ºC***
b)	Microorganisms consistent with infectious endocarditis from persistently positive blood cultures	3	Vascular phenomena (example: major arterial emboli, septic pulmonar infarcts, Janeway's lesions)
2	Imaging positive for infectious endocarditis	4	Immunological phenomena (example: Osler's nodes)
		5	Microbiological evidence: positive blood culture but does not meet a major criterion
1 major criterion plus 1 minor criterion – Possible infective endocarditis			

Adapted from: Habib G, et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). Eur Heart J. 2015;36:3075-128.[1]

After 48 hours of sustained fever, a holosystolic murmur grade II/VI in the pulmonary focus was detected, and methicillin-sensitive *Staphylococcus aureus* (MSSA) was isolated in blood cultures. All other exams requested were negative. Considering the modified Duke criteria for the diagnosis of IE[1], the patient met one major criterion (positive blood cultures for MSSA) and one minor criterion (fever > 38ºC), indicating possible endocarditis (Table 1).

Given this hypothesis, and since the patient was edentulous and without macroscopic lesions of the mouth and oropharynx, observation by Otorhinolaryngology was waived. The only etiological source founded to the MSSA isolation was the skin wound.

New blood cultures were collected, directed antibiotic therapy with flucloxacillin (2 g every 6/6 hours) was started and a TTE was requested. MSSA was again isolated and TTE showed circumferential pericardial effusion of moderate dimensions and a vegetation of the pulmonary valve with 3.56 x 7.37 mm (Fig. 2). With 2 major criteria (MSSA isolation and vegetation detected in TTE), a definitive diagnosis of endocarditis was established (Table 2).[1]

Concerning RSIE embolic potential, a thoracic CT

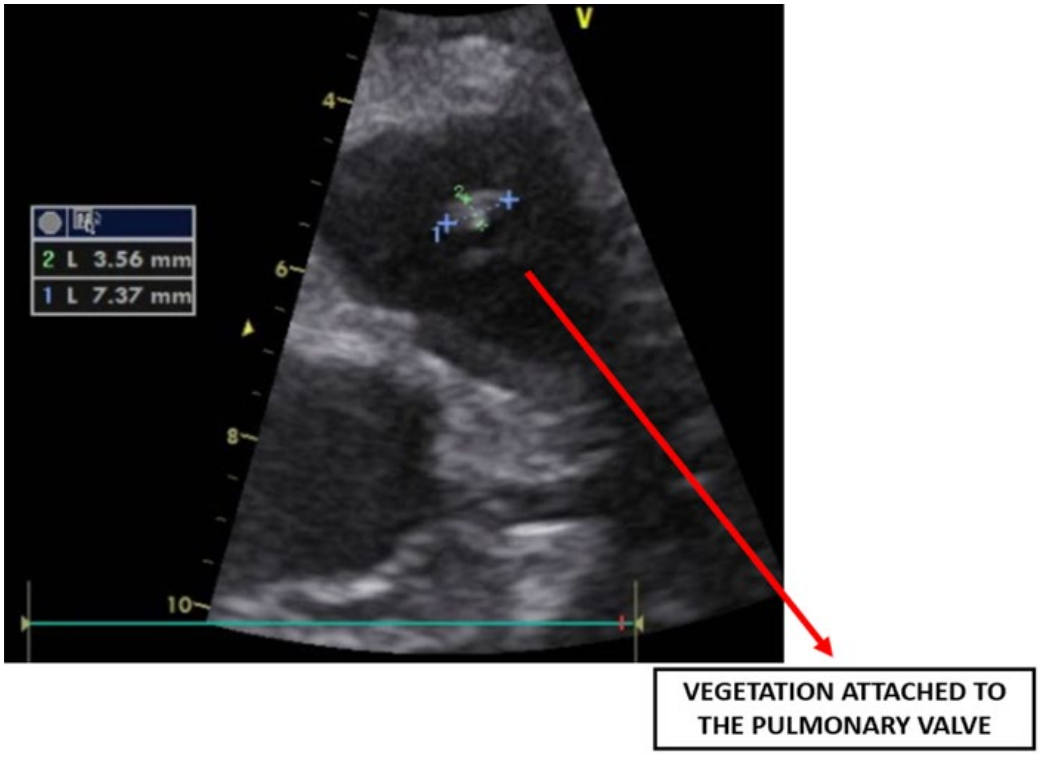

Figure 2 -Transthoracic echocardiography basal short axis view showing a vegetation of size 3.56 x 7.37 mm attached to the pulmonary valve (red arrow). The yellow V signals the transducer marker.

Table 2: Modified Duke criteria presented by the patient after transthoracic echocardiography (in bold and italic).

Major criteria		Minor criteria	
1	***Blood cultures positive for infectious endocarditis***	1	Predisposition such heart condition or injection drug use
c)	***Typical microorganisms from 2 separate blood cultures: Staphylococcus aureus***	2	Fever: temperature > 38ºC
d)	Microorganisms consistent with infectious endocarditis from persistently positive blood cultures	3	Vascular phenomena (example: major arterial emboli, septic pulmonar infarcts, Janeway's lesions)
2	***Imaging positive for infectious endocarditis***	4	Immunological phenomena (example: Osler's nodes)
		5	Microbiological evidence: positive blood culture but does not meet a major criterion
2 major criteria – Definite infective endocarditis			

Adapted from: Habib G, et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). Eur Heart J. 2015;36:3075-28.[1]

angiography was performed, which revealed continued pericardial effusion and bilateral pleural effusion, with passive atelectasis of the adjacent lung, parenchymal condensation of the lingula (Fig. 3), and excluded embolic phenomena.

Recrudescence of fever was observed after 72 hours and blood cultures were negative. After 2 weeks, TTE was repeated, showing reduction of the vegetation dimensions (3.32 x 3.76 mm, Fig. 4). The patient remained hemodynamically stable and without compromise of right ventricular function. Intravenous antibiotic therapy of flucloxacillin was carried out for 6 weeks with full resolution of the clinical condition.

Discussion

It is known that most cases of PVIE are related to typical risk factors, however, in 28% of cases no risk factor is identified.[12,13] This patient, besides old age, has no other apparent risk factors for native PVIE.

Being in a nursing home, might have contributed to the acquiring a healthcare associated infection – a possible predisposing factor. This and the finding of a skin wound, could have lead to the MRSA screening upon admission. However, given the absence of other risk factors, such as hospitalization or administration of antibiotics in the previous 6 months, this was not

