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Introduction

Obesity is a known feature of chromosome 22q11 deletion syndrome, with a ~35% prevalence in adults, emerging in adolescence or adulthood. However, there is limited published literature about weight trends among patients with the reciprocal recombination. However, anecdotal evidence and rare reports suggest that obesity may also be associated with 22q11 duplication. Herein we describe four pediatric patients followed at our institution who have 22q11 duplication syndrome and are overweight (body mass index [BMI] 85-95 centile) or obese (BMI ≥95 centile).

Methods

Clinical databases of patients followed in the General Genetics Clinic or Genetic Obesity Clinic at Texas Children's Hospital (TCH) were queried to identify patients with 22q11 duplication syndrome who are overweight or obese. In cases with available information, we further characterized the obesity onset as early (before age 5), childhood (between ages 5-12), and adolescent (between ages 13-19) and described the inheritance of the duplication and weight phenotype of the family members carrying the duplication.

References

PMID: 28605459 PMID: 39616274 PMID: 22711268
 PMID: 25411582 PMID: 27184501 PMID: 17618498
 PMID: 30509170 PMID: 29441128 PMID: 25411582
 PMID: 27537705 PMID: 38308768 PMID: 30509170
 PMID: 40822943 PMID: 28605459 PMID: 29441128
 PMID: 28963451

Results

	Individual 1	Individual 2	Individual 3	Individual 4
Age, Sex	6yo F	4yo M	3yo F	17yo F
Duplication	2.6Mb at 22q11.21 LCR-A to LCR-D	2.6 Mb at 22q11.21 LCR-A to LCR-D	1.1Mb at 22q11.21q11.22	1.3Mb at 22q11.23
Inheritance	Maternal	Paternal	Unknown	Maternal
Other genetic results	Obesity panel – negative tGS - duplication	tES – VUS's in non- obesity genes	dES – Pathogenic variant in <i>RB1</i>	None
Birth parameters	Appropriate for gestational age (AGA)	LGA	AGA	SGA
Age at overweight, obesity	Overweight at 9m Obese at 12m	Obese at 45m	Overweight at 15m Obese at 18m	Overweight at 15m Obese at 28m
Current BMI Z-score	6.26	1.74	2.10	3.54
Family history	Mother – childhood- onset obesity	Father – unknown	N/A	Mother – childhood- onset obesity Affected half-brother – BMI Z-score -2.01

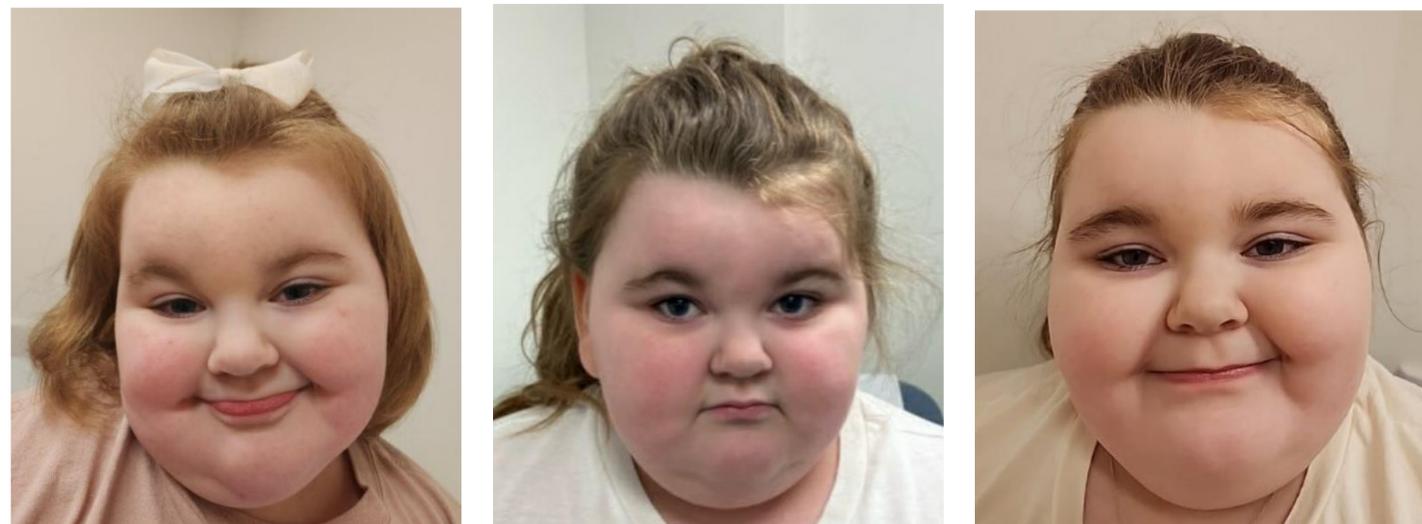


Figure 1. Individual 1 at 3.5y, 5.5y, and 6.25y old (family provided permission to publish photos)

Conclusion

We have identified four children with 22q11 duplication syndrome who exhibited childhood-onset obesity. Two inherited the duplication from a parent with childhood-onset obesity. One inherited the duplication from a parent whose weight is not known. One has an affected sibling with the familial duplication and low weight. Further investigation is needed to determine the overall prevalence of obesity, overweight, and poor weight gain among individuals with 22q11 duplication syndrome.

Future Directions

- Identify more patients with 22q11 duplication syndrome and obesity
- Please email murali@bcm.edu!
- Publish an illustrative case series
- Propose that patients presenting for evaluation of monogenic obesity undergo these tests:

