IS CLOZAPINE SAFE TO REINITIATE IN A PATIENT WITH PREVIOUS COVID-19 VACCINE MYOCARDITIS? A CASE REVIEW

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Introduction
Clozapine-induced myocarditis (CIM) is a rare but potentially life-threatening adverse event seen to occur in approximately 7 in every 1000 cases of clozapine exposure1, most commonly between 14-21 days after drug initiation2. General prescribing guidelines recommend a degree of caution when initiating clozapine in patients with prior cardiovascular complaints.

COVID-19 mRNA vaccine-induced myocarditis (VIM) is a recently identified phenomenon seen to occur up to a rate of 3.2 per 100,000 in the high-risk subgroup of males aged 12-39 years of age, post-mRNA dose 2. The demographics of this subgroup overlap considerably with the demographics of the average outpatient prescribed clozapine, found in one Canadian study to be males aged 39.5 ± 11.8.

It is important to note that patients on clozapine are recognized to be at increased risk of COVID-19 infection and subsequent poor outcomes3, and there is a resounding consensus that the benefits of vaccination outweigh the risks. Complicating matters is the observation that COVID-19 vaccination can be associated with transient toxic clozapine levels, believed to potentially be driven by inflammation-mediated cytochrome P450 1A2 activity4.

Due to the overall uncertainty and differing hypotheses for the mechanisms behind both CIM and VIM, it is difficult to predict mechanistically if a diagnosis of one adverse reaction would be expected to predispose a patient to the other. Here, we present a case that highlights an approach to this uncertainty, and we review the paucity of literature discussing the relationship between these two rare adverse drug outcomes.

Literature Review
A focused systematic review was conducted to identify any prior studies or communications in the literature that specifically addressed a potential relationship between vaccine-induced myocarditis and clozapine-induced myocarditis. MEDLINE, PubMed, EMBASE, CENTRAL and PsycInfo were searched using the search strategy “(COVID-19 OR ‘COVID-19 Vaccines’) AND ‘Clozapine’ AND ‘Myocarditis’”. Identified studies were screened and subsequently reviewed by two independent reviewers for relevancy; discrepancies were discussed (Figure 1). This search protocol ultimately yielded one relevant communication (Dawson et al., 2021)5 discussed here.

Clozapine was safely reinitiated and uptitrated in a patient with a history of probable vaccine-induced myocarditis.

Case Summary
A 21-year-old man with treatment-resistant schizophrenia, previously maintained on clozapine in the community for three years, was admitted to hospital for medication non-compliance and psychiatric decompensation. Aside from clozapine-induced tachycardia, for which he had been prescribed a beta blocker, he had no history of adverse reactions to clozapine. Four months prior to this admission he was seen by Cardiology and diagnosed with probable mild vaccine-induced myocarditis after he received a second dose of the Moderna COVID-19 mRNA vaccine.

Upon re-initiation of clozapine, a low but persistently elevated troponin T was observed (39 - 99 ng/L). He consistently showed no signs or symptoms of myocarditis however, and a repeat ECG was normal. As advised by Cardiology, up-titrination was continued. Over the following two months the patient responded well to a maximum dose of 475 mg. The unexplained findings of persistently elevated troponin were ultimately determined to be a lab error due to assay antibody interference. Subsequent troponin I tests were normal.

Against medical advice, the patient received a third dose of COVID-19 mRNA vaccine while on a pass near the end of his admission. Aside from a briefly elevated CRP, no other clinical evidence of recurrent myocarditis was observed.

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References