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Liraglutide therapy in an adolescent with Prader-Willi syndrome and concomitant diabetes mellitus

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A 14-year-old male patient was admitted to our hospital because his blood glucose levels had been high for a day. His fasting venous blood glucose level was 24.52 mmol/L, glycated haemoglobin (12.5%; RR: 4–6%), and β-hydroxybutyric acid (0.83 mmol/L; RR: 0.03–0.3 mmol/L), and he had xerostomia, polydipsia, polyuria, and weight loss. Seven years earlier, the patient was diagnosed with Prader-Willi syndrome (PWS)/Angelman syndrome in the Paediatric Department of the Second Affiliated Hospital of Xi'an Jiaotong University through genetic analysis. At that time, he had normal blood glucose levels and pancreatic islet function. There was no related medical history in his family. His height was 140 cm; body weight, 61.5 kg; and body mass index (BMI), 31.4 kg/m^2. He had an unusual face, almond-shaped eyes, a childish voice and appearance, and mental retardation. He had a short penis, cryptorchidism, and scrotal dysplasia, with no axillary and pubic hair. Based on the above findings, the patient was diagnosed with a special type of diabetes mellitus associated with PWS. During hospitalization, he was treated with an insulin pump and metformin to control blood glucose. His fasting blood glucose levels varied in the range 12–18.2 mmol/L, and his postprandial blood glucose levels were between 14.4 and 26.5 mmol/L within one week of treatment. After liraglutide therapy was approved by the Ethics Committee of our hospital, it was started with a dose of 0.3 mg. No discomfort or abnormalities in biochemical indices were found after 3 days of liraglutide therapy. Therefore, the liraglutide dose was progressively increased to 1.2 mg. The patient experienced mild nausea, but his appetite was relatively decreased, and blood glucose control was markedly improved. At 3- and 6-month follow-up, the patient tolerated liraglutide well and had no evident gastrointestinal symptoms such as nausea, vomiting, and diarrhoea. Additionally, no severe complications such as hypoglycaemia and pancreatitis occurred during the course of treatment (Tab. 1).

PWS is a rare disorder caused by the loss of function of imprinted genes in the 15q11.2-q13 region of the paternal chromosome. As a result of advances in medical treatments and technologies over the years, the mortality of infant patients has been steadily declining and, accordingly, the number of adolescent and adult patients with PWS has been increasing progressively [1]. The prognosis of PWS is poor, and there is no specific treatment available. In this study, we report the case of a 14-year-old patient with PWS caused by aberrant gene methylation in the 15q11-q13 region. PWS is associated with hyperphagia and life-threatening morbid obesity, and it is the most common cause of symptomatic obesity among known genetic disorders. With respect to blood glucose management, diet control and weight loss are essential for the treatment of PWS patients. However, PWS patients exhibit a certain degree of hypomentia and uncontrolled eating [2]; therefore, drug intervention and strict food management by caregivers are both necessary for their treatment. Liraglutide is a long-acting glucagon-like peptide-1 (GLP-1) receptor agonist that stimulates insulin secretion, represses glucagon secretion, and reduces appetite [3]. In recent years, the use of liraglutide for the treatment of adult PWS patients has been reported in a few countries, including China, and it has been generally associated with satisfactory outcomes [4]. However, its application in adolescents with PWS has

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Table 1. *Changes in the physical and biochemical indices and pancreatic islet functions of our patient before and after treatment with liraglutide*

Time	Weight [kg]	Blood pressure [mm Hg]	Abdominal circumference [cm]	Fasting blood glucose [mmol/L]	Haemoglobin A1c [%]
Baseline	61.5	113/82	106	10.38	12.5
3 months	60	115/78	103	8.49	7.5
6 months	58.6	112/75	99	7.60	7.1
Time	**Alanine transaminase [U/L]**	**γ-Glutamyl transferase [U/L]**	**Creatinine [μmol/L]**	**Albumin/Creatinine [mg/gCr]**	**Low-density lipoprotein cholesterol [mmol/L]**
Baseline	43	69	27	Normal	3.21
3 months	36	74	32	Normal	3.20
6 months	42	76	41	Normal	3.16
Time	**Triglyceride [mmol/L]**	**Cholesterol [mmol/L]**	**Fasting C-peptide [ng/mL]**	**1-h C-peptide [ng/mL]**	**2-h C-peptide [ng/mL]**
Baseline	4.21	5.27	3.41	11.85	7.36
3 months	3.31	4.69	1.00	–	–
6 months	2.97	4.22	1.01	–	–
Time	**Free triiodothyronine [pmol/L]**	**Free thyroxine [pmol/L]**	**Thyroid stimulating hormone [μIU/mL]**	**Testosterone [ng/mL]**	**Blood amylase [U/L]**
Baseline	4.83	24.81	2.53	0.137	42
3 months	–	–	–	0.34	31
6 months	3.69	22.23	1.01	–	36

— not detected

not been reported. Because China has not approved the use of liraglutide for adolescent patients with type 2 diabetes mellitus, we provided all the information about this treatment to his guardian before treatment and obtained their informed consent. Additionally, the therapeutic regimen was approved by the Ethics Committee of our hospital. The use of liraglutide was found to be safe and effective in our patient based on close observation of its curative effect, biochemical indices, vital signs, and symptoms. In summary, the application of liraglutide, a GLP-1 receptor agonist, achieved a satisfactory effect in improving glucose metabolism in an adolescent patient with PWS and concomitant diabetes mellitus. This report can help guide the treatment of adolescent PWS patients with concomitant diabetes mellitus in the future.

Conflict of interests

The authors declare no conflict of interest.

Ethics approval

The study has been approved by the Ethics Committee of our hospital.

Informed patient consent

This work does not contain personal information about an identifiable living individual.

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