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Case report

Right ventricular endomyocardial fibrosis: atypical presentation of a rare disease. Case report

Laura Valentina López Gutiérrez[1,a], **Mauricio Andrés Murillo Moreno**[2,b], **Luisa Fernanda Durango**[3,c,d], **Jhon Fredy Salamanca Montilla**[4,c,d,e], **Clara Inés Saldarriaga Giraldo**[1,f]

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Author´s affiliation
[1] Departamento de Cardiología, Clínica CardioVID, Medellín, Colombia.
[2] Departamento de Medicina Interna, Universidad CES, Medellín, Colombia.
[3] Clínica CardioVID, Medellín, Colombia.
[4] Universidad Pontificia Bolivariana, Colombia.
[a] Cardiology Fellow.
[b] Internal Medicine Resident.
[c] Internist.
[d] Cardiologist.
[e] Echocardiography Fellow.
[f] Clinical Cardiologist.

Correspondence
Mauricio Andrés Murillo Moreno.
Circular 4#72-24 Laureles, Medellín, Colombia.

E-mail
maomoreno9410@gmail.com

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ABSTRACT

Endomyocardial fibrosis or Davies' disease is a rare cause of restrictive cardiomyopathy. It is characterized by the deposition of fibrous material in the endocardium, leading to rapidly progressive heart failure. Both ventricles are most commonly affected, with isolated involvement of the right ventricle being less common. The clinical presentation of this condition is based on symptoms of right heart failure, although arrhythmias and conduction disturbances may also be present. The treatment is determined by the control of congestion and surgical intervention in symptomatic patients. We present the first case of isolated right ventricle endomyocardial fibrosis in Colombia, describing the clinical, etiological, imaging and management characteristics, in order to provide the medical community with an approximate understanding of this disease, focusing on an unusual form of presentation.

Keywords: Endomyocardial Fibrosis; Cardiomyopathy, Restrictive; Ventricular Dysfunction, Right (Source: MeSH-NLM).

RESUMEN

Fibrosis endomiocárdica aislada de ventrículo derecho: presentación atípica de una rara enfermedad. Reporte de caso

La fibrosis endomiocárdica o enfermedad de Davies es una causa poco frecuente de miocardiopatía restrictiva. Se caracteriza por el depósito de material fibroso en el endocardio que conlleva a insuficiencia cardiaca rápidamente progresiva. Con mayor frecuencia se comprometen ambos ventrículos, siendo menos común el compromiso aislado del ventrículo derecho. La presentación clínica de esta entidad se basa en síntomas de falla cardiaca derecha, aunque las arritmias y los trastornos de la conducción también pueden estar presentes. El tratamiento está determinado por el control de la congestión y la intervención quirúrgica en pacientes sintomáticos. Presentamos el primer caso de fibrosis endomiocárdica aislada del ventrículo derecho en Colombia, describimos las características clínicas, etiológicas, imagenológicas y de manejo, con el fin de entregar a la comunidad médica una comprensión aproximada de esta enfermedad enfocándonos en una forma inusual de presentación.

Palabras clave: Fibrosis Endomiocárdica; Cardiomiopatía Restrictiva; Disfunción Ventricular Derecha (DeCS-BIREME).

Introduction

Endomyocardial fibrosis (EMF) is a rare cause of restrictive cardiomyopathy [1]. Despite being first reported 75 years ago [2], it remains a poorly studied and underdiagnosed condition. [1] The etiology is unclear, but it is thought to be associated with nutritional, infectious, or autoimmune factors. [1-3,4] The natural history of the disease includes an acute inflammatory phase with necrosis, a transitional phase, and a chronic phase characterized by endocardial fibrosis. [1-5] While biventricular involvement is the typical presentation, isolated right ventricular involvement is less common. [6] We present the first reported case of isolated right ventricular EMF in Colombia, highlighting its clinical and imaging characteristics, etiology, and available management options for right ventricular involvement. This report aims to provide the medical community with valuable insights into this rare and poorly understood condition, enhancing its diagnosis and management.

