Case Report

Role of Liraglutide in improving diabetes and suppressing appetite in Biedl-Bardet syndrome

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SUMMARY

Biedl-Bardet syndrome (BBS) is a rare autosomal recessive disorder that is characterized by severe abdominal obesity, intellectual disability, polydactyly, male hypogonadism, visual impairment and functional or structural abnormalities of the kidneys. Traditionally, lifestyle changes and bariatric surgery has been used to manage obesity in Biedl-Bardet syndrome while oral hypoglycemic agents and insulin has been used for management of diabetes. Recently, Setmelanotide has been approved for management of chronic weight management in adults and children more than 6 years old with Biedl-Bardet syndrome. We report the case of an adolescent male with BBS who was initiated on liraglutide not only to manage his diabetes but also to suppress his appetite, thus helping in weight loss. To the best of our knowledge, this case is one of the few successful uses of a glucagon like peptide-1(GLP-1) agonist in an adolescent male with Biedl-Bardet syndrome and type 2 diabetes mellitus with the aim of controlling his hyperphagia as well as his diabetes.

Learning Points:

- Biedl-Bardet Syndrome is a rare autosomal recessive disorder characterized by obesity, insulin resistance, diabetes mellitus and hyperphagia.
- Conventional ways of treating diabetes in adolescent with Biedl-Bardet syndrome such as insulin leads to weight gain and worsening of insulin resistance.
- GLP-1 agonist can be used not only to control diabetes but also to suppress hyperphagia in Biedl-Bardet Syndrome.

BACKGROUND

Biedl-Bardet syndrome (BBS) is a rare autosomal recessive disorder that is characterized by severe abdominal obesity, intellectual disability, polydactyly, male hypogonadism, visual impairment and functional or structural abnormalities of the kidneys.[1] Rapid weight gain usually begins after one year of age with hyperphagia being the most probable cause.[2] Obesity-related co-morbidities such as diabetes mellitus, hypertension, and hypercholesterolemia are also common in BBS.[3] We present the case of an adolescent male with BBS who was initiated on liraglutide not only to manage his diabetes but also to suppress his appetite, thus helping in weight loss. To the best of our knowledge, this case is one of the few successful uses of a GLP-1 (glucagon like peptide-1) agonist in an adolescent male with Biedl-Bardet syndrome and

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type 2 diabetes mellitus with the aim of controlling his hyperphagia as well as his diabetes.

CASE PRESENTATION

A 17-year-old male with Biedl-Bardet syndrome [comprising of obesity, diabetes for the past three years with no diabetic complications, hyperphagia, polydactyly (Fig.1), intellectual disability, and delayed milestones] presented to the Endocrinology clinic with complaints of hyperphagia, weight gain and poor diabetes control. He was already taking Regular human insulin (R) 50 units three times without basal insulin per day with meals. On examination, his blood pressure was 140/90 mmHg, weight was 125 kg and BMI was 39.2. Polydactyly of one hand had been surgically corrected in the past. He had signs of insulin resistance such as acanthosis nigricans. He didn't complain of any visual symptoms or genitourinary issue.

Investigations: Investigations revealed total triglycerides: >885 mg/dL (normal: <150 mg/dL), HbA1c: 9.7% (normal: < 5.7%) and creatinine: 1.32 mg/dL (normal: 0.72 - 1.25 mg/dL). Liver function tests were not performed on this indication as it would not have altered the management.

Treatment: On the account of his complaints of hyperphagia and obesity as well as associated history of type 2 Diabetes mellitus and signs of insulin resistance, he was prescribed Liraglutide after taking his father's consent at the dose of 0.6 mg daily and increased to 1.2 mg after one week which he tolerated well without any GI side effects. He was advised to stop regular human insulin (R) and was instead prescribed insulin glargine 40 units once daily along with metformin extended release 750 mg once daily.

Outcome and Follow up: At his follow up visit after 2 months, he reportedly felt better, and his appetite was appropriately suppressed. His weight remained 125 kg though HbA1c had improved to 8.3%. He did not attend his subsequent follow up visits due to Corona virus pandemic but was assessed 1 year later. At this visit his weight had now gone down by 5 kg to 121 kg, his appetite remained suppressed, and his HbA1c had improved to 7.1%.

