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CASE REPORT

Dysendocrinism Linked to Ring Chromosome 7 with 7q36 Deletion – A Unique Case

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Abstract

Background Ring chromosome 7 has been associated with developmental delay, mental disability, growth failure, and numerous developmental organ anomalies. To date, very few cases have been described, but none have any endocrine manifestations.

Case presentation Here, we report a 23-year-old male suffering from ring chromosome 7 due to deletion of 7q36.1-36.3, who presented with young-onset diabetes mellitus and pituitary microadenoma in addition to the usual features of gene deletion defects.

Conclusion This is the first reported case in the literature having endocrinopathies in association with ring chromosome 7 syndrome.

Keywords Ring chromosome 7 · 7q36 deletion · Young-onset diabetes mellitus · Pituitary microadenoma

Introduction

Ring chromosome formation is a rarely reported entity in the literature. It is formed by the fusion of two ends of a chromosome's short and long arms, and there may be associated deletions of the terminal segments of the arms. Persons who acquire ring chromosomes present some common phenotypic features depending upon the chromosome involved. Thus, it is also known as ring syndrome [1, 2].

The formation of the ring at chromosome 7 was reported in only 22 cases in the literature. All the cases were characterized by growth failure, delayed developmental milestones, mental retardation, dysmorphism of the skull, along with midline facial defects, skin changes, and developmental anomalies of other organs [3].

Endocrine disorders associated with ring chromosome 7 have not been reported in the literature. Here, we present a case of young-onset diabetes mellitus with preserved pancreatic β-cell function and pituitary microadenoma in a patient with a 7q36 deletion and subsequent ring formation, along with other similar phenotypical characteristics.

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Case

A 23-year-old Bengali male born by consanguineous marriage presented with a history of delayed tooth eruption at 2 years of age and global developmental delay (e.g., monosyllabic words by 2 years of age and walking without support by 4 years of age). There was history of birth asphyxia. Additionally, his mother reported poor height gain from the age of 14 and the appearance of pubic and axillary hair from the age of 16. The patient had a history of bilateral tonsillectomy at 14 years of age due to recurrent tonsillitis and tonsillar enlargement. He had suffered from chronic serous otitis media (CSOM) with frequent watery discharge from both ears for the last 4 years. The patient had been diagnosed with diabetes mellitus 1 month before presentation and was on oral anti-diabetes agents. No other family member had a similar presentation and also did not have diabetes.

On examination, the patient was normotensive; his height was 144 cm, body weight was 52.4 kg, arm span was 152 cm, upper and lower segment ratio was 64:80 (i.e., 0.8). The head circumference was 45 cm, and the waist circumference was 94 cm. On genital examination, he had normal male genitalia with a stretch penile length (SPL) of 12 cm, and both testes were palpable in the scrotal sac with a volume of 10 ml each; there was no gynecomastia. His pubic and axillary hairs were in Tanner stages 3 and 1, respectively. Additionally, the patient had (Figure 1) sparse scalp hair, bilateral immature cataracts, a squint in the right eye, maloccluded teeth, black firm papular swelling in the middle of the hard palate, grade 2 acanthosis, bilateral perforated tympanic membranes, bimanual synkinesis, and nevi in the right parotid region and chest. He had severe intellectual disability with an intelligence quotient of 27 ± 5.

His bone age was approximately 17 years. There was sclerosis of the bilateral mastoid bones on computed tomography scan. The liver was found to be enlarged with grade I fatty infiltration on ultrasound. His complete hemogram, renal, and liver function tests were within the normal range. All other biochemical reports are listed in Table 1.

On magnetic resonance imaging (MRI) of the sella, the pituitary gland was slightly prominent, measuring $9 \times 12.1 \times 7$ mm with postcontrast small hypointensity on the right side (7 mm), which was suggestive of pituitary microadenoma (Figure 2). The patient's karyotype (50 cells) revealed 46, XY, r (7) (p22q36) (Figure 3). His whole exome sequencing (average coverage > 100X, read quality > Q30) suggested a heterozygous partial deletion of the chr7q36.1–36.3.3 region (Supplementary Figure 1) involving the following 20 genes: XRCC2 (X-ray Repair Cross Complementing 2), ACTR3B (Actin-related protein 3B), DPP6 (Dipeptidyl-Peptidase 6), PAXIP1 (PAX interacting protein 1), HTR5A (Serotonin type 5 A receptor), INSIG1

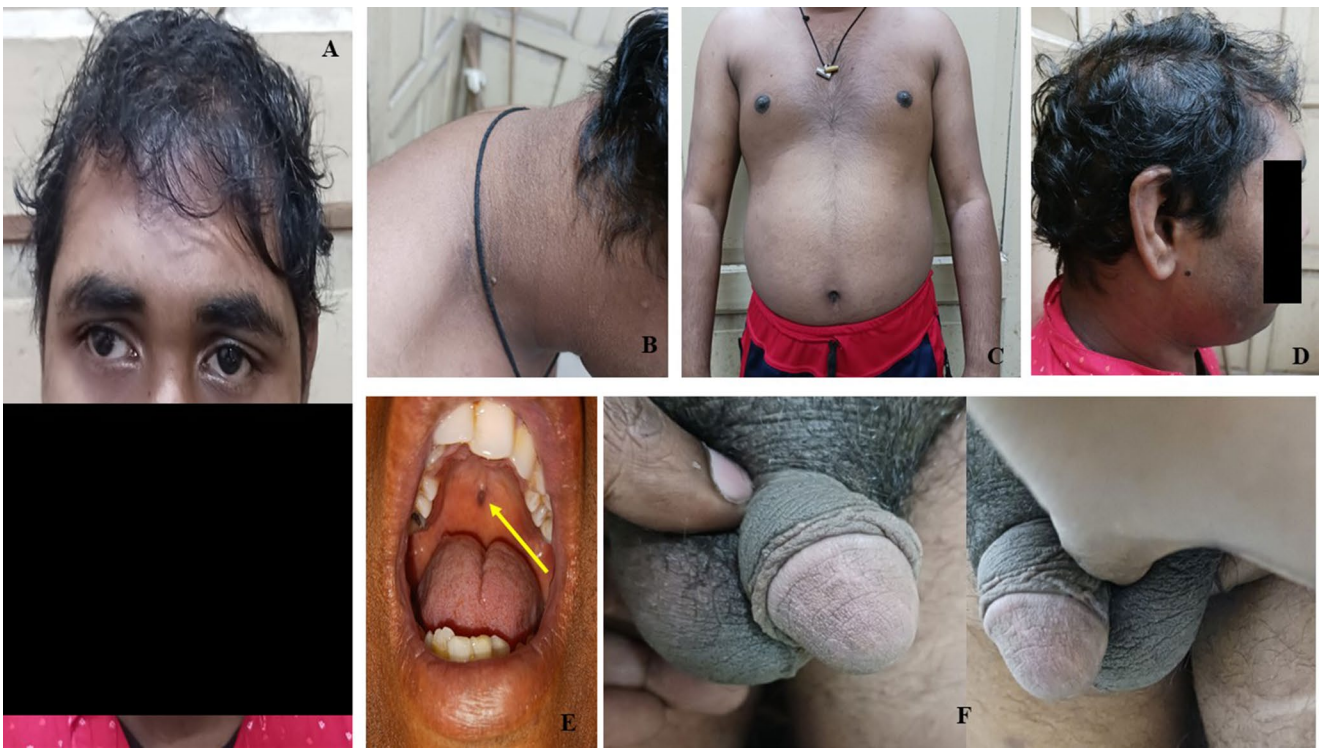


Fig. 1 Clinical features of the patient, **A** – Exotropia of the right eye and sparse scalp hair, **B** – Acanthosis, **C** – Truncal obesity and moles on chest skin, **D** – one mole at the right parotid region, **E** – A black popular lesion in the middle of the hard palate (yellow arrow) and malocclusion of teeth, **F** – Bilateral testicular volume of 12 ml (measured by Prader orchidometer)

Table 1 Biochemical and hormonal parameters of the reported patient at the initial presentation. ACTH – Adrenocorticotropic hormone, FSH – Follicular-stimulating hormone, GAD – Glutamic acid decarboxylase, HbA1c – Glycated hemoglobin, HDL – High-density lipoprotein, IA-2 – Islet tyrosine phosphatase 2, IGF1 – Insulin-like growth factor 1, LH – Luteinizing hormone, TSH – Thyroid-stimulating hormone, T4 – Thyroxine, ZnT8 – Zinc transporter 8

