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Fulminant myocarditis as a late sequelae of DRESS-2 cases

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To the editor:

Case 1

A 31 year-old African-American woman was diagnosed with drug-induced hypersensitivity syndrome/ drug rash with eosinophilia and systemic symptoms (DIHS/DRESS) following a presentation of fevers, facial edema, cervical lymphadenopathy, a diffuse morbilliform eruption (Figure 1), leukocytosis with 11% eosinophilia, acute renal failure, and hepatitis. A biopsy of her eruption showed a vacuolar interface dermatitis with numerous apoptotic keratinocytes throughout the epidermis. She was treated with systemic corticosteroids, cyclosporine, and IVIG due to a relapsing-remitting course of disease. Her new medications at original presentation consisted of trimethoprim-sulfamethoxazole for a respiratory tract infection and zonisamide for migraines. She had a history of a prior drug reaction to celecoxib.

Four months after her initial presentation, she presented to the ER with acute EKG inferior ST-T segment elevations and elevated cardiac enzymes. Although a rash was still present, she had a normal level of peripheral eosinophils. Immediate cardiac catheterization showed normal coronary arteries and a decreased ejection fraction. Shortly after catheterization, the patient suffered cardiac arrest. She was successfully resuscitated, but further evaluation showed worsening LV function and development of a pericardial effusion. Two days later, the patient died due to a second cardiac arrest shortly after an intra-aortic balloon pump was placed for refractory hypotension and pericardial tamponade. Post-mortem examination showed cardiomegaly with geographic mottling within the myocardium and punched-out liquefactive necrosis. Histologically, there was a diffuse eosinophilic myocarditis with mononuclear infiltrate, scattered giant cells, and secondary liquefactive necrosis.

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Conflicts of interest: The authors have no conflict of interest to declare.

Case 2

A 28 year-old African-American woman was diagnosed with DRESS/DIHS following several months of a waxing and waning diffuse morbilliform eruption. She originally presented with facial edema, fevers, cervical lymphadenopathy, hepatitis, and leukocytosis with 30% eosinophilia. These clinical signs appeared shortly after a new medication, sulfasalazine, was started. A skin biopsy revealed a perivascular infiltrate of lymphocytes and eosinophils. She was treated with varying doses of oral prednisone for a number of months.

Four months after her original presentation, she was seen at the ER with diffuse ST-T segment elevations on EKG and elevated cardiac enzymes. Her skin was clear however, her labs revealed a marked leukocytosis with eosinophilia of 30%. Treatment with intravenous corticosteroids was begun, but the patient rapidly decompensated. An urgent cardiac catheterization revealed normal coronary arteries but a diffusely hypokinetic left ventricle and a profoundly decreased ejection fraction. At that time, an intra-aortic balloon pump was placed.

Approximately 24 hours after arrival, the patient suffered cardiac arrest. She was successfully resuscitated and was taken for open myocardial biopsy and placement of a left-ventricular assist device (LVAD). The biopsy showed a lymphocytic and eosinophilic infiltrate, consistent with myocarditis. She was treated with high dose IV methylprednisolone (1gm/day), IVIG (1gm/kg/day $\times$ 2 doses), and mycophenolate mofetil during her hospital course. Serial echocardiograms showed slow but progressive improvement in left ventricular ejection fraction, and the LVAD was explanted after 53 days. A mitral-valve replacement was also performed at this time, due to ruptured chordae tendinae.

The patient continued to improve and was discharged 71 days after admission. She currently is doing well after two years but required mycophenolate mofetil and low dose prednisone for one year as several attempts to taper off the immunosuppressive agents resulted in elevation of the hepatic transaminases and ESR.

Acute necrotizing eosinophilic myocarditis (ANEM) is a severe form of myocarditis that can occur in DRESS as demonstrated by these two cases. The presentation of ANEM is similar to an acute coronary event with chest pain, ST-segment elevation, elevated cardiac markers, but with normal coronary arteries on angiography. The course progresses rapidly into a fulminant heart failure. Mortality is greater than 50%, and median survival is a few days. Definitive diagnosis is with an endomyocardial biopsy that reveals an eosinophilic and lymphocytic infiltrate with associated myocyte necrosis although the infiltrate may be patchy in nature.¹ The treatment is high-dose corticosteroids with pharmacologic and/or mechanical ventricular support, as used in our second case.^{2, 3}

To our knowledge, this is the first case of DRESS-associated ANEM treated with a ventricular assist device, and we recommend its use as a life-saving treatment if rapidly deteriorating cardiac function develops in these patients.

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Figure 1.
Patient 1. Diffuse erythematous and violaceous papules coalescing into plaques