Case report

A 72-year-old female patient, from an urban area, with a history of hypertension and no recent travel history, presented with 20 days of dyspnea and lower limb edema. She was admitted in generally good condition, with a blood pressure of 139/100 mmHg, a heart rate of 67 beats per minute, a respiratory rate of 20 breaths per minute, and an oxygen saturation of 97%. Physical examination revealed jugular venous distention, rhythmic heart sounds without murmurs, clear breath sounds, and lower limb edema.

Diagnostic tests were performed, including a transthoracic echocardiogram, which showed normal anatomy and function of the left ventricle and atrium, an enlarged right atrium, and a dilated right ventricle at the basal portion with obliteration of the distal portion. The basal contractility was normal, but there was restricted mobility in the mid and apical segments of the free wall, with alterations in the free wall architecture in these segments, showing heterogeneous echogenicity and mild pericardial thickening. The contrast-enhanced imaging with microbubbles

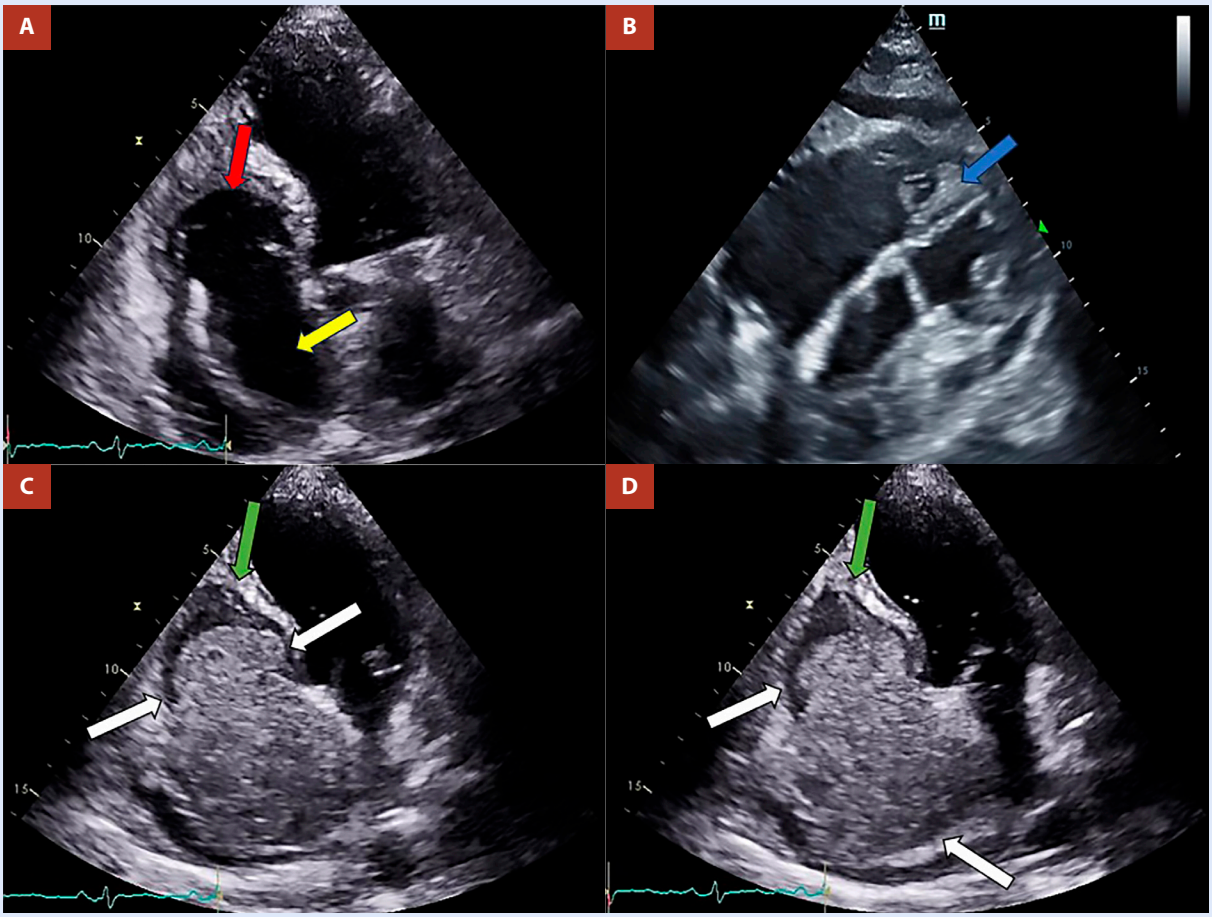

Figure 1. Transthoracic echocardiogram. Obliteration of the right ventricle (1A, red arrow), increased density of the moderator band (1B, blue arrow), endomyocardial plaques >2 mm thick (1C, green arrow), dilation of the right atrium (1A, yellow arrow) without involvement of the left ventricle. The agitated saline test clearly defined the endocardial border (1C-D, white arrow).

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more clearly delineated the affected area **(Figure 1)**, while other echocardiographic parameters are listed in **Table 1**. Laboratory tests revealed eosinophilia, elevated blood urea nitrogen (BUN) suggesting acute kidney injury, elevated N-terminal pro B-type natriuretic peptide (NT-proBNP) as an indicator of cardiac congestion, and hyperlactatemia as a sign of tissue hypoperfusion **(Table 2)**.

Based on the clinical, laboratory, and echocardiographic findings, isolated right ventricular EMF was suspected. Cardiac magnetic resonance imaging (MRI) showed late gadolinium enhancement in the subendocardial region, with additional findings in the right ventricle and atrium, confirming the presence of EMF **(Figure 2)**. A biopsy of the right ventricle demonstrated fibrous thickening of the right ventricular wall **(Figure 3)**. Due to the presence of eosinophilia, additional studies were conducted, including anti-neutrophil cytoplasmic antibodies (ANCA), IgG levels, vitamin B12 levels, liver profile, serial stool tests, flow cytometry, urinalysis, and chest CT, all of which returned normal results.

The patient was started on therapy with furosemide and ivermectin. After a few days, the eosinophilia resolved. Given the severe involvement of the right ventricle, heart transplantation was considered as a curative treatment. However, the patient had surpassed the age limit for this therapy, and thus the intervention was not pursued. Symptomatic management with inotropic support was offered. She received levosimendan infusion, resulting in a decrease in serum creatinine, improved lactate clearance, and clinical improvement. She was discharged with furosemide, spironolactone, losartan, and empagliflozin, with a plan for intermittent inotropic support with levosimendan.

Table 1. Transthoracic echocardiogram.

Echocardiographic parameter	Result	NV
Ejection fraction	55%	>50%
Left ventricular mass index	40 g/m^2	43-95 g/m^2
LV fractional shortening	55%	27-45%
Septum in diastole	0,7 cm	0,6-0,9 cm
RV/LV ratio	0,7	0,6-0,8
RV free wall thickness	10 mm	1-5 mm
Average mitral E/e' ratio	8.01	<15%
RV free wall strain	-17,4	-20 to -38%
TAPSE	13 mm	17-31 mm
RV TDI	7 cm/s	9,5-18,7 cm/s
Fractional area change	30%	35-63%
PSAP	33 mmHg	18-30 mmHg
Indexed left atrial volume	18 mL/m2	16-35 mL/m^2
Indexed right atrial volume	46 mL/m2	15-27 mL/m^2
Estimated CVP	8 mmHg	2-6 mmHg
Estimated cardiac output	2,1 L/min/m^2	2,4-4,2 L/min/m^2
Pericardium adjacent to RV wall	5 mm	<2 mm

LV: left ventricle. RV: right ventricle. TAPSE: tricuspid annular plane systolic excursion. TDI: tissue doppler imaging. PSAP: pulmonary systolic artery pressure. CVP: central venous pressure. NV: normal value.

Table 2. Laboratory results.

Parameter	Result	NV
Complete blood count		
Leukocytes	8,25 x10^3/uL	3,8 - 10,8 x10^3/uL
Neutrophils	4,58 x10^3/uL	1,82 - 7,47 x10^3/uL
Lymphocytes	1,77 x10^3/uL	1,16 - 3,33 x10^3/uL
Eosinophils	1,9 x10^3/uL	0,02 - 0,32 x10^3/uL
Hemoglobin	13 g/dL	10,8 - 13,3 g/dL
Hematocrit	44%	33,4 - 40,4 %
Platelets	175 x10^3/uL	150 - 445 x10^3/uL
Serum creatinine	1,99 mg/dL	0,2 - 1,2 mg/dL
Blood urea nitrogen	28,7 mg/dL	7 - 18 mg/dL
NT-proBNP	3789 pg/dL	< 300 pg/dL
Serum lactate	2,5 mmol/L	< 1,2 mmol/L

NT-proBNP: N-terminal pro B-type natriuretic peptide. NV: normal value.

