Growth hormone deficiency as a cause of persistent hypoglycaemia in a child with Turner mosaic and Kabuki Syndrome

Michal Ajzensztejn[1,2], Pratik Shah[3], Noina Abid[2], Jane Hurst[4], Deborah Morrogh[4], Shane McKee[5], Khalid Hussain[3]

[1] Paediatric Endocrinology Department, The Evelina London Children's Hospital, [2] Paediatric Endocrinology Department, The Royal Belfast Hospital for Sick Children, [3] Paediatric Endocrinology Department, Great Ormond Street Hospital for Children NHS Trust, [4] Genetics Department, Great Ormond Street Hospital for Children NHS Trust, [5] Northern Ireland Regional Genetics Department, Belfast City Hospital

Introduction:

We report the first known case of a child with mosaic Turner syndrome (TS) with ring X chromosome abnormality with features of Kabuki like syndrome (*KDM6A* deletion) presenting with hypoglycaemia secondary to severe growth hormone (GH) deficiency.

When the XIST locus is present in ring X Turner's mosaic, the chromosome is inactivated. There is a threshold which needs to be met in order to inactivate XIST, if this is not reached there in no inactivation. The KDM6A gene deletion associated with Kabuki Syndrome escapes X-inactivation as it falls below the threshold required to manifest the inactivation. This results in a more severe phenotype than Turner's monosomy.

Case History:

We describe a girl diagnosed antenatally with a lumbar myelomenigocele and spina bifida. She was born at term with intra-uterine growth restriction and noted to be dysmorphic.

Karyotype confirmed Turner's mosaic syndrome 46XrX(p11;q13)[22]/ 45X[8]arrXp22.33p11.2x1,Xp11.1q13.3x2-3,Xq13.3q28x1 with a small r(X). Several facial features were suggestive of Kabuki syndrome (everted lateral lower lid, arched eyebrows, depressed nasal tip, spinal anomalies, developmental delay and IUGR) see Photographs. CGH array confirmed that KDM6A was deleted on her ring X chromosome. She developed recurrent asymptomatic hypoglycaemia around the ages of 20-25weeks with concurrent gastroenteritis, which was resistant to treatment with standard TS dose GH therapy. She underwent formal pituitary assessment aged 18 months confirming GH deficiency.

Peak Growth hormone 4.7 mcg/L (>7.5)

Discussion:

Children with TS develop postnatal short stature. They usually have normal GH levels but show end organ resistance to it. Hypoglycaemia has been associated with Kabuki syndrome from various aetiologies including GH deficiency. Two recent case reports describe children with combined Turner Mosaic and Kabuki syndrome presenting with hyperinsulinaemic hypoglycaemia, but no reported cases due to severe growth hormone deficiency alone. The combination of GH deficiency and end organ GH resistance is likely to have led to the severity and resistance to treatment seen in this case, which rectified on treatment with a high dose of growth hormone given in two divided doses (0.07mg/kg/day).

Conclusion:

From this case, we recommend a low threshold for monitoring blood glucose levels in children with this phenotype and if evident, growth hormone provocation testing should be performed.

Photograph of patient aged 18 months.

Permission to use photograph provided by parents