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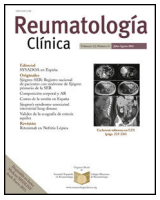

Case report

Takotsubo Syndrome in a Rheumatoid Arthritis Patient Under Tofacitinib: A Case Report

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ABSTRACT

We describe a case of a 57-year-old white woman treated for rheumatoid arthritis (RA) with tofacitinib 10 mg daily (started one year ago) and prednisolone 5 mg daily. She presented to the emergency department with a tight squeezing chest pain and shortness of breath for 7 h and the clinical evaluation revealed regional systolic dysfunction of the left ventricle, mimicking a myocardial infarction, in the absence of angiographic evidence of obstructive coronary artery disease or acute plaque rupture. All changes were transient and resolved completely within 4 days. The diagnosis of Takotsubo cardiomyopathy (TKM) was established. This is, as far as we know, the first report of a case of TKM in a RA patient taking tofacitinib. Although the association has not been previously described and the precise cause cannot be identified in this patient, the association with tofacitinib should be considered given the etiopathogenic rationale and the absence of any other identifiable cause.

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Síndrome de takotsubo en un paciente con artritis reumatoide tomando tofacitinib: reporte de un caso

Palabras clave:
Artritis reumatoide
Tofacitinib
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Cardiomiopatía

RESUMEN

Describimos el caso de una mujer blanca de 57 años tratada por artritis reumatoide (AR) con tofacitinib 10 mg al día (iniciado hace un año) y prednisolona 5 mg al día. Acudió al servicio de Urgencias con dolor torácico opresivo y dificultad para respirar durante 7 h y la evaluación clínica reveló disfunción sistólica regional del ventrículo izquierdo, simulando un infarto de miocardio, en ausencia de evidencia angiográfica de enfermedad arterial coronaria obstructiva o aguda. rotura de placa. Todos los cambios fueron transitorios y se resolvieron por completo en 4 días. Se estableció el diagnóstico de miocardiopatía de takotsubo (TKM). Este es, hasta donde sabemos, el primer informe de un caso de TKM en un paciente con AR que toma tofacitinib. Aunque la asociación no se ha descrito previamente y no se puede identificar la causa precisa en este paciente, la asociación con tofacitinib debe considerarse dada la justificación etiopatogénica y la ausencia de cualquier otra causa identificable.

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Introduction

Concerns of adverse cardiovascular events with the use of tofacitinib have been raised, but no case of cardiomyopathy has been reported so far.[1,2]

We describe a rare case of Takotsubo cardiomyopathy (TKM) in a rheumatoid arthritis (RA) patient treated with tofacitinib.

Clinical observation

A 57-year-old white woman was diagnosed with a seropositive for anti-citrullinated protein antibody RA 5 years ago. She was treated with tofacitinib 10 mg daily (started one year ago) and prednisolone 5 mg daily. Initially, the patient experienced adverse events with the first 2 attempted csDMARDs (liver toxicity under methotrexate and hypertension with leflunomide) and was refractory to multiple biologic agents (etanercept, golimumab and tocilizumab, were consecutively tried) and her disease was refractory to multiple biologic agents (etanercept, golimumab and tocilizumab). She had no other cardiovascular risk factors. Previous electrocardiogram (ECG) was unremarkable.

She presented to the emergency department with an acute onset tight squeezing chest pain lasting for 7 h. Upon admission, we observed the following vital signs: blood pressure of 110/60 mmHg, heart rate of 90 beats per minute, respiratory rate of 18 breaths per minute and oxygen saturation of 98% on room air with a pulse oximeter. Her heart sounds were regular with no murmurs and lung examination was normal. Her cardiac enzymes were elevated, presenting with a creatine phosphokinase-MB of 5.7 ng/mL (normal < 5 ng/mL) and a troponin I of 1.16 ng/mL (normal < 0.04 ng/mL). She had a normal complete blood count. Thyroid function and cortisol levels were normal. ECG showed pathologic Q-waves in leads V1-V3 and a negative T-waves in lead V4. Cardiac catheterization was performed, demonstrating normal coronary arteries, circumferential akinesia of the apex and a poor left ventricular systolic function (LVEF) (of approximately 40%], consistent with the diagnosis of TKM. Myocardial perfusion scintigraphy performed on day 6 showed no alterations; LVEF was estimated at 38%.

The patient received supportive care and had an uneventful hospital stay with complete resolution of symptoms and normalization of cardiac enzymes in 48 h. Three days after, prior to hospital discharge, she performed an echocardiogram that revealed a preserved LVEF (estimated at 55%), with normal wall thickness and absence of wall motion abnormalities.

Treatment with tofacitinib was stopped and the patient started abatacept. One year later, the patient was reassessed with a cardiac magnetic resonance, showing no abnormalities in segmental motility/contractility or areas of late gadolinium enhancement, estimating LVEF at 58%.

Discussion

The diagnosis of TKM was made in this patient once all four Mayo Clinic diagnostic criteria were present: transient left ventricular systolic dysfunction, absence of obstructive coronary disease, new electrocardiographic abnormalities and absence of pheochromocytoma.[3]

Several pathophysiological mechanisms have been proposed for TKM, but one of the most unanimous is a catecholamine surge, supported by a number of features, including its association with emotional stress and with the exposure to supratherapeutic doses of catecholamines.[4–6] In a 2017 article, reviewing all the 157 drug-induced TKM cases published in the literature until then, the authors conclude that over two-thirds of drug-induced TKM cases were due to catecholamine stimulation.[7] Moreover, a recent study in rats, who were given tofacitinib, evaluated the relationship between cardiovascular hemodynamics and plasma norepinephrine (NE) levels, showing a dose-dependent increase in circulating NE levels, which was maintained during 14 days of tofacitinib administration. However, this increase in plasma NE concentrations presumably reflects a reflex response to direct vasodilation.[8] Further studies in humans, are needed to clarify this finding. It may represent the link between tofacitinib and TKM.

This is, to our knowledge, the first report of a case of TKM in a patient taking tofacitinib. A cause cannot be clarified with certainty, however the association with tofacitinib should be considered given the etiopathogenic rationale and the absence of any other identifiable cause.

Conflict of interest

None.

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