Discussion

Over the past 75 years since the first case of EMF was described, its prevalence has increased in sub-Saharan Africa, with isolated cases reported in India [2], Asia, and Latin America, including Colombia. [7,8] It affects both men and women equally [9], with ages of presentation ranging from 24 to 67 years. [6] Biventricular involvement is the most common, occurring in 53% of cases, followed by isolated left ventricular involvement in 29%, and only 18% with isolated right ventricular disease [6], indicating that our case falls within the less frequent category and is the first reported in Colombia to date.

The etiology remains unclear, though associations have been found with magnesium deficiency and high consumption of cerium, which is present in tubers such as cassava. There also appears to be an association with diseases such as eosinophilic leukemia, Löffler's disease [4], Behçet's disease [3], and parasitic infections like *Schistosoma mansoni*. [1] In our patient, eosinophilia

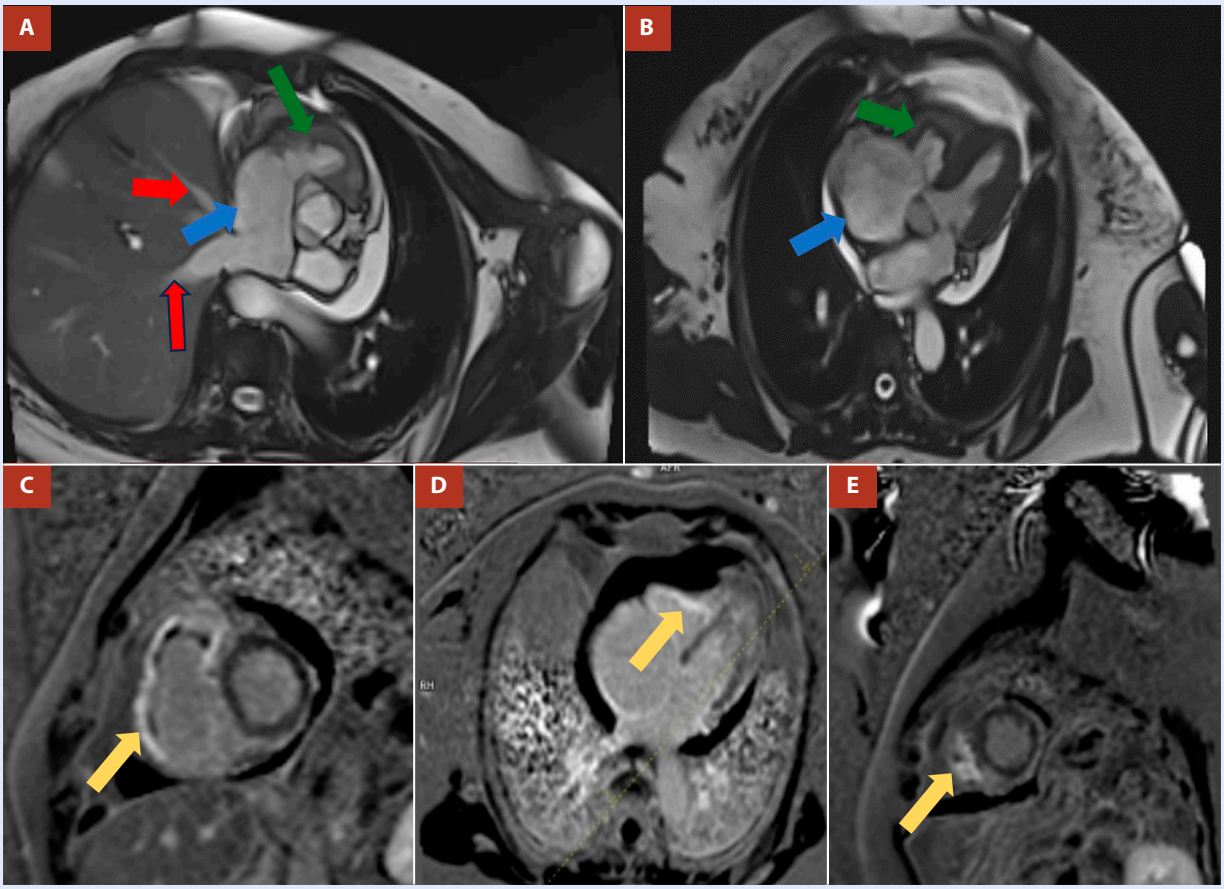

Figure 2. Cardiac magnetic resonance imaging. Dilation of the right atrium (blue arrow), obliteration of the right ventricle (green arrows), contrast reflux into the dilated hepatic veins (red arrows) due to increased systemic venous pressures, subendocardial enhancement in the mid and apical regions of the right ventricle representing areas of fibrosis (yellow arrows).

was observed, but it resolved, and no secondary etiology was found despite various tests. While EMF is classified as a tropical disease, which correlates with the tropical climate of Colombia (the patient's region of origin), isolated right ventricular involvement has been reported in non-tropical areas, somewhat questioning this hypothesis. [5] Ethnic origin, poverty, and age are also risk factors associated with the disease. [6]