Blood Parameters (units)	Patient's value	Reference/ Target range
Fasting plasma glucose (mg/dl)	197	≥126
Postprandial plasma glucose (mg/dl)	385	≥200
HbA1c (%)	5.9%	≥6.5%
Fasting C-peptide (ng/ml)	1.55	>0.26
Post-mixed meal C-peptide (ng/ml)	5.2	>0.6
Islet autoantibodies (GAD-65, IA-2, ZnT8)	Negative	-
Total cholesterol (mg/dl)	104	<200
Triglyceride (mg/dl)	80	<150
HDL (mg/dl)	30	>50
Non-HDL (mg/dl)	74	<130
Free T4 (ng/dl)	1.2	0.89–1.8
TSH (µIU/ml)	3.6	0.35–4.6
IGF 1 (ng/ml)	200	107–316
FSH (mIU/ml)	13.5	0.7–11.1
LH (mIU/ml)	5.7	0.8–7.6
Total testosterone (ng/dl)	573	227–1030
Morning serum cortisol (µg/dl)	5.3	5–25
Plasma ACTH (pg/ml)	95	< 120
ACTH-stimulated cortisol (µg/dl)	60 min: 19.1 120 min: 20.5	>19.5
Serum calcium (mg/dl) (albumin corrected)	9.8	8.6–10.2
Serum phosphate (mg/dl)	3.8	2.5–4.5
Serum 25-hydroxy vitamin D (ng/ml)	38	10–65

(Insulin-induced gene 1), EN2 (Engrailed Homeobox 2), CNPY1 (Canopy FGF signaling receptor 1), RBM33 (RNA binding motif protein 33), RNF32 (Ring finger protein 32), LMBR1 (Limb development membrane protein 1), NOM1 (Nuclear protein with MIF4G domain 1), MNX1 (Motor neuron and pancreatic homeobox 1), UBE3C (Ubiquitin protein ligase E3C), DNAJB6 (DnaJ (Hsp40) homolog, subfamily B, member 6), PTPRN2 (Protein tyrosine phosphatase, receptor type, N polypeptide 2), NCAPG2 (Condensin-2 complex subunit G2), ESYT2 (Extended synaptotagmin-like protein 2), WDR60 (WD repeat domain 60), VIPR2 (Vasoactive intestinal peptide receptor 2).

The patient experienced the onset of adrenal insufficiency after a follow-up period of 1.5 years. The recent morning serum cortisol was 5.1 µg/dl, plasma ACTH was 32.6 pg/ml, and ACTH-stimulated serum cortisol values were 14.5 (at 60 min) and 15.7 (at 120 min). Up until now, the hydrocortisone supplementation dose was set at 5 mg/m^2 body surface area per day, and regular monitoring of signs of glucocorticoid excess or deficiency has been carried out. A follow-up imaging of the sellar region showed late enhancement of contrast in the dynamic study on the right side, suggestive of a pituitary microadenoma of 9.2 mm in size with stalk deviation to the opposite side (Supplementary Figure 2).

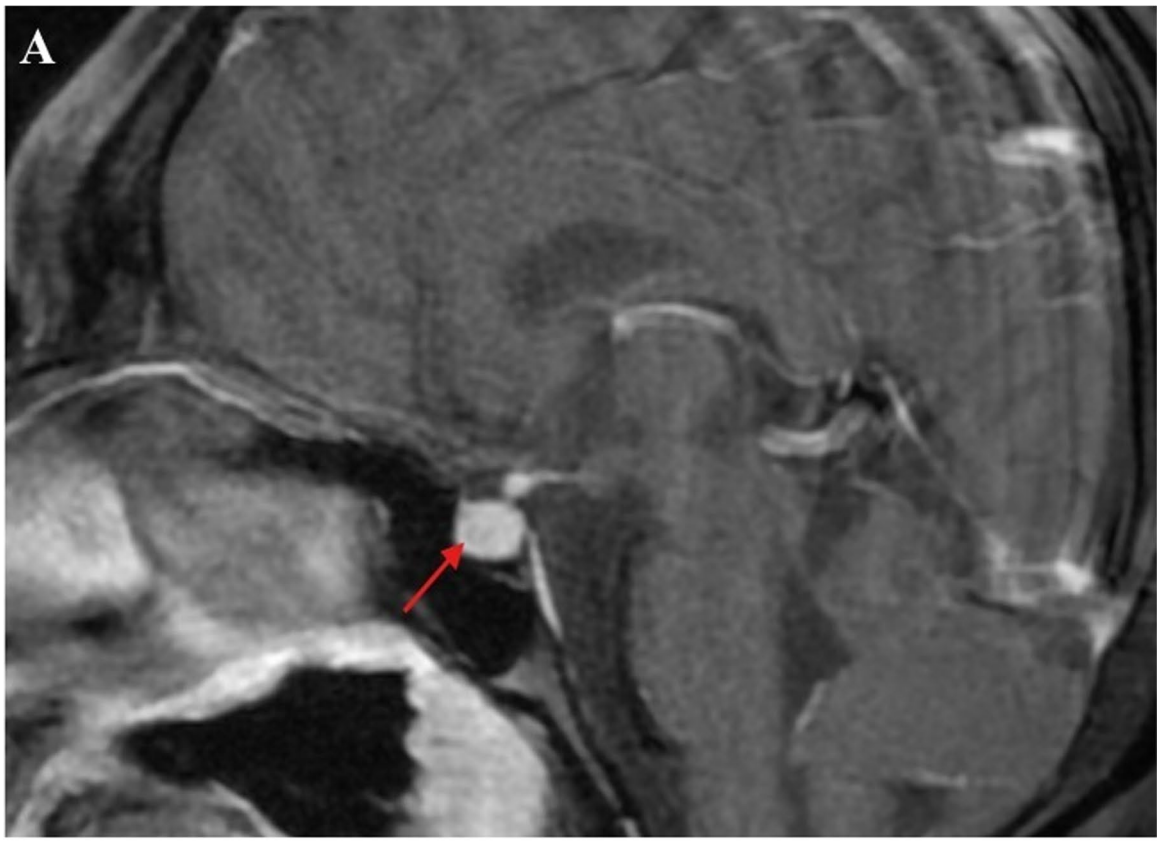
Discussion

As per the case discussed, the patient's height was below the 3rd percentile (−4.46 standard deviation score) compared with the adult height chart of the Indian standard. He was obese as per the Asian standard of body mass index (25.3). In addition to the delayed appearance of sexual hair, the difference between arm span and height was more than 5 cm. Although he had normal adult SPL, testicular volume (Tanner stage 3), normal total testosterone, and gonadotropin levels, the coexistence of reversible hypogonadotropic hypogonadism may be considered, as he had delayed onset of puberty and had a eunuchoid body habitus. For the evaluation of his short stature, all pituitary hormonal evaluations were performed and found to be within the normal range (baseline cortisol, which was at the lower end of the reference range, crossed the cutoff value of 19.5 µg/dl after stimulation). Thus, the pituitary microadenoma was considered nonfunctional, without any hormonal excess or deficit initially. Later, the patient developed adrenal insufficiency, probably due to the compressive effect of the tumor (Supplementary Figure 2).

With respect to the evaluation of the patient's diabetes mellitus, his pancreatic β-cell function was preserved with normal C-peptide values. There was no history of hyperglycemic crisis. He was initially managed with multiple subcutaneous insulin injections, and upon glycemic control, he was shifted to sulfonylurea, biguanide, and dipeptidyl-peptidase 4 inhibitor.

Other phenotypical features, such as developmental delay, severe intellectual disability, microcephaly, exotropia, midline palatal defects, multiple nevi, and eardrum defects, were similar to those reported previously [3]. The karyotype was sent in suspicion of chromosomal defect. His karyogram was suggestive of the presence of a ring chromosome 7 involving regions p22 and q36, along with one normal chromosome 7 in all the cells analyzed. Among all 22 reported cases in the literature, the male-to-female ratio was 17:5 (excluding the present case), and the prevalence of all possible clinical characteristics is depicted in Fig. 4.

