DiGeorge Syndrome: Summary of Neurologic Issues

By Terry O. Harville, MD, PhD

IN PREVIOUS issues, we discussed features of DiGeorge syndrome (DGS) and partial DGS (PDGS) resulting from the consequences of improper timing of the sequence of events during early phases of embryonic development. We began with a discussion of the genes affected by chromosome 22q11.2 hemizygosity, and how some of these genes may be involved with the neurologic features of this complicated disease. In this column, we will summarize the major neurologic and behavioral issues associated with DGS/PDGS.

As with many medical disorders, the initial primary concerns involve the most serious features and how to provide the best treatment. With DGS/PDGS, the initial concern is the heart since before the introduction of PGE1, many infants died of cardiac malformations. Also of initial concern are immune dysfunction, which is recognized as relevant, nondetectable or mild in many, but severe and life-threatening in some; hypocalcemia due to parathyroid dysfunction; and obvious features such as cleft lip or cleft palate.

Because some DGS/PDGS infants require surgery for heart conditions, resulting in significant time spent in the ICU and sometimes prolonged periods of time on ventilators, neurologic and behavioral issues were initially considered a secondary consequence, rather than a direct consequence, of the disease and, therefore, not necessarily requiring earlier intervention. However, after DGS/PDGS patients began living longer and were monitored, it was discovered these patients expressed behavioral, neurologic and psychiatric issues that correlated with having the 22q11.2 deletion found in DGS/PDGS. Subsequently, specific genes from this region were identified (e.g., COMT and CRKL), which are implicated in neurologic and psychiatric diseases.

Unfortunately, essentially all patients with DGS/PDGS will be at risk for some form of neurologic or behavioral problems, and these can include psychiatric issues.

Therefore, children with DGS/PDGS must be evaluated early and enrolled in special education programs to offset these deficits.

While relatively rarer in children, it is thought that 60 percent of patients with DGS/PDGS will eventually be diagnosed with a psychiatric illness by adulthood. Those with lower IQ levels are at higher risk. As such, children with DGS/PDGS should be evaluated by psychiatric specialists to assess their risks, and followed over time so that a transition into psychiatric disease is not missed and specific treatment can begin earlier in the course of disease.

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Today, it is known that neurologic problems and subsequent psychiatric disease are major complications in patients with DGS/PDGS, and more needs to be done earlier to mitigate these issues.

In the next issue, we will discuss more of the problems and issues that occur due to improper timing of the sequence of events during early phases of embryonic development.

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