CASE REPORT

Bardet-Biedl syndrome: a multisystem disorder with rare dermatological manifestations

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Abstract

Bardet-Biedl syndrome (BBS) is a disorder of primary ciliary dysfunction, having a wide range of systemic and dermatological manifestations. We report the case of a nine-year-old patient having multiple erythematous plaques over the dorsal surface of both feet, scalp seborrhoea,, keratosis pilaris, and polydactyly, associated with night blindness and central obesity. Initial workup correlated well with BBS reporting metabolic syndrome, retinal dystrophy, and gonadal dysfunction. Genetic testing for disease confirmation was not done due to the limited hospital resources. Multidisciplinary symptomatic management was carried out for the patient, along with counselling of the parents regarding possible complications of the disease. This case was reported at the Dermatology Department of Medical Teaching Institute-Hayatabad Medical Complex, Peshawar.

Keywords: Bardet-Biedl syndrome, Cone-rod dystrophy, Ciliopathic disorder, Polydactyly, Acanthosis nigricans, Keratosis pilaris.

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Introduction

Ciliopathies comprise a group of disorders associated with genetic mutations encoding defective proteins, which result in either abnormal formation or function of cilia, manifesting clinically as retinal degeneration, renal disease, cerebral anomalies, congenital fibrocystic diseases of the liver, diabetes, obesity, and skeletal dysplasias. Bardet-Biedl syndrome (BBS) is a rare disorder of cilia, affecting children born from consanguineous marriages, with autosomal recessive mode of inheritance due to mutations in 21 identified genes (BBS1-BBS21).[1] Beales et al. proposed a clinical diagnostic criterion for BBS enlisted in Table 1.[2,3]

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BBS presents dermatologically as seborrheic dermatitis, keratosis pilaris, and obesity-related cutaneous disorders.[4] Prevalence ratio of BBS in European countries is around one in 160,000.[1] In Pakistan, 18 families have been reported with this disorder according to the available clinical data.[5] The management of BBS relies mainly on weight reduction and on multidisciplinary approach to prevent its associated complications.[6]

This clinical case tends to highlight the need of a better diagnostic protocol for such rare genetic disorders, in a clinical setting of resource-limited hospitals with poor or inaccessible molecular diagnostic facilities.

Case Presentation

A nine-year-old female patient presented to the Dermatology Department of Hayatabad Medical Complex, Peshawar, in October 2023, with multiple erythematous oozy plaques over the dorsal surface of both feet that had been recurring since a year, with disease aggravation for one week, and responding fairly well to wound care with systemic antibiotics. The patient also had central obesity with polydactyly, without any history of polyuria or polyphagia. She had night blindness and learning difficulties as reported by her parents. It was a consanguineous marriage, with normal health status of the other four siblings.

Figure-1: Clinical manifestations of Bardet-Biedl syndrome (BBS)
A. Facial dysmorphism showing moon-like face, broad nasal bridge, deep-set eyes
B. Polydactyly in both hands
C. Central obesity with infected eczematous plaques over bilateral feet

