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CASE REPORT

Loss of Muscle Mass in Delayed Diagnosis of Renal Cysts and Diabetes Syndrome: A Case Report

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Abstract: Renal cysts and diabetes syndrome (RCAD) is a rare disease caused by abnormalities in the HNF1B gene, which often leads to dysfunction in the renal, genital tracts, and pancreas. In this report, we present a rare case of a 27-year-old female with muscle mass loss who experienced a delayed diagnosis of RCAD. The patient had been misdiagnosed as "type 1 diabetes" for a long period. Her main clinical manifestations included muscle loss, renal magnesium loss, and an incomplete longitudinal uterus. Ultimately, the diagnosis of RCAD syndrome was confirmed through genetic testing. Reduction of muscle mass, although rarely reported, can progress to sarcopenia. Therefore, early intervention should be strongly emphasized. Furthermore, in future research, it is crucial to explore the mechanisms and relationships underlying these patients and their unusual manifestations.

Keywords: muscle loss, special type diabetes, maturity-onset diabetes of the young type 5, 17q12 deletion syndrome, renal cysts and diabetes syndrome, case report

Introduction

Renal cysts and diabetes (RCAD) syndrome is a rare disease with hepatocyte nuclear factor-1-beta (HNF1B) gene mutations.[1] According to reports, the syndrome often involves the urinary tract, diabetes mellitus (maturity-onset diabetes of the young type 5, MODY 5), reproductive system malformations, hypomagnesemia and neuropsychiatric disorders.[1,2] Here, we firstly report a case of a delayed diagnosis of renal cysts and diabetes syndrome with loss of muscle mass loss.

Case Presentation

A 27-year-old woman was diagnosed with "type 1 diabetes" with negative of GADA, IA-2A, ZnT8A and IAA for 3 years. The patient was first referred for diabetic ketosis and had a low C-peptide level (0.96 ng/mL, chemiluminescence Roche Cobas e601 Analyzer) and glycated haemoglobin (6.4 mmol/L, Premier Hb9210, Primus) at the time of admission. Initial insulin therapy was effective. However, her blood glucose levels fluctuated widely, and a postprandial hypoglycaemic coma developed. Low blood magnesium levels were persistent during the course of diabetes, but the physician did not pay great attention to it. Her menstrual cycle was irregular, as her last menstrual period occurred six months prior. There was no history of conception. Her mother and grandmother were diagnosed with "type 2 diabetes".

On admission, she was lean with a body mass index of 18.6 kg/m^2, while the albumin, prealbumin, serum lipid showed a normal range. Laboratory tests revealed a blood magnesium concentration of 0.54 (normal range 0.75–1.02, Beckmann AU5800) mmol/L and a 24-hour urinary magnesium concentration of 3.19 (normal range 0.98–10.49, Beckmann AU5800) mmol, suggesting renal magnesium loss. The luteinizing hormone concentration was 9.70 (corpus luteum phase, normal range 1.2–12.86) mIU/mL, follicle-stimulating hormone concentration was 2.28 (corpus luteum phase, normal range 1.79–5.12) mIU/mL, the oestrogen concentration was 241.70 (corpus luteum phase, normal range

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30.3–274.2) pg/mL, and testosterone concentration was 0.74 (normal range 0.1–0.75). The sex hormones above were detected by Beckman DXI800. A renal ultrasound was completed and revealed a left renal cyst. As the patient had abnormal levels of sex hormones, a gynaecological ultrasound was performed and revealed an incomplete longitudinal uterus and polycystic ovary. Moreover, due to the patient's low BMI, further body composition analysis was refined by bioimpedance analysis (InBody 770, Korea, InBody Co, Lid). The results showed a height of 1.64 m, body weight of 50.0 kg, and skeletal muscle mass of 17.8 kg (normal range 22.0–27.0), suggesting muscle loss (Figure 1a). Fat mass was 15.7 kg (normal range 11.6–18.5), and the body fat rate was 31.4% (normal range 18–28%). The left arm muscle mass was only 1.30 kg (normal range 1.46–2.19), the right arm muscle mass was 1.37 kg (normal range 1.46–2.19), which was notably reduced, the right leg muscle mass was 5.62 kg (normal range 5.20–6.36), the left leg muscle mass was 5.64 kg (normal range 5.20–6.36), the trunk muscle mass was 14.6 kg (normal range 14.97–18.29) (Figure 1b), and the fat-free mass index was 6.6 kg/m^2 (normal range 13.3–17.8).[3]