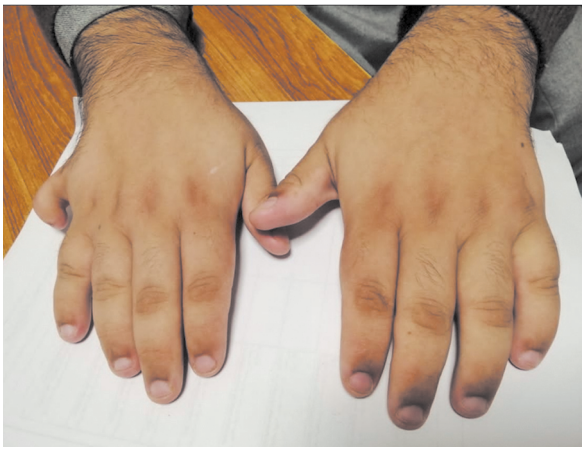

Fig.1: Polydactyly of right hand with surgical correction of left hand.

DISCUSSION

Biedl-Bardet syndrome belongs to a family of ciliopathies and can be diagnosed clinically if at least 4 out of 6 primary diagnostic features are present, and if only 3 primary features are detected, then 2 secondary features are also required to confirm a diagnosis of BBS[4] (Table-I). However, due to clinical overlap with other causes of syndromic obesity, genetic testing is also usually employed.[5] Obesity is the second major feature of BBS with a frequency of 72-96% depending on measurement criteria[2] and therefore its management is of paramount importance. Studies in BBS mouse models have shown that obesity is associated with increased food intake, decreased mobility, defects in leptin action[6] and disrupted energy homeostasis due to alteration in resting energy expenditure (REE).[7]

Sleeve gastrectomy is safe and effective for the treatment of morbid obesity in adult patients with BBS.[8]

Table-I: Primary and secondary diagnostic features of Biedl-Bardet syndrome.

	Primary Diagnostic Features	*Secondary Diagnostic Features*
Biedl-Bardet Syndrome	Rod-cone dystrophy	Developmental delay
	Polydactyly	Speech deficit
	Obesity	Brachydactyly or syndactyly
	Genital abnormalities	Dental defects
	Renal defects	Ataxia or poor coordination
		Olfactory deficit
	Learning difficulties	Diabetes mellitus

It leads to significant weight loss, thereby improving diabetes, hypertension, and non-alcoholic fatty liver disease. The effects of sleeve gastrectomy in patients with BBS are similar to those in polygenic obese patients. A recent review of previous literature assessed patients with BBS that were treated with several different surgical procedures, such as laparoscopic sleeve gastrectomy, Roux-en-Y gastric bypass, and adjustable gastric banding. Their meta-analysis reveal that at 26 months after sleeve gastrectomy, patients regain weight along with recurrence of diabetes and dyslipidemia requiring medication resumption.[9]

We describe an adolescence patient with Biedl-Bardet syndrome whose main concerns were hyperphagia and poor diabetes control. He was on higher doses of regular insulin which was not only contributing to his weight gain but also might be responsible for his complaints of hyperphagia through hypoglycemic episodes, though we were unable to confirm this by looking at his blood glucose readings. Tightening his diabetes control through addition of basal insulin and adjustment of his regular insulin might have improved his diabetes control but would have contributed to more weight gain.

Given the potential of liraglutide as an anti-obesity as well as anti-diabetic agent and its recent approval to be used in adolescents with type 2 diabetes between the ages of 12-18 years, we thought of liraglutide as an appropriate therapy in our patient. By explaining the rationale behind using liraglutide to patient and his parents, liraglutide was added along with insulin Glargine and metformin, while at the same time stopping his regular insulin. This not only resulted in better glycemic control but also contributed to appetite suppression and weight loss. We suspect that this suppression in appetite is due to a combination of direct action of liraglutide on the appetite center in the hypothalamus and a reduction in hypoglycemic episodes due to reduction in dose as well as switching to appropriate type of insulin use.

While GLP-1 agonists have proven to be effective for weight loss in syndromic obesity, there is no reported case of GLP-1 agonist use in Biedl-Bardet syndrome to date to the best of our knowledge. Liraglutide can therefore be used as an adjunct medicine in patients who have BBS, whether they underwent bariatric surgical procedure or not, and have solely presented with hyperphagia and obesity. Our findings cannot be generalized to other patients at this stage and further studies are needed to determine whether liraglutide can be used as an effective treatment option for patients with BBS. Nevertheless, our case highlights the need to study the role of liraglutide as an adjunctive treatment to bariatric surgery in patients with BBS.

Conflict of Interest: There are no potential conflicts of interest, financial or otherwise.
Disclosure: There is nothing to disclose.

Patient Consent: Written informed consent was obtained from patient and his parents for publication of patients' clinical details and clinical image.

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