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## Genetic Services Policy Project

### Multiple Congenital Anomalies: A Vignette

Marty Lewis is a genetic counselor in Washington state. She first met the Moore family when their newborn baby was being evaluated for multiple congenital anomalies. Peggy Moore was a healthy 27-year-old woman. Her husband, Jack, was 31 years old and also healthy. For the most part, Peggy had experienced an uneventful first pregnancy that included normal screening tests for Down syndrome, Trisomy 18, and neural tube defects during the second trimester. An early ultrasound exam for dates was also normal, and a second trimester ultrasound was offered but declined. At 36 weeks gestation, the Moores presented to their local hospital in Sitka, Alaska after Peggy's water broke. Fetal monitoring demonstrated that the baby was experiencing distress, so a caesarean section was performed. On delivery, Peggy's family physician who was overseeing her obstetrical care, noted a hypotonic (floppy) male infant with dysmorphic (abnormal) facial features, a cleft lip/palate, and a heart murmur. The infant was given supportive care and immediate arrangements were made to transport the child by air to Seattle, given the limited availability of tertiary services in Alaska.

Once in Seattle, the child was admitted to the Neonatal Intensive Care Unit and evaluated by a cardiologist, geneticist, orofacial team, and feeding specialist, in addition to the neonatal intensivist, and the rest of the NICU team. The cardiac ultrasound demonstrated a large ventricular septal defect. This heart defect in addition to the other anomalies suggested the presence of a syndrome. Dr. James, the geneticist, ordered several lab tests to pinpoint a diagnosis, including a traditional karyotype study. He and Marty met with the Moores to discuss other testing options including newly available chromosomal microarray (CMA) testing. The testing required blood samples from both parents and the baby. The advantage of this testing is the ability to test for multiple conditions in one test with rapid availability of results. However, health insurance plans were not yet universally covering this testing. Other options included multiple fluorescence *in situ* hybridization (FISH) tests for the most likely syndromes. The Moores decided to pursue the new testing and, after discussion with Dr. James, the family's health insurance plan pre-authorized the \$1,900 testing at 80 percent coverage.

A week later, the CMA test results came back demonstrating an abnormality (subtelomeric microdeletion) of chromosome 1p and the infant was diagnosed with 1p36 deletion syndrome. The chromosomal abnormality was not present in either of the parents' samples, suggesting a "de novo" deletion. This abnormality was not detected on the karyotype, which eventually came back normal.

Marty and Dr. James met with the Moores to discuss the results. Marty informed the couple of the low risk of recurrence and assured the Moores that nothing they did caused this abnormality. She told them that despite their lack of family history or other risk factors, 1 out of every 33 babies is born with one or more birth defects. The prevalence of this particular condition was 1 in 10,000 to 1 in 5,000; although relatively rare, it is the most common terminal deletion

syndrome. Clinical course was variable, but the majority of affected children experienced moderate to severe developmental delay and mental retardation. Seizures were a common complication but could typically be controlled with medication.

Because of financial concerns, Peggy stayed in Seattle with the baby while her husband returned to Alaska for work. During this time, Peggy began to experience significant episodes of sadness and anxiety. Concerned about post-partum depression, Marty recommended a mental health provider, but Peggy preferred to wait to see her physician when she got home to Alaska.

The infant fared moderately well and was discharged at 4 weeks of age. Arrangements were made for the baby to receive Children with Special Health Needs support services and early intervention services in Sitka. Arrangements were also made for roll-up with the geneticist who travels to Sitka twice yearly for a public health sponsored genetics clinic as well as with a neurologist and cardiologist in Anchorage. Future evaluation and treatment by the cardiac and orofacial surgery teams back in Seattle would be required. Marty provided Peggy with contact information for other families with affected children. Discharge planning included involvement of the family physician from Sitka through a conference call. Records from the infant's hospitalization were forwarded to the family physician to take over routine care.

In reflecting on the case, Marty wondered how things might have been different if the diagnosis were made prenatally. Would the Moores have continued the pregnancy knowing the prognosis? How will their son's condition affect their lives in the days ahead? Will this special child bring more joy than sorrow as similar children have done in many families? Marty made a note to contact the Moores in a week or so to check on their progress and to encourage Peggy and Jack to call upon the resources they need.

This case study highlights the following points:

- Although congenital anomalies may be identified through prenatal screening and diagnosis (maternal serum screening, ultrasound, chorionic villus sampling, amniocentesis), the test results may be normal or the tests may not be done at all (because of patient preference, provider practice patterns, etc.). In one recent study from Hawaii, only 16 percent of congenital anomaly cases were identified prenatally. Recent changes in professional screening recommendations and the availability of newer testing techniques may increase the number of anomalies that are identified prenatally. Options would then include pregnancy termination or continuation of pregnancy with enhanced fetal monitoring and ability to plan for a high-risk delivery. Pregnancy termination has numerous social, ethical and cultural implications. Cost-effectiveness studies of prenatal screening that demonstrate cost savings from screening assume that a large percentage of couples will choose pregnancy termination for affected fetuses.
- Availability of services, including genetic services, may be limited because of geography. In this case, services were not immediately available and the child/family needed transportation out-of-state. Follow-up services may also require travel (either the specialist coming to the area or the family traveling to the services). States have developed a variety of arrangements to assist with these concerns, including contracting

with out-of-state geneticists and other specialists who will conduct outreach clinics on a periodic basis.

- New techniques, such as high-resolution chromosomal microarray tests that can identify a large number of conditions in one test, are emerging. These tests allow for more accurate and timely diagnosis of congenital anomalies (either in the pre- or postnatal period). Professional guidelines for use of these new technologies have not yet been established, and ethical concerns have been raised about the prenatal use of these tests.
- Multiple providers are involved in the care of children with congenital anomalies and their families, including geneticists and genetic counselors, specialists, and primary care providers. Coordination of care and support services are often needed.
- Family issues and needs are complex and vary among families. The time commitment as well as the physical and emotional strain of having a child with complex health needs can be significant. Because of hormonal changes, depression and other mental health concerns in mothers are not uncommon in the perinatal period and may be exacerbated by stress. Family separation and financial concerns are also issues in this case.

## REFERENCES

Wei U, Ballif B, Kashork C, et al. Development of a comparative genomic hybridization microarray and demonstration of its utility with 25 well-characterized 1p36 deletions. *Hum Mol Genet* (2003);12(17):2145-2152.