



Coexistence of Kabuki Syndrome and Autoimmune Thyroiditis

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Dear Editor,

Kabuki syndrome (KS) is a multiple congenital anomalies/intellectual disability syndrome characterized by developmental delay, specific facial features, skeletal and visceral abnormalities. This syndrome is caused by mutations in *MLL2* and *KDM6A* gene. Autoimmune abnormalities such as idiopathic thrombocytopenic purpura, hemolytic anemia, thyroiditis, and vitiligo have been described very rarely in patients with KS (1,2,3). Herein, we present a very rare condition, KS in association with autoimmune thyroiditis and vitiligo due to a *de novo* heterozygous p.R2471* mutation in *MLL2* gene.

Case report: A female patient aged 7 7/12 years presented with short stature. There was no consanguinity between her parents. She was born as a term neonate weighing 2100 g as the product of a twin pregnancy and had no perinatal complications. On physical examination, the patient was noted to have large and low-set ears, broad and arched eyebrows, elongated palpebral fissures with eversion of the lateral third of the lower eyelid, as well as high and narrow palate. She also had other phenotypic malformations such as numerous vitiligo lesions of different sizes in the neck, brachydactyly, prominent fetal finger pads, and hyperlaxity in her joints. Her height was 116.3 cm (-1.85 standard deviation score [SDS]) and weight was 21.7 kg (-0.78 SDS). She had sensorineural hearing loss (left 65 dB, right 55 dB) and moderate mental retardation (Stanford-Binet intelligence scale total score was 43). She had a normal female karyotype (46,XX). A clinical diagnosis of KS was considered.

Additionally, laboratory findings revealed autoimmune thyroiditis [thyroid-stimulating hormone (TSH): 242 mIU/L (reference range: 0.55-6.7) and free thyroxine (fT₄) was

0.42 ng/dL (reference range: 0.91-1.92), Anti-microsomal antibody: 450.6 U/mL (reference range: 0-9), anti-thyroglobulin antibody: 2766 U/mL (reference range: 0-4)]. Thyroid ultrasonography demonstrated a rough pattern, consistent with thyroiditis. Levothyroxine (50 µg/day) replacement therapy induced a euthyroid state (TSH: 3.65 mIU/L and fT₄: 1.15 ng/dL).

The main causes of KS are point mutations with large intragenic deletions and duplications of the histone methyl transferase *MLL2* gene (1,4,5). We detected a *de novo* heterozygous p.R2471* (c.7411C>T) mutation in this patient. No mutations were detected in *MLL2* gene in her parents and her brother. This mutation causes an early stop codon and a truncated protein. It severely affects the protein structure. To our knowledge, this mutation was not reported in KS patients to date. As this is a truncating mutation, it is most probably a disease causing mutation.

In several patients, KS was reported to be associated with autoimmune abnormalities such as idiopathic thrombocytopenic purpura, hemolytic anemia, thyroiditis, and vitiligo (3,5). The autoimmune disorders may be manifestations of abnormal immune regulation. Ming et al (3) conclude that KS is associated with an increased incidence of autoimmune disorders. In our patient, the vitiligo lesions in the neck and thyroiditis were considered to be signs revealing an autoimmune condition. We recommend that all KS patients be investigated for possible coexistence of autoimmune disorders.

Keywords: Kabuki syndrome, *MLL2* gene, autoimmune thyroiditis, vitiligo

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