

# Left Ventricular Noncompaction Cardiomyopathy in a Patient with Congenital Atransferrinemia

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## ABSTRACT

Congenital atransferrinemia is an extremely rare autosomal recessive inherited disorder characterized by a transferrin deficiency and results with hypochromic microcytic anemia and hemosiderosis. Left ventricular noncompaction is uncommon and results from the arrest of the myocardium's normal compaction process in the early stages of fetal development. Here, we reported a congenital atransferrinemia who was first diagnosed at nine months with left ventricular noncompaction cardiomyopathy.

**Keywords:** Atransferrinemia, echocardiography, iron, left ventricular noncompaction, magnetic resonance imaging.

## KONJENİTAL ATRANSFERRİNEMİ OLAN OLGUDA SOL VENTRİKÜLER NONKOMPakte KARDİYOMİYOPATI

### ÖZET

Konjenital atransferrinemi, transferrin yetersizliği ile karakterize, hipokromik mikrositer anemi ve hemosideroz ile sonuçlanan son derece nadir görülen otozomal resesif geçişli kalıtsal bir hastalıktır. Sol ventrikül nonkompaksiyonu nadirdir ve fetal gelişimin erken evrelerinde miyokardın normal kompaksiyon sürecinin durdurulması ile karakterizedir. Biz burada, ilk defa dokuz aylıkken konjenital atransferrinemi tanısı alan beraberinde sol ventriküler non kompakte kardiyomyopatisi olan bir kız çocuğunu sunduk.

**Anahtar sözcükler:** Atransferrinemi, ekokardiyografi, demir, sol ventrikül nonkompaksiyon, manyetik rezonans görüntüleme

Congenital atransferrinemia (CAT) is one of the rare causes of microcytic hypochromic anemia (1). This is an autosomal recessive inherited disorder, and various mutations result in defects in transferrin (TRF), the iron carrying protein in the body (2). Moderate to severe microcytic hypochromic anemia with normal serum iron levels, high serum ferritin values, and a significantly low total iron-binding capacity (TIBC) can be seen in CAT or acquired by an atransferrinemia patient (3). The absence of TRF leads to iron accumulation in various organs, including the liver, heart, kidney, joints, and thyroid. Left ventricular noncompaction cardiomyopathy (LVNC) is a congenital disorder affecting endomyocardial development and results in excessive trabeculations in the left ventricle (4). Different mutations in protein-encoding genes are the etiology of LVNC in children and adults (5,6). Left ventricular noncompaction cardiomyopathy is uncommon and occurs as a result of the arrest of the normal myocardium compaction process in the early stages of fetal development

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**Received :** September 30, 2018  
**Revised :** September 30, 2018  
**Accepted :** March 10, 2019

(7). We here report a case of atransferrinemia with accompanying LVNC. To the best of our knowledge, this is the first case in the literature reporting the co-occurrence of atransferrinemia and LVNC.

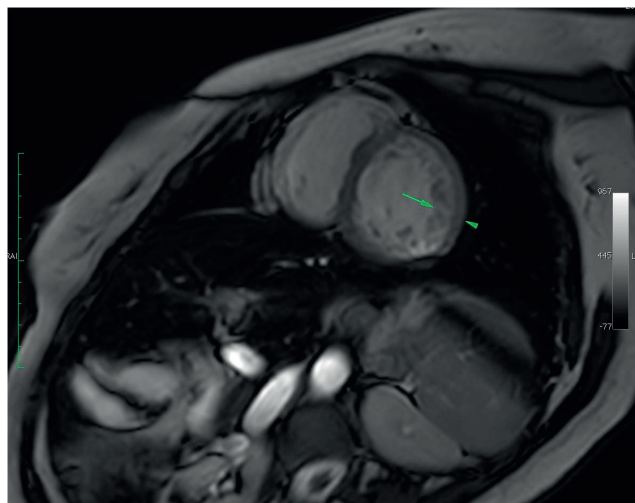
## Case

An 18-year-old girl that was followed up for atransferrinemia and LVNC was admitted to our hospital for routine control. She was diagnosed when she was nine months old and admitted because of growth retardation and recurrent respiratory tract infections. At the first physical examination when she was nine months old, generalized and symmetrical loss of subcutaneous fatty tissue and paleness in the skin and mucous membranes was revealed. On laboratory examination, the hemogram revealed the following: hemoglobin 3.1 mg/dl, hematocrit 27.8 %, mean corpuscular volume (MCV) 71 fL, and red blood cell distribution width (RDW):39.2. These values were low compared to normal ranges, indicating hypochromic microcytic anemia, which was confirmed by microscopic examination. A bone marrow biopsy and aspiration were performed. Normal cellular bone marrow was detected without atypical cells. Parameters determining the iron metabolism were also evaluated. The measured ferritin level was 726.5 ng/mL, which is extremely high compared to the normal range (4.63-204 ng/mL). Total iron-binding capacity was 11.9 µg/dL (normal range: 245-450 µg/dL), and the unsaturated iron-binding capacity was 6 µg/dL, which is very low (normal range: 130-375 µg/dL). Ferritin saturation was 49.6%. Transferrin was 35.9 mg/dl. The final diagnosis was atransferrinemia. On routine physical examination, a systolic murmur at the mitral valve was detected at six years of age. Echocardiography (echo) was performed due to the cardiac murmur, and it revealed increased trabeculations in the lateral wall of the left ventricle and the apex of the right ventricle. The anterior leaflet of the mitral valve was bulging into the left atrium, suggesting mitral valve prolapse. LVNC was diagnosed due to the findings of the echo.

