

# Transient complete atrioventricular block in a patient with Blackfan-Diamond anemia due to severe hypothyroidism

## Blackfan-Diamond anemili hastada ciddi hipotiroidizme bağlı gelişen geçici tam kalp bloğu

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### ABSTRACT

We report a 14-year-old boy with a previous diagnosis of Blackfan-Diamond anemia (BDA) who presented with the complaint of bradycardia. Electrocardiogram (ECG) showed complete atrioventricular (AV) block with the mean heart rate 51 bpm on admission. Laboratory data revealed endocrine abnormalities and severe hypothyroidism. Soon after chelation and levothyroxine therapy, AV block was disappeared gradually.

**Key words:** Blackfan-Diamond anemia, hypothyroidism, complete atrioventricular block

### ÖZET

Burada bradikardi semptomları ile başvuran Blackfan-Diamond anemisi tanılı 14 yaşında erkek hasta sunulmaktadır. Başvuru sırasında çekilen elektrokardiyografide ortalama kalp hızının 51/dk olduğu tam atriyoventriküler blok saptanmıştı. Laboratuvar verileri endokrin anormallikleri ve ağır hipotiroidiyi göstermekteydi. Tanıdan sonra uygulanan şelasyon ve levotiroksin tedavisi sonrası atriyoventriküler blok aşamalı olarak kayboldu.

**Anahtar kelimeler:** Blackfan-Diamond anemisi, hipotiroidizm, tam atriyoventriküler blok

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### INTRODUCTION

Cardiac disease and its associated complications are the most serious side effects of hypothyroidism. Although bradyarrhythmic conduction disturbance in thyroid disorders is frequently encountered in clinical practice, AV conduction disorders (especially complete AV block) are rare. In such patients reversion of the conduction abnormality to normal sinus rhythm is usually seen several days to weeks after thyroxine supplementation therapy.

### CASE REPORT

A 14-year-old boy presented to our emergency department with long-standing fatigue, paleness, marked bradycardia and growth retardation. In the months prior to the presentation the patient had been feeling progressive weakness.

His medical history revealed that he had been diagnosed as having BDA with a hemoglobin (Hb) level of 2.3 g/dL at the age of 4 months. When he was 2 years old, deferoxamine therapy was started for the

prevention of subsequent iron overload but the compliance of the family to this treatment had been insufficient. Unfortunately, patient was not present at regular follow-ups during the following years.

He was admitted to our outpatient clinic with the complaint of severe fatigue, paleness and dyspnea. Transthoracic echocardiographic (ECHO) imaging revealed dilated cardiomyopathy (DCMP) and minimal pericardial effusion. Therefore anticongestive therapy was started. His symptoms relieved partially during his hospital stay, but patient's daily follow-up revealed marked bradycardia with a heart rate below 30 bpm, especially at nights.

He was referred to our center with a possible indication of a cardiac pacemaker implantation. On physical examination, he was found (figure 1) to be pale, sleepy with a coarse facial features, dry puffy skin, slow and hoarse speech, hypertrichosis especially at his back. His sexual development was prepubertal and the testicular volume was measured as 3 mL. An increase in lumbar lordosis, hepatosplenomegaly and short stature were detected during his physi-

cal examination. Patients' bone age was compatible with 8 years. His weighed 21.5 kg (<3. p, -2.5 SDS), his height was 114.5 cm (<3. p, -5.6 SDS) and axillary body temperature 36.5 C. Cardiac auscultation revealed a normal S1 and S2, arrhythmia and a soft systolic murmur (I/VI) heard at the left sternal border. Standart 12-lead electrocardiogram (ECG) revealed a complete AV block with a rate of 54 bpm. The width of QRS complex was not more than 0.1 second. On echocardiographic examination, wall motion was uniformly reduced and left ventricular end-diastolic diameter (LVED) increased up to 4.5 cm (normal value is between 2.4-3.8 cm) and ejection fraction was decreased (EF: 40%). Minimal pericardial effusion was also detected. Holter ECG showed complete AV block with the mean heart rate of 51 bpm

Laboratory findings were as follows: Hb: 9.8 gr/dL, Hct: 27.9%, AST: 114 (N:10-34) U/L, ALT:187 (N: 9-43) U/L, LDH:606 (N: 210-425)U/L. Comb's test was negative, reticulocyte count was 1.3% (N: 0.50-2.50). Biochemical parameters including auto-antibodies concerning connective tissue disorders,