Ring formation on any chromosome usually occurs when the two ends of the short and long arms of a chromosome fuse with each other to form a ring shape. Breakages in the


A

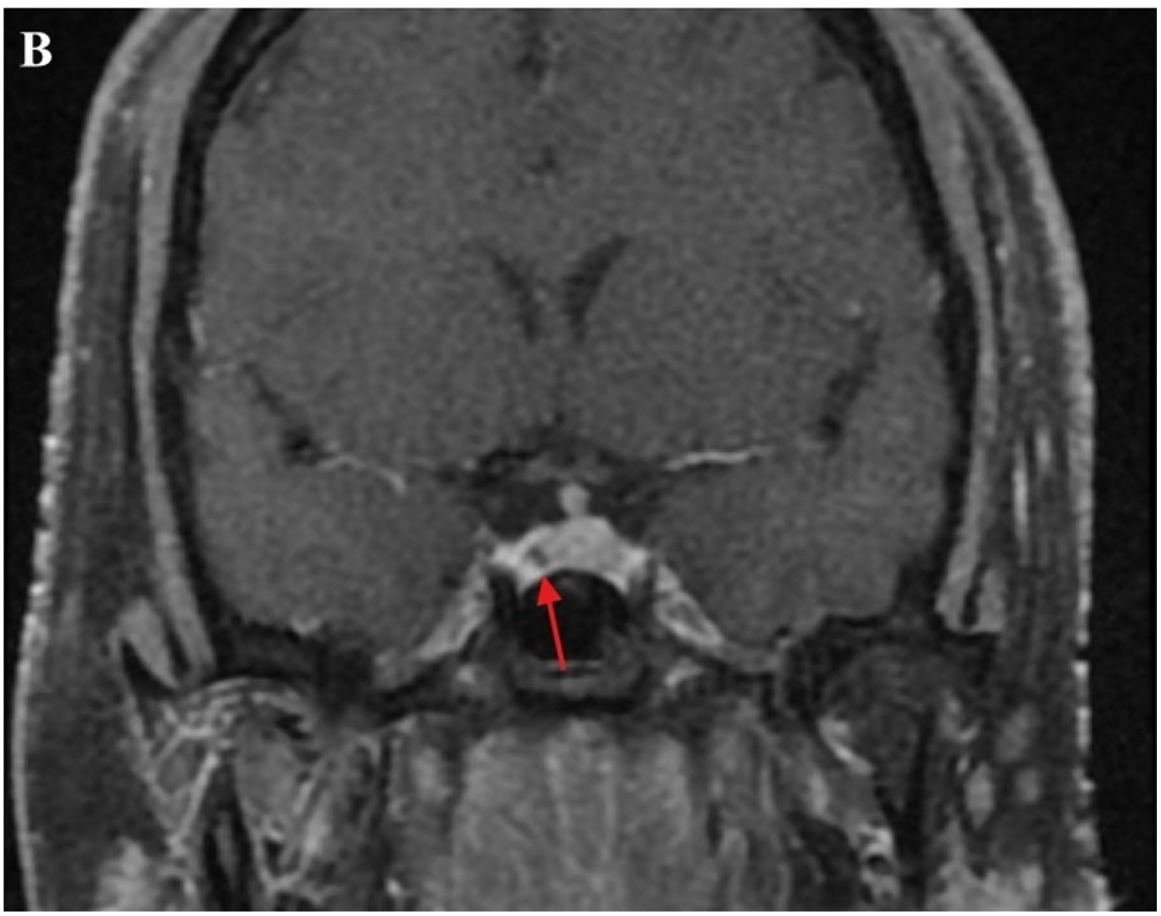

B

Fig. 2 Sagittal (**A**) and coronal (**B**) sections of the sellar MR image showing a microadenoma of the pituitary (*red arrows*)

chromosome arms, mostly due to loss of distal segments, occur with a fusion of the proximal broken ends, the exact mechanism of which is not yet well understood. Telomerase dysfunction without any loss of chromosomal segments can also cause ring formation in certain cases [4].

The findings of exome sequencing revealed that the 7q36 deletion syndrome affects 20 genes mentioned earlier. Previously reported cases of 7q36 deletion were characterized by hypoplasia of the corpus callosum, downslanting palpebral fissure, bulbous nasal tip, flat nasal bridge, deep-set ears, cleft lip, cleft palate, growth retardation, speech delay, hearing defects, and hand defects [5–7]. Some of these features were found in the index case, but the endocrine associations as described here were not reported in the literature. Also, none of the previously reported cases were found with exome sequencing, so we proceeded with the test to find out any possibility of monogenic diabetes.

