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CASE REPORT

Fulminant Necrotizing Eosinophilic Myocarditis Successfully Treated With Veno-Arterial Extracorporeal Membrane Oxygenation and High-Dose Steroids

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Abstract

Fulminant necrotizing eosinophilic myocarditis (FNEM) is a rare form of EM characterized by biventricular heart failure with hemodynamic deterioration, often requiring inotropes or mechanical circulatory support.

Here, we report a case of a 43-year-old healthy woman with FNEM who was admitted with acute heart failure that rapidly progressed to cardiogenic shock and electrical storm, culminating in cardiac arrest. Early diagnosis and prompt administration of corticosteroids in combination with veno-arterial extracorporeal membrane oxygenation allowed complete recovery of biventricular systolic function.

Case report

A 43-year-old woman with a history of idiopathic thrombocytopenia was admitted to the emergency department with sudden onset of orthopnea and paroxysmal nocturnal dyspnea. She reported progressively worsening dyspnea and peripheral edema in the last week. Her only medication was oral contraceptives.

At admission, she was afebrile and presented a blood pressure of 95/64 mmHg, a regular pulse of 120 b.p.m., elevated jugular venous pressure and signs of pulmonary congestion. Electrocardiogram showed sinus tachycardia, T-wave inversion in leads V4-V6, and low voltage in peripheral leads (Video 1). Laboratory investigation revealed an inflammatory state with absolute hypereosinophilia (leukocytes at 17.6 x 10^3/uL, N:4.8-10.8 x 10^3/uL; eosinophils at 5.1 x 10^3/uL, N:0-0.49 x 10^3/uL), increased C-reactive protein (138 mg/L,N: < 3 mg/L), mild thrombocytopenia (109 x 10^3/uL, N:150-350 x 10^3/uL), myocardial injury (troponin I of 4.5 ng/mL, N: <0.045 ng/mL), and increased prohormone of brain natriuretic peptide (28618 pg/mL, N: < 125 pg/mL). Computed tomography angiography excluded pulmonary embolism.

Transthoracic echocardiogram revealed increased thickness and echogenicity of the myocardial walls and moderate compromise to left ventricular systolic function due to global hypokinesia. Right ventricular systolic function was impaired (tricuspid annular plane systolic excursion [TAPSE] 15 mm), but without dilation. There was a small pericardial effusion and moderate functional mitral regurgitation. (Figure 2, Panel A-B; Videos 1, 2 and 3) Considering the clinical presentation, analytical data, and echocardiographic findings, the diagnosis of eosinophilic myocarditis (EM) was considered highly probable. Within a few hours of admission, the patient's condition deteriorated rapidly, evolving to cardiogenic shock with increasing hyperlactacidemia (3.3 mmol/L) and severe compromise to left ventricular systolic function. She was promptly transferred to a tertiary hospital for endomyocardial biopsy and possible mechanical circulatory support under dobutamine and noradrenaline. Systemic corticosteroid therapy was immediately initiated with intravenous methylprednisolone (1 mg/kg/day).

Endomyocardial biopsy of the right ventricle was performed and coronary angiography excluded epicardial coronary disease. In the post-procedural period, the hemodynamic profile suddenly worsened, requiring increasing doses of inotropic and vasopressor support. Transthoracic echocardiogram showed

Keywords

Myocarditis; Biopsy; Steroids; Extracorporeal Membrane Oxygenation.

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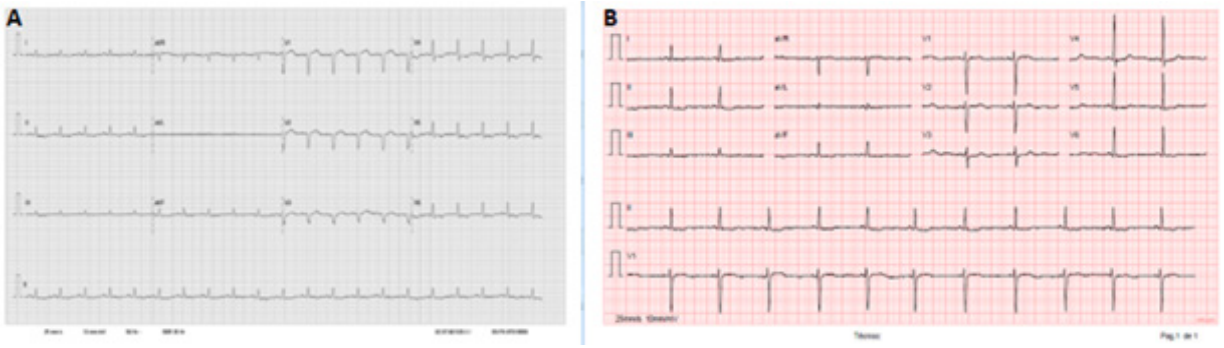


