Not the usual suspects: DRESS secondary to carvedilol

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Carvedilol, a dual alpha and beta receptor blocker, is a treatment choice in heart failure with reduced ejection fraction with proven mortality benefit. Pharmacodynamic reactions, such as dizziness and bradycardia, occur frequently; however, idiosyncratic reactions are rare. We describe a case of probable drug reaction with eosinophils and systemic symptoms (DRESS) secondary to carvedilol.

DRESS is a potentially life-threatening reaction, generally due to liver failure, and has an estimated mortality rate of 5–10%. It is a predominantly clinical diagnosis, which complicates assessment. The European Registry of Severe Cutaneous Adverse Reactions (RegiSCAR) have devised a scoring system based upon symptoms, organ involvement and clinical course.

A literature search identified four case reports of idiosyncratic reactions to carvedilol. Liver derangement and pruritus, toxic epidermal necrolysis, Stevens-Johnson and pneumonitis were described.

Case report

A 74-year-old New Zealand European woman was diagnosed with idiopathic left ventricular failure. Carvedilol, furosemide, cilazapril, atorvastatin and aspirin were initiated.

One month later, she presented with a week history of progressive nausea, vomiting, upper abdominal pain and diarrhoea, with no rash or fever. Weight had decreased 4kg due to furosemide titration. Examination revealed mild abdominal tenderness in the right upper quadrant; there was no rash or lymphadenopathy. The white blood count was elevated (16.7x10⁹/L), eosinophils 1.5x10⁹/L. Eosinophils peaked at 15.8x10⁹/L, five days into admission. She had acute kidney injury (creatinine of 232μmol/L) and LFT derangement, which peaked four days into admission (ALP 394U/L, ALT 114U/L, AST 79U/L, GGT 145U/L, bilirubin normal). Abdominal ultrasound was unremarkable.

Cilazapril was stopped two days prior to admission, furosemide on admission, and carvedilol the following day.

Differentials for the eosinophilia, including parasitic infection, atopy, vasculitis and eosinophilic myocarditis, were investigated. Stool specimen was negative for giardia, cryptosporidium. Strongyloides serology and ANCA testing were negative. Cardiac MRI confirmed severe left ventricular systolic impairment, but showed no evidence of myocarditis or infiltrative disease.

Her only pre-existing medications were omeprazole and colecalciferol. She had self-ceased aspirin after 1–2 weeks as she thought it unnecessary. Atorvastatin was continued throughout.

Symptoms improved following carvedilol cessation. Eosinophils gradually improved to 4.7x10⁹/L 15 days later. Furosemide was reintroduced prior to discharge, and cilazapril one week after discharge, given symptoms had only improved after cessation of carvedilol. Eosinophils and LFT have normalised two months following discharge without symptom recurrence.

Discussion

The diagnosis of DRESS is difficult due to the initiation of multiple new medications concurrently and gradual symptom onset. The normal eosinophils and LFTs during her initial heart failure admission provide an objective measure for delayed onset. Carvedilol is the most likely culprit given the proximity to symptom onset and the...
resolution of both clinical and biochemical abnormalities on cessation, as well as the sustained response after restarting furosemide and cilazapril.

In terms of organ involvement, there is definite liver involvement, and probable gastrointestinal involvement based on symptoms. It is difficult to determine if the kidney injury is purely the result of furosemide in the context of dehydration, or whether this also represents organ involvement.

Based on the RegiSCAR scoring system, a score of 4 would be assigned; 1 for lack of fever, 2 for eosinophilia, 2 for organ involvement of liver, gut and kidney, 1 for negative investigations. This would be consistent with a probable diagnosis of DRESS.

**Conclusion**

Carvedilol is the likely cause of probable DRESS given the temporal relationship to the symptoms, eosinophilia and LFT derangement, that resolved on cessation. This is the first time this medication has been associated with DRESS. It presents an important learning point regarding consideration of not just carvedilol, but all medications in cases of DRESS, not just the ‘typical’ drugs.

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**Competing interests:**
Nil.

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