After an extensive literature search, we found that a few genes at the terminal end of chromosome 7 may be associated with diabetes and metabolic syndrome; some have been described in animal models, and also in human studies. Like, ACTR3B downregulation may predict type 2 diabetes and Alzheimer's disease [8]. DPP6 has been found to be involved in nanobody tracer uptake on human β and α cells [9]. HTR5A, a serotonin receptor gene, has been shown to play a role in the regulation of body lipids, especially triglyceride levels. A direct association with diabetes mellitus has not been demonstrated [10, 11]. INSIG1 functions to suppress high glucose-induced SREBP-1c transcription and, in turn, decrease the generation of free fatty acids. A study has shown that the overexpression of INSIG1 protects pancreatic β cells from the effects of chronic glucolipotoxicity [12]. The LMBR1 gene has been associated with type 2 diabetes mellitus in a previous study [13]. Downregulation of NOM1 is associated with decreased insulin secretion at significant amounts when cultured with high glucose concentrations [14]. The MNX1 gene plays an important role in pancreatic β-cell development, and mutations in this gene have been found in association with permanent neonatal diabetes mellitus [15]. Although no direct relationship between UBE3C and diabetes has been reported; the genetic mutation is associated with the deterioration of renal function in individuals with diabetes mellitus [16]. The PTPRN2 gene encodes an autoantigen against pancreatic islet cells in the pathogenesis of type 1 diabetes mellitus and has a role in metabolic syndrome [17]. Knockdown of VIPR2 in mouse models has been associated with an altered glucose response under metabolic stress [18]. In addition, no other deleted genes are associated with the dysendocrinism found in the patient.

Our patient had been diagnosed with young-onset diabetes mellitus 1 month before presentation, with signs of insulin resistance (acanthosis and central obesity) and preserved pancreatic β-cell function. There was no familial trend of diabetes, and the patient's pancreatic exocrine function was normal from the clinical viewpoint and sonographic features of the pancreas. No known genetic defect associated with monogenic diabetes was detected via exome sequencing. To date, the patient maintains a good glycemic status with oral anti-diabetes agents and is followed up by other disciplines for specific health issues.

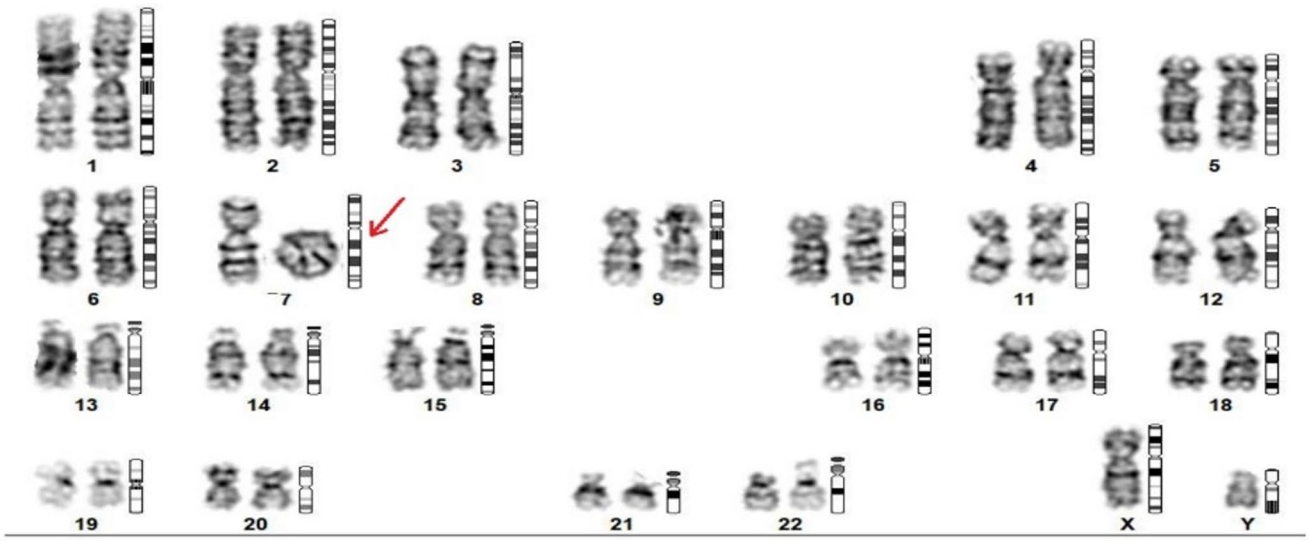


Fig. 3 Karyogram of the patient showing ring formation (*red arrow*) at chromosome 7

