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Kasuistika | Case report

Late recurrence of fulminant myocarditis related to HSS/DRESS

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SOUHRN

Hypersenzitivní syndrom (hypersensitivity syndrome)/DRESS (drug rash with eosinophilia and systemic symptoms, DRESS) syndrom (jiný termín i polékový hypereozinofilní syndrom) je vzácně se vyskytující alergický, život ohrožující nežádoucí účinek některých léků postihujících i srdeční funkci, s vysokou mortalitou a dlouhodobým srdečním selháním.
U 28leté ženy došlo dva měsíce po stanovení diagnózy DRESS na podkladě podávání sulfasalazinu k rozvoji fulminantní eozinofilní nekrotizující myokarditidy. Po intenzivní multiorgánové podpoře se pacientka zotavila a její srdeční funkce se normalizovala. O osm měsíců později došlo k recidivě s rychlou progresí k refrakternímu kardiogennímu šoku a úmrtí.
V článku upozorňujeme na vzácné a nedostatečně diagnostikované onemocnění s nepříznivou prognózou, které je nutno včas odhalit a léčit.

ABSTRACT

Hypersensitivity Syndrome or Drug Reaction with Eosinophilia and Systemic Symptoms (HSS/DRESS) is a rare pharmacological hypersensitivity reaction that may include cardiac involvement, with high mortality and long-term heart failure.
A 28-year-old woman, two months after the diagnosis of DRESS secondary to sulfasalazine, developed fulminant eosinophilic necrotizing myocarditis. After intensive multiorgan support, recovery and cardiac function normalization were observed. Eight months later presented a recurrence with fast progression to refractory cardiogenic shock and death.
We alert to a rare and underdiagnosed pathology, with adverse prognosis, needing timely identification and treatment.

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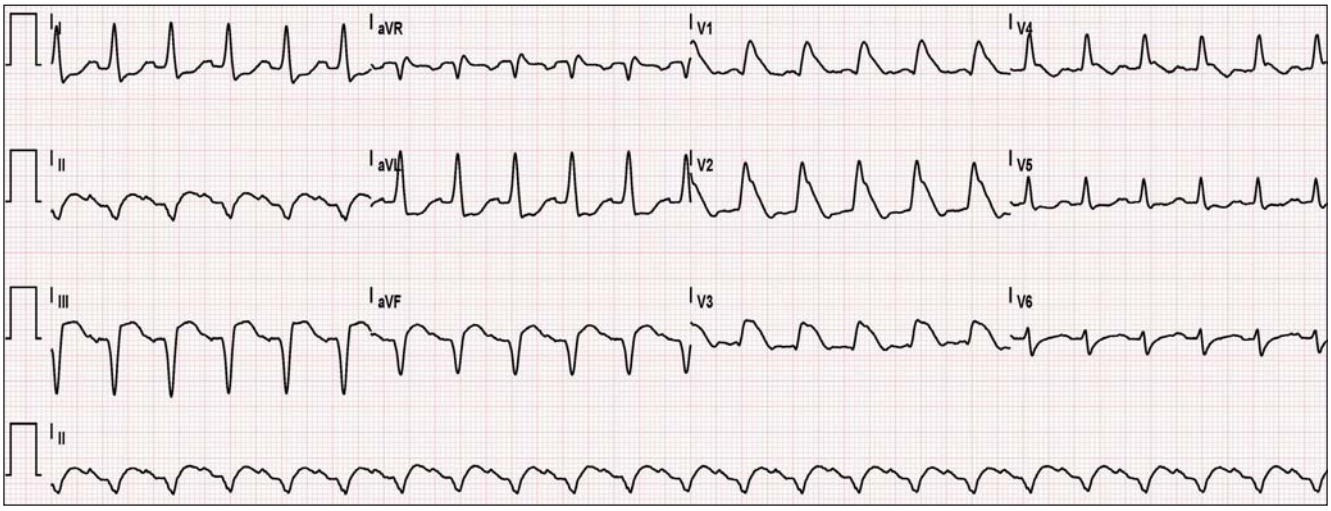

Fig. 1 – EKG on admission – atrial tachycardia with aberrant ventricular conduction.

Introduction

Hypersensitivity Syndrome or Drug Reaction with Eosinophilia and Systemic Symptoms (HSS/DRESS) is a rare reaction of delayed pharmacological hypersensitivity [1]. In its pathogenesis appear to be relevant a drug-specific T-cell mediated immune response and the sequential reactivation of Herpes virus [2].

Myocarditis is an underdiagnosed complication with high mortality and long-term heart failure, that may present as hypersensitivity myocarditis (less severe, without myocardial necrosis) or eosinophilic necrotizing myocarditis (mortality >50%). Mortality can be reduced with early diagnosis, immediate interruption of the responsible drug and treatment with immunosuppressants [1].

