



End Stage Renal Failure and Radial Artery Tortusity: Two Uncommon Manifestations in Bardet-Biedl Syndrome

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Bardet-Biedl Syndrome (BBS) is an autosomal recessive disorder characterized by retinitis pigmentosa, obesity, polydactyly, brachydactyly, hypogonadism and mental retardation. Renal involvement is frequent and is usually presented as minor structural or functional defects. However, end stage renal failure is rare. More importantly radial artery tortusity has not been reported in BBS yet.

Twenty-year-old girl with BBS was admitted to emergency department with complaints of malaise, nausea, seizures and muscle cramps. Initial evaluation revealed severe hypocalcemia (Ca: 3.6 mg/dl) and uremia. Calcium replacement therapy was initiated, and she was hospitalized to the endocrinology department. Detailed investigation revealed end stage renal failure and radial artery tortusity in addition to classical finding of retinopathy with near blindness, brachydactyly, speech deficiency and glucose intolerance. Etiologic investigations pointed out renal failure as cause of hypocalcaemia. Fistulization operation was tried twice, but failed. Doppler ultrasonography of radial artery showed that there was insufficiency in radial artery flow and it had a tortuous appearance. Therefore, continuous ambulatory peritoneal dialysis (CAPD) was initiated and she tolerated it very well.

Key Words: Bardet-Biedl Syndrome, Renal failure

Son Dönem Böbrek Yetmezliği ve Radial Arter Tortusitesi: Bardet-Biedl Sendromunun Nadir Görülen İki Bulgusu

Bardet-Biedl Sendromu (BBS) retinitis pigmentosa, obezite, polidaktili, brakidaktili, hipogonadizm ve mental retardasyon ile karakterize otozomal resesif geçiş gösteren bir hastalıktır. Renal tutulum sık görülür ve daha çok hafif yapısal ve fonksiyonel bozukluklar şeklindedir. Ancak son dönem böbrek yetmezliği çok nadir görülür. Daha da önemlisi radial arter tortusitesi bildirilmemiştir.

Yirmi yaşındaki BBS'li bayan hasta bulantı, kasılma ve kas krampları ile acil servise başvurdu. Hastanın ilk değerlendirilmesinde ciddi hipokalsemi (Ca: 3.6 mg/dl) ve üremi tespit edildi. Kalsiyum replasman tedavisi başlandı ve hasta Endokrinoloji bölümüne yatırıldı. Yapılan ileri tetkiklerinde retinopati, brakidaktili, konuşma bozukluğu ve glikoz tolerans bozukluğu gibi klasik bulgularının yanında son dönem böbrek yetmezliği ve radial arter tortusitesi mevcuttu. Hastanın sonuçları hipokalseminin böbrek yetmezliğine bağlı olarak geliştiğini işaret etmekte idi.

Fistülizasyon operasyonu iki kez yapılmasına rağmen başarısız oldu. Yapılan Doppler ultrasonunda radial arterde yetmezlik ve tortusite saptandı. Bundan dolayı sürekli ambulatuar peritoneal dializ tedavisi başlandı ve hasta tedaviyi iyi tolere etti.

Anahtar Kelimeler: Bardet-Biedl Sendromu, Böbrek yetmezliği

Bardet Biedl Syndrome (BBS) is a multi system autosomal recessive disorder, characterized by rod cone dystrophy, dystrophic extremities, renal dysplasia, hypogonadism, central obesity, learning disabilities and diabetes mellitus.^{1,2} Hepatic fibrosis, short stature, behavioral and speech abnormalities are other features of the disease that can be seen in varying frequency.¹ BBS occurs throughout the world with varying frequencies, and its prevalence rate in North America and Europe ranges from 1:140 000 to 1:160 000 live births.³ However, the rate is much higher in Kuwait and Newfoundland with a prevalence of 1:13 500 and 1: 17 500.²

In 1920 George Bardet while preparing his thesis about hypothalamic obesity, realized that some of his cases had unusual features like polydactyly, retinitis pigmentosa and obesity.⁴ Meanwhile, Arthur Biedl published a case report of two siblings with congenital deformities including retinitis pigmentosa, polydactyl, hypogonadism and mental retardation.⁵ Then Laurence and Moon (LM) went on to consider these conditions to be the same then they called the syndrome Laurence Moon Bardet Biedl, however it was discovered that Laurence Moon and Bardet Biedl are two related but separate syndromes. Because polydactyl, which occurs in 75 % of patients with BBS, is extremely rare in LMS.^{1,2} On the contrary the neurological signs involving spasticity, ataxia is rare in BBS, but is dominated in LMS.^{1,2}

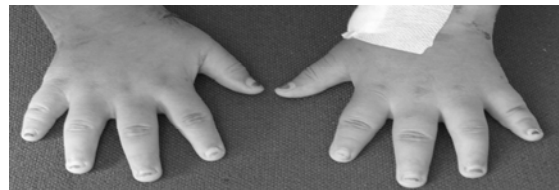
Renal disease occurs in 30%-60% of BBS cases.⁶ Recent studies indicated that renal involvement usually consists of minor structural or functional defects. On renal imaging, structural defects are demonstrated as communicating cysts and dilatation of collecting ducts and calyces. Among these patients, only 5% develop end stage renal failure and require dialysis or transplantation.¹