Figure 1 – Panel A: 12-lead electrocardiogram at presentation, showing sinus tachycardia with T-wave inversion in the V4-V6 leads and low voltage in the peripheral leads; Panel B: Electrocardiogram 4 weeks after recovery, showing sinus rhythm with resolution of repolarization changes.

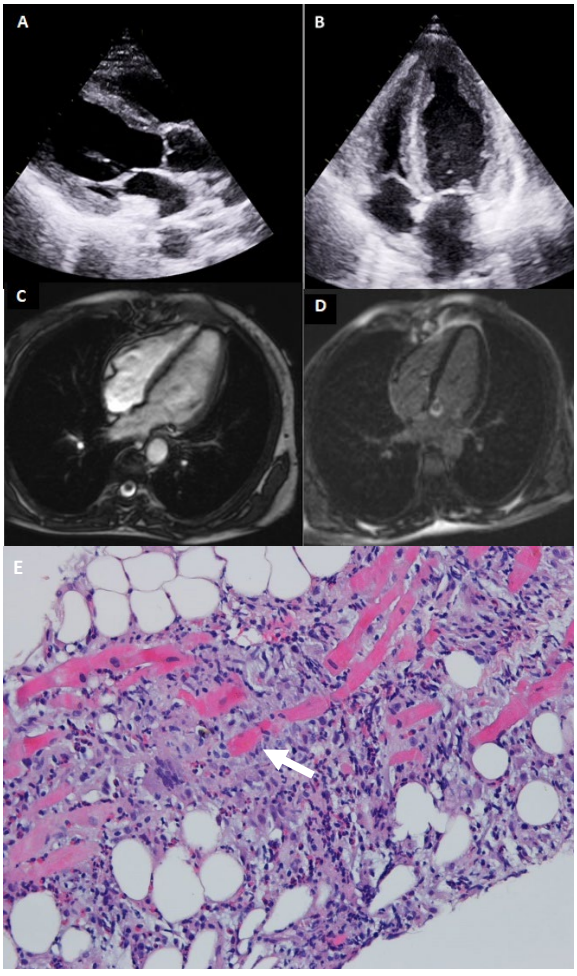
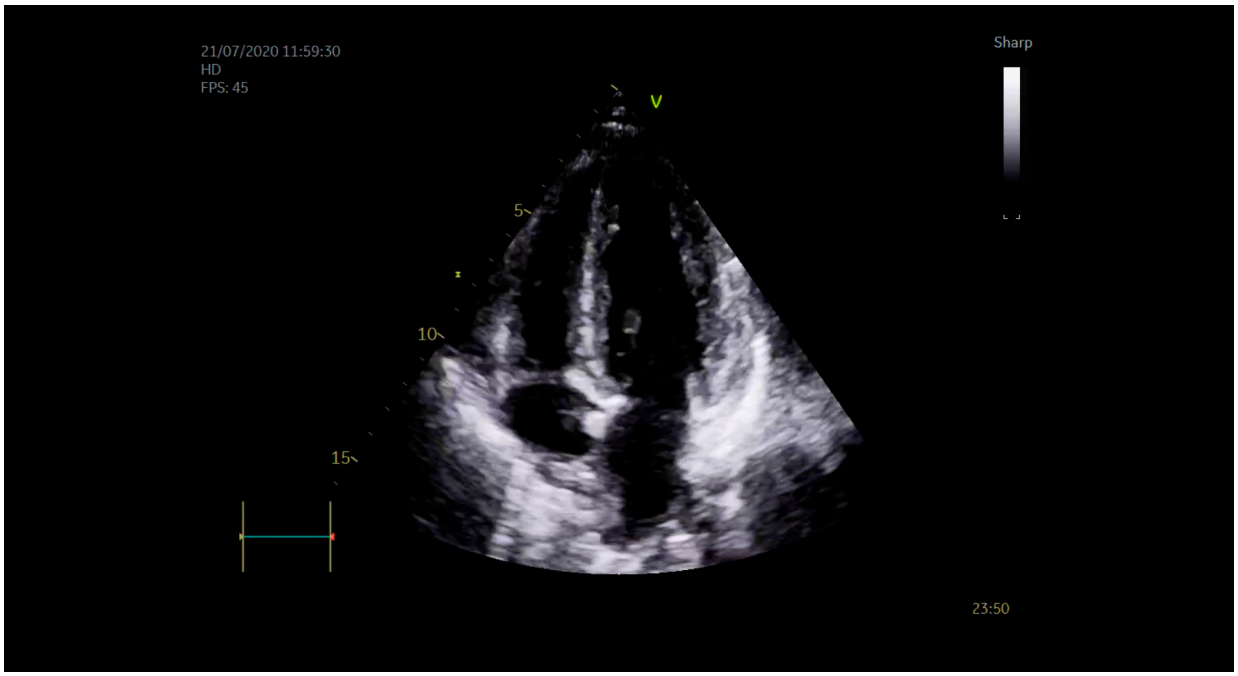
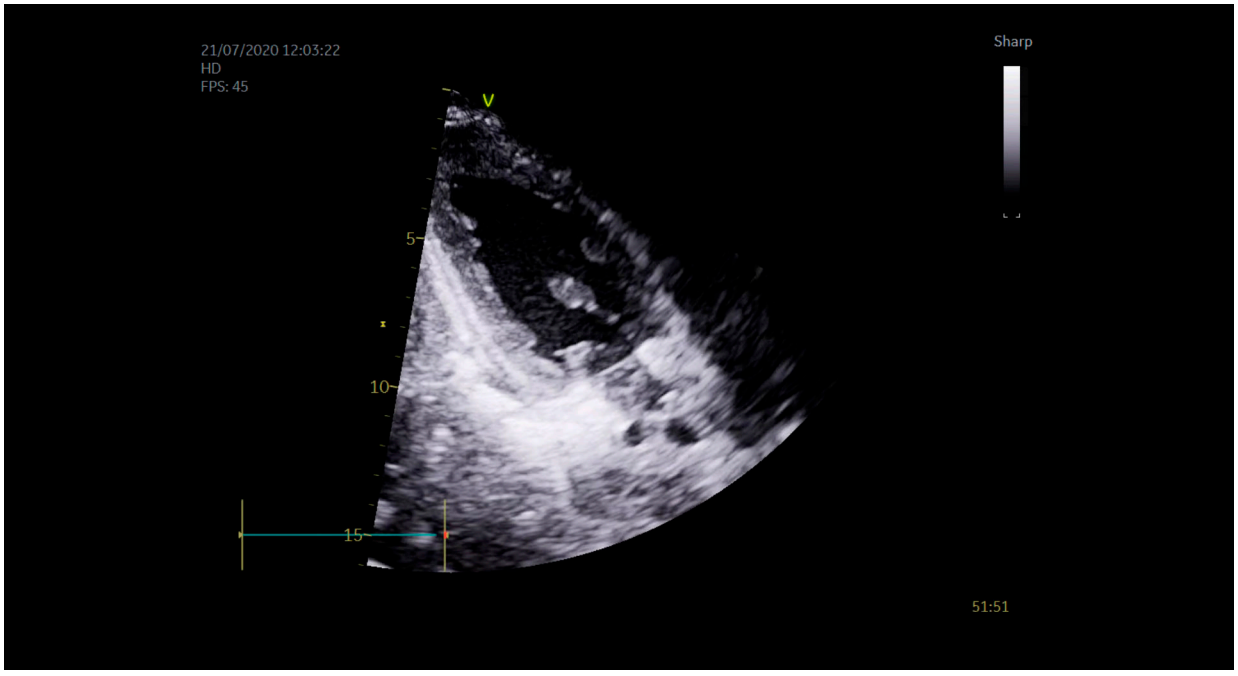