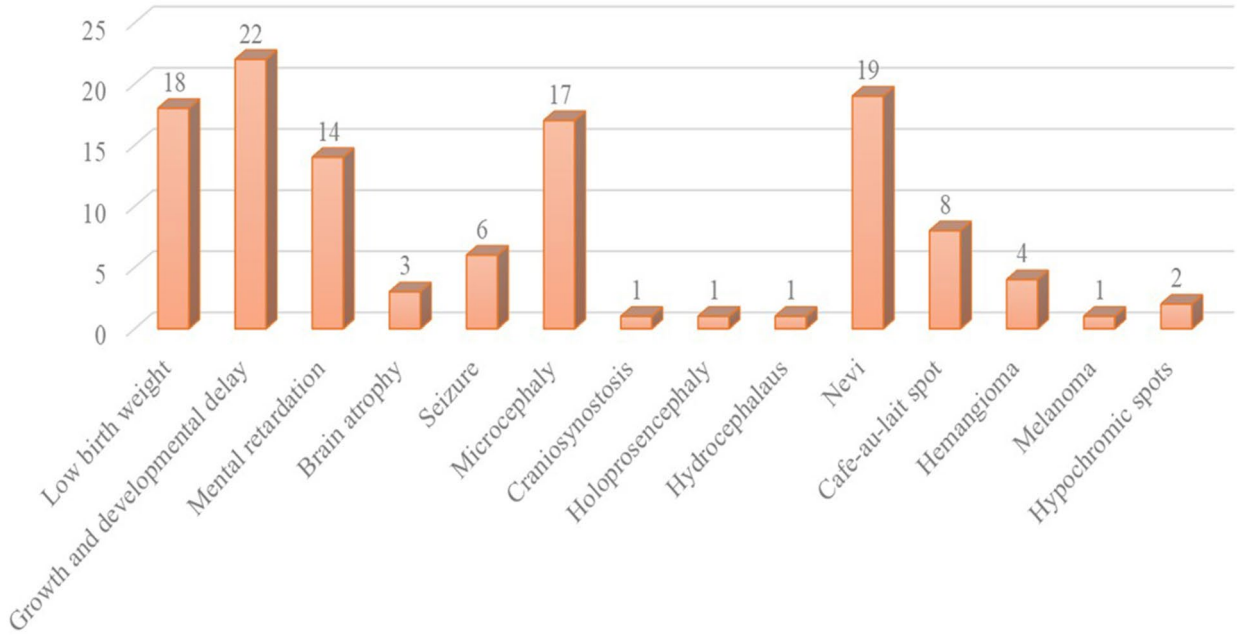


Fig. 4 Major clinical features documented in previously reported cases ($N = 22$) [3]

Conclusion

After an extensive literature search, we conclude that this is the first case found with endocrine manifestations in the 7q36 deletion and ring formation of chromosome 7. Although a case report adds very little value to the literature, we still hope that this unique case can highlight the association of genes present at the distal end of chromosome 7 with endocrine dysfunctions, especially young-onset diabetes mellitus and pituitary microadenoma.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s42399-025-02163-0.

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Author Contributions R.B. wrote the main manuscript (original draft) and edited it; A.B. and S.M. (1) reviewed and edited it; A.B. and N.S. participated as project administrators and supervised the whole investigation and treatment process; S.G. and S.M. (2) conceptualized the case details; K.S. and J.D. were involved in investigating and following up.

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Data Availability No datasets were generated or analysed during the current study.

Code Availability Not applicable.

Declarations

Ethics Approval and Consent to Participate Not applicable.

Consent for Publication The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's mother has consented to his investigation images (name masked) and other clinical information to be reported in the journal. His mother understood that his name and initial would not be published, and due efforts would be made to conceal their identity.

Competing interests The authors declare no competing interests.

References

1. Zackai EH, Breg WR. Ring chromosome 7 with variable phenotypic expression. Cytogenet Genome Res. 1973;12(1):40–8. https://doi.org/10.1159/000130436.
2. Kosztolányi G. Does ring syndrome exist? An analysis of 207 case reports on patients with a ring autosome. 1987;75(2):174–9. https://doi.org/10.1007/bf00591082
3. Bangun K, Kreshanti P, Tania V, Ariani Aswin Y, Menna C, Aurino L. Bilateral cleft lip and palate in ring chromosome 7 syndrome: a case report and review of clinical characteristics. Cleft Palate Craniofac J. 2024;61(3):527–33. https://doi.org/10.1177/10556656221149243.
4. Gisselsson D. Ring chromosomes: vicious circles at the end and beginning of life. Atlas Genet Cytogenet Oncol Haematol. 2001;6:59–66.
5. Caselli R, Mencarelli MA, Papa FT, Ariani F, Longo I, Meloni I, et al. Delineation of the phenotype associated with 7q36.1q36.2 deletion: long QT syndrome, renal hypoplasia and mental retardation. Am J Med Genet Part A. 2008; 146:1195–9.

