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DOI: 10.17235/reed.2023.9950/2023
Link: PubMed (Epub ahead of print)

Please cite this article as:

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Transient second-degree type 2 atrioventricular block after infliximab infusion in a patient with Crohn’s disease and heterozygous familial hypercholesterolemia

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Keywords: Crohn's disease. Familial hypercholesterolemia. Infliximab. Cardiac arrhythmias.

Conflict of interest: the authors declare no conflict of interest.

Dear Editor:
Current treatments for patients in the active phase of Crohn's disease (CD) include conventional treatments and biological treatments. Infliximab (IFX), a TNF-α antagonist, is recommended to induce remission in patients with moderate-to-severe CD who have not responded to conventional therapy. IFX terminates the inflammatory cascade by inhibiting the nuclear factor-κB (NF-κB), mitogen-activated protein kinase (MAPK), and caspase signaling pathways and increases the apoptosis of activated T cells in inflamed tissues (1).

Here, we report a 17-year-old male who experienced chronic left lower abdominal pain and diarrhea for two years and was diagnosed with CD (A2L2B1) (Fig 1.A). The patient develops sudden palpitations 8 days after the second infusion of IFX and exhibited no dizziness, syncope, amaurosis or other symptoms. The electrocardiograph (ECG) of the patient was generally normal, but the laboratory workup showed elevated myocardial enzymes and myoglobin, which returned to
normal levels on Day 3. The 24-hour ambulatory ECG revealed a second-degree type 2 atrioventricular (AV) block (Fig 1.B). In further interviews, the patient revealed that his mother died of severe dyslipidemia and metabolic disorders. Elevated levels of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) were noted in the patient’s medical records, and a diagnosis of heterozygous familial hypercholesterolemia (HeFH) with a low-density lipoprotein receptor (LDLR) mutation was confirmed. He was started on a treatment regimen of mesalazine and atorvastatin calcium. After 3 weeks of treatment, the 24-hour ambulatory ECG showed a second-degree type 1 AV block (Fig 1.C).

Familial hypercholesterolemia (FH) is characterized by hyper-LDL-C, premature coronary artery disease, and tendon and skin xanthomas and is classified into HeFH or homozygous FH (HoFH) according to genetic tests. Increased levels of plasma LDL due to a reduction in the levels of functional LDLR increase the risk of sudden arrhythmias in patients with FH. According to statistics, the incidence of HeFH is 1:200-250, and an insufficient understanding of dyslipidemia can easily lead to the missed diagnosis of HeFH (2, 3). When we stopped IFX therapy and oral atorvastatin, palpitations did not recur at the six-month follow-up, and second-degree type 1 AV block was detected. These findings suggest that this condition was likely caused by both IFX and HeFH. The levels of plasma lipoprotein should be measured, the safety and efficacy of IFX for use in patients with CD combined with dyslipidemia should be emphasized, and a 24-hour ambulatory ECG should be performed before administering biological therapies.

References
Figure 1. (A) Histology image of Crohn's disease. (B) The 24-hour ambulatory ECG showed a second-degree type 2 atrioventricular block 8 days after the second infusion of IFX. (C) The 24-hour ambulatory ECG revealed a second-degree type 1 atrioventricular block 3 weeks after IFX suspension.