CASE REPORT

Bardet-Biedl syndrome with vulva carcinoma presented with acute renal failure: a case report

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Abstract
Background: Bardet-Biedl syndrome is a rare disorder characterized by retinal dystrophy, obesity, kidney dysfunction, polydactyly, hypogonadism and cognitive impairment. It can be accompanied by systemic findings such as malignancy, hypertension, diabetes mellitus, constitutional and functional disorders of urogenital system and liver fibrosis.
Case report: A 35-year-old woman with Bardet-Biedl syndrome was referred to our outpatient nephrology clinic with dysuria, acute renal failure, and urinary tract infection. A sized 2 x 1 cm mass between labia major and minor was noted, while CT scan showed a lesion that encompassed uterus and extended to the posterior side of the bladder in the left adnexal region and a 3 cm lesion in the liver. Excisional biopsy of the mass revealed a well-differentiated, squamous cell carcinoma. Dysuria resolved with insertion of urinary catheter after bougie dilatation and the patient was referred for radiotherapy.
Conclusion: It should be kept in the mind that renal failure may develop due to constitutional urogenital anomalies such as vulva carcinoma. This can be an important cause of morbidity and mortality in patients with Bardet-Biedl syndrome. Hippokratia 2015; 19 (2):176-178.

Keywords: Bardet-Biedl syndrome, malignancy, renal failure

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Introduction

Laurence-Moon-syndrome (LMS) and Bardet-Biedl-syndrome (BBS) have traditionally been referred as a single condition with the name of Laurence-Moon-Bardet-Biedl-syndrome (LM/BBS)[1,2]. It is now accepted that BBS is a distinct clinical entity similar to, but different from LMS and separated from LMS mainly by the absence of spastic paraplegia and presence of polydactyly. Typical findings in BBS are developmental and progressive degenerative defects such as retinal dystrophy, obesity, polydactyly, kidney dysfunction, hypogonadism and cognitive impairment[2-5].

LM/BBS is a rare autosomal recessively inherited disorder. It can be accompanied by systemic findings including hypertension, diabetes mellitus, structural and functional disorders of urogenital system and hepatic fibrosis[6]. Rarely, urogenital system malignancies such as endometrial carcinoma can be encountered in patients with LM/BBS[7,8]. Nephropathy is one of the most common involvements seen in LM/BBS and is accepted as the most important cause of morbidity and mortality[9-11]. We report a BBS case with vulva carcinoma that presented with acute renal failure due to urinary obstruction, which has never been reported in the literature previously.

Case report

A 35-year-old woman with BBS was referred to our outpatient nephrology clinic with dysuria, acute renal failure, and urinary tract infection. In her medical history, we noted that she had visual loss, obesity, mental retardation and underwent an operation for polydactyly at childhood. She had amenorrhea for the last three years. On physical examination blood pressure was 110/70 mmHg; pulse was 75/minute and body temperature was 36.6 ºC. She was obese (height: 1.60 m; weight: 92 kg; body mass index: 35.9 kg/m^2) with a short neck, rounded face, short limbs and fingers. Visual examination revealed retinitis pigmentosa. In her genitourinary examination, we detected a solid, painless, mobile mass with a size of 2 x 1 cm that was localized between labia major and minor.

Laboratory data were as follows: Hemoglobin: 8.6 g/dl (normal range:12-16), Hematocrit: 29.2% (35-52), white blood cell: 12,340 /mm^3 (4,800-10,800) platelet count: 431,000 /mm^3, glucose: 115 mg/dl (74-106), blood urea nitrogen: 30 mg/dl (6-20), creatinine: 1.9 mg/dl (0.7-1.2), uric acid: 7.1 mg/dl (3.4-7,0), albumin: 3.9 g/dl (3.97-4.94), potassium: 5.9 mmol/l (3.5-5.1), erythrocyte sedimentation rate: 96 mm/h (0-20), C-reactive protein: 18.6 mg/dl (0-0.5), estradiol: 29 pg/ml (0-39),

follicle-stimulating hormone: 2.53 mIU/ml (25.8-134.8), luteinizing hormone: 0.86 mIU/ml (7.7-58.5), urinary erythrocyte count: 4 /high power field, urinary leukocyte count: 106 /high power field. Serum calcium, total protein, sodium, parathormone, ferritin and lipid levels were normal. There was no bacterial growth in urine culture. In addition, evaluation for acid-resistant bacilli was negative.