**Figure 1.**

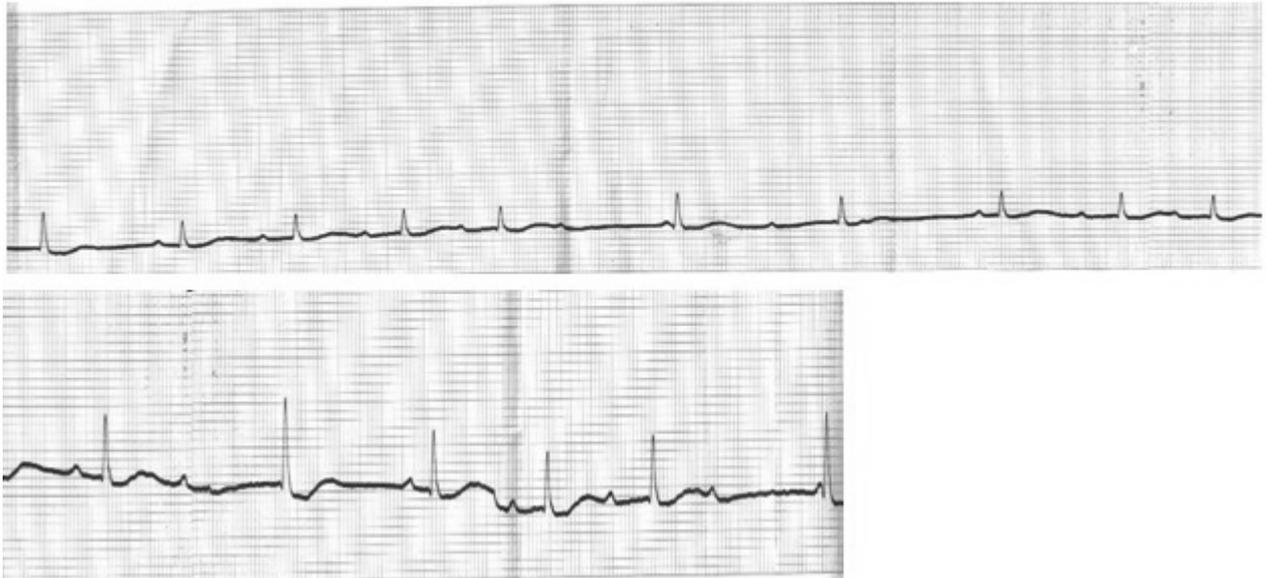


Figure 2.

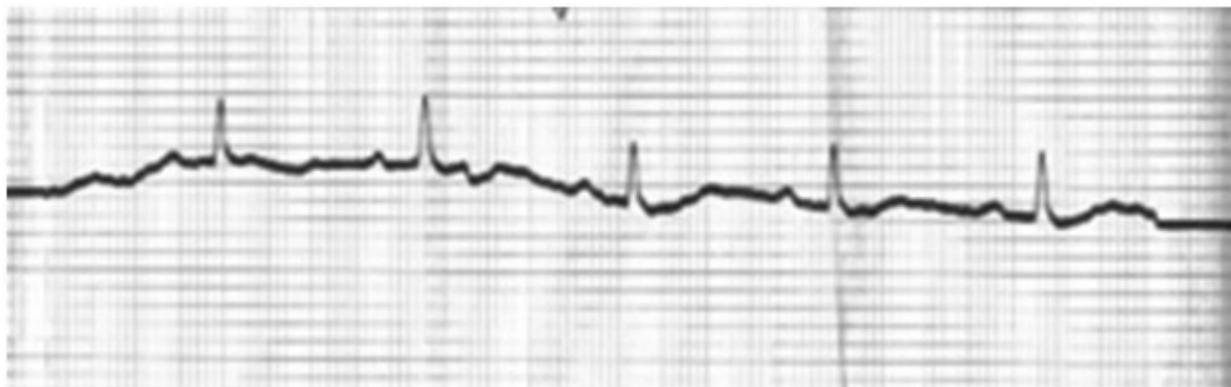


Figure 3.

plasma LH and FSH values, cortisol level and other biochemical parameters were in normal ranges.

Serum levels of testosterone (30 ng/dL (N: 300-1.000)), parathyroid hormone (14 pg/ml (N: 16-87)) and calcium (7.0 mg/dL (N: 8.4-10.2)) led us to the probable diagnosis of hypoparathyroidism, therefore calcium and active D3 replacement therapy were started. His thyroid function tests revealed hypothyroidism with diagnostic serum free thyroxin (FT4) 0.4 pmol/L; (N: 9-25) and thyrotropine (TSH) 526.4 mIU/L; (N: 0.27-4.20) levels. The thyroid sonography was unremarkable, apart from a mild decrease in thyroid volume. Iron level was 162 (N: 50-170)  $\mu$ g/

dL, TIBC: 184 (N: 250-410)  $\mu$ g/dL and ferritin level was 8562 mcgr (N: 60-110).

These results suggest that hemosiderosis due to iron overload in the heart and the endocrine organs might be responsible for the hypothyroidism, hypoparathyroidism and DCMP in our case; hence chelation therapy was intensified by increasing the desferrioxamine dosage.

To rule out digoxin intoxication as the cause of the arrhythmia, digoxin therapy was terminated. Digoxin blood level was found as 0.8 ng/mL (N: 0.8-2) before termination of the therapy.

