Meet Sophia*

During pregnancy, an ultrasound identified an abnormal umbilical cord attachment. Once identified, Sophia's mom received weekly nonstress tests to monitor fetal heart rate and bloodwork for NIPS, which returned low risk for aneuploidies. A follow-up 38-week ultrasound showed no new concerns.

Birth

Sophia was born full term with an uncomplicated delivery.

While in the nursery, the care team noted difficulty closing her right eye and iris coloboma. Nurses also noted signs of multi-suture craniosynostosis. She was then transferred to the NICU and experienced a seizure-like episode during transport.

Day 2

Upon NICU admission, Sophia received:

- Echocardiogram
- Brain MRI
- Skull X-ray
- Genetics consult

Findings showed:

- **Echo:** Complex congenital heart disease (CHD) including Shone's complex variant with multiple hypoplastic left-sided structures, small atrial septal and ventricular septal defects, and bilateral superior vena cava without bridging vein
- **MRI:** Findings concerning for cortical and migration malformations
- **Skull X-ray:** Confirmed multi-suture craniosynostosis
- **Bloodwork:** Thrombocytopenia
- **Genetics:** Microcephaly, facial dysmorphisms, and neck/interdigital webbing which led to them ordering a chromosomal microarray (CMA)

Day 6

Cardiology and Neurology care teams met to review findings and discuss next steps.

The surgical team preferred to wait for the CMA results to come back before making surgical recommendations, as genetic findings could influence surgical planning and peri-operative risk. However, the CMA results were still 13 days out.

Day 7

Given the time-sensitive nature of Sophia's condition and the need for rapid diagnostic clarity, the genetics team met with the family to obtain consent for ultraRapid genome sequencing. Results were returned in 48 hours.

UltraRapid genome sequencing identified a de novo pathogenic multi-gene deletion (11q23.3q25). This confirmed a molecular diagnosis of Jacobsen syndrome which is associated with:

- **Congenital heart disease**
- **Thrombocytopenia**
- **MRI abnormalities** (consistent with Sophia's findings)
- **Developmental and intellectual disability**

The result provided a unifying diagnosis and directly enabled the surgical team and family to make timely decisions. Without it, the team would have waited on CMA results for two more weeks, delaying critical decisions about whether to pursue surgery or withdraw care.

Sophia ultimately received ultraRapid genome sequencing in the NICU, but testing was not ordered until a week after clinical presentation. For critically ill patients, rapid comprehensive genetic testing can provide the clarity needed to make expedited care decisions.

*Case study is based on GeneDx patient testing, with all identifying information removed.

Photos do not represent actual patients.

GeneDx