Considering that the patient exhibited renal magnesium loss with a left renal cyst and an incomplete longitudinal uterus, RCAD syndrome was suspected. According to the Consensus Report,[4] the next-generation sequencing was performed to confirm RCAD syndrome. There was a heterozygous fragment deletion of 1.3 Mb in size on 17q12 at the interval from chr17: 34806179 to 36104883, of which hepatocyte nuclear factor-1-beta (HNF1B) and 21 other genes were missing, including MYO19, and ACACA. Subsequently, we found that the patient's mother also had a fragment deletion on 17q12, which suggested that it was inherited from her mother.

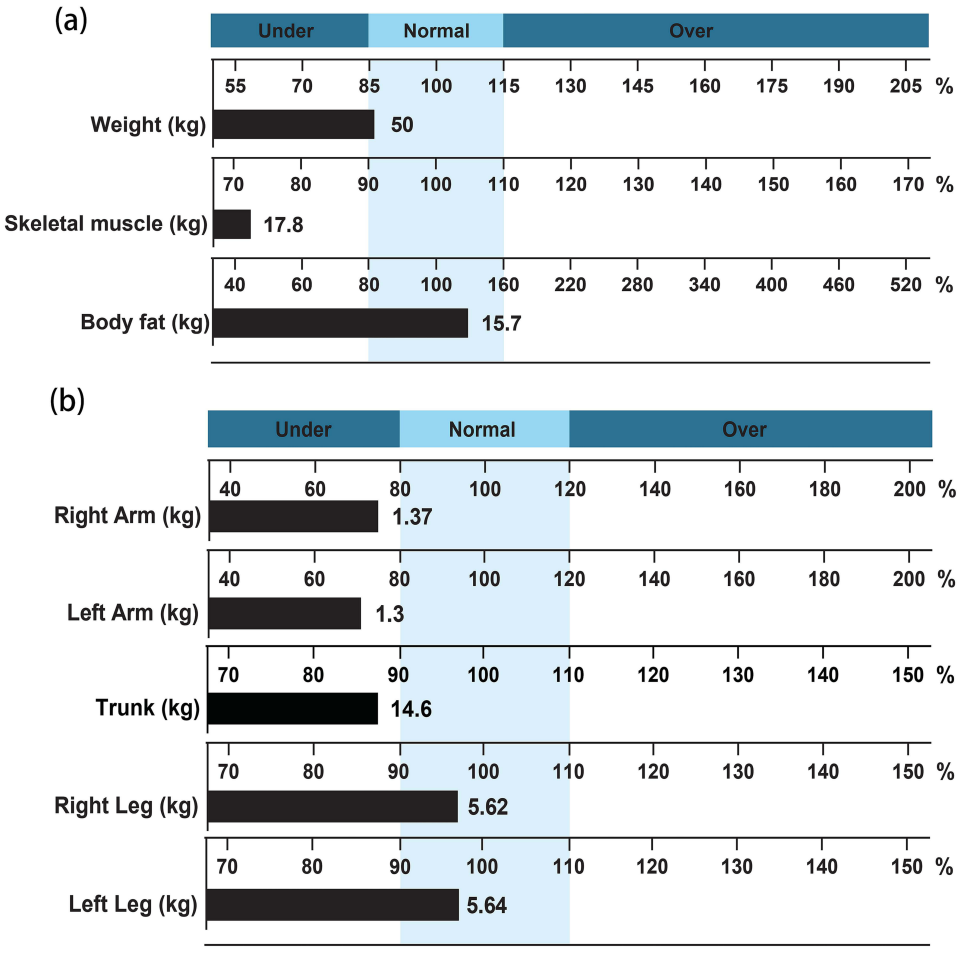

Figure 1 Body composition analysis of the patient. (**a**) A graph of muscle-fat analysis of the skeletal muscle mass detected by InBody 770 (Korea, InBody Co, Lid). (**b**) A graph of segmental lean analysis of the arm and trunk muscle mass detected by InBody 770 (Korea, InBody Co, Lid).

