Mild autistic spectrum disorder in a 33 year-old male Japanese patient with Temple syndrome

Shuichi Yatsuga[1], Masayo Kagami[2], Keiko Matsubara[2], Takuro Kimura[1], Chiho Yatsuga[3], Rio Mukasa[1], Takako Matsumoto[1], Yasutoshi Koga[1]

1.Department of Pediatrics and Child Health, Kurume University School of Medicine, Kurume, Fukuoka, Japan
2.Department of Molecular Endocrinology, National Research Institute for Child Health and Development, Tokyo, Japan
3.National Hospital Organization Hizen Psychiatric Center, Saga, Japan

Nothing to disclose

Introduction

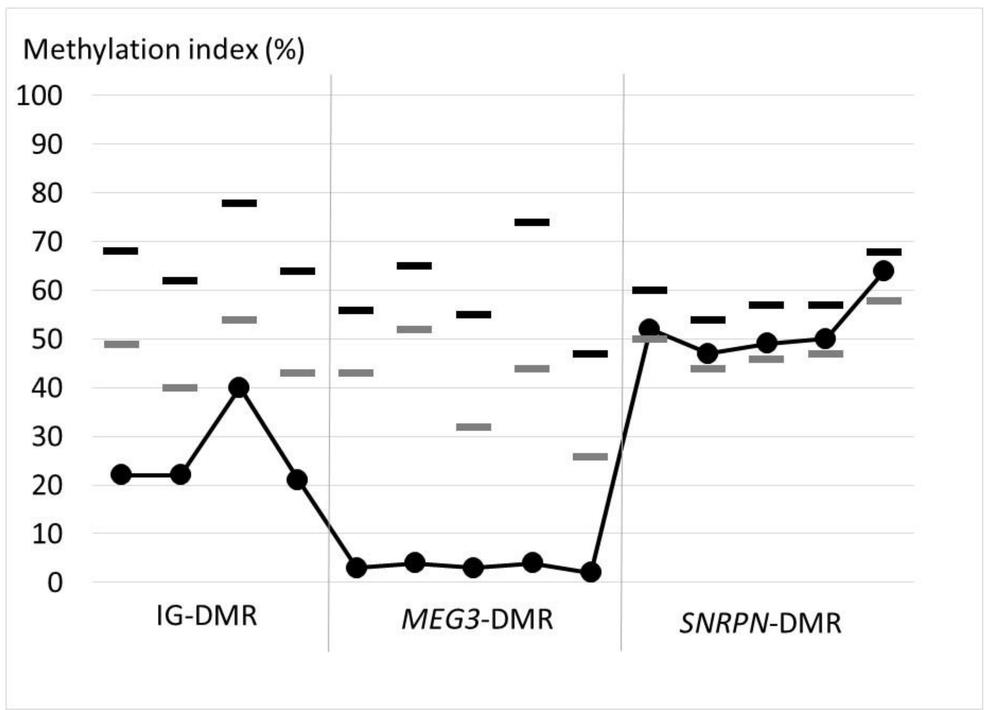
Temple syndrome (TS14) caused by maternal uniparental disomy chromosome 14 (UPD(14)mat), paternal deletions and the imprinting defect affecting the 14q32.2 imprinted region is associated with non-specific symptoms such as growth failure, precocious puberty, obesity, and diabetes mellitus (DM).[1,2] Some TS14 cases are misdiagnosed as having Prader–Willi syndrome (PWS).[1] In TS14, patient's intelligence quotient (IQ) is usually normal, and autism spectrum disorder (ASD) is a rare comorbidity.[3]

Case

A male patient was born at 39 weeks and was not small for his gestational age. He was clinically diagnosed with PWS owing to hypotonia during infancy. After infancy, he received no regular follow up. He exhibited precocious puberty, transient obesity, and DM. His final height was within normal limits at 159 cm (-2.0 SD). At 33 years of age, he visited our hospital to receive a genetic diagnosis and social welfare. He showed the normal methylation levels of the *SNRPN*-DMR on chromosome 15 and hypomethylation of the IG-DMR and *MEG3*-DMR at the 14q32.2 imprinted region without UPD(14)mat and maternal microdeletion involving the 14q32.2 imprinted region, and was diagnosed with TS14. At age 33, his total IQ was 97; verbal IQ was 104, and performance IQ was 88 (Wechsler Adult Intelligence Scale-III). Although his scores of ASD assessment scales (Pervasive Developmental Disorders ASD Rating Scale-Text Revision and Autism Spectrum Quotient) were low, we clinically diagnosed with ASD, with both verbal and nonverbal communication impairments.

Conclusion

We report a patient who was diagnosed as TS14 at the age of 33, with post-natal growth failure, obesity and DM. Comorbidity of ASD was also diagnosed, which is the second case reported. This case also highlights the importance of genetic analysis for differentiating TS14 from PWS. Hypotonic infants with unknown etiology should be considered for genetic analysis of TS14. Additionally, long-term follow up is needed, not only to observe precocious puberty and DM, but also to identify problems associated with developmental disorders, such as ASD.

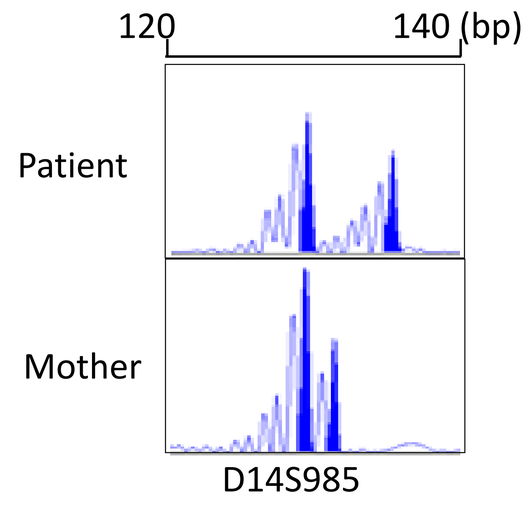


A. The results of methylation analysis using pyrosequencing
Black and gray dotted lines depict upper and lower limit values of the reference range, respectively. The methylation levels of the IG-DMR and MEG3-DMR were bellow the lower limit values of the reference range.