On ultrasonographic evaluation, the right kidney size was measured 70 mm, whereas parenchyma thickness was 9 mm. A grade 1-2 increase in the echogenicity of renal parenchyma was noted. The right ureteral wall was thickened, and the right renal pelvis was dilated. Also, millimetric cysts and calcifications were detected. The size of the left kidney was 93 mm, whereas parenchyma thickness was 16 mm. In addition to the presence of lobulated contours, parenchymal echogenicity was increased by grade 1-2. An anechogenic cyst with a diameter of 4.5 cm was observed in the left ovary, which passed over its' contours. On Computed Tomography scan, a hypodense mass lesion with a diameter of 3 cm was seen in the liver, which showed a peripheral enhancement during the arterial phase and became isodense to the liver tissue during the venous phase. No contrast passage was observed in the collecting duct system of the right kidney. Also, an asymmetric thickening of the right lateral wall of the bladder was detected. Moreover, a septated hypodense lesion with 5 cm diameter and multi-loculated complicated cystic lesions with intense peripheral enhancement, thar encompass uterus and extend to the posterior side of the bladder in the left adnexal region, were shown. Fluid collection around the endometrial region and a few enlarged lymph nodes at the obturator region were also detected. On magnetic resonance imaging, a complex mass lesion sized 58 x 68 x 100 mm and consisting of solid and cystic components was observed at cervix uteri localization. A septated cystic mass with multi-lobulated appearance was detected in the left adnexal region, which was 42 x 58 mm in size. An excisional biopsy of the mass between labium major and minor was performed, which was reported as a well-differentiated, squamous cell carcinoma in the pathological evaluation.

Intravenous antibiotic treatment with Ceftriaxone (2 x 1 g) was administered. In cystoscopy, a urethral stenosis was detected and a Foley urinary catheter was inserted, after bougie dilatation. Dysuria was resolved; the patient had fever (38 ºC) occurring at an interval of 2-3 days, which was relieved with antipyretics. Blood urea nitrogen, creatinine and C-reactive protein levels were 18 mg/dL, 1.3 mg/dL, and 182 mg/L, respectively while urine leukocyte was found to be 2 /high power field.

The patient was referred to the Departments of Medical and Radiation Oncology after improvement of her renal function tests, and radiotherapy was planned for vulva carcinoma.

Discussion

Eventhough LMS and BBS have traditionally been referred as a single condition, it is now accepted that BBS is a distinct clinical entitiy. BBS has typical manifestations such as developmental and progressive degenerative defects characterised by retinal dystrophy, obesity, polydactyly, kidney dysfunction, hypogonadism and cognitive impairment as it was the case in our patient[2-5]. Moreover, renal dysfunction, hypertension, diabetes mellitus, heart failure, hepatic fibrosis, hyperuricemia, hyperfibrinogenemia, thrombocytosis and/or increased vascular risk may be seen[9-11].

The most common cause of mortality in patients with LM/BBS is nephropathy. Lower urinary tract obstruction, pyelonephritis, glomerulonephritis and hypertension are frequently seen in these patients, whereas recurrent urinary infections may cause chronic pyelonephritis and renal failure. Renal cysts, diverticulum, calyceal deformities and diffuse cortical loss may be also seen. The presence of vesicoureteral reflux can exacerbate these findings[9-11]. In the patient reported, renal failure at presentation was due to urethral stenosis, which was resolved by urinary catheter insertion. However, there was bilateral, structural renal disorder on the radiological evaluation, suggesting previous injuries. It should be kept in mind that renal failure is the most important cause of mortality in these patients. Recurrent urinary infections and obstructions increase the risk for development of renal failure. However, relieving obstruction and effective treatment of infections may prevent renal failure.