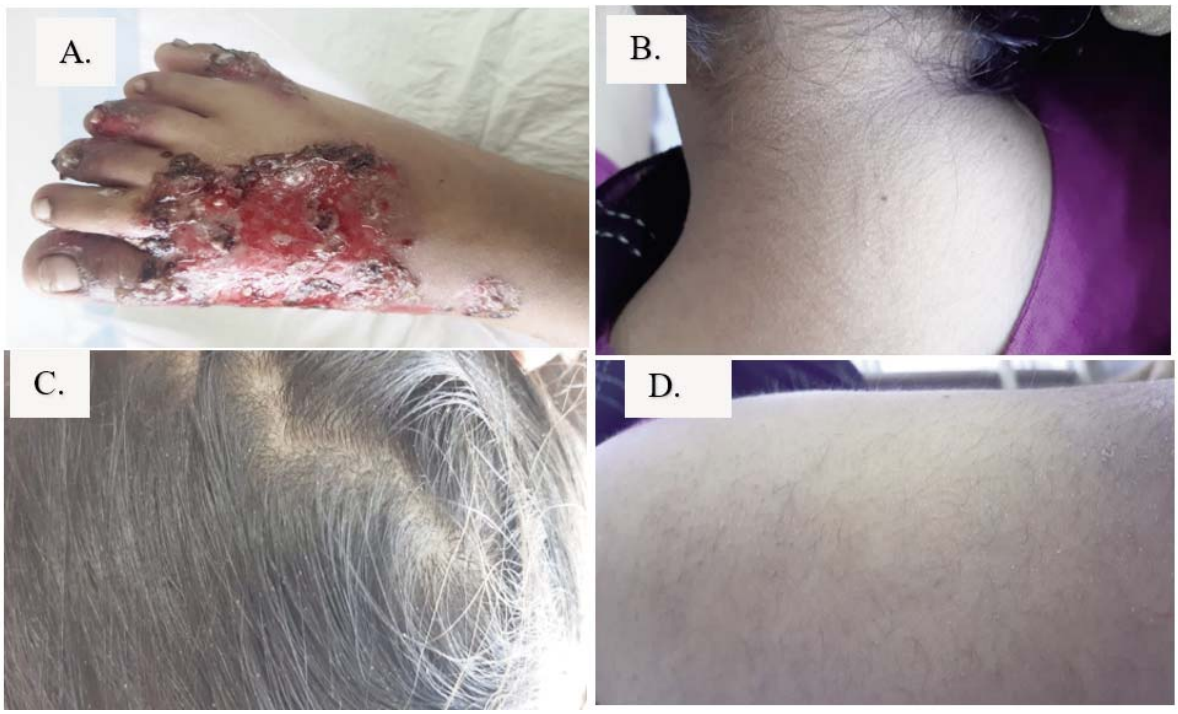

Figure-2: Dermatological manifestations of Bardet-Biedl Syndrome (BBS)
A. Multiple eroded erythematous oozy plaques with yellowish-brown crusts at the edges involving the dorsum of foot and few toes, with polydactyly.
B. Acanthosis Nigricans over neck.
C. Scalp Seborrhea.
D. Keratosis Pilaris over upper arm with surrounding xerosis.

On examination, she was vitally stable and afebrile, with body mass index (BMI) of 30, fasting blood glucose level of average 105 mg/dL, regular pulse rate and rhythm, blood pressure of 120/70 mmHg, and a normal respiratory rate. The patient had a moon-like face with central obesity, facial dysmorphism, and polydactyly (Figure 1). Dermatological examination revealed multiple erythematous non-indurated plaques, bilateral symmetrically over dorsal surface of the feet and toes (the largest one measured approximately 9x6cm), with pus discharge and thick brown crusting at the margins, along with oedema of the surrounding skin. Additional features were keratosis pilaris over both the upper arms, generalised xerosis, acanthosis nigricans over the neck, diffuse scalp seborrhea, and dysmorphic facial features, with deep-set eyes and broad nasal bridge (Figure 2). The rest of the dermatological examination was unremarkable. Eye examination revealed bilateral Bull's eye maculopathy, with arteriolar attenuation and bony spicules. Systemic examination was insignificant, with no neurological or cardiovascular defect.

Her wound culture yielded Methicillin-resistant Staphylococcus Aureus (MRSA), with drug sensitivity to Vancomycin, Imipenem, Linezolid, Doxycycline, and Gentamicin. Her HbA1C was in pre-diabetic range of 6.02% with deranged lipid profile. She had no cardiac anomaly on echocardiogram. However, her ultrasound of

Table-1: Beales et al. diagnostic criteria for Bardet-Biedl syndrome (BBS).

PRIMARY FEATURES	Cone-Rod Dystrophy
	Polydactyly
	Truncal Obesity
	Learning Difficulties
	Renal Anomalies
	Hypogonadism In Males
	Genital Malformations in Females
SECONDARY FEATURES	Speech Disorder / Delay
	Strabismus / Cataract / Astigmatism
	Brachydactyly / Syndactyly
	Developmental Delay
	Polyuria / Polydipsia
	Ataxia / Poor Coordination / Imbalance
	Mild Spasticity
	Diabetes Mellitus
	Hepatic Fibrosis
	Congenital Heart Disease / Left Ventricular Hypertrophy
	Dental Crowding / Hypodontia/ Small Roots / High Arched Palate

For clinical diagnosis, the following is required:
Four Primary Features OR Three Primary + Two Secondary Features

Table-2: Laboratory reports.

Tests	Normal Range	Patient's Level
Hb, g/dL	11.5 – 17.5	12.2
MEAN CELL VOLUME, fL	76-96	81
WBC, x10.e3/µL	4 – 11	13.5
EOS, %	0 – 6	2.9
PLATELETS, x10.e3/µL	150 -450	218
BLOOD UREA, mg/dL	18 -45	20.8
CREATININE, mg/dL	0.42-1.06	0.49
TOTAL BILIRUBIN, mg/dL	0.1-1.0	0.28
ALT/GPT, U/L	10-50	39.5
ALKALINE PHOSPHATASE, U/L	40-129	204
TSH, IU/mL	0.3 – 4.2	3.99
HbA1C, %	Pre-Diabetes: 5.7- 6.4%	
Diabetes Mellitus: >6.5%	6.02%	
TRIGLYCERIDES, mg/dL	<200	211
CHOLESTEROL, mg/dL	<200	205
HDL CHOLESTEROL, mg/dL	35-65	27
URINE RE WBCs, 0-5/HPF	0-5	10-12
URINE CULTURE	No Growth Yielded	
WOUND CULTURE	Growth of MRSA sensitive to Linezolid, Vancomycin, Doxycycline, Imipenem, Gentamicin	

Baseline investigations were done at the time of admission. Normal laboratory values taken from the Department of Pathology, Hayatabad Medical Complex, Peshawar, KPK, Pakistan

the abdomen and pelvis revealed a non-existent uterus and fatty liver with increased parenchymal echogenicity. Moreover, her optical coherence tomography (OCT) confirmed cone-rod dystrophy. The rest of the baseline and hormonal investigations were unremarkable as enlisted in Table 2.

Keeping in view her cutaneous manifestations, differential diagnoses of infected eczema, atopic dermatitis, and hyperimmunoglobulin-E syndrome (HIES) were proposed. However, the clinical and laboratory correlation, along with facial dysmorphism, hypogonadism, and cone-rod dystrophy were consistent with BBS. Genetic analysis required for confirmation of this disorder was not performed due to the unavailability of this facility in our clinical setting.

There is no specific therapy for BBS till date. The patient in this case study was managed symptomatically, after consultation with multiple clinical disciplines. Weight reduction and nutritional counselling were advised for metabolic syndrome. Her fasting blood glucose level was regularly monitored during the hospital stay. She received the basic wound care including saline soaks and saline washes, along with a 10-day course of topical and systemic antibiotic as per the pus culture and sensitivity report. For generalised xerosis, liberal use of bland emollients was advised. The skin lesions responded well to the management and showed significant progress towards healing, with removal of crusts and reduction in exudate and erythema. Her cone-rod was not managed during this consultation. Parents were advised to bring the child for regular follow-up to monitor for any possible complication.

Discussion

Bardet-Biedl Syndrome (BBS) is a ciliary dysfunctional disorder usually noticed by the parents at pre-pubertal age, as the affected children depict slightly low intellect at school.[7]

The case presented in this report was clinically diagnosed as BBS according to the Beales et al. diagnostic criteria,[4] with features of hypogonadism, cone-rod dystrophy, central obesity, polydactyly, and learning difficulties. Cutaneous features of this case were also suggestive of BBS, including acanthosis nigricans, keratosis pilaris, and seborrheic dermatitis, which were in agreement with another study conducted by Robert M. et al exploring the cutaneous features of BBS.[4] The genetic mutations (BBS1-BBS21) associated with this disorder require molecular analysis for identification. However, the probable diagnosis in resource-limited setting of tertiary care hospitals in Pakistan is based on the history, clinical examination, and the available investigations of the patient.

A multidisciplinary approach is required for the management of BBS. Patients should be offered educational programmes for learning difficulties and adaptive living skills for cone-rod dystrophy. In addition to this, genetic counselling and surveillance for the associated complications is mandatory for improving the disease outcome.[8]

Conclusion

Bardet-Biedl Syndrome (BBS) is a ciliopathic disorder affecting multiple systems that usually remains undiagnosed due to its rarity and lack of genetic analysis and diagnostic facility. The present case report signifies that diagnostic correlation from multiple clinical disciplines, along with genetic counselling, is required for better prognosis and effective management of rare disorders like BBS.

Consent: Written informed consent was obtained from the patient's guardian for publication of the details of her medical case and the accompanying images in this study.

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AUTHOR'S CONTRIBUTION:
GU: Concept and design.
SS: Data acquisition, analysis and interpretation.
HM & MQ: Drafting and revision.
FF: Final approval.
MS: Agreement to be accountable for all aspects of the work.