Discussion

RCAD syndrome is a rare recurrent chromosomal aberration that can be caused by deletion of the long arm region of chromosome 17. The diagnosis of this syndrome relies on genetic testing. In this patient, the expression of 22 genes, including the HNF1B gene, was affected.

Notably, decreased muscle mass was the prominent clinical manifestation in this patient. Previous understanding suggested that age-related factors contribute to muscle mass loss, but recent studies have highlighted the involvement of multiple mechanisms, including mitochondrial dysfunction, satellite cell dysfunction, neuromuscular dysfunction, reduced anabolic hormone production or sensitivity, undernutrition, and increased inactivity.[5,6] Additionally, various systemic diseases, such as cancer, cardiovascular disease, and metabolic diseases, can also lead to muscle mass and strength reduction.[7,8] The reduction of muscle protein homeostasis occurs when muscle protein breakdown exceeds muscle protein synthesis, and decreased dietary protein intake can further facilitate muscle mass loss. However, in the case of the 27-year-old female patient with a regular diet described here, laboratory tests showed normal levels of albumin, prealbumin, and serum lipids, indicating fair nutritional status. Thus, it is evident that other factors are involved in the breakdown of muscle protein homeostasis. First, glucose metabolism disorder in this patient contributed to chronic inflammation and mitochondrial metabolism oxidative stress, leading to muscle injuries.[9] In addition, a heterozygous deletion of the MYO19 gene fragment was identified. MYO19 is a myosin related to mitochondria that provides power for muscle contraction,[10] and mitochondrial metabolism plays a crucial role in skeletal muscle mass and function.[11] Moreover, another heterozygous gene, ACACA, was located in the deleted fragment. Pathogenic variants in ACACA cause acetyl-CoA carboxylase deficiency, characterized by hypotonia and motor and intellectual developmental delays.[12] Acetyl-CoA carboxylase 2, primarily expressed in the heart and skeletal muscles, is coupled to the mitochondrial outer membrane, and muscle weakness has been reported in patients with acetyl-CoA carboxylase deficiency.[13] Furthermore, an in vivo study demonstrated that Mg^{2+}-deficient rats exhibited various ultrastructural changes in skeletal muscle tissue, including swelling mitochondria and disorganization of the sarcoplasmic reticulum network.[14] In summary, multiple mechanisms may be involved in the reduction of muscle mass. The ratio of luteinizing hormone and follicle-stimulating hormone was observed to be increased in this patient with polycystic ovary changes, leading us to believe that polycystic ovarian syndrome and reproductive system abnormalities may cause her irregular menstrual cycles.

The progression of muscle mass loss can result in sarcopenia, which increases the risk of falls, fractures, frailty, cognitive impairment, and mortality. This, in turn, leads to a reduced quality of life for patients and a significant increase in economic burden and health care costs.[15,16] Therefore, it is crucial to recognize and intervene early in patients with 17q12 deletion syndrome to prevent muscle mass loss.

Conclusion

RCAD syndrome is a rare type of diabetes that requires attention because it can be easily misdiagnosed as type 1 or type 2 diabetes. Hypomagnesemia may serve as a clue for diagnosis. Additionally, due to the involvement of multiple genes in the deletion, multiple systems can be affected. Here, we highlight a young woman with 17q12 deletion syndrome who experienced muscle mass loss. Early intervention should be emphasized for such patients. The underlying mechanisms of the relationship between the conditions of these patients and their unusual manifestations should be further explored in the future.

Ethical Approval and Consent

The institution has given approval for this article to be published in this journal. A written consent was obtained from the patient included in the study for publication.

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Disclosure

The authors report no conflicts of interest in this work.

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