CASE

20-year-old female patient presented with malaise, nausea, seizures and muscle cramps. She had had these symptoms over the previous 2 months. She had brachydactyly in hands and feet. (Picture 1) Her secondary sex characteristics were delayed. Her breast development was at Tanner 3 stage. (Picture 2) She had menarche when she was 15 years old (compared to her mother and sister, it was delayed). She had nocturnal enuresis up to 17 years of age. At ophthalmological examination, retinitis pigmentosa, optic atrophy and cataract were detected. Optic atrophy was confirmed by visual-evoked potential responses. She had a history of night blindness that had begun in early childhood and progressed toward severe impairment of vision. She had speech deficiency; her voice was breathy and nasal. She had short stature (height: 152 cm, weight: 62.2 kg and body mass index: 27 kg/m²). On admission, laboratory tests included Ca: 3.6 mg/dl, P: 8 BUN:99 mg/dl, Glu:106mg/dl, Cre:10.6 mg/dl, K:4.9 mmol/l, albumin: 3,6 g/dl, T. Protein 7,3 g/dl and micro total protein/creatinin:7,7g. Her urine density was 1015 mg/dl. After Ca replacement therapy, her clinical status improved. Glomerular filtration rate was calculated as 5.4 ml/min, ultrasonographic examination showed bilateral atrophic kidneys (right

one was 6.2x3.4, left one was 7.6x3 cm), and PTH level was 312 pg/ml. All these findings were consistent with end stage renal failure and secondary hyperparathyroidism. For urgent therapy, she was commenced on hemodialysis via jugular vein catheter. Then she was operated for permanent AV fistulization via radial artery and cephalic vein, but the operations were not successful. Doppler ultrasonography of radial artery revealed tortuous appearances and decreased flow in it (flow volume in right and left radial artery- snuffbox is 2.7-14.4; peak systolic velocity is 22-37). Consequently, CAPD was tried, and she tolerated it well.

Picture 1. Brachydactyly



DISCUSSION

In this case report, we described a unique case with Bardet Biedl Syndrome. Our diagnosis was based on classical clinical features (retinopathy, brachydactyly, obesity, development delay, glucose intolerance and speech deficiency). In addition to these features, our case had three uncommon features that were hypocalcaemia, end stage renal failure and radial artery tortuosity.

The ocular disease is progressive and the prognosis for visual function is poor and usually leads to blindness before the age of 20.¹ Retinitis pigmentosa is a common finding; other ophthalmological signs, which may be present, include nystagmus, myopia, optic atrophy, macular dystrophy, strabismus, glaucoma and cataracts.^{1,2} Consistent with these reports our case had retinitis pigmentosa, cataracts and optic atrophy.

Postaxial polydactyl is present in 69% of the cases, and it ranges from a single skin tag to a fully formed digit on all four limbs. Brachydactyly is common and is more frequent in the feet than in the hands. However, syndactyly is much less frequently seen.¹ Our case had brachydactyly in hands and feet without syndactyly.

The causes of obesity appear to be due to both pituitary and hypothalamic abnormalities. Obesity usually begins in childhood and the severity increases

with age. Distribution of adipose tissue is mostly prominent in the trunk and proximal limbs. However our case was overweight, not obese.

Picture 2. Short stature and delayed breast maturation



Although many studies described mental retardation as a major feature, more recent IQ tests revealed that only a minority of patients are mentally retarded.¹ Similarly, our case was not mentally retarded and was student in high school.

Diabetes mellitus is present in 6-32% of the patients.^{1,2} We performed oral glucose tolerance test to our case and revealed impaired glucose tolerance.

Genetic background is important in BBS. It is heterogeneous with 6 gene loci having been mapped to date 11q13 (BBS1), 16q21 (BBS2), 15 q 22 (BBS4) and 3p12 (BBS3), 2q31 (BBS5), 20p12 (BBS6). BBS1 is the most common causative locus.³ We planned genetic screening for the entire family, but they did not give consent for this evaluation.

Renal involvement is frequently associated with BBS, but progression to end stage renal failure is rare. It usually consists of minor structural and functional defects. Beales et al. did the largest extensive study involving 109 BBS patients and their families. Fifty-seven patients had undergone any radiological investigation of the renal tract, and 26 of them were found to have renal abnormalities, but six of patients had chronic renal failure.¹ Hamett et al. studied 20 patients. Three of them had chronic renal impairment.⁷ Linne et al. examined six patients and two of them had end stage renal disease.⁸

Ambulatory peritoneal dialysis is reported to be an effective method for BBS with end stage renal failure. Ulusoy et al. reported a patient with end stage renal failure on hemodialysis.⁹ Roussel et al. described a 6-year-old patient who had CAPD.¹⁰ In our patient, we planned hemodialysis, but could not managed AV fistulization due to radial artery tortusity and decreased radial artery blood flow. Thus, we tried CAPD, and she tolerated it well.

Congenital renal artery abnormalities, like bilateral arterial occlusions and micro aneurysms, were reported previously,⁶ but to our knowledge, no study reported radial artery tortusity and decreased radial artery blood flow. It is difficult to know whether this vascular abnormality is related to the syndrome. However renal arterioler abnormalities, that was described before,⁶ made us to speculate that the abnormality of radial artery might be a part of vascular abnormalities.

In summary, we suggest that patients with BBS should be investigated for radial artery abnormalities

beside the renal abnormalities especially in patients with end stage renal failure before radial artery AV shunt operation.

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