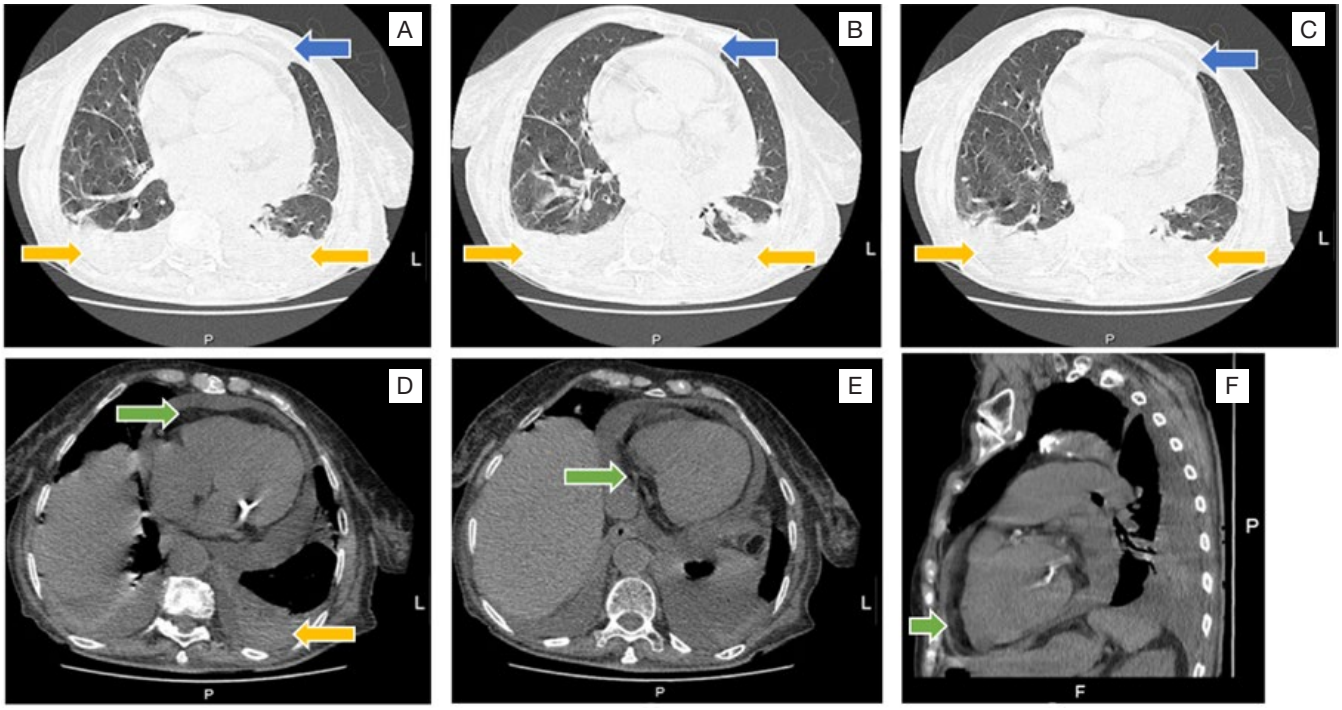

Figure 3 - (**A**), (**B**) and (**C**) Computed tomography angiography using pulmonary view showing bilateral pleural effusion (yellow arrows) and parenchymal condensation of the lingula (blue arrow). (**D**), (**E**) and (**F**) Computed tomography angiography using mediastinal view showing circumferential pericardial effusion (green arrows) and pleural effusion (yellow arrow) (F - Front, L – Left, P – Posterior).

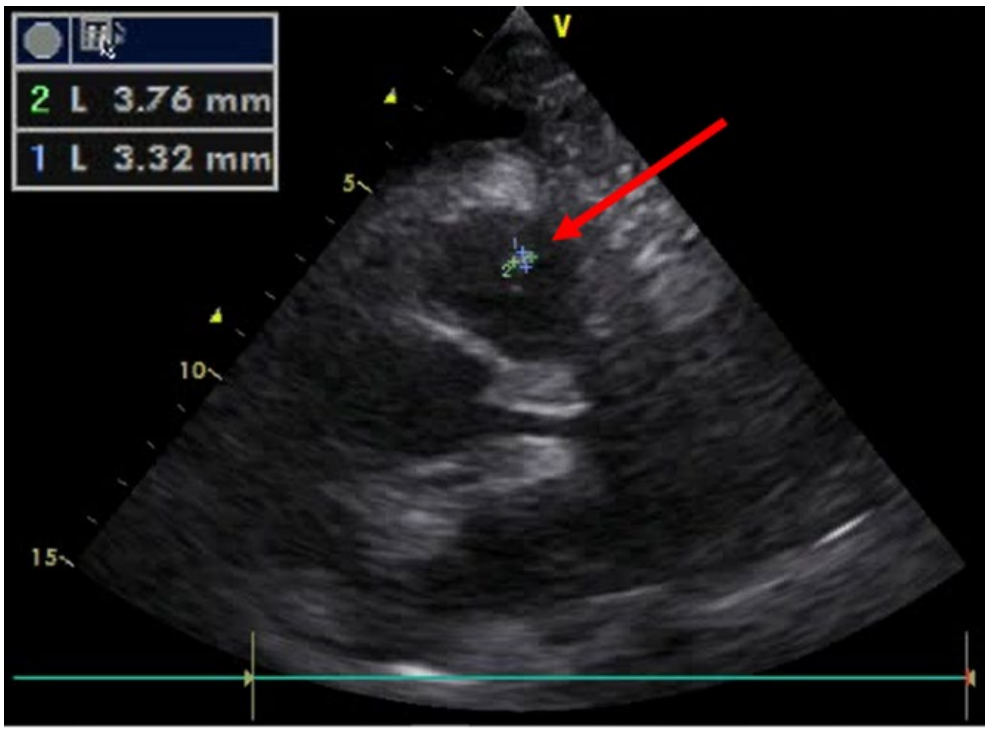

Figure 3 -Transthoracic echocardiography basal short axis view showing reduction in the vegetation size (3.32 x 3.76 mm) attached to the pulmonary valve (red arrow). The yellow V signals the transducer marker.