The natural history of the disease progresses in three stages. The first is a phase of necrosis resulting from an acute inflammatory response (pancarditis), followed by a transient phase with the formation of endocardial thrombi, and finally a chronic phase with the deposition of fibrous material in the endocardium, leading to rapidly progressive heart failure with systemic congestion, as seen in our patient. Echocardiographic, MRI, and histopathological findings suggest that the patient is in the final stage of the disease. [1-5]

In cases of isolated right ventricular involvement, fibrosis extends from the ventricular apex to the subvalvular apparatus, without affecting the tricuspid valve. Valve insufficiency may occur due to defects in coaptation. Additionally, the inflow tract and papillary muscles are affected, but the right ventricular outflow tract remains unaffected, as observed in the reported case. [1-4] Histologically, there is endocardial thickening due to the deposition of dense fibrous tissue that extends into the underlying myocardium, forming septa and surrounding intramyocardial vessels, similar to what was seen in the biopsy of our patient. [10]

Isolated right ventricular involvement may present in asymptomatic patients or those with signs and symptoms of right heart failure. Atrial fibrillation occurs in more than 30% of cases, and ventricular arrhythmias and conduction abnormalities, such as first-degree atrioventricular block and/or right bundle branch block, are common. [1-9] Intracavitary thrombi, pulmonary embolism, and subsequent pulmonary hypertension [5] may also be present. Of these findings, only signs and symptoms of right heart failure were observed in our case, with no evidence of conduction abnormalities or arrhythmias. Transthoracic echocardiography suggests the diagnosis, while MRI is the preferred technique in developed countries. [4] Imaging reveals right ventricular endocardial thickening resembling "artificial flooring", obliteration of the trabecular portion, reduced cavity volume, tricuspid annular dilation, and regurgitation. In advanced

