

22q11.2 Deletion

Understanding the test, the result, and the clinical concerns

Associated Cardiovascular Anomalies

- -Tetralogy of Fallot, 16%.
- -Truncus arteriosus, 34%
- -VSDs, 5-10%.
- -Interrupted aortic arch, type B, 52%.
- -Right aortic arch without intracardiac defect, 8%.

Screening for congenital heart disease

- -Aggressive fetal imaging.
- -TOF specifics.
 - Absent pulmonary valve.
 - Right aortic arch.
 - Pulmonary atresia with multiple aortopulmonary artery collaterals.

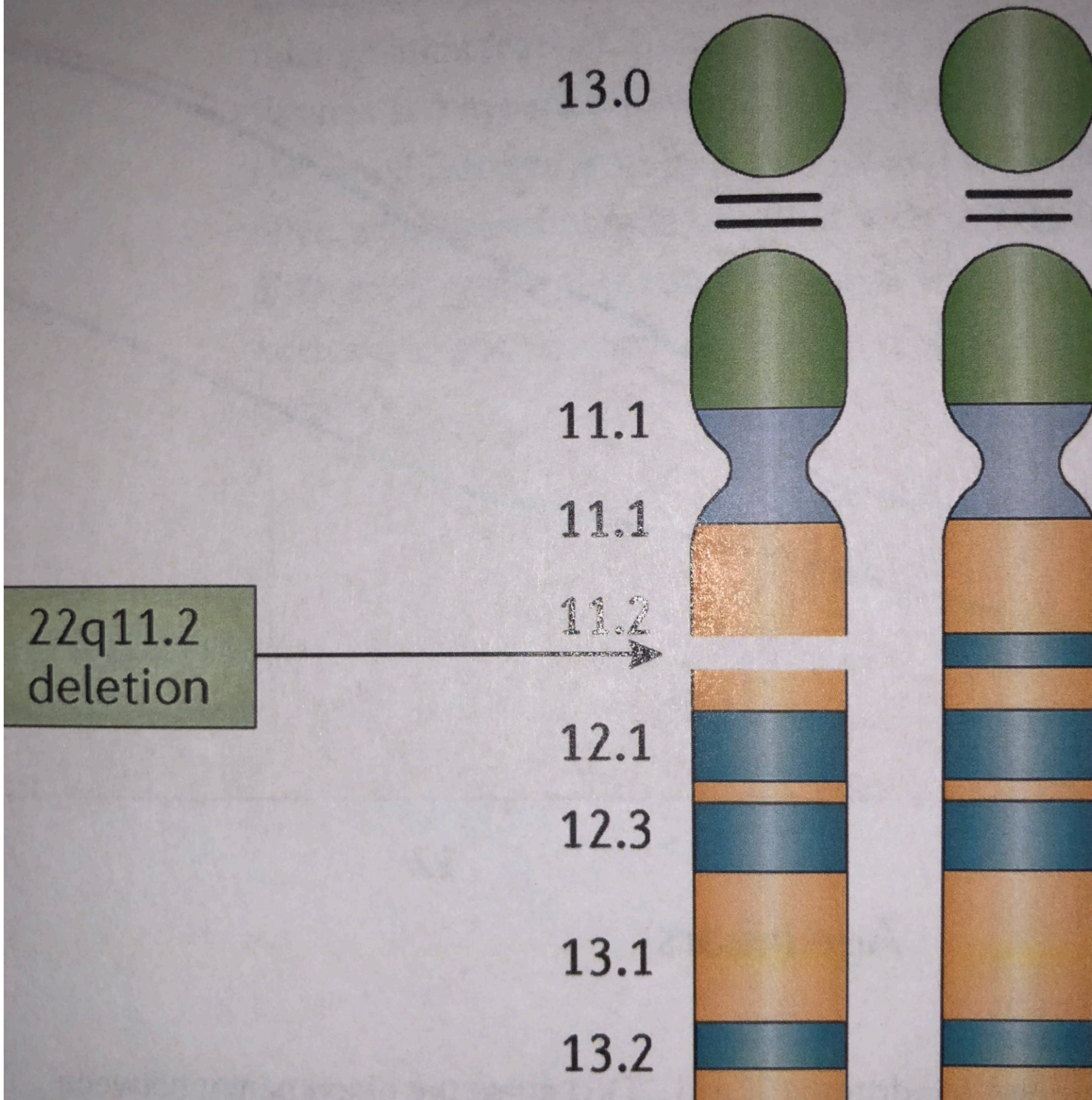
You suspect, you order the test

- -Microarray. Now the standard.
- -Genetic testing has been available since late 1980s.
- -More than 90 genes within the commonly deleted region of chromosome 22q11.2. Most common chromosomal micro deletion disorder.
- -90% of the time it is a de novo defect.

DiGeorge Syndrome

- -Angelo DiGeorge described the clinical triad of immunodeficiency, hypoparathyroidism, and congenital heart disease.
- -Facial features: long face, hypertelorism, retrognathia, narrow palpebral fissures, prominent nose with large tip and hypo plastic nares, small mouth with everted upper lip, small teeth, low-set dysmorphic ears, short philtrum.

Chromosome 22



Embryology

- In early embryologic development, cranial neural crest cells migrate, distribute, and form those tissues and organs of the pharyngeal arch systems, including the aortic arch and its branches, outflow tracts, thymus, parathyroid and parts of the palate, pharynx, and face.

Made my heart diagnosis, but...

- -At least 180 clinical features.
- -CHD, 80%.
- -Development delay, 90%.
- -Palatal defects, 76%
- -Immunodeficiency, 77%.
- -Hypocalcemia, 49%.
- -Renal anomalies, 36%.
- -Dysphagia, 35%.
- -Mental health, 25%.
- -Orthopedic issues, 5%.

Immunodeficiency

- -Low T cell numbers in at least 75% of infants with 22q11.2 DS.
- -In most cases, T cell count is moderately decreased and does not impact surgical procedures.
- -susceptible to bacterial superinfection.
