High Degree Atrioventricular Block Following COVID-19 Vaccination

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KEY WORDS: atrioventricular block, complication, coronavirus disease 2019 (COVID-19) vaccination, high degree

IMAJ 2022; 24: 627–628

The coronavirus disease 2019 (COVID-19) pandemic has resulted in more than four million deaths globally. In addition to the lower respiratory system, a wide range of major organ injuries have been reported among patients infected with COVID-19. These injuries include cardiac involvement. The spectrum of cardiac manifestations includes cardiac injury, heart failure, cardiogenic shock, acute coronary syndrome, myocarditis, tachyarrhythmias, and bradyarrhythmia [1]. Different degrees of atrioventricular blocks have been reported [2].

The pathogenesis of these complications is not fully understood. Different mechanisms are proposed, including direct myocyte injury, interstitial inflammation and fibrosis, cytokine storm, plaque destabilization, and and/or hypoxia [3]. Many countries have worked toward mass vaccination using the Pfizer BioNTech (BNT162b2) COVID-19 vaccine, including Israel. We report a case of high degree atrioventricular block (AVB) following vaccination with the COVID-19 BNT162b2 vaccine.

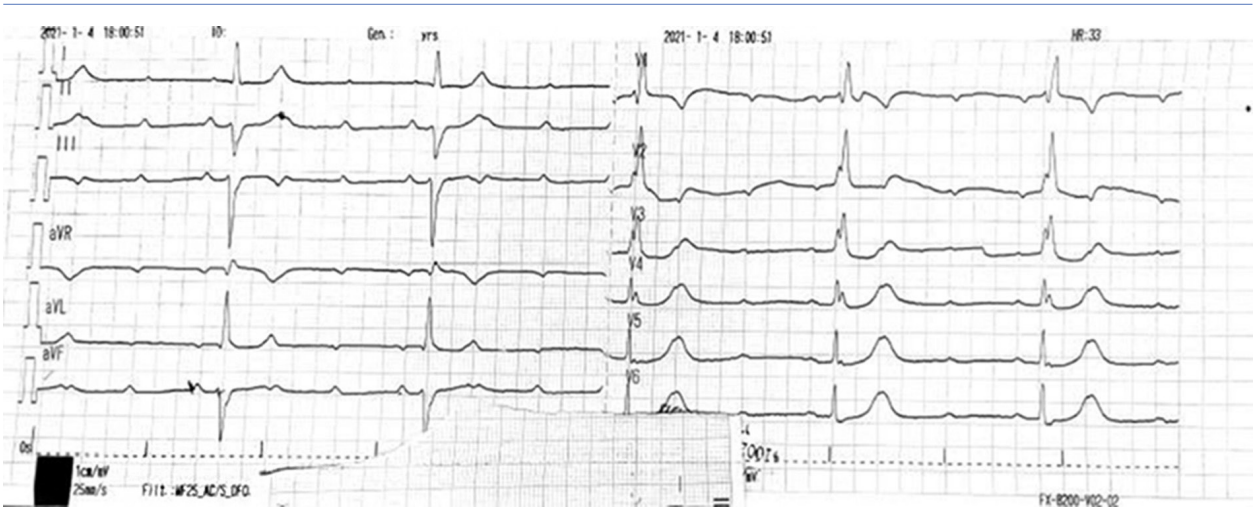
PATIENT DESCRIPTION

A 67-year-old healthy male, with no medical history or consumption of medication, was admitted to our hospital after a 4-day history of weakness and pre-syncope that started 2 days following his first vaccine dose (Pfizer, USA). The patient did not undergo any kind of treatment or use eye drops. He had no family history of heart problems. He also denied olfaction problems. He had not been outside of the country during the last year. He had no recent electrocardiogram or echocardiogram results.

In the emergency department, the patient was alert and conscious, blood pressure was 179/58 mmHg, regular pulse was 33 beats per minute (bpm), temperature was 36.4°C, heart sounds were normal, and lungs were clear. No neurological findings were evident. White blood count was 13.2 K/ml, hemoglobin level 15.2 g%, platelet count was 233 K/ml, neutrophils were 50.1%, lymphocytes were 42.7%, creatinine was 1.5 mg%, potassium was 4.1 mmole/L, C-reactive protein was 3.2 mg/L (normal 0–5), first troponin was 15.6 ng/L (normal 0–14), and repeated troponin level 13 hours later was 21.

