

Growth hormone deficiency and phenotypic features in four cases of 22q11.2 deletion syndrome

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Background

- 22q11.2 deletion syndrome (22q11DS) displays a wide phenotypic spectrum.
- It is the most common deletion syndrome with an estimated incidence of 1 in 4000 children¹.
- Short stature is a phenotypic feature of the spectrum.
- Uncommonly, growth hormone deficiency (GHD) has been identified as a cause of short stature within this population².
- We present a case series of four 22q11DS patients with concurrent GHD that have been followed up in our paediatric endocrinology clinics.

Case Series

All four patients were referred to clinic for short stature with heights below the 0.4th centile. They subsequently underwent GH provocation testing (Table 1) and were diagnosed with GHD. No other pituitary hormone deficiencies were identified and coeliac screen was negative in all four patients.

Patient 1 (Older brother of Patient 2)

- Male patient, born at 37 weeks gestation by emergency caesarean section to non-consanguineous parents. Birth weight 2.72 kg. Background of left hemiparesis secondary to right polymicrogyria, global developmental delay and congenital heart disease. Inherited 22q11.2 deletion from father. Mid-parentile centile = 9th with range < 0.4th to 50th. Dysmorphic features consistent with 22q11.2 deletion. Bone age reported as 5-6 years at chronological age 8.3 years. Started on daily recombinant human growth hormone (r-hGH) at age 4.5 years. Both Patients 1 and 2 had a period of non-compliance to treatment.

Patient 2 (Younger brother of Patient 1)

- Male patient, born prematurely at 34 weeks gestation, labour was induced for polyhydramnios. Birth weight of 2.47 kg. Background of left hemiparesis secondary to right polymicrogyria, autism, global developmental delay and congenital heart disease. Dysmorphic features consistent with 22q11.2 deletion. Started on daily r-hGH at age 5 years.

Patient 3

- Male patient, born premature at 33+4 weeks gestation by emergency caesarean section to non-consanguineous parents. Birth weight 2.2 kg. Hypocalcaemic at birth. Background of cryptorchidism of left testis requiring orchidopexy, complex congenital heart disease, subcutaneous cleft palate, severe GORD and left vocal cord palsy. Both parents did not have 22q11.1 deletion on genetic testing, although paternal cousin was found to have 22q11DS. Dysmorphic features consistent with 22q11.2 deletion. Feeding difficulties requiring prolonged NG feeding. Started on daily r-hGH at age 3.3 years.

Patient 4

- Female patient. Birth history unavailable. Birth weight 3.18 kg. Non-consanguineous parents. Mid-parental height 160.5 cm. Background of complex congenital heart disease. 22q11.2 deletion inherited from mother. Dysmorphic features consistent with 22q11.2. Started on daily r-hGH at age 8 years

Growth charts of height pre and post r-hGH³

Figure 1. Patient 1

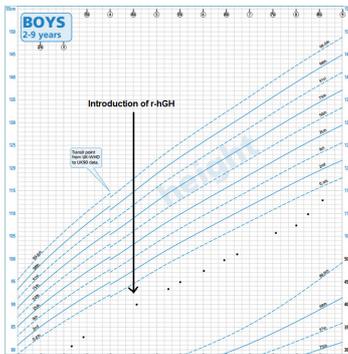


Figure 2. Patient 2

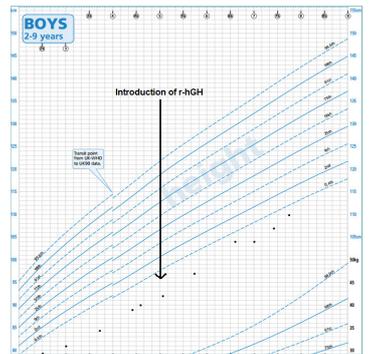


Figure 3. Patient 3

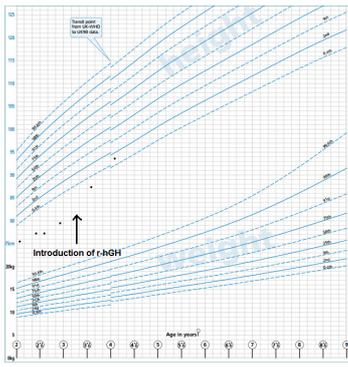
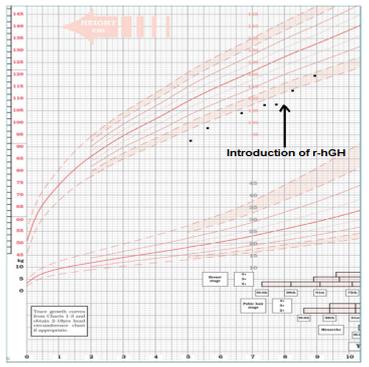


Figure 4. Patient 4



Conclusion

- The patients were all commenced on GH replacement therapy, with an excellent response (Figures 1-4).
- Our data suggest that 22q11DS patients with short stature should be appropriately investigated for GHD if they manifest poor growth.
- Early treatment with r-hGH may help optimise height.

References

1. Botto et al. *Pediatrics* 2003. 112;101-117.
2. Weinzimer et al. *Pediatrics*. 1998 May;101(5):929-32.
3. Growth charts taken from RCPCH website. <http://www.rcpch.ac.uk/child-health/research-projects/uk-who-growth-charts/uk-growth-chart-resources-2-18-years/school-age> & <http://www.healthforallchildren.com/shop-base/shop/growth-charts/uk90-four-in-one-charts-duo-decimal/>

Table 1. Evaluation for Growth Hormone Deficiency

Patient	Age (years)	MRI Brain and Pituitary appearance	Source of 22q11 Deletion	GH peak (ug/l)	IGF-1	IGFBP-3
1	3	Right-sided polymicrogyria	Paternal	5.8	7.1 pmol/l (4-20)	Not tested
2	3	Small anterior pituitary and right-sided polymicrogyria	Paternal	3.2	19 pmol/l (4-20)	Not tested
3	2.7	Small anterior pituitary, normal posterior pituitary and stalk	Sporadic	5.0	29 ng/ml (49-289)	1.55 mg/L (0.9-4.3)
4	7.16	Normal	Maternal	6.5	30 ng/ml (45-302)	1.78 mg/L (1.6-6.5)