

A case with monogenic diabetes mellitus caused by *RFX6* mutation in a 14-year-old girl



Goo Lyeon Kim¹, Soo Heon Kwak², Jeesuk Yu¹

¹Department of Pediatrics, Dankook University Hospital, Dankook University College of Medicine, Cheonan, Korea

²Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea

Introduction

Recently, the incidence of type 2 diabetes mellitus (DM) increased explosively in children and adolescents. The underlying mechanism of childhood-onset type 2 DM may be different from the adult-onset type 2 DM. It is important to investigate the genetic causes in children with clinical features of type 2 DM to understand the mechanism of glycemic dysregulation as well as for management of diabetes mellitus. The gene Regulatory factor X6 (*RFX6*), which is located at chromosome 6q22.1, is associated with the development of beta cells in the pancreas and regulates the homeostasis of the blood glucose level by activating the insulin secretory pathway. It also matures pancreas beta cells by silencing the 'disallowed' genes. In the presence of the *RFX6* gene mutation, the GIP, which promotes insulin secretion, decreases after a meal, resulting in impaired insulin secretion. This study reports a case with monogenic diabetes mellitus caused by *RFX6* mutation in a 14-year-old female patient.

Case

A 14-year-old-girl was diagnosed as having type 2 DM. Initially, she was presented with glycosuria, polydipsia, and polyuria. Initial HbA1c was 11.7%. She had no specific past medical problems. Her weight was 66.3kg (95 percentile) and height was 148.3cm (3 percentile). Acanthosis nigricans was detected in neck and axillary areas. Her mother was also diagnosed as DM and on medication.

Blood levels of glucose, insulin, and C-peptide were 345 mg/dL, 27.2 uIU/mL, and 8.7 ng/mL, respectively. There was neither ketonuria nor acidosis. Blood lipid profile showed 200 mg/dL of cholesterol, 45 mg/dL of HDL cholesterol, and 144 mg/dL of triglyceride. Thyroid function test showed normal. Long-acting insulin and oral hypoglycemic agent (MetforminTM) were started (Fig.1). Her HbA1c level was 9.3% at one year after the diagnosis.

To find the candidate gene, targeted exome sequencing which included 29 genes associated with monogenic DM was performed. Nonsense mutation of the gene *RFX6* was found (c.2661T>A, p.Tyr887*)(Fig.2A). Her mother showed same mutation of *RFX6* gene (Fig.2C). The mutation of gene *RFX6* was reported to contribute to beta-cell dysfunction and associated with lower fasting and stimulated gastric inhibitory polypeptide (GIP) levels.