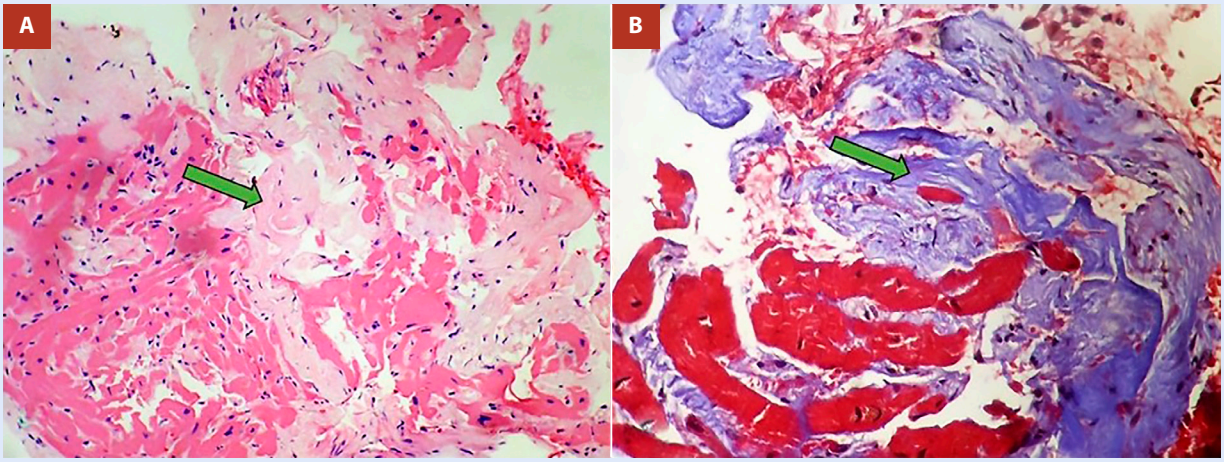

Figure 3. Right ventricle biopsy. Fibrosis of the right ventricle (A-B, green arrow), without inflammatory infiltrate, few elastic and reticular fibers, and abundant acellular collagen, without eosinophils.

stages, an apical notch due to right ventricular retraction, right atrial thrombi, pericardial effusion, and late gadolinium enhancement of the endocardium suggest the presence of endocardial fibrosis, as observed in our patient's images. [7]

The use of contrast microbubbles in echocardiography can more clearly delineate the true endocardial border and clarify the apical thrombo-inflammatory material, as seen in our case [5]. Echocardiographic diagnostic criteria include six major criteria (endomyocardial plaques >2 mm; thin endomyocardial patches (≤1 mm) in more than one area of the ventricular wall; obliteration of the ventricular apex; thrombi without severe ventricular dysfunction; right ventricular apical notch and atrioventricular dysfunction; and valvular dysfunction secondary to valve adhesion to the ventricular wall) and seven minor criteria (a ventricular wall affected by endomyocardial patches; restrictive flow through the atrioventricular valves; diastolic opening of the pulmonary valve; diffuse thickening of the anterior mitral valve leaflet; enlarged atrium with a normal-sized ventricle; M-motion of the interventricular septum and flat posterior wall; and increased density of the moderator band or other intraventricular bands).

To establish the diagnosis of EMF, two major criteria or one major and two minor criteria are required. [1-11] Our patient met one major and two minor criteria, including obliteration of the ventricular apex, the presence of endomyocardial patches on the ventricular wall, and increased density of the moderator band, respectively. Furthermore, the involvement was limited to the right ventricle **(Table 1)**. MRI, in addition to diagnosing EMF, allows for monitoring of medical and surgical treatment and more precisely delineates the fibrotic zones, which can be observed as a double V sign at the ventricular apex (appearance of three layers of normal myocardium, enhanced and thickened endocardium, and overlying thrombus). [1-7]

Medical treatment consists of managing fluid overload with diuretics and nitrates [6] and anticoagulation in cases of intracavitary thrombosis or atrial fibrillation. [12] Despite a high surgical mortality rate (10-30%), surgery can improve survival and functional capacity in the long term compared to medical treatment. [5] Surgery should be offered as soon as the patient presents symptoms, as most patients in the terminal stage have a worse postoperative prognosis and are not eligible for surgery. Surgical interventions described to date include complete endomyocardial decortication with tricuspid valve replacement and extracorporeal membrane oxygenation (ECMO) support in patients with critical hemodynamics [12], endocardiectomy with bidirectional cavopulmonary shunt [4-13], bidirectional cavopulmonary shunt without endocardiectomy [13], and total cavopulmonary connection. [14] The prognosis depends on early surgical intervention, as outcomes are poor once symptoms have worsened. [4] In our patient, medical management was chosen due to advanced age and frailty, with intermittent levosimendan support, and no further hospitalizations have occurred to date.

In conclusion, EMF is a rare and poorly understood disease that leads to restrictive cardiomyopathy with rapidly progressive heart failure and poor prognosis. Isolated right ventricular involvement is the least frequent form. Our case is the first reported in Colombia, where we highlight the advanced presentation, imaging and histopathological findings, and, through a literature review, contribute to the medical community a better understanding of this atypical presentation to improve the approach and management of this disease.

Authors' contributions

MM: conceptualization, investigation, methodology, writing - original draft, writing - review & editing. **LL:** investigation, visua-

lization. **JS:** conceptualization, resources. **LD:** conceptualization, methodology. **CS:** conceptualization, supervision, methodology, project administration.

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