carried out.[15] Moreover, the age related immunosenescence might induce immunosuppression, leading to greater susceptibility to infection.

MSSA bacteremia, should raise RSIE as a diagnostic hyphotesis.[9] In this case, MSSA bacteremia, persistent fever and appearance of a pulmonary murmur raised the hypothesis of IE, then confirmed by the echocardiographic finding of a vegetation in the pulmonary valve. The skin wound in the left hand might constitute the etiologic source of MSSA bacteremia.

Despite fever, bacteremia and respiratory symptoms are the most common symptoms in PVIE,[1,4,7] the physical findings initially presented by the patient were relatively nonspecific, with fever being the predominant symptom.

Renal dysfunction may occur in 6% to 30% of IE, with one of the possible manifestations being nephritic syndrome – with hematuria and proteinuria, corresponding to immune complex deposition and glomerulonephritis.[1] The hematuria initially detected and later excluded by the systematic repetition of the urine analysis, could corresponded to the first manifestation of endocarditis.

Initial hypoxemia, which ceased after fever resolution, might have masked pulmonary involvement. The imaging findings of pleural and pericardial effusion could also have led to an earlier clinical suspicion of IE, and consequently, to earlier diagnosis. The pulmonary murmur identified can be considered a late physical finding.[4,11]

The thoracic CT angiography requested excluded pulmonary embolism. However, it showed the presence of pleural effusion and pneumonia of the lingula confirming synchronous pulmonary involvement, probably acquired through the hematogenous route.

Although studies have reported a lower sensitivity of the modified Duke criteria for the diagnosis of RSIE,[5] they were applied before and after TTE, and led to a definitive diagnosis. TTE is of great value due to right heart structures anterior location and their relative proximity to the transducer.[3,9] Regarding transesophageal echocardiogram (TOE), studies disagree on its higher diagnostic yield[3] and TOE is not mandatory in isolated RSIE in the presence of quality TTE with unequivocal findings.[6,9] In this case, TTE was sufficient to identify the vegetation and TOE was not required.

Negative blood cultures and repeated TTEs demonstrated the absence of complications and the reduction of the vegetation dimensions, confirming the therapeutic efficacy of the targeted antibiotic therapy. TTE at the end of antibiotic therapy was not performed, given the favorable echocardiographic evolution and the absence of new signs or symptoms, associated with hemodynamic stability. Some studies show that performing TTE at the end of therapy may not be necessary in all patients with IE, being more relevant in the face of maintenance or worsening of previous signs and symptoms.[14] After discharge, the patient was referred for follow-up at outpatient clinic.

Conclusion

This case represents a rare finding of isolated PVIE, in an individual with no other predisposing factors to native valve IE, beyond old age. Isolated PVIE has low incidence and its

diagnosis could be difficult in the setting of unspecific physical findings, also given the absence of direct clinical guidelines. This highlights the relevance of high clinical suspicion, early identification and management, which, even in older individuals, might prevent complications and ultimately reduce mortality.

From an Internal Medicine point of view, this case highlights the increasing importance of understanding and being aware of age-related immunosenescence, particularly with regard to its clinical consequences, namely, increased susceptibility to infections. ■

Declaração de Contribuição

CM, SB – Redação do artigo
TSM, PF – Revisão do caso
IL – Aquisição de imagem e revisão do caso.
Todos os autores aprovaram a versão final a ser publicada.

Contributorship Statement

CM, SB – Drafting of the article
TSM, PF – Case review
IL – Image acquisition and case review
All authors approved the final draft

Responsabilidades Éticas

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