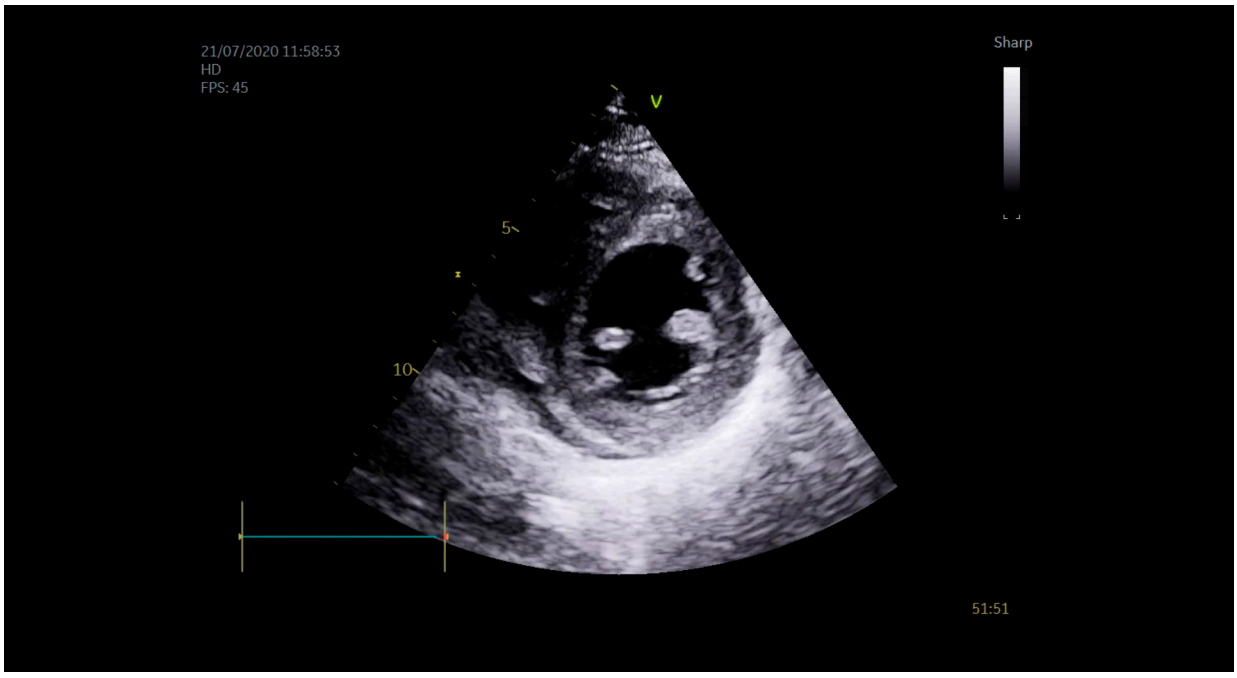
Figure 2 – Panels A-B: Transthoracic echocardiography performed in the emergency department, showing increased thickness and echogenicity of the myocardial walls; Panels C-D: Cardiac magnetic resonance (A-cine diastole and B-late gadolinium enhancement) performed on the 40th day after hospitalization, showing normal thickness and dimensions of the cardiac chambers (C) and no late gadolinium enhancement (D); Panel E: Endomyocardial biopsy showing inflammatory cell infiltration with a high number of eosinophils (white arrow) (Hematoxylin-eosine, 200x amplification).



Video 1 – https://ijcscardiol.org/supplementary-material/2023/36/2023-0071_video_1a.mp4



Video 2 – https://ijcscardiol.org/supplementary-material/2023/36/2023-0071_video_1b.mp4



Video 3 – https://ijcscardiol.org/supplementary-material/2023/36/2023-0071_video_1c.mp4

moderate to severe pericardial effusion, mainly in the right cardiac chambers, which caused cavity collapse, and hyperechoic mobile material in the right ventricle free wall, suggestive of a fibrin clot. On suspicion of a myocardial perforation, surgical subxiphoid drainage of pericardial effusion was performed (600 ml of hemorrhagic fluid), although the source of the bleeding could not be identified.