The relationship between LM/BBS and increased cancer risk is controversial. Beales et al[12] reported three cases of renal cell carcinoma among 180 identified parents of 109 patients. This was estimated to represent a 17-fold increased risk of renal carcinoma. In contrast, data from Hjortshoj et al[13] did not support the suggested increased risk for renal cancer, in these patients. In the literature, there are case reports including LM/BBS patients with malignancies such as intracranial malignancy, uterine, testicular, renal and endometrial carcinoma[7,8,14]. Obesity and insulin resistance may affect development of malignancy in these patients. Herein, we report a BBS patient with vulva carcinoma, presented with acute renal failure due to urinary obstruction, which has never been reported previously in the literature.

Conclusion

The present case shows that renal failure may develop due to constitutional urogenital anomalies such as vulva carcinoma. Also, careful assessment should be undertaken in terms of malignancy, due to increased risk of cancer, related to obesity in BBS patients.

Conflict of Interest

The authors have no any conflict of interest and any funding support.

References

1. Anadoliiska A, Roussinov D. Clinical aspects of renal involvement in Bardet-Biedl syndrome. Int Urol Nephrol. 1993; 25:

509-514.
2. Sheffield VC. Use of isolated populations in the study of a human obesity syndrome, the Bardet-Biedl syndrome. Pediatr Res. 2004; 55: 908-911.
3. Sapp JC, Nishimura D, Johnston JJ, Stone EM, Heon E, Sheffield VC, et al. Recurrence risks for Bardet-Biedl syndrome: Implications of locus heterogeneity. Genet Med. 2010; 12: 623-627.
4. Riise R, Tornqvist K, Wright AF, Mykytyn K, Sheffield VC. The phenotype in Norwegian patients with Bardet-Biedl syndrome with mutations in the BBS4 gene. Arch Ophthalmol. 2002; 120: 1364-1367.
5. Lofterod B, Riise R, Skuseth T, Storhaug K. Laurence-Moon-Bardet-Biedl syndrome. Nord Med. 1990; 105: 146-148.
6. Green JS, Parfrey PS, Harnett JD, Farid NR, Cramer BC, Johnson G, et al. The cardinal manifestations of Bardet-Biedl syndrome, a form of Laurence-Moon-Biedl syndrome. N Engl J Med. 1989; 321: 1002-1009.
7. Peiker G, Böhm W, Carol W. Laurence-Moon-Bardet-Biedl syndrome and endometrial carcinoma. Zentralbl Gynakol. 1978; 100: 1126-1130.
8. Schwab G, Kriz K. [Two sisters with Laurence Bardet-Biedl-Moon syndrome and concomittant carcinoma of the body of the uterus (author's transl)]. Geburtshilfe Frauenheilkd. 1980; 40: 279-281.
9. Harnett JD, Green JS, Cramer BC, Johnson G, Chafe L, McManamon P, et al. The spectrum of renal disease in Laurence-Moon-Biedl syndrome. N Engl J Med. 1988; 319: 615-618.
10. Riise R. The cause of death in Laurence-Moon-Bardet-Biedl syndrome. Acta Ophthalmol Scand Suppl. 1996; 219: 45-47.
11. Ulusoy S, Kaynar K, Gul S, Ukinc K. Renal failure due to Bardet-Biedl syndrome. A case report. Med Princ Pract. 2004; 13: 380-382.
12. Beales PL, Reid HA, Griffiths MH, Maher ER, Flinter FA, Woolf AS. Renal cancer and malformations in relatives of patients with Bardet-Biedl syndrome. Nephrol Dial Transplant. 2000; 15: 1977-1985.
13. Hjortshøj TD, Grønskov K, Rosenberg T, Brøndum-Nielsen K, Olsen JH. Risk for cancer in patients with Bardet-Biedl syndrome and their relatives. Am J Med Genet A. 2007; 143A: 1699-1702.
14. Yamada K, Miura M, Miyayama H, Sakashita N, Kochi M, Ushio Y. Diffuse brainstem glioma in a patient with Laurence-Moon-(Bardet-)Biedl syndrome. Pediatr Neurosurg. 2000; 33: 323-327.