Bardet-Biedl syndrome and subaortic membrane: co-occurrence of two rare conditions

Bardet-Biedl sendromu ve subaortik membran: Ender görülen iki beraberlik

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Summary– Bardet-Biedl Syndrome (BBS) is a rare autosomal recessive disorder with multiple morphological abnormalities. Clinical diagnosis is based on the presence of central obesity, polydactyly, rod-cone dystrophy, varying degrees of learning disability, hypogonadism (in men) and renal abnormalities. Cardiac involvement is a rare condition. We present a 28-year-old male with complaints of progressive dyspnea and palpitation diagnosed as BBS and subaortic discrete membrane. Careful echocardiographic evaluation of patients with BBS, such as in this case report, may allow us to discover novel cardiac abnormalities in this patient population.

Özet– Bardet-Biedl sendromu (BBS) birden fazla morfolojik bozukluk içeren ve nadir görülen otozomal resesif bir hastalıktır. Klinik tanı merkezi obezite, polidaktili, rod-cone distrofisi, öğrenme bozuklukları, hipogonadizm (erkelerde) ve böbrek bozuklukları ile konur. Kalp tutulumu ise nadir bir durumdur. Bu yazıda, çarpıntı ve giderek artan nefes darlığı yakınması ile başvuran BBS ve subaortik membran tanısı konmuş 28 yaşında erkek hasta sunuldu. Bu olguda olduğu gibi, BBS'li hastaların ekokardiyografik değerlendirmesi kardiyak anormalliklerin değerlendirilmesi için büyük önem taşımaktadır.

Bardet-Biedl syndrome (BBS) is a rare autosomal recessive disorder characterized by central obesity, polydactyly, rod-cone dystrophy, various degrees of learning disabilities, hypogonadism (in men) and renal abnormalities. Clinical diagnosis is based on the presence of four of these primary features. Other manifestations include diabetes mellitus, congenital heart disease, hepatic fibrosis, neurological features and dental abnormalities.[1]

Although BBS is a heterogenous disease, cardiac involvement in BBS is a rare conditition.[1] There are no previously described cases of BBS with subaortic membrane. Here we discuss a patient with BBS and subaortic discrete membrane admitted with acute atrial fibrilation.

CASE REPORT

A patient, 28-year-old and male, presented with complaints of progressive dyspnea and palpitations lasting for three days. He did not have any prior history of palpitations. He did not have chest pain or syncope. He was born out of a consanguineous marriage as a full term normal vaginal delivery. There was no history of any illnesses in his neonatal period. He had poor school performance and progressive visual decrement.

Abbreviations:

AS	*Aortic stenosis*
BBS	*Bardet-Biedl syndrome*
LVOT	*Left ventricular outflow tract*
VSD	*Ventricular septal defect*

His weight was 78 kg and height 162 cm (body mass index 29 kg/m^2). His blood pressure was 120/70 mmHg and pulse rate 120/min on physical examination. He had polydactyly in the upper limbs and right lower limb (Fig. 1a, b) and micropenis (<2.5 cm). In auscultation a systolic ejectional murmur was heard at the aortic site. In addition, bilateral impaired distant vision and bilateral strabismus was observed. In laboratory examination, glucose was 241 mg/dL, BUN 32 mg/dl, cretinine 1.35 mg/dl, serum sodium 137

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mmol/L, serum potassium 3.9 mmol/L and BNP 374 pg/ml. Hemogram, thyroid and hepatic function parameters, basal gonadotrophins and steroid hormones were normal. Bilateral retinitis pigmentosa (Fig. 1c, d) was observed on retinal examination. In abdominal computed tomography, the right kidney was hypoplastic. ECG was consistent with atrial fibrillation with high ventricular response. Echocardiography showed normal ejection fraction with left ventricular hypertrophy, left atrial enlargement, mild aortic regurtitation and a mean 86 mmHg gradient between left ventricle and aorta. On transesophageal echocardiography, a discrete subaortic membrane was detected as the cause of severe left ventricular outflow gradient