At follow-up, our patient responded very well

with an acceleration of the heart rate, transitional periods of heart rhythm from complete AV block (Figure 2) to type 2 second-degree AV block, and then first degree AV block were observed before recovery to the normal sinus rhythm (Figure 3). He also responded well to treatment with levothyroxine. Pacemaker implantation was not required during his hospital stay.

Holter ECG showed improved heart rate with sinus rhythm, but rarely first and second degree AV block were observed. Echocardiographic examination revealed EF: 51% and pericardial effusion was resolved but other associated findings were still present. His symptoms resolved rapidly and the patient, who was bed dependent, started to walk without assistance by the 9th day hospitalization.

FT4 had increased to 5.6 pmol/L but TSH didn't change significantly. The patient was discharged on the 13th day of hospitalization without any need for a pacemaker. The patient had been followed-up for three months. His serial ECG and control holter ECG revealed improved heart rate without any recurrence of AV block or other arrhythmias.

## **DISCUSSION**

Blackfan-Diamond anemia is described as a rare disorder of impaired red cell production in children.

Most of these patients respond to corticosteroids but for many patients regular erythrocyte transfusions are required. Chronic blood transfusion therapy causes excessive iron accumulation in different organs such as the heart, thyroid, and parathyroid glands <sup>(1)</sup>.

We encountered a case of BDA with hypothyroidism who presented with a complete heart block. TSH level was very high in our patient. After the replacement therapy with levothyroxine and intensive chelation, lasting for less than two weeks, heart rate normalized and the complete AV block was resolved completely. We know that iron overload causes thyroid damage in addition to the effects of excessive or insufficient thyroid hormones on the cardiovascular system. Significant arrhythmia, poor

cardiac contractility and even heart failure are cardiovascular manifestations of hypothyroidism <sup>(2)</sup>. Although a rare entity hypothyroid patients with a complete AV block, can be seen <sup>(3)</sup>. Reasons for occurrence of disturbances of intracardiac conduction in association with hypothyroidism are not well known but they are attributed, in a part, to various histopathologic changes in the myocardium and especially in blood vessels supplying the conduction system <sup>(4)</sup>.

It has been suggested that the use of intensive chelation therapy can reverse iron load to normal levels, and also plays a leading role in the prevention and/or reversal of hypothyroidism and the other endocrinopathies secondary to iron overload (Gamberini et al, 2008) <sup>(5)</sup>. Additionally this treatment regimen may prevent the progression from absence of clinical symptoms to marked hypothyroidism and may also help treating marked hypothyroidism. In one case report of hereditary hemochromatosis, low thyroid levels increased after iron depletion, suggesting that even iron-induced damage of the thyroid might be reversible (Hudec et al, 2008) <sup>(5)</sup>.

Also, cardiac involvement in iron overload can manifest as a toxic cardiomyopathy or an arrhythmia. Usual rhythm disturbances are supraventricular or ventricular premature contractions. Besides, first- or second-degree and rarely complete heart block occurs in end-stage iron overload cardiomyopathy (IOC). It seems to be the most common cause of death in these groups of patients <sup>(6)</sup>. Many studies showed iron induced cardiomyopathy can be reversible after treatment by chelation therapy, but it is not universally accepted due to the high mortality rate of these patients despite chelation treatment <sup>(7)</sup>.

To eliminate the role of this disorder as an underlying cause of the severe cardiac bradyarrhythmias in our patient, he was screened for evidence of an iron overload. Serum ferritin values were much higher than the normal limits, which could have been caused cardiac siderosis. If IOC was the cause of the heart block in our case, the patient would have a very poor prognosis. Also AV block would continue despite our

treatment modalities and often in these cases it would result in death<sup>(8)</sup>. In our patient, since the cardiac findings were reversed quickly after chelating and levothyroxine therapy, we did not diagnose him as IOC, although it was in our differential diagnosis list. As a conclusion, we believe that in our case the severe iron overload probably had been the cause of hypothyroidism that led to complete AV block which was resolved soon after treatment by chelating and levothyroxine.

Jong and Lewis<sup>(9)</sup> reported a 72-year-old man with a complete AV block, myxedema and syncope that responded very well to thyroid extract therapy within 6 weeks. Also Schoenmakers and Graaff<sup>(10)</sup> reported a similar case that was a 90-year-old man presented with complete AV block secondary to severe hypothyroidism. Recovery to sinus rhythm after treatment with levothyroxine was also reported.

To the best of our knowledge, this is the first case report of a complete AV block associated with hypothyroidism in a young patient with a diagnosis of BDA who recovered after levothyroxine and chelating therapy. Our case demonstrates that thyroid function abnormalities should always be considered in the differential diagnosis of patients presenting with AV conduction block so that unnecessary pacemaker implantation could be avoided.

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