A Rare Case of Bardet Biedl Syndrome with Cirrhosis of the Liver

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Abstract: Bardet-Biedl syndrome (BBS) is an autosomal recessive condition that impacts multiple body systems. The cardinal features of BBS are Central obesity, Cognitive impairment, renal anomalies, polydactyly, retinal degeneration and male hypogonadism(1). BBS affects males and females in equal numbers. Here we present a rare case of BBS with cirrhosis of the liver and splenomegaly, in a 27 year old man born out of consanguineous marriage. We described that the cirrhosis of liver can be a rare complication of BBS and emphasized the need for early diagnosis and multidisciplinary approach to reduce mortality and morbidity. We also did a brief review of the literature on BBS and other syndromes that closely resemble BBS.

I. Background:
In 1886, Lawrence and Moon described a family with retinitis pigmentosa, obesity, and cognitive impairment who later developed a spastic paraparesis. In 1920 and 1922, respectively, doctors Georges Bardet and Artur Biedl independently described two families with obesity, retinitis pigmentosa, and polydactyly. In previous years, it was believed that both the cases were the same and are described by the term Laurence-Moon-Bardet-Biedl syndrome (LMBBS). In recent years LMBBS has been recognized as inaccurate because the cases exhibit mutations in different genes and are now considered as two distinct: BardetBiedl syndrome (BBS) and Laurence-Moon syndrome (LMS)(2).

II. Case Description:
A 27 year old male presented to outpatient clinic with abdominal distension and yellowish discoloration of eyes for one month. He has a background of delayed developmental milestones and learning difficulties for which he had dropped out of school as reported by his mother. He had a history of difficulty in seeing in the dark for the past six years, which was worsening. He had reduced hearing and increased the frequency of micturition for 6 months. He was born out of consanguineous marriage and no other member of the family had similar complaints.

His vitals were stable and BMI was 31.7 kg/m². On examination, he had icterus, central obesity, a moon-shaped face, polydactyly, small testicular size and absence of the pubic and axillary hair. An abdominal examination showed shifting dullness with splenomegaly. His vision was restricted to the perception of hand movements.

Figure: 1
Post axial Polydactyly of hands(fig:1) and feet (fig:2)
INVESTIGATIONS:
His complete blood picture, renal function tests, liver function tests were normal but ascitic fluid analysis showed high SAAG low protein. His fasting blood sugar was 164mg/dl, post prandial blood sugar was 246mg/dl. Fundus examination showed retinitis pigmentosa with glaucomatous optic atrophy. Audiometry showed mild sensorineural deafness. Testosterone levels were low (173.9ng/dl). Ultrasound abdomen showed altered echotexture of the liver with splenomegaly.
**DIFFERENTIAL DIAGNOSIS:**

**Laurence-Moon syndrome (LMS):**
LMS is an inherited autosomal recessive disorder associated with learning difficulties, diminished sex hormones, and stiffness of the muscles and joints. BBS and LMS are very similar but are considered different because LMS patients do not show signs of extra digits or obesity in the abdomen. For those with Laurence-Moon syndrome, life expectancy is usually shorter than other people. The most common cause of death is linked to renal or kidney issues.(3)(4)(5)

**Alstrom syndrome:**
It is a rare autosomal recessive disorder characterized by vision and hearing abnormalities, childhood obesity, diabetes mellitus, and slowly progressive kidney dysfunction. It usually presents with the initial symptoms of Nystagmus an insensitivity to light(3)(4)(5).

**Meckel syndrome:**
It is an autosomal recessive disorder with a characteristic finding of encephalocele. Polydactyly, scarring-fibrosis of the liver and genital abnormalities are the overlapping symptoms with BBS(3)(4)(5).

**III. Discussion:**
The Bardet–Biedl syndrome is an autosomal recessive disorder with a variable expression of symptoms. The patients with same genotype and even siblings manifest symptoms differently. We diagnosed BBS based on the modified diagnostic criteria proposed by Beales et al.

**Modified diagnostic criteria for diagnosis of BBS proposed by Beales et al., (6)**

<table>
<thead>
<tr>
<th>Primary features</th>
<th>Secondary features</th>
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<tbody>
<tr>
<td>Rod cone dystrophy</td>
<td>Speech disorder/delay</td>
</tr>
<tr>
<td>Post axial polydactyly</td>
<td>Strabismus/cataracts/astigmatism</td>
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<tr>
<td>Central obesity</td>
<td>Brachydactyly/syndactyly</td>
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<tr>
<td>Learning disabilities</td>
<td>Developmental delay</td>
</tr>
<tr>
<td>Male hypogonadism</td>
<td>polyuria/polydipsia</td>
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<tr>
<td>Renal anomalies</td>
<td>ataxia/ poor coordination/imbalance</td>
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<td></td>
<td>Mild spasticity</td>
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<tr>
<td></td>
<td>Diabetes mellitus</td>
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<td></td>
<td>Dental crowding/hypodontia/high arched palate</td>
</tr>
<tr>
<td></td>
<td>Left ventricular hypertrophy/congenital heart disease</td>
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<td></td>
<td>Hepatic fibrosis</td>
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Diagnosis: Four primary features / three primary + 2 secondary features
The rare associations include hypothyroidism, Hirschsprung’s disease, epilepsy, genital anomalies, anal stenosis and abnormal dentition. Our patient had polydactyly, obesity, retinitis pigmentosa, hypogonadism, mental retardation and Diabetes Mellitus i.e five primary and one secondary clinical feature. The patient had cirrhosis of the liver which made this case a rare one.

Numerous sub types of BBS have been identified, with mutations in more than 20 different genes. Of these, BBS1 accounts for ~25-30% cases. The exact pathogenesis of BBS was unknown for a long time. It has recently been recognized that the proteins which are coded for by the BBS4, BBS6, BBS8, and the BBS10 genes are expressed in the basal body of the cilia and that BBS is now regarded as one of the ‘ciliopathies’. The gene products are probably involved in the signaling pathway in the cilia; and the abnormalities interfere with normal development, resulting in the diverse pathological effects of the syndrome. Currently, the management of BBS is supportive and it includes training and rehabilitation for blind patients and for those with specific learning disabilities, hearing aids for deafness, dietary changes and exercise for obesity. Aggressive management of diabetes and metabolic syndrome is necessary to prevent secondary effects on already vulnerable organ systems in BBS. There is a need for annual multidisciplinary review by an ophthalmologist, Nephrologist, Endocrinologist, Psychologist, Dietitian, Speech and language therapist which helps in risk assessment and effective management.

Renal failure is very common and is the most likely cause of death in Bardet-Biedl syndrome. Managing renal issues can improve life expectancy and quality of life. In recent years, there has been a significant advance in the development of therapeutic modalities like Gene Therapy, Readthrough Therapy, Exon Skipping Therapy, Targeted therapy(6)(7).

IV. Conclusion::

The diagnosis of Bardet-Biedl syndrome should be considered in patients with the characteristic phenotype of retinitis pigmentosa, post axial polydactyly, and central obesity. Cirrhosis of the liver can be a rare complication.

References: