

ABSTRACT

Bardet Biedl syndrome is a rare autosomal recessive disorder with variable clinical presentation and challenging diagnosis. Recognition of orofacial features might help in the diagnosis. Dental management of affected patients might be complicated by renal, cardiac, metabolic, neurosensory, and cognitive defects.

KEY WORDS: Bardet Biedl syndrome, dental, gingival enlargement, rare diseases

Oral healthcare management in Bardet Biedl syndrome

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Introduction

Bardet Biedl syndrome (BBS) is a rare autosomal recessive disorder. Described in 1920s by G. Bardet of France and A. Biedl of Germany,¹ the syndrome is characterized by a wide spectrum of features including retinal dystrophy, learning disability, cognitive defects, renal dysfunction, obesity, and postaxial polydactyly, genital, cardiac, and dental anomalies.² BBS shares many phenotypic features with Laurence-Moon syndrome described by Laurence and Moon of England in 1866,¹ and the disorders were previously considered the same—being referred to as the Laurence-Moon-Bardet-Biedl syndrome. However, clinical and genetic studies have identified differences between the two, and BBS is now considered a separate entity.² Nevertheless, there remains considerable terminological confusion in the literature.

The diagnosis of BBS is challenging because of variable clinical features and the presence of significant inter- and intrafamilial variation.³⁻⁵ Beales *et al.* proposed criteria for diagnosis of BBS (Table 1); clinical diagnosis is established if at least four major features or three major and two minor features are present in a patient.⁶ BBS is genetically heterogeneous, and to date 19 genes (*BBS1-19*) have been identified to account for the majority of clinically diagnosed BBS.⁷ Interestingly, recent studies demonstrated that mutations of certain genes, such as *BBS12*, are linked to a more severe phenotype.⁸ A higher prevalence of BBS has been reported in communities with high rates of

consanguineous marriage such as those of the Middle East (1:13,000) and Newfoundland (1:18,000).^{3,4} BBS is far less common in North American, African, and European populations (1:140,000-160,000).⁵

Orofacial anomalies are minor diagnostic criteria for BBS and include crowding, missing teeth, small teeth and short dental roots, and high-arched palate,⁶ but few reports have formally described the oral manifestations, though recognition of orofacial anomalies might help differentiate BBS from similar syndromes such as Alstrom syndrome and McKusick-Kuffman syndrome.⁹⁻¹¹ In addition, patients with BBS presenting for oral healthcare might require special

Table 1. Diagnostic criteria of BBS.

Major features
Red cone dystrophy
Postaxial polydactyly
Obesity
Genital anomalies
Renal anomalies
Learning difficulty
Minor feature
Speech delay
Developmental delay
Diabetes mellitus
Dental anomalies
Congenital heart disease
Syndactyly
Ataxia/poor coordination
Anosmia

management considerations because of the associated cognitive defects and renal, metabolic, or cardiac complications. In this report, we describe the oral/dental findings of a 27-year-old male with BBS, and discuss the management.

Case report

A 27-year-old male presented with complaints of toothache, oral malodor and gingival bleeding. The patient was the third child of consanguineous (paternal cousins) parents. His birth at full term was a normal delivery with birth weight around 3 kg. He was born with six toes (postaxial polydactyly) in each feet; the sixth toe of the right foot was surgically removed at the age of 2 years. At the age of 12 years, he suffered from early-onset renal failure which was managed by hemodialysis for a period of 6 years followed by renal transplantation at the age of 19 years. Interestingly, his older brother had died at the age of 8 years from chronic renal failure; other family members were apparently healthy with no chronic medical issues. His current medications included ciclosporin, prednisolone, and atenolol.

Upon systemic examination, the patient had learning disability and showed lack of attention and autistic-like

behaviors. The patient had impaired vision with inability to see during the night due to red cone dystrophy. He had short and broad limbs with postaxial polydactyly involving the left foot; no evidence of other skeletal abnormalities was detected. His body mass index was 31.4, and he had truncal obesity and hypogonadism (Figure 1).

Extraoral head and neck examination showed mild hypertelorism, strabismus of the right eye, a long philtrum, hypotony of the upper lip, and mouth breathing. Cranial nerve examination showed impaired olfaction only. Complete blood count indices and kidney function tests were within normal ranges.

Intraoral examination revealed bilateral posterior cross-bites, dental spacing, plaque accumulation, and multiple proximal and occlusal caries involving teeth no 2, 4, 6, 7, 8, 9, 10, 11, 15, 18, 19, 28, 29, and 30. OPG examination revealed short dental roots, particularly of the lower anterior teeth, and congenitally missing third molars



Figure 1. Postaxial polydactyly of the left foot.

and lower lateral incisors (Figure 2). Generalized gingival enlargement was evident, particularly involving the upper labial and palatal gingivae (Figure 2).

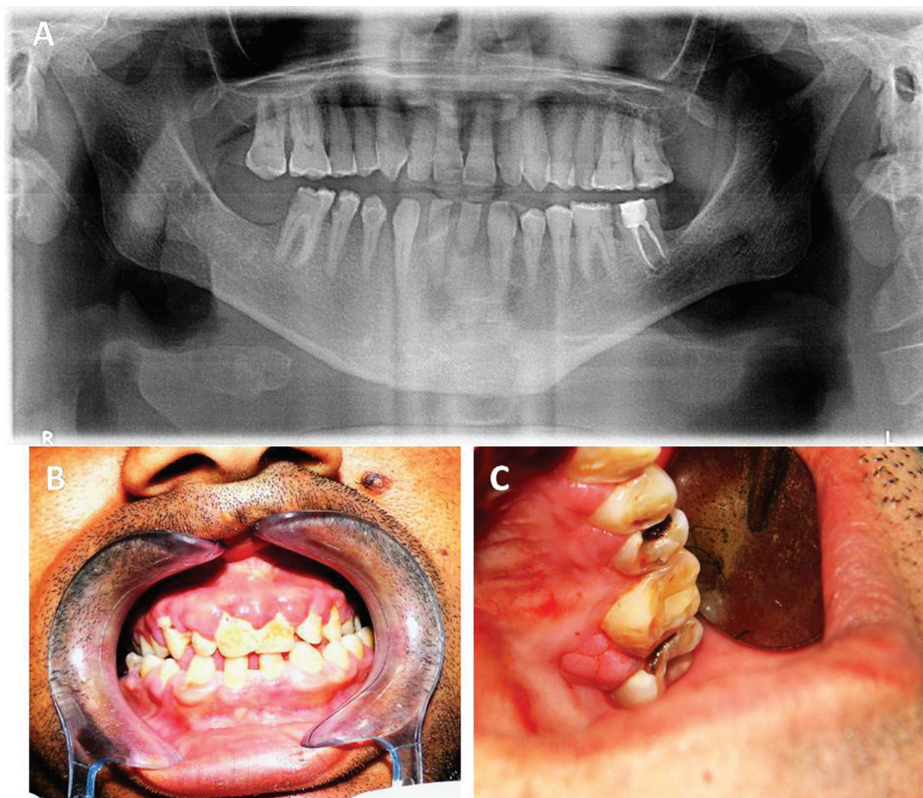


Figure 2. (A) OPG showing missing lower lateral incisors and short dental roots, particularly of lower anterior teeth. (B) Gingival enlargement of upper labial gingivae. (C) Gingival enlargement involving upper palatal gingiva.

Soft tissue examination revealed leu-koedema of both buccal mucosae.

The patient showed good cooperation with the dental team and was tolerant to dental treatment; therefore, all procedures were performed under local anesthesia without any need for sedative drugs. An internal bevel gingivectomy was performed in one surgical session. The patient was instructed to double his daily dose of prednisolone at the day of surgery to prevent adrenal crisis, and was given 2 g amoxicillin 1 hour before gingivectomy to avoid secondary infection associated with immunosuppression. The patient was instructed to rinse with 0.12% chlorhexidine gluconate twice a day for 1 week, and was prescribed paracetamol to control postoperative pain. Instructions on oral hygiene and advice on low-sugar, fiber-rich diet was given to the patient and his parents, and periodontal maintenance was scheduled every other month (Figure 3). Restorative work was performed in multiple sessions without any need for antibiotic or steroid prophylaxis. At 10-month follow-up, there were no signs of recurrence of the gingival enlargement; but the patient showed evidence of gingivitis, probably due to irregular attendance at periodontal maintenance appointments, mouth breathing and difficulty in plaque removal because of his visual problems (Figure 3). The nephrologist was consulted regarding the possibility of changing the immunosuppression regimen since it might be implicated in the observed gingival enlargement; but the decision was to

keep the patient on the same regimen provided no recurrence of gingival enlargement became evident.

Discussion

BBS is a rare autosomal recessive disorder of variable clinical features and genetic heterogeneity whose diagnosis is based primarily on clinical diagnostic criteria.⁶ Molecular confirmation of the diagnosis can be obtained in nearly 80% via direct sequencing of BBS gens (*BBS1-19*).^{1,6}

Our patient demonstrated all the major diagnostic features of BBS including visual impairment, postaxial polydactyly, obesity, genital anomalies, renal dysfunction, and learning difficulty. In addition, he exhibited minor diagnostic features including developmental delay, anosmia, and orodental anomalies.

Dental anomalies have been reported in nearly 50% of patients with BBS, and include missing teeth, short roots, arched palate, gingival enlargement, incompetent lips, retrognathic mandible, and taurodontism.^{1,10} In a recent study of 39 patients with BBS, Andersson *et al.* examined 82.9% to have taurodontism, suggesting that taurodontism anomaly should be included in the diagnostic criteria of BBS.¹¹ Recognition of orodental features might help to distinguish BBS from similar syndromes such as Laurence-Moon syndrome, Cohen syndrome, Alstrom syndrome, and McKusick-Kuffman syndrome; dentists therefore can have an important role in the diagnosis.

Our patient demonstrated ciclosporin-induced gingival enlargement which was aggravated by plaque accumulation and mouth breathing. The reported prevalence of ciclosporin-induced gingival enlargement is between 8% and 100%, depending on genetic susceptibility, age, dose of drug, duration of drug therapy, and presence of dental plaque.¹² Gingivectomy with oral hygiene instructions and periodontal maintenance is the standard management of bothersome gingival enlargement. Liaison with the nephrologist is required to plan treatment and to consider modifying the immunosuppression regimen, particularly in cases of severe and recurrent drug-induced gingival overgrowth. Our patient responded favorably to gingivectomy and showed no recurrence at 10-month follow-up, however, he showed evidence of gingivitis, probably due to irregular attendance at periodontal maintenance appointments, mouth breathing, lack of compliance with dietary advice, and difficulty in plaque removal because of his associated visual problems.

Patients with organ transplants are usually prescribed systemic steroids for immunosuppression. Traditionally, prophylactic steroid cover was recommended before dental procedures to avoid the potential occurrence of adrenal crisis. However, the recent World Workshop of Oral Medicine VI (2015) on the controversies in the management of medically compromised patients concluded that there is no strong scientific evidence to support or refute this practice.¹³ The general trend from expert opinion is not to provide steroid supplement for most routine dental procedures under local anesthesia, and reserving steroid supplementation for more stressful procedures, those performed under general anesthesia, and when the patient's health is poor.^{14,15} There are diverse regimens for preoperative steroid supplementation. In this case, we decided to double the daily dose of steroid at the day of gingivectomy since the procedure was judged to be moderately stressful and required little time to complete. Steroid supplementation was not given for routine restorative

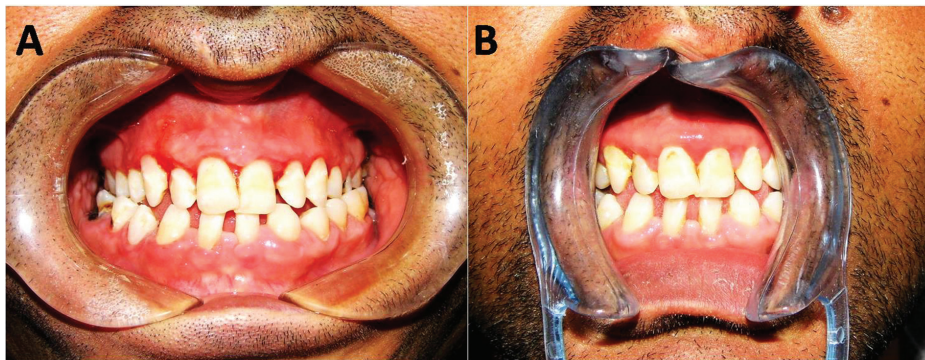


Figure 3. (A) Gingival healing 1 week following gingivectomy. (B) Ten-month follow-up showing plaque accumulation and mild gingivitis with no recurrence of gingival enlargement.

work and periodontal maintenance. Transplant patients may also present issues related to blood-borne viral infections.

Patients with BBS have variable degrees of learning disability and cognitive deficit. Patients with BBS are often reported to have labile behaviors and, like autists, prefer to have a fixed routine, speech delay, and may have elements of obsessive compulsive behavior and poor social communication;¹⁶ compliance with dental treatment might therefore be compromised. Our patient showed attention problems and autistic-like behaviors, however, his compliance with the dental treatment proved to be satisfactory, and all dental procedures were performed under local anesthesia alone. Cases with more severe cognitive and behavioral deficit might need the use of adjunct sedation techniques to perform dental treatment. Visual impairment due to red cone dystrophy is a cardinal feature of BBS;^{1,17} affected patients therefore might have difficulties accessing dental facilities and performing adequate oral hygiene.

It has been reported that 7% to 50% of patients with BBS might have cardiac abnormalities including valvular stenosis, patent ductus arteriosus, and cardiac myopathies.^{6,18} Dentists should therefore consult the physician if there is any evidence of cardiac involvement. Furthermore, dentists are required to follow guidelines applicable in their region regarding endocarditis prophylaxis.¹⁹

Summary

BBS is a rare autosomal recessive disorder with variable clinical presentation and challenging diagnosis. Recognition of orofacial features might help in diagnosis. Dental management of affected patients might be complicated by renal, cardiac, metabolic, neurosensory, and cognitive defects. Special-need dentists might be consulted regarding the oral

features and dental management planning of affected patients.

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Conflict of interest

None declared.

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