

## Case Report: Atrioventricular Block Related to Glucosamine/Chondroitin in a Patient Presented with Syncope Complaint

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### Abstract

Drug toxicity and coronary artery disease are the most frequent causes of degenerative atrioventricular (AV) complete block in adults. In the present study, development of AV block subsequent to Glucosamine/Chondroitin sulfate use in a 42 year-old male patient was evaluated. A patient with an osteoarthritis in his medical history applied to the emergency department with syncope, and an A-V block was diagnosed in the evaluation of his electrocardiogram. The patient was admitted to the coronary intensive care unit, and underlying etiology was investigated. Coronary angiography was in normal range. AV nodal functions in the electrophysiological study were considered normal. Glucosamine/Chondroitin sulfate intake was suspected as the causative factor, and sinus rhythm was achieved at the 4th hour following the cessation of the supplement.

Since there is no report on the literature indicating the use of this supplement may cause AV blocks, we aimed to emphasize the necessity of being watchful for an AV block in case of Glucosamine/Chondroitin use.

**Keywords:** Drug toxicity; Coronary artery disease; Atrioventricular; Osteoarthritis; Electrocardiogram; Glucosamine

### Introduction

Glucosamine (GlcN) is an amino-monosaccharide, and it was believed that it modifies progression of osteoarthritis (OA) as a constituent of glucosaminoglycans in joint cartilage [1]. Although it is not a FDA-approved drug, it is on the market in the form of Glucosamine/Chondroitin sulfate as a nutrition supplement in United States and Turkey [1].

Chondroitin sulfate (CS) is the essential constituent of the connective tissue extracellular matrix in hyaline cartilage of which it is responsible for the maintenance of elasticity [1]. It has antiinflammatory effects on cartilage metabolism. In long-term use, the recommended dose is 800 mg/day. In human chondrocyte cultures, it has been shown that it increases the proteoglycan density in pericellular matrix, and decreases the collagenolytic activity in a dose dependent manner [2]. Although side-effect profile of GlcN is non-specific, gastrointestinal symptoms, headache and skin-related symptoms have been observed, but no side effect myocardial conduction has been reported to date [3].

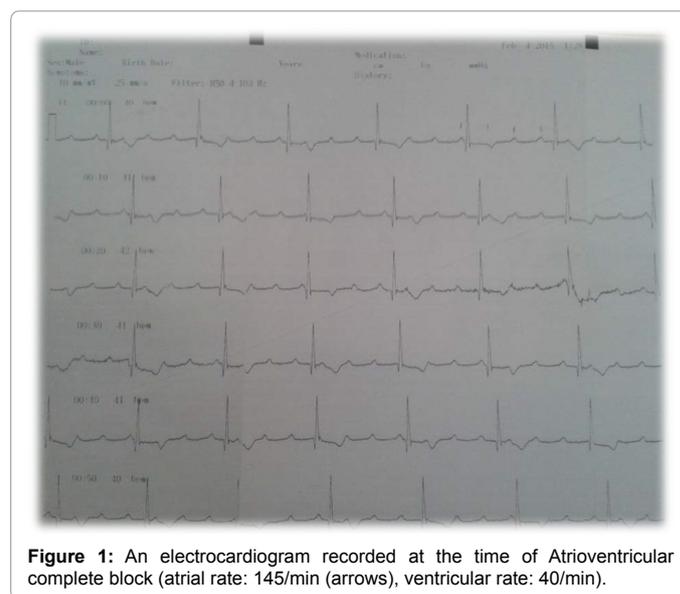
Atrioventricular (AV) complete block is a bradyarrhythmia, and it may result in mortal consequences if left untreated [4]. AV complete block may arise due to various reasons including acute myocardial infarction (AMI), chronic ischemic heart disease, myocarditis, collagen tissue diseases, trauma, infiltrative diseases, neuromuscular defects, myxedema, medications and electrolyte imbalance [5]. In literature, development of AV block related to use of a number of medications has been reported such as carbamazepine [6], amphotericin B [7] and somatostatin [8]. However, a case with AV block by reason of Glucosamine/Chondroitin (GlcN-CS) use has not yet been reported to date. In this case report, we aimed to present a patient with AV complete block developed after GlcN-CS use.

### Case

A 42-year-old male patient presented to the emergency department with syncope lasting less than a minute followed by dizziness and nausea. He denied any history of a similar syncopal episode. In his medical history, he stated that he had been diagnosed with osteoarthritis, and admitted the use of a supplement containing GlcN-CS as the active ingredient beginning 3 days before presentation. He

denied taking any other medications or supplements. There was no significant disease other than hypertension in his family history. In his physical examination, he had a blood pressure of 126/86 mmHg, and a lower heart rate of 40 beats/min. A-V complete block was diagnosed on the 12-lead ECG (Figure 1). Blood potassium level was 3.4 mEq/L.

In transthoracic echocardiography, there was no pathology other than left ventricular hypertrophy. In applied coronary angiography



**Figure 1:** An electrocardiogram recorded at the time of Atrioventricular complete block (atrial rate: 145/min (arrows), ventricular rate: 40/min).