Clinical case

A 28-year-old woman with psoriatic arthritis was diagnosed with DRESS (definite RegiSCAR score of 6) secondary to sulfasalazine. Serologies demonstrated past contact (IgG+/IgM–) with Epstein-Barr virus (EBV), Cytomegalovirus (CMV) and Human herpesvirus (HHV) types 6 and 7. High titers of HHV-6 were detected in the blood.

Two months later, still under corticosteroid and without re-exposure to sulfa compounds, started to suffer from fatigue, malaise and retrosternal pain. She presented with regular tachycardia (160 bpm), a blood pressure of 124/67 mmHg and no clinical signs of heart failure (HF). The electrocardiogram (EKG) (Fig. 1) showed atrial tachycardia with aberrant ventricular conduction. The echocardiogram revealed diffuse left ventricular (LV) hypokinesia (ejection fraction [EF] of 40%), but no other changes. There was neutrophilic leukocytosis (but no eosinophilia) and increased values of C-reactive protein (CRP) and troponin. Ionogram, renal function and thyroid function were normal.

Myocarditis, possibly related to DRESS, was considered the most likely diagnosis and beta-adrenergic blocker and corticosteroid were started. However, there was a rapid evolution to cardiogenic shock and multiorgan failure. Electrophysiological study identified the site of atrial tachycardia, which stopped with the mechanical pressure of the catheter, remaining in sinus rhythm.

In the first 24 hours, she kept deteriorating, requiring increasing doses of inotropes, invasive mechanical ventilation and continuous kidney replacement technique. Eosinophilic necrotizing myocarditis became the most plausible diagnosis.

During the next 3 days, clinical recovery was observed and multiorgan-support therapies were tapered and stopped. Signs of HF improved significantly over the next 10 days, under beta-blocker, angiotensin-converting-enzyme inhibitor and diuretics, and functional LV systolic recovery (LV EF of 64%) was also observed. Serological reactivation of CMV was observed (IgG+/IgM+) and high titers of CMV and EBV were detected in the blood (but not HHV-6). Human immunoglobulin and valganciclovir were added to therapy. Myocardial biopsy revealed multifocal interstitial lymphocytic infiltrate with focal necrosis and viral genomes of EBV and Parvovirus B19 were identified in the samples. Cardiac magnetic resonance imaging (CMR) didn't show myocardial inflammation or fibrosis.

The patient was discharged at day 23 under therapy with prednisolone, valganciclovir, carvedilol, perindopril, furosemide and spironolactone. She was regularly monitored during follow-up, showing increasing effort tolerance, normal LV EF and laboratorial stability. Diuretics and perindopril were discontinued and corticosteroid was tapered, maintaining valganciclovir prophylactically.

Eight months after the myocarditis onset (11 months after the inaugural episode of DRESS), still under prednisolone (15 mg/day) and valganciclovir, and with persistently negative viral loads, she acutely developed fatigue, malaise and palpitations. She was abroad and the situation evolved again to cardiogenic shock and multiorgan failure, requiring air transference to the closest tertiary center, where extracorporeal membrane oxygenation was performed. However, after sedation withdrawal,

there was no consciousness recovery, justified by anoxic encephalopathy. She died two weeks later and autopsy was not performed.

Discussion

In this patient, the myocardial biopsy allowed the confirmation of myocarditis in probable relation with DRESS. The absence of eosinophilic infiltrate might be attributed to the often focal nature of infiltrates, the use of corticosteroids and the delay on the myocardial biopsy execution (after 2 weeks of therapy) [3,4]. CMR was also performed only after 2 weeks of therapy, which may also explain the absence of changes [5].[5]

The remarkably fast improvement after the interruption of tachyarrhythmia (which was probably caused by atrial inflammation) suggests it might have also contributed to the HF condition.

It is interesting to notice that sequential reactivation of Herpes virus occurred, with demonstrated HHV-6 in the first episode and EBV and CMV in the second episode. This corroborates the theory that, in DRESS, sequential activation of Herpes virus perpetuates inflammation in a process that is similar to that seen in graft versus host disease and is likely to be responsible for the development of multi-organ failure following discontinuation of the causative agent [2].

It remains controversial whether viral reactivation is a causative factor or a consequence of cell activation [1]. Valganciclovir is only recommended in severe cases with demonstrated reactivation of HHV-6 or CMV [6] and human immunoglobulin is even more controversial [7]. Usage of these two drugs was a joint decision between specialists in cardiology and infectious diseases.

The case reported had an unfavorable outcome despite a multidisciplinary, evidence-based approach. Late recurrences of DRESS occur in up to 20% of cases, even without re-exposure, with late fulminant myocarditis as a possible complications [6]. We point out to a very rare and severe condition to which timely identification is critical.

Conflict of interest
None declared.

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Ethical statement
Authors state that the research was conducted according to ethical standards.

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