In the immediate post-operative period, the patient had a sustained monomorphic ventricular tachycardia that required electrical cardioversion. Amiodarone was initiated as an antiarrhythmic. At that point, transthoracic echocardiogram showed that the pericardial effusion had resolved, although left ventricular systolic function continued to be severely compromised and right ventricular systolic function worsened (TAPSE 10 mm). There was rapid recurrence of pulseless ventricular tachycardia, which degenerated into ventricular fibrillation and led to cardiac arrest. Cardiopulmonary resuscitation was initiated, the patient was intubated, and femoral-femoral cannulation to veno-arterial extracorporeal membrane oxygenation was initiated within 5 minutes of cardiopulmonary resuscitation. The total low flow period was 25 minutes. The patient returned to spontaneous circulation 3 times during cardiopulmonary resuscitation, and neurological recovery occurred during the first attempt. Anticoagulation with unfractionated heparin was initiated. Subsequent clinical evolution was favorable and she was extubated the next day.

Histopathological analysis confirmed the diagnosis of FNEM (Figure 2; Panel E). Treatment with high-dose glucocorticoids allowed normalization of the eosinophil count within 24 hours and progressive improvement in biventricular systolic function after 7 days (LVEF35%; TAPSE 14 mm). Daily echocardiographic assessment excluded pericardial effusion. On the seventh day, methylprednisolone was transitioned to prednisone 60 mg orally per day, which was maintained for 1 month.

On the 11th day after admission, moderate to large asymmetrical pericardial effusion recurred over the right atrium, associated with clinical tamponade. Subxiphoid pericardiocentesis was unsuccessful and an emergency median sternotomy was performed, with 500 ml of hemorrhagic pericardial fluid drained. The active bleeding source could not be identified. The patient remained stable for some hours but, again, her clinical condition worsened, with sudden hemodynamic instability, new abdominal pain, and a drop in hemoglobin. Suspecting hemoperitoneum as the cause of the hemorrhagic shock, an exploratory

laparotomy was performed, which confirmed the diagnosis; 3 L of hemorrhagic fluid was drained. Although the source of the hemorrhage was not clearly identified, the visualization of perihepatic clots raised suspicion of a suprahepatic laceration and perihepatic packing was performed. During this period, the patient received a massive blood transfusion. The patient finally stabilized after surgery.

Following clinical improvement, serial echocardiographic exams revealed a daily increase in biventricular systolic function. The patient was decannulated on the 16th day of hospitalization.

One month after her initial presentation, biventricular systolic function and myocardial thickness had fully normalized. Repeated biomarker measurements revealed a troponin I level of 0.083 ng/ml and normal electrocardiogram (Figure 1 B).

To investigate EM etiology, the patient underwent a myelogram and bone marrow biopsy, which excluded primary hematologic disease. Autoimmune, infectious, and neoplastic investigations were also negative.

After 38 days of hospitalization, she was transferred back to the referring hospital for functional rehabilitation and slow tapering of steroids while prednisolone was maintained at 30 mg per day.

Cardiac magnetic resonance was performed on the 40th day of hospitalization, which confirmed normal biventricular systolic function, with no evidence of myocardial edema or fibrosis (Figure 2, Panel C-D).

At 2 years of follow-up, she remains asymptomatic and without complications, with a normal eosinophil count and normal biventricular systolic function.

Discussion

EM is a relatively uncommon form of myocardial inflammation, although its incidence may be underestimated.[1] The degree of myocardial eosinophilic infiltration depends on the stimulus attracting the eosinophils, as well as the degree and duration of eosinophilic exposure; nevertheless, in 25% of cases, peripheral eosinophilia is absent, which makes diagnosis challenging.[1-3]

The clinical spectrum of EM is broad, ranging from paucisymptomatic cases to FNEM, but it can also present later as chronic restrictive cardiomyopathy.[3] Hypereosinophilia may have multiple causes, such as infections, malignancies, vasculitis, hypereosinophilic syndromes or drug hypersensitivity, with the latter being the most common etiology of FNEM.[2,4,5]

FNEM is a rare form, mainly affecting adolescents and young adults.[4] It is often a fatal condition that can manifest as fulminant heart failure or sudden cardiac arrest, with death or transplantation rates up to 50%.[5] In this case, low voltage electrocardiographic criteria, hyperechoic myocardial wall thickening, and hypereosinophilia in a patient with acute heart failure raised suspicion of EM, which was critical for timely transfer to a center with mechanical circulatory support.[1]