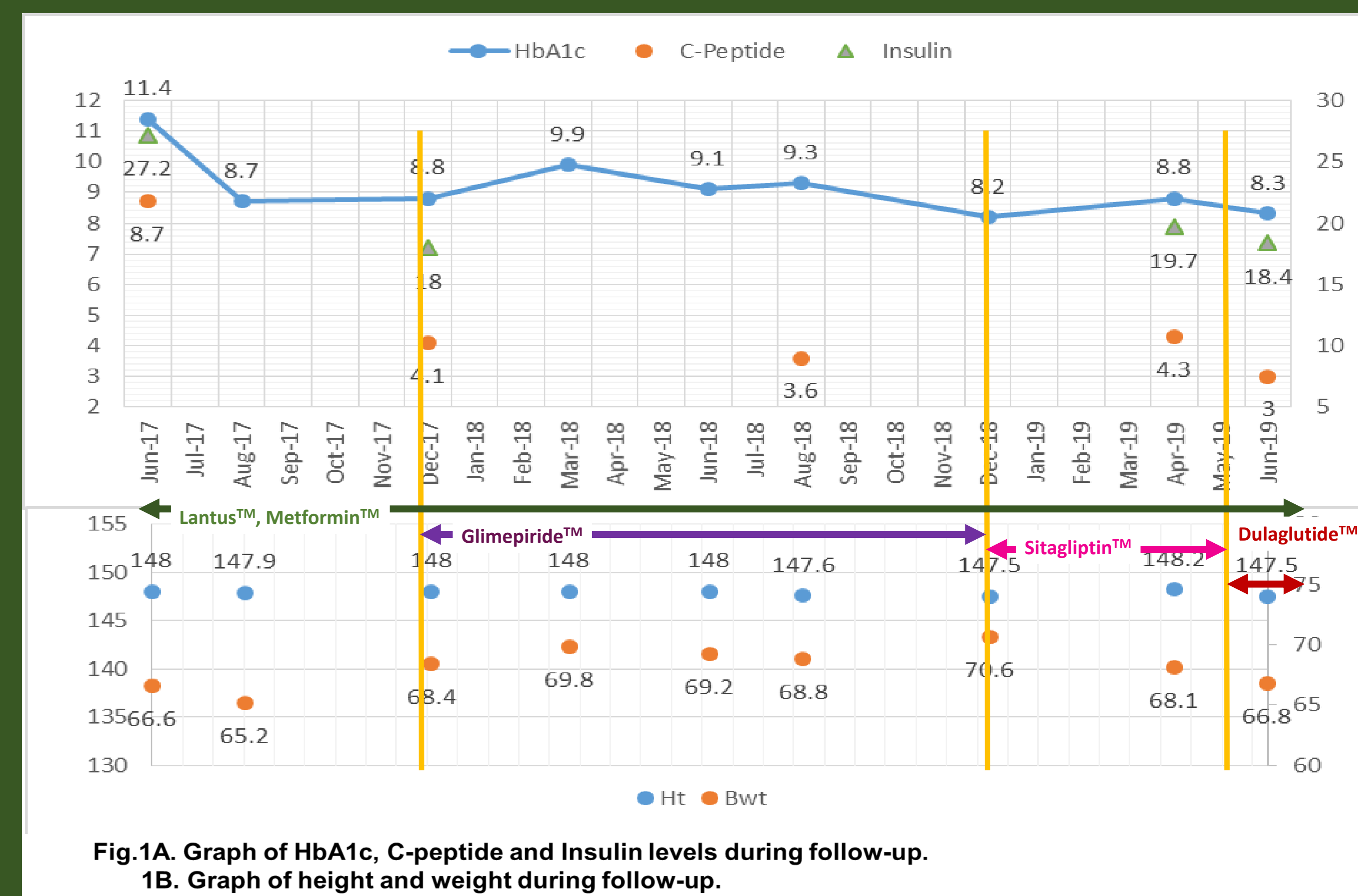
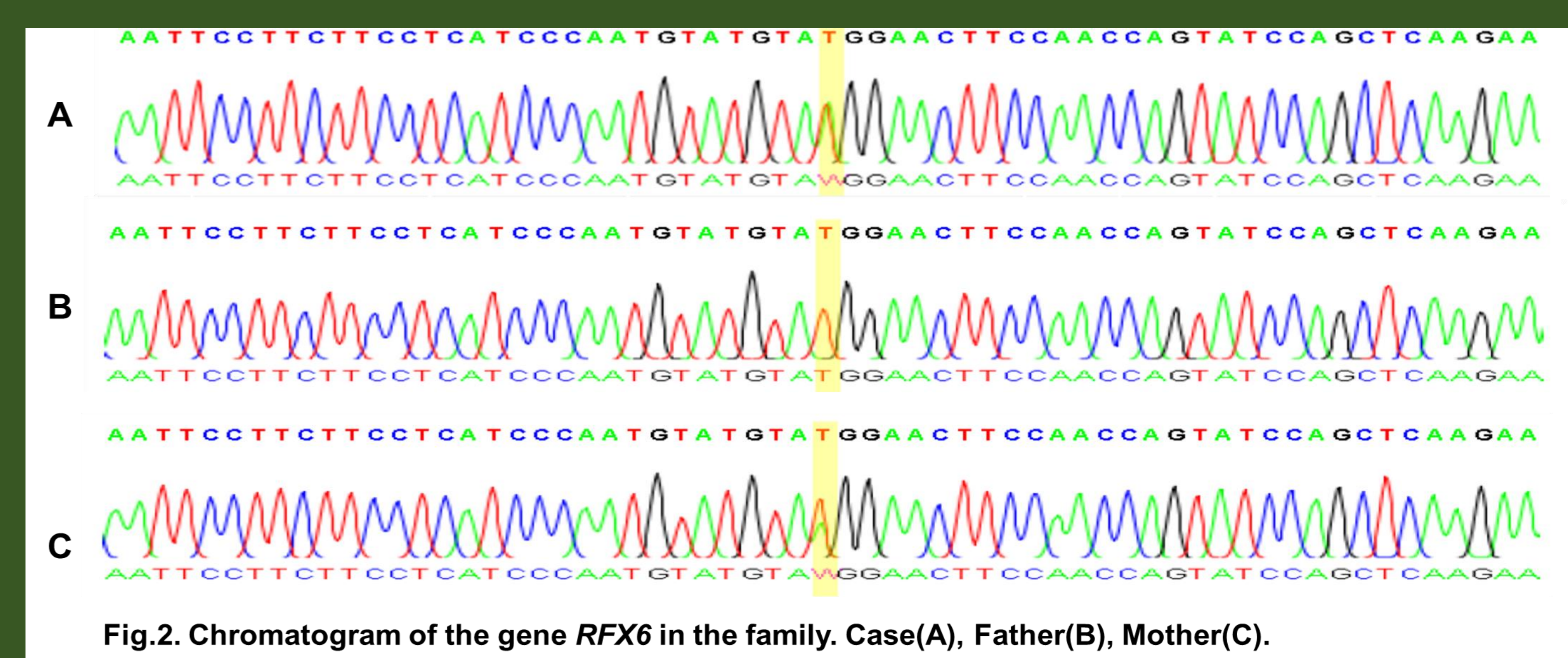


Fig.1A. Graph of HbA1c, C-peptide and Insulin levels during follow-up.
1B. Graph of height and weight during follow-up.



Conclusion

It may be recommended to perform the genetic test to find the candidate gene of type 2 diabetes mellitus which developed in children and adolescents. Here we report a case with monogenic diabetes caused by *RFX6* mutation in a 14-year-old girl.

References

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