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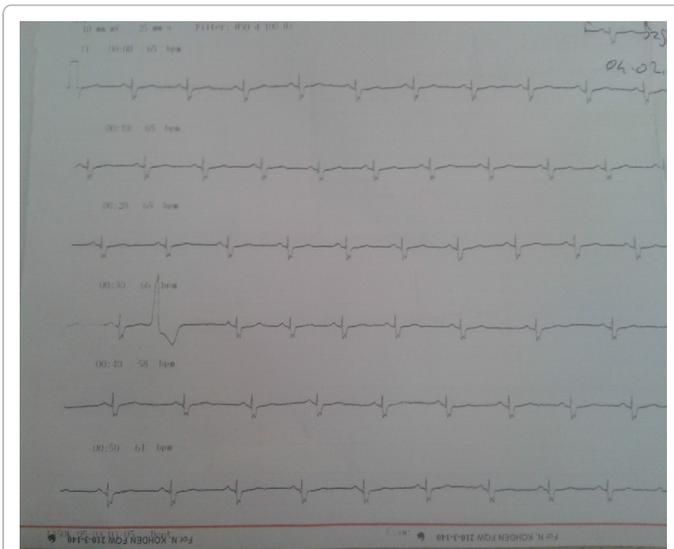


Figure 2: An electrocardiogram recorded when sinus rhythm returned in the patient.

aiming to exclude AV complete block caused by ischemia, no critical coronary stenosis was detected, and temporary cardiac pacemaker was not inserted since his hemodynamics were stable. The patient was transferred to the coronary Intensive Care Unit (ICU) and began to be monitored. At the 4th hour of his follow up in the ICU, the patient reverted to a normal sinus rhythm” (Figure 2). The patient was monitored for the following 72 hours with no abnormality in holter recordings, and was discharged from the hospital. In the electrophysiological evaluation carried out after discharge, AV nodal functions were determined as normal.

## Discussion

AV complete block is a cardiac rhythm disorder caused by interrupted transmission of atrial impulse to the ventricles [9]. Atria and ventricles are electrically stimulated independently from each other, and their contractile functions are sustained. An escape rhythm from any focal area at the distal side of the Atrioventricular node provides electrical depolarization to the ventricles in order to retain blood supply to the critical organs. If the focus providing ventricular depolarization is at the distal of AV node or within the bundle of His, generated ventricular pulses are formed with narrow QRS complexes. If located inferior, QRS waves are broad [9]. In our patient’s electrocardiogram recorded at the time of diagnosis with AV complete block, QRS waves were narrow (80 ms) suggesting that the escape rhythm during AV complete block was originated from the distal to the AV node or within the bundle of His.

Aylan et al. [10] investigated 191 cases in their clinical study, and have reported that the most frequent cause of AV complete block is AMI (38%). They could not find any causative reason in 23.6% of the patients. In 41.1%, 26.7% and 13.1% of those cases, permanent, temporary and initially-temporary-then-permanent pacemakers were implanted, respectively. Interestingly, they could not find the certain cause of AV complete block in 45.1% of the patients within the group with permanent pacemaker. Other causes of AV block are collagen tissue diseases, trauma, infiltrative diseases, neuromuscular disorders, myxedema, medications and electrolyte imbalance.

In the present case, AMI diagnosis was disregarded due to the lack of chest pain, negative troponin level and no wall motion abnormality

on the echocardiography. In further step, coronary angiography performed to evaluate possible coronary artery disease was reported normal. AV block caused by electrolyte imbalance was eliminated since his electrolyte levels were within the normal ranges. AV block triggered by myxedema due to hypothyroidism was suspected, and thyroid hormone levels were evaluated in the patient, with normal findings. Infection-related AV block was not consistent with our case since the patient had no leukocytosis, no fevers and a normal erythrocyte sedimentation rate. No trauma history and the lack of neuromuscular disease symptoms let us disregard those causes in the etiology. GlcN-CS use was primarily suspected as the primary cause of AV complete block.

GlcN-CS is typically taken in pill form orally, and 90% of the content is absorbed across the small intestine [11]. The majority of this supplement is metabolized in liver during the first-pass. Just 26% of orally taken glucosamine can be absorbed into the blood [12]. When taken 23.1 mg/kg per day, it attains the steady-state concentration in human. At this dose level, the serum concentration of GlcN-CS is about 0.06 mmol/L (11). As considered being a safe-to-use supplement, the toxic dose of GlcN-CS is quite high (around 7.2 gr), and it is usually tolerated pretty well [13]. Despite 13 studies examining GlcN-CS use on 800 participants observed for over 40 weeks, no significant alterations have been recorded in cardiovascular parameters, blood pressure and heart rate [13]. In those studies, though, nonspecific adverse effects including constipation, diarrhea, dyspepsia, nausea, abdominal wall tension, bellyache, headache, itch and skin rash have frequently been reported [3]. In our case, we thought that AV complete block occurred due the use of total 4500 mg GlcN-CS in 3 days (20 mg/kg per day). The drawback of the present study is that we could not evaluate blood glucosamine level in our patient. Since no other reason we could find that might be causative for AV block in our case, and the attainment of sinus rhythm shortly after the cessation of the supplement led us to think this bradyarrhythmia was caused by GlcN-CS.

In the treatment of AV block, if the patient’s hemodynamics is unstable, a transient pacemaker is implanted. Following this, studies are carried out to reveal its etiology. Ischemia, electrolyte dysregulation and medication use, for instance, are investigated as possible causes, and found reasons are aimed to be ameliorated. When a certain etiologic factor cannot be determined or AV complete block lasts over 48 hours even though detected possible causes are fixed, a permanent pacemaker can be implanted [10]. Since this patient’s hemodynamics were stable, a pacemaker was not implanted, and he was admitted to the ICU for follow the heart rhythm. Studies intended for determination of underlying causes were performed in the ICU setting, while the patient was closely monitoring. With no worsening in the hemodynamics of the patient during this period, sinus rhythm was achieved 4 hours after presentation.

In conclusion, the first case with AV complete block related to GlcN-CS has been presented in the current study. We aimed to raise awareness on the likelihood of arising of AV block from GlcN-CS use since it is strongly suggestive that an AV complete block occurred in this patient due to the ingestion of GlcN-CS in a total dose of 4500 mg in 3 days, and there has been no study to date reported a similar adverse effect.

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