6. Hyohyeon C, Lee CG. A 13-year-old boy with a 7q36.1q36.3 deletion with additional findings. Am J Med Genet A. 2015;167A(1):198–203. https://doi.org/10.1002/ajmg.a.36792.
7. Pelegrino KO, Sugayama S, Catelani AL, Lezirovitz K, Kok F, Chauffaille MdL. 7q36 deletion and 9p22 duplication: effects of a double imbalance. Mol Cytogenet. 2013;6:2. https://doi.org/10.1186/1755-8166-6-2.
8. Alamro H, Bajic V, Macvanin MT, Isenovic ER, Gojobori T, Essack M, et al. Type 2 diabetes mellitus and its comorbidity, Alzheimer's disease: identifying critical MicroRNA using machine learning. Front Endocrinol. 2023;13:1084656. https://doi.org/10.3389/fendo.2022.1084656.
9. Balhuizen A, Massa S, Mathijs I, Turatsinze JV, Vos JD, Demine S, et al. A nanobody-based tracer targeting DPP6 for non-invasive imaging of human pancreatic endocrine cells. Sci Rep. 2017;7:15130. https://doi.org/10.1038/s41598-017-15417-2.
10. Yuan X, Yamada K, Ishiyama-Shigemoto S, Koyama W, Nonaka K. Identification of polymorphic loci in the promoter region of the serotonin 5-HT2C receptor gene and their association with obesity and type II diabetes. Diabetologia. 2000;43(3):373–6.
11. Zhang Y, Smith EM, Baye TM, Eckert JV, Abraham LJ, Moses EK, et al. Serotonin (5-HT) receptor 5A sequence variants affect human plasma triglyceride levels. Physiol Genomics. 2010;42(2):168–76. https://doi.org/10.1152/physiolgenomics.00038.2010.
12. Chen K, jin H, Hh X, Yh X, Xy MX. Overexpression of Insig-1 protects β cell against glucolipotoxicity via SREBP-1c. J Biomed Sci. 2011;18:57. https://doi.org/10.1186/1423-0127-18-57.
13. Lu Y, Li Y, Li G, Lu H. Identification of potential markers for type 2 diabetes mellitus via bioinformatics analysis. Mol Med Rep. 2020;22(3):1868–82. https://doi.org/10.3892/mmr.2020.11281.
14. Yu L, Wang H, Guo Z, Li F, Cui H. Role of nucleolar protein NOM1 in pancreatic islet β cell apoptosis in diabetes. Exp Ther Med. 2016;12:2275–80. https://doi.org/10.3892/etm.2016.3576.
15. Aly HH, De Franco E, Flanagan SE, Elhenawy YI. MNX1 mutations causing neonatal diabetes: review of the literature and report of a case with extra-pancreatic congenital defects presenting in severe diabetic ketoacidosis. J Diabetes Investig. 2023;14(4):516–21. https://doi.org/10.1111/jdi.13968.
16. Chen YC, Wu MY, Yu ZL, Chou WH, Lai YT, Kao CC, et al. Association of *UBE3C* variants with reduced kidney function in patients with diabetic kidney disease. J Pers Med. 2020;10(4):210. https://doi.org/10.3390/jpm10040210.
17. Lee S. The association of genetically controlled CpG methylation (cg158269415) of protein tyrosine phosphatase, receptor type N2 (*PTPRN2*) with childhood obesity. Sci Rep. 2019;9:4855. https://doi.org/10.1038/s41598-019-40486-w.
18. Kozlova EV, Bishay AE, Denys ME, Chinthirla BD, Valdez MC, Spurgin KA, et al. Gene deletion of the PACAP/VIP receptor, VPAC2R, alters glycemic responses during metabolic and psychogenic stress in adult female mice. J Neuroendocrinol. 2023;35(11):e13354. https://doi.org/10.1111/jne.13354.