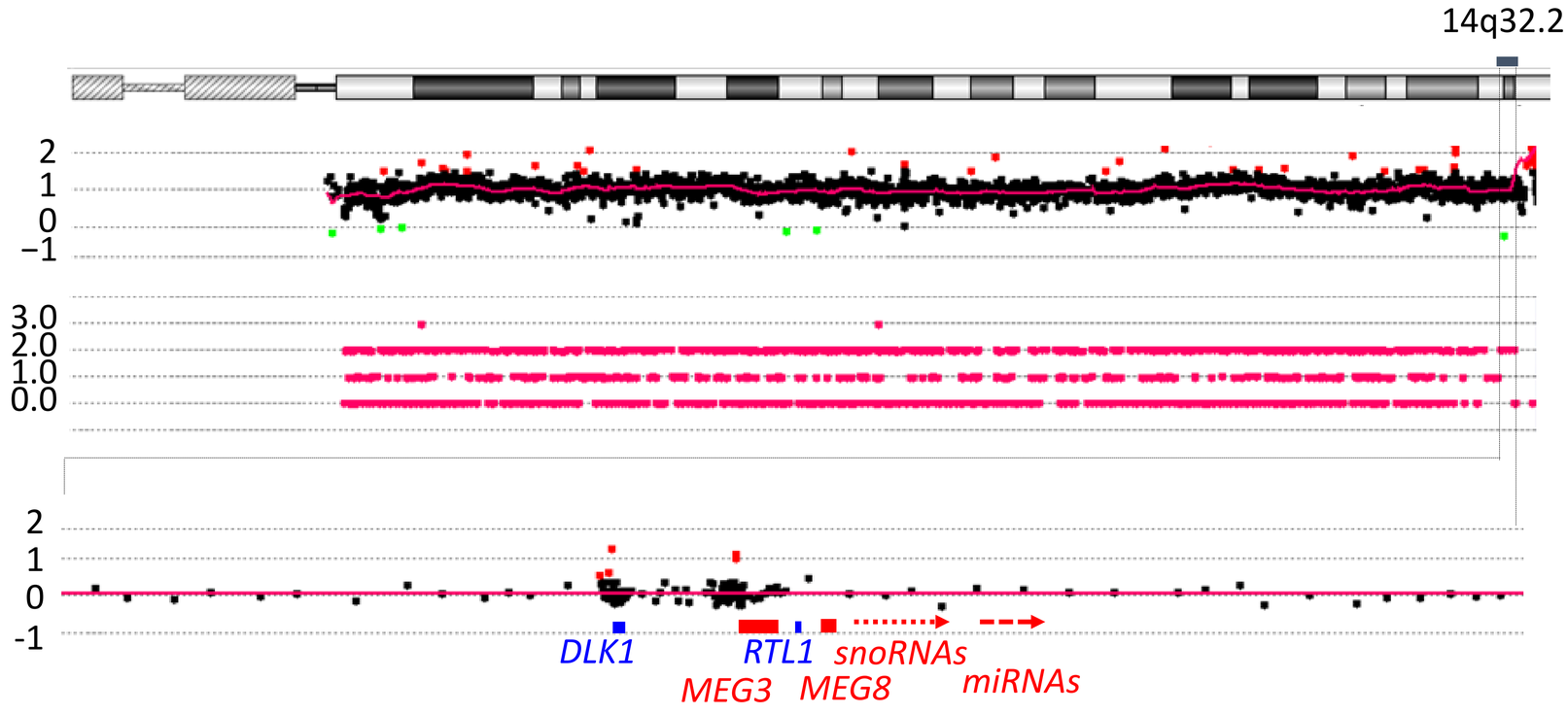
B. Microsatellite analysis for chromosome 14
Left:
summary of microsatellite results.
Right:
representative microsatellite results.

N.I.; not informative

	Cytogenetic localization	Patient	Mother	Assessment
D14S608	14q12	213/221	209/213	Biparental
D14S588	14q23-24.1	114	114	N.I.
D14S258	14q24.2	170/172	170/176	Biparental
D14S617	14q32.12	140/162	140/166	Biparental
D14S267	14q32.1-32.2	211/213	213/215	Biparental
D14S250	14q32.2	155/167	161/167	Biparental
D14S1006	14q32.2	126/136	136/138	Biparental
D14S985	14q32.2	130/136	130/132	Biparental
D14S1007	14q32.33	120/124	120/124	N.I.



C. CGH+single mucleotide polymorphism (SNP) microarray profiles for chromosome 14.
We performed a single nucleotide polymorphism (SNP) array analysis the SurePrint G3 ISCA CGH+SNP Microarray Kit (catalog number G4890A, Agilent Technologies).



References
1. Kagami, M., et al. 2017. Temple syndrome: comprehensive molecular and clinical findings in 32 Japanese patients. *Genet. Med.* **19**:1356-1366.
2. Ioannides, Y., et al. 2014. Temple syndrome: improving the recognition of an underdiagnosed chromosome 14 imprinting disorder: an analysis of 51 published cases. *J Med Genet* **51**: 495-501.
3. Lande, A., et al. 2018. Temple syndrome as a differential diagnosis to Prader–Willi syndrome: Identifying three new patients. *Am J Med Genet A* **176**: 175-180.