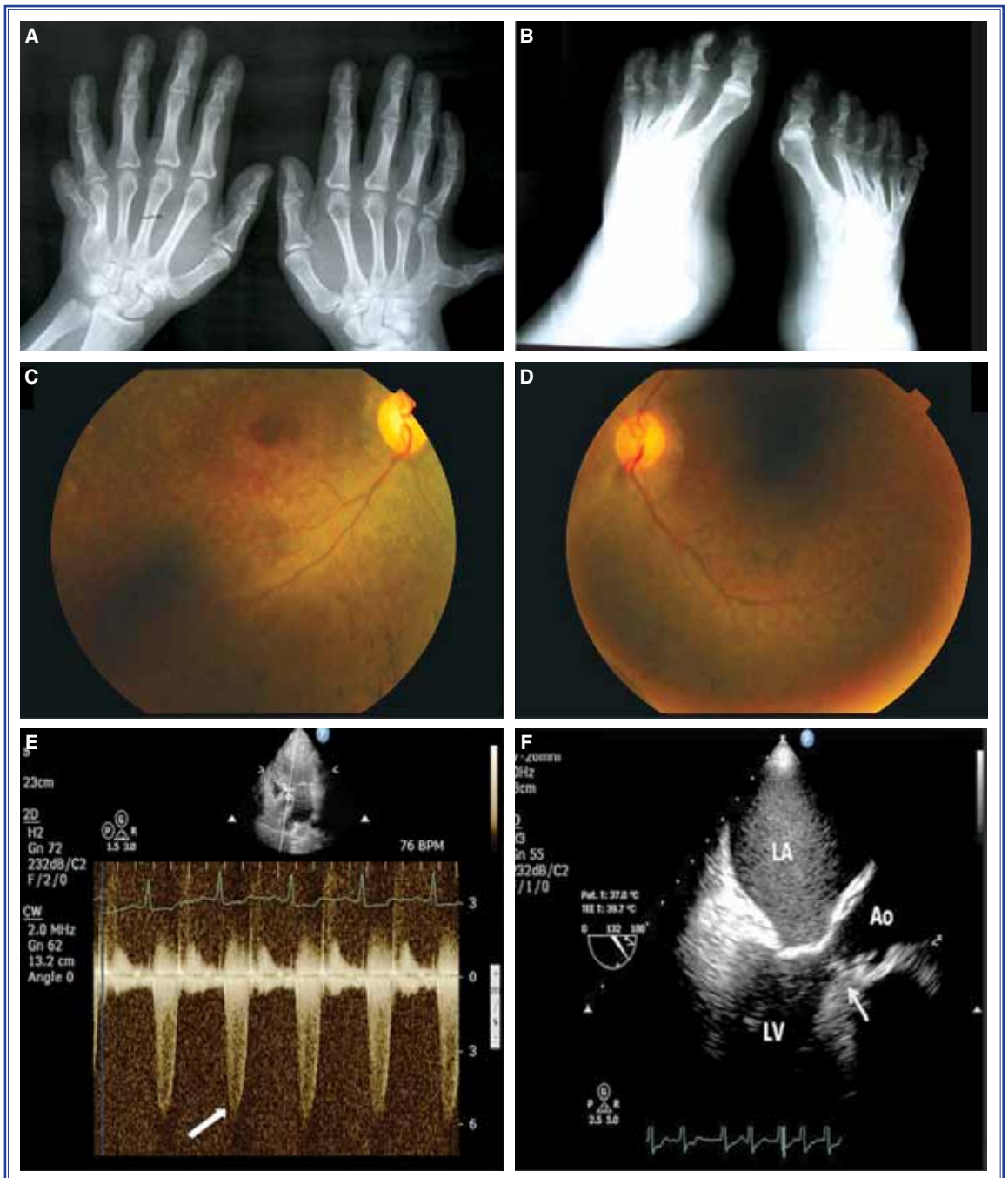

Figure 1. Polidactily in **(A)** upper limbs and **(B)** right lower limb. Retinitis pigmentosa in **(C)** right and **(D)** left eyes. **(E)** High LV outflow velocity in apical five-chamber view in transtorasic echocardiography (white arrow), **(F)** subaortic discrete membrane in transesophageal ecocardiography (white arrow).

(Fig. 1e, f). Since no thrombus formation was seen in the left atrial appendage, DC cardioversion was performed with 100 J to terminate atrial fibrillation and normal sinus rhythm was maintained. He was diagnosed as BBS with severe subaortic stenosis due to a discrete subaortic membrane. Heart failure treatment was started and finally the patient underwent surgery for subaortic membrane.

DISCUSSION

Bardet-Biedl syndrome is both phenotypically and genetically heterogeneous. Its incidence has been estimated to be 1 in 150.000 to 160.000 individuals in North America and European populations, but is much higher in some populations with a high level of consanguinity.[2] The diagnosis of BBS is established by clinical findings. Renal failure is the major cause of morbidity and early mortality in BBS.[3] To date, fourteen BBS genes have been cloned (BBS1-BBS14).[4] About 7-50% of cases with BBS have cardiac involvement.[1,5] Common cardiac abnormalities observed in BBS are left ventricular hypertrophy, aortic valve anomalies, atrial septal defect, pulmonary stenosis and dilated cardiomyopathy.[1,5] Subvalvular aortic stenosis (AS) is the second most common form of aortic stenosis. Among children with congenital AS, subvalvular AS accounts for 10% of cases. Similar to valvular AS, subvalvular AS is more common in males.[6] Since subvalvular AS develops after birth and progresses over time, it is considered an acquired pathology rather than congenital.[7,8] In some patients, it may remain undetected for one to six years after surgical correction of ventricular septal defect (VSD) or aortic coarctation.[8,9] There are some hypotheses regarding mechanisms contributing to the development of subvalvular AS. Turbulence created by an underlying abnormality in left ventricular outflow tract (LVOT) architecture may contribute to progressive thickening, fibrosis, and scarring of LVOT and otherwise normal aortic valve.[10] Some observations are consistent with congenital mechanisms predisposing development of subvalvular AS. First, among children who undergo surgery for VSD or aortic coarctation, specific LVOT geometric abnormalities, such as alterations of the angle between the aortic outflow and the long axis of the ventricular septum,[11] have been identified on echocardiography, which may predispose to subsequent development of subvalvular AS.[9] Secondly, familial occurrence of subvalvular AS has been described, which may indicate a genetic predisposition.[12] Although co-occurrence of subaortic membrane and BBS may be a coincidental finding, hypotheses mentioned above may reflect a genetic association between the two conditions. Although a combination of BBS and other cardiac abnormalities are well known, a subaortic membrane in a patient with BBS has not been described before. Careful echocardiographic evaluation of patients with BBS, such as in this case report, may allow us to discover novel cardiac abnormalities in this patient population.

Conflict-of-interest issues regarding the authorship or article: None declared

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Key words: Atrial fibrillation; Bardet-Biedl syndrome/diagnosis; echocardiography; heart defects, congenital; kidney/abnormalities.

Anahtar sözcükler: Atriyum fibrilasyonu; Bardet-Biedl sendromu/tanı; ekokardiyografi; kalp defektleri, doğumsal; böbrek/anormallik.