Exploring the Mysteries of 22Q Deletion Syndrome

Objectives

- To discuss common issues present in persons diagnosed with 22q Deletion Syndrome
- To explore what may lead to suspicion of and testing for 22q Deletion Syndrome
- To review treatment of Endocrine disorders present in 22q Deletion Syndrome

Introduction

- 22q Deletion Syndrome
  - a chromosomal disorder that results in poor development of several body systems
  - features vary widely, even among members of the same family.
  - original classifications included DiGeorge sequence/syndrome, velocardiofacial syndrome, Shprintzen syndrome, Sedlackova syndrome, and conotruncal anomaly face syndrome.
- This syndrome is caused by the deletion of a small piece of chromosome 22; the International 22q11.2 Foundation, through its "Same Name Campaign", advocates for the name 22q11.2 deletion syndrome.
The genetic information is found in the center of the cell.

- **p** = short arm
- **q** = long arm

**Typical Pair of Chromosomes 22**

**Pair of Chromosomes 22 with a deletion**

**22q11.21 deletion syndrome**

**Atypical Deletions** include both Central and Distal deletions.
Case Study

• RW was born on 8/30/12.
• She was the 4th child together for her 24 y.o. mother and 23 y.o. father.
• Mother was on Zofran for morning sickness.
• Pre-term labor at 29 weeks led to bedrest.
• Ultrasound showed fetus was smaller than expected, as well as had a prenatal arrhythmia.
• She arrived at 37 weeks by spontaneous vaginal delivery, weighing 5 pounds, 4 ounces. Length unknown.

Presentation to Genetics Clinic

RW was referred for a genetics consult at 3½ months of age due to:
– slow growth
– developmental delay
– nasal regurgitation
– dysmorphic features
– history of tracheomalacia with a possible laryngeal cleft
– failed hearing tests since birth

At the Genetics appointment, her length, weight, and HC were at the 50th percentile for a 1 month old.

Genetics findings

• Wide spaced eyes
• Small, unusually shaped ears
• Prominent parietal bones
• Thin ala nasi (the cartilaginous flap on either side of the nostrils)
• Long slender fingers
• Decreased tone
• Diagnosed with 22q Deletion Syndrome on 12/12/12.
22q Deletion Syndrome

- Present in 1 out of every 1,000 live pregnancies, in 1 in 68 children with congenital heart disease, and in 5 to 8 percent of children born with cleft palate
- 22q11.2 Deletion Syndrome is almost as common as Down syndrome.
- Potential to affect almost every system
  - can cause a wide range of health problems
  - no two people are ever exactly alike

22q Deletion Syndrome

- Though not always present, the key characteristics of this syndrome include combinations and varying degrees of:
  - heart defects
  - palate differences
  - feeding and gastrointestinal difficulties
  - immune system deficiencies
  - kidney problems
  - growth delay
  - hearing loss
  - low calcium and other endocrine issues
  - cognitive, developmental and speech delays
  - behavioral, emotional and psychiatric differences (ADHD, autism, anxiety, etc.)

Cardiac

- A congenital heart defect is present in 75-80% of patients with 22q Deletion Syndrome
- The most frequently seen cardiac malformations are "conotruncal" defects, including tetralogy of Fallot, pulmonary atresia with ventricular septal defect, truncus arteriosus, interrupted aortic arch, and ventricular septal defect.
Immunology

- 22q11.2 Deletion syndrome is the most common congenital chromosome deletion syndrome
  - associated with developmental defects including hypoplasia or abnormal migration of the thymus
  - patients have variable defects in T-cell immunity with an increased incidence of infection and autoimmune disease.
- The thymus gland is located behind the sternum and is responsible for the maturation of T-cells to fight infections.

Thymus Gland

Three major immunological concerns can complicate 22q11 deletion syndrome.
1. The most severe clinical scenario: complete absence of the thymus, alymphocytosis and SCID-like phenotype. This is rare and affects fewer than 1% of patients with 22q11 deletion.
2. The most common clinical scenario: patients have small, often atopic, thymus development and present with T-lymphocytopenia and recurrent sinusopulmonary infection in early childhood, which usually resolves by adolescence.
3. An increasingly recognized scenario: autoimmunity, a common feature of many immunodeficiencies.
GI

Feeding difficulties
- Nasal regurgitation, which may happen because of a cleft palate
- Spitting up or vomiting due to esophageal dysmotility
- Gastroesophageal reflux disease (GERD)
- Tracheoesophageal fistula

Gastrointestinal problems
- Mild to severe constipation
- Intestinal malrotation
- Hirschsprung’s disease
- Diaphragmatic hernia
- Inguinal and umbilical hernia

Development and Behavioral

- Delayed development
  - Mild speech delays
  - Delay in emergence of language
  - Delayed motor skills development

Endocrine

- Midline defects are common
- 3 major Endocrine concerns:
  - Calcium
  - Thyroid
  - Growth
Thyroid

- The thyroid gland is in front of the neck and is shaped like a butterfly or bowtie. The main job of the thyroid is to make thyroid hormones (T4 and T3). Thyroid hormones help maintain normal metabolism, growth, and development.
- A thyroid disorder may be present at birth (congenital) or might develop later in life. The thyroid may make too little hormone (hypothyroidism) or too much (hyperthyroidism).

Thyroid Concerns

- Congenital hypothyroidism
  - May be transient
  - Higher etiology of being autoimmune
  - May be less likely to come off treatment

Thyroid treatment

- Monitor with TSH and Free T4 in order to not miss a central hypothyroidism
- Standard treatment for hypothyroidism or hyperthyroidism
RW was found to have central hypothyroidism on 8/5/13. First Endocrine evaluation on 8/7/13.

TSH 0.4 mciU/ml (0.35-7.6)
Free T4 0.6 ng/dL (0.8-1.9)

Hypocalcium

• Hypocalcemia is almost always related to hypoparathyroidism

Calcium - Hypoparathyroidism

• The four parathyroid glands are located adjacent to the thyroid gland in the neck and regulate calcium in the blood through the production of parathyroid hormone.
Hypoparathyroidism

- Hypoparathyroidism is the presence of a low calcium level in the presence of an inappropriately normal or low PTH
- Congenital hypoparathyroidism tends to be transient

Treatment of Hypoparathyroidism

- Treatment is 2-fold:
  - Calcium
  - Calcitriol
Calcium

• Obtain a baseline renal ultrasound

Calcium

• 50-100 mg elemental calcium/kg/day divided into 3-4 doses
  – Use gut when possible
  – The intestine can only absorb so much.
• Titrate to target a slightly low to normal calcium level.

Calcitriol

• Calcitriol is the active form of Vitamin D.
  – PTH converts the inactive to the active form of Vitamin D. With a low PTH level, this conversion is unable to take place.
• Calcitriol helps retain calcium in the body.
Growth

- Concerns with growth hormone needs
- Celiac disease
Conclusion
• This disorder is autosomal dominant - A person with 22q Deletion Syndrome has a 50% chance of passing the syndrome on to any offspring.

Conclusion
• 22q Deletion Syndrome can affect many different bodily systems.
• Endocrine Concerns
  – Calcium
  – Thyroid
  – Growth