Brief Report

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Pericardial effusion: A rare side effect of clozapine

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Abstract

A pericardial effusion is a rare but very serious side effect of clozapine. We present a case of a 50-year old female, who developed fever and tachycardia during the initial period of treatment with clozapine. This case highlights the importance of having a high degree of suspiciousness for occurrence of a pericardial effusion.

Key words: pericardial effusion, clozapine, schizophrenia

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Introduction

Among patients diagnosed to have schizophrenia, about 30% are known to develop resistant schizophrenia, for which clozapine is currently considered the drug of choice (1). Clozapine use is reported to be associated with agranulocytosis, weight gain, insulin resistance, seizures, as well as cardiac side effects such as myocarditis or cardiomyopathy (1). We report a case of a patient who developed pericardial effusion while on clozapine treatment, which is considered as a rare side effect, with only a few published reports (2).

Case Report

A 50-year-old female, diagnosed to have resistant schizophrenia, was started on treatment with clozapine. Treatment was commenced after an initial workup, which included full blood count, liver and renal function tests, C-reactive protein (CRP), electrocardiogram (ECG) and echocardiography, all of which were normal. She developed a fever spike (101.1 F) on the fourth day of clozapine while on a daily dose of 75 mg of clozapine. There were no systemic or other constitutional complaints and the physical examination was unremarkable, except for hyperthermia (101.1 F) and a tachycardia (104 b.p.m). Her total white cell count (WBC) was 14140/µl, with a neutrophil count and eosinophil count of 8730/µl and 1060/µl respectively. Her CRP value continued to increase from 121.2 mg/l on day 4 to 132.5 mg/l on day 5. Her erythrocyte sedimentation rate (ESR) also increased from 60 mm/hr on day four to 80 mm/hr on day 6. The septic screening, which included urine and blood cultures, were negative. Serological analysis for viral infections such as Epstein Barr virus, cytomegalovirus and HIV were negative. The ECG depicted a sinus tachycardia of 110 b.p.m, with no other abnormalities. High sensitive troponin was negative (0.004 ng/ml). Echocardiography done on the 5th day demonstrated a thin rim of pericardial effusion, with normal right and left ventricular systolic function. There was no echocardiographic evidence of myocarditis or endocarditis.

In the absence of any other aetiological agents, clozapine was considered as the most likely cause for the pericardial effusion and was therefore stopped. With discontinuation of clozapine, the fever spikes receded, along with the tachycardia. Furthermore, the white cell count, CRP and ESR gradually normalized within a week. Echocardiography repeated a week after discontinuation of clozapine demonstrated no residual pericardial effusion. There was no evidence of myocarditis or evidence of myocardial dysfunction.

Discussion

Clozapine is a dibenzodiazepine used in resistant schizophrenia (1). It is known to be more effective than other antipsychotics in resistant schizophrenia and is also known for its anti-suicidal effects (1).

Orthostatic hypotension and tachycardia are reported as common side effects of clozapine, while cardiovascular adverse effects such as myocarditis, pericarditis and cardiomyopathy are also documented, albeit less commonly (1). Pericardial effusion is a rare and serious adverse effect of clozapine therapy, and there are a few reported cases of sudden cardiac death attributed to myocarditis or tamponade, due to the pericardial effusion (3).

Pericardial effusion can occur as early as in the first week of initiating clozapine, hence can be hypothesized to be an acute drug reaction (4). The clinical presentation of pericardial effusion can range from mild viral-like illness to sudden death from cardiac tamponade (3). Patients usually present with fever, shortness of breath and pleuritic chest pain, while common examination findings are tachycardia and tachypnea with muffled heart sounds, depending on the size of effusion (2). Inflammatory markers are usually elevated, though troponin elevation is seen only in those with myocardial injury (2). Our patient had fever and tachycardia, but no breathing difficulties or other signs, which could be explained by the small size of the effusion found on echocardiography. Given that features such as fever and tachycardia are common and self-limiting during the initiation phase of clozapine therapy (1), a high degree of clinical suspiciousness and investigation findings will help reach the correct diagnosis (1).

In our patient, all the symptoms and investigations became less and disappeared within a week of discontinuation of clozapine, without any other intervention, which also supports the existing evidence regarding clozapine-induced pericardial effusion (5). As there is a lack of evidence regarding clozapine re-challenge following pericardial effusion, and given the seriousness of the side-effect that occurred, the patient was thereafter treated with amisulpride (3).

Conclusions

Clozapine induced pericardial effusion is a rare manifestation, and can occur as early as in the first few weeks of treatment. The condition may present with a wide range of clinical symptoms, and could be lethal if not detected. Discontinuation of clozapine results in resolution of the pericardial effusion without the need for further intervention. Baseline ECG and echocardiography should be performed in all patients to be started on clozapine treatment, and a having a high degree of clinical suspiciousness will minimize adverse outcomes.

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Statement of contribution

PDLRW, RJ and FHDSS jointly conceived and prepared the manuscript.

Declaration of interest

None declared.

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