Endomyocardial biopsy is recommended in high-risk clinical scenarios, such as acute myocarditis presenting with acute heart failure or cardiogenic shock, myocarditis complicated by severe myocardial dysfunction and associated with ventricular arrhythmias or high-degree atrioventricular block, and in some specific scenarios as myocarditis associated with peripheral eosinophilia.[1,6]

In hemodynamically stable patients, cardiovascular magnetic resonance can be considered an alternative diagnostic tool to biopsy, although a definite diagnosis of EM can only established through endomyocardial biopsy.[2,3]

In the present case, fluoroscopy-guided biopsies were taken from the right ventricle, as per hospital protocol, but they could also have been taken from the left ventricle or both ventricles. Most evidence suggests a higher diagnostic yield in the latter 2 options.[7-9] This case demonstrates the possibility of complications from endomyocardial biopsy, even in a specialized high-volume center with major complication rates < 1%.[6,9] Left ventricular biopsy has been associated with a lower incidence of cardiac perforation than right ventricular biopsy, probably because the right ventricular wall is thinner.[8]

Identifying the underlying etiology is also a very important step for EM patients, since it allows specific treatment. In this case, we could not determine the etiology, which is not rare, since up to 35% of EM cases are considered idiopathic.[2,3]

Mechanical circulatory support, immunosuppression, and standard medical therapies for heart failure are the basis of FNEM treatment. Due to the rarity of FNEM, there are no solid evidence-based guidelines regarding initial steroid dosage or

optimal treatment length.[2,3] Steroids should be given as soon as the diagnosis is confirmed or even highly suspected, since their immediate initiation is the key to successful treatment. The majority of patients usually respond to corticosteroids but, in some cases, a second immunosuppressive agent is needed, such as azathioprine or mycophenolate mofetil.[4,5] In the present case, after endomyocardial biopsy, we began empirical treatment with high-dose corticosteroids while waiting for the histological results, with gradual tapering over 12 months.[1,2]

Our patient had a fulminant clinical course that rapidly progressed to cardiogenic shock, complicated by electrical storm, which culminated in cardiac arrest. Veno-arterial extracorporeal membrane oxygenation has an invaluable role in resuscitation and it provides biventricular support as a bridge to transplant or recovery while anti-inflammatory treatment takes effect.[10] In fact, despite the high rate of in-hospital mortality among patients with fulminant EM, recovery after mechanical circulatory support is common.[3]

Beyond the spectrum of myocarditis, extracorporeal membrane oxygenation has been applied in different clinical scenarios that culminate in electrical storm, severe heart failure, cardiogenic shock, or cardiac arrest.[10-12] Its role in cardiopulmonary arrest is growing, with extracorporeal cardiopulmonary resuscitation emerging as a means of improving resuscitation during refractory cardiac arrest:[11] the mean survival rate is ~30% (higher values for in-hospital cardiorespiratory arrest patients).[11,12] Patients whose initial rhythm is shockable have shorter low flow times, and those with lower intra-arrest blood lactate levels are more likely to benefit from extracorporeal cardiopulmonary resuscitation in both hospital and non-hospital settings.[12] Despite its more generalized use, extracorporeal membrane oxygenation-related complications remain low, the most common being hemorrhage, limb ischemia, pulmonary edema, and mechanical issues related to the circuit.[11,12]

In conclusion, FNEM is a rare life-threatening disease that is eminently treatable if identified at an early stage. The key to survival is a rapid systematic assessment using endomyocardial biopsy to establish the diagnosis, initiating steroids as soon as the diagnosis is suspected; mechanical circulatory support devices provide time for patients to recover or until other treatments, such as cardiac devices or transplantation, can be performed.[3,4]

Author Contributions

Conception and design of the research and writing of the manuscript: Pereira T, Tinoco M, Faria B, Azevedo O; acquisition of data and analysis and interpretation of the data: Pereira T, Tinoco M, Azevedo O; critical revision of the manuscript for intellectual content: Pereira T, Tinoco M, Faria B, Azevedo O, Albuquerque RR, Lourenço A.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Hospital Senhora da Oliveira Guimarães under the protocol number 176/2023. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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*Supplemental Materials

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