Throat and nose swaps for COVID-19 polymerase chain reaction were negative

Figure 1: Electrocardiogram of the patient at admission to the emergency department



on two consecutive days, thyroid stimulating hormone was 2.4 μIU/ml (normal 0.2–4.7), electrocardiogram showed second degree 3:1 Mobitz II AVB, with ventricular rate of 33 bpm [Figure 1], chest X-ray was normal, echocardiography showed good left ventricular function with ejection fraction of 60%, no diastolic dysfunction was noted, normal valvular function was seen, and no pericardial effusion was determined. The patient was given four infusions of atropine, 0.5 mg each, with no response. The patient had a temporary external pacemaker for few hours, then a dual chamber permanent pacemaker was implanted (Biotronik Enitra 6-DR-T, Germany) without any complications. The patient was discharged the next day feeling well. The last follow-up appointment was 3 months later. The patient still presented with second degree AVB with atrial beats of approximately 80 bpm and the patient remained pacing dependent.

COMMENT

High degree AVB is an emergency cardiac manifestation that could occur secondary to ischemic heart disease, cardiomyopathies, medications, cardiac surgery, or infection. Our patient had no evidence of any cause known to be associated with high degree AVB; however, he had a COVID-19 vaccination two days prior to the development of his symptoms.

There are many reports in the literature of patients who developed different symptoms and signs following vaccination similar to those caused by the virus itself, like the classic example following influenza vaccination [4]. These symptoms and signs could develop during the first few days following the vaccination. The mechanism of these symptoms and signs is thought to be an immunologic reaction to a component of the vaccine [5]. It seems that the level of block in our case is infranodal.

Although the COVID-19 vaccine is produced using a different technology than the influenza vaccine, its clinical implementation has just started. Medical personnel should be aware of unusual manifestations following the vaccination that could lead to possible adverse effects, especially in a climate where hundreds of millions of people are expected to receive this type of vaccine.

Previous COVID-19 infection could be a possibility in our case; however, patients with COVID-19 infection who develop cardiac manifestations are usually very symptomatic. Our patient had no clinical or lab evidence of infection. Unfortunately, serological testing for COVID-19 was not performed at our hospital or at the community health clinic because such studies were not performed for those who were vaccinated.

The sequence of events in our case, the lack of risk factor for developing high degree AVB, and the fact that high degree AVB is one of the cardiac complications of acute COVID-19 infection, make the association between high degree AVB in our patient and Pfizer COVD-19 vaccination a possibility. However, such an association cannot be proven unless more cases are reported.

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Capsule

Type I IFNs promote cancer cell stemness by triggering the epigenetic regulator KDM1B

Cancer stem cells (CSCs) are a subpopulation of cancer cells endowed with high tumorigenic, chemoresistant and metastatic potential. Nongenetic mechanisms of acquired resistance are increasingly being discovered, but molecular insights into the evolutionary process of CSCs are limited. **Musella** and colleagues showed that type I interferons (IFNs-I) function as molecular hubs of resistance during immunogenic chemotherapy, triggering the epigenetic regulator demethylase 1B (KDM1B) to promote an adaptive, yet reversible, transcriptional rewiring of cancer cells towards stemness and immune escape. Accordingly, KDM1B inhibition prevents the appearance of IFN-I-induced CSCs, both in vitro and in vivo. Notably, IFN-I-induced CSCs are heterogeneous in terms of multidrug resistance, plasticity, invasiveness and immunogenicity. Moreover, in breast cancer patients receiving anthracycline-based chemotherapy, KDM1B positively correlated with CSC signatures. This study identifies an IFN-I → KDM1B axis as a potent engine of cancer cell reprogramming, supporting KDM1B targeting as an attractive adjunctive to immunogenic drugs to prevent CSC expansion and increase the long-term benefit of therapy

Nature Immunol 2022; 22: 1379
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