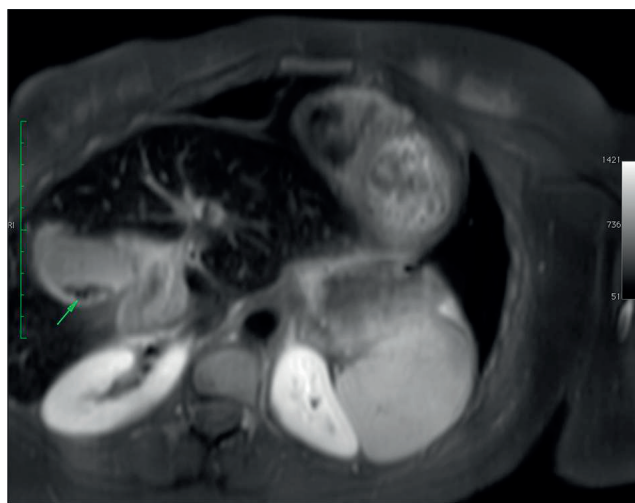
The patient was followed up with routine abdominal ultrasonography (US) and echo to detect possible complications over 18 years. Cardiac magnetic resonance imaging (MRI) was performed for left ventricular function at 18 years. Increased trabeculations in the apex and lateral wall of the left ventricle were seen in the cardiac MRI. The ratio of noncompacted myocardium to compacted myocardium was 2.4; this finding was consistent with LVNC (Figure 1). The ventricular wall motion was normal in cine images. In the left ventricular functional analyses of cardiac MRI, ejection fraction was 52%, end-diastolic volume was

105 ml, end-systolic volume was 51 ml, stroke volume was 54.3 ml, and cardiac output was 5.2 L/min. A post-contrast series did not show pathological contrast enhancement. A T2 weighted MRI series also showed a marked decrease in the signal intensity of the liver. Also, several stones were seen in the gallbladder (Figure 2).

On laboratory examination, a hemogram showed hemoglobin 7.8 mg/dl, hematocrit 25.1%, MCV 62.4 fL, and RDW:23.8 on the final check at 18 years of age. Biochemistry tests, including liver, kidney, and thyroid functions, were normal. Thus, a routine follow-up with complete hemogram, biochemistry tests, and echo was offered to the patient due to her being asymptomatic. Verbal informed consent was obtained from the patient and her family.



**Figure 1.** A balanced turbo field-echo sequence (BTFE) MR image shows left ventricular noncompaction in short-axis views. Arrows point to noncompacted myocardium, and the arrowhead points to compacted myocardium.



**Figure 2.** T1-weighted fat saturated MR image shows multiple stones (arrow) in the gallbladder and diffuse low signals in the liver due to iron storage.

## Discussion

Left ventricular noncompaction cardiomyopathy is uncommon and occurs as a result of the arrest of the myocardium's normal compaction process in the early stages of fetal development (7). The American Heart Association (AHA) classifies LVNC as primary genetic cardiomyopathy. In children, the familiar type is common and follows an X-linked, autosomal-dominant, or mitochondrial-inheritance pattern (in children) (7). Gene defects identified in patients with LVNC have been limited and infrequent, suggesting genetic heterogeneity (8). LVNC usually affects the left ventricle, but can also affect the right ventricle. Biventricular noncompaction cardiomyopathy can also be seen. Multiple forms of LVNC occur, and these include primary myocardial forms, a form associated with arrhythmias, and LVNC-associated with congenital heart disease (CHD), including septal defects, hypoplastic left heart syndrome, and right heart obstructive abnormalities, such as pulmonic stenosis and Ebstein's anomaly, among others (9). In the present case, LVNC was not associated with CHD. Additionally, there is nothing available in the literature about LVNC associated with CAT.

Although LVNC can be asymptomatic, it may still cause ventricular arrhythmia, thromboembolism, heart failure, and sudden cardiac death in patients. The echo is the most commonly used diagnostic tool because it is inexpensive, non-invasive, and easy to perform (10). The transthoracic echo shows a trabeculated, sponge-like appearance of the left ventricular apical and inferolateral segments. This

appearance is very important in the diagnosis of the LVNC. Also, a cardiac MRI is extremely useful in making a diagnosis. The most accepted cardiac MRI criteria of the LVNC are the following: 1) absence of coexisting cardiac abnormalities, and (2) segmental thickening of the myocardial wall of the left ventricle with two layers, a thin epicardial layer and a thick endocardial layer with prominent trabeculations and deep recesses. The ratio of noncompacted myocardium to compacted myocardium at the end of diastole is  $> 2:1$  (3,11,12). The trabeculae are usually located on the apical/lateral, middle/bottom walls of the left ventricle. Also, most noncompacted segments are hypokinetic (11,12). The diagnostic value from cardiac MRI is highly sensitive (86%) and highly specific (99%) for LVNC diagnosis (13).

The prognosis of LVNC varies because of the presence of thromboembolism, CHF, and arrhythmia (14). In our case, medical treatment was not given because the patient was asymptomatic, and left ventricular ejection fraction was 52%. Therefore, she was followed up with a complete hemogram and biochemistry tests for atransferrinemia and given a yearly echo for LVNC.

Herein, we described the case of an 18-year-old girl who had atransferrinemia with accompanying LVNC. We also discussed the LVNC diagnosis and cardiac MRI findings.

**Declaration of Conflicting Interests:** The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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