- -Decreased humoral response.
- -Susceptible to autoimmune disease.
- -Higher incidence of malignancy.

Palatal Anomalies

- -11% have overt cleft palate.
- -65% have milder but often medically actionable manifestation contributing to feeding issues, speech and articulation issues.
- -recurrent sinus and middle ear infections.

Endocrine Abnormalities

- -Hypoparathyroidism resulting in hypocalcemia, 50-65% of patients.
- -Hypothyroidism in 20% of adults.
- -Hyperthyroidism in 5% of adults.
- -Growth hormone deficiency, 4 to 15% of patients.

Developmental Delay

- -Gross and fine motor difficulties, and expressive language delays and speech problems dominate in infants.
- -Mean IQ is 70. Range generally is 55-85.
- -Prevalence of anxiety, attention-deficit, and autism spectrum disorders.
- -Significant mental health issues. Up to 25% develop schizophrenia.

Orthopedic Issues

- Cervical abnormalities in almost all patients. Sometimes require cervical decompression.
- Scoliosis in 60%. 5-6% require surgical intervention.
- Club foot, polydactyly, syndactyly.
- Juvenile rheumatoid arthritis. Up to 50 times more likely.

Sometimes Inherited

- Case report demonstrating 3 generation pedigree and paternal transmission demonstrating intrafamilial phenotypic variability.
- Index patient was adult man living in residential setting for people with moderate to severe intellectual disability.
- This patient's younger brother had 4 year old daughter with significant delay.
- Both the father and grandfather of this girl had 22q11.2 DS. Grandfather had right aortic arch. Father had TOF.

Heterogeneous Clinical Presentation

- As a cardiologist, it's pretty straightforward that microarray is ordered. Hey, does anybody know what the microarray showed?
- If positive genetic screen, parents will have a lot of questions and I will not have that many answers. In fact, will likely add to parents' anxiety.
- If there are no obvious cardiac issues, diagnosis may be delayed.