


50 Years Ago in The Journal of Pediatrics

Familial Holoprosencephaly with Endocrine Dysgenesis


Seploptic dysplasia (SOD) is a rare, heterogeneous disorder occurring in 1 in 10,000 live births. It is classically diagnosed when at least 2 of the following features are present: midline brain defects, pituitary hormone abnormalities, and optic nerve hypoplasia. Historically known as de Morsier syndrome, the definition of SOD has evolved as imaging techniques have advanced combined with the growing recognition of endocrine abnormalities in this syndrome.

In the 1960s, reports appeared characterizing findings associated with holoprosencephaly, such as midfacial malformations and radiologic abnormalities. However, few of these reports described endocrinopathies, and, if described, they typically were discovered on autopsy. In 1968, Hintz et al described 2 cases of holoprosencephaly occurring in siblings. The older sibling died on the first day of life, and autopsy revealed an absent pituitary and adrenal hypoplasia. Testing on the younger sibling diagnosed endocrinopathies involving both anterior and posterior pituitary hormones. The authors were the first to report a thorough endocrine evaluation of an infant with holoprosencephaly. Their recommendations for a careful search for neuroendocrine deficiencies in similar patients remains pertinent advice for contemporary pediatric care.

Today, the diagnosis of these siblings would fall in the spectrum of SOD. Clinical presentation includes hypopituitarism, visual deficits, seizures, developmental delay, and autism. Current management involves a multidisciplinary approach with ophthalmology, endocrinology, neonatology, and neurodevelopmental teams to identify and address these issues. Evaluation includes ophthalmologic examination, brain imaging, and pituitary hormone screening. Magnetic resonance imaging has replaced cerebral ventriculograms as the preferred imaging modality, and genetic testing is an option. Although progress has been made, the etiology remains unclear in more than 99% of cases. However, development in the field of genetics has discovered 2 genes implicated in SOD, HESX1 and SOX2, which regulate pituitary gland and forebrain development.

This report holds particular significance for our division, as this was Dr Hintz’s first publication, and he served for many years as chief of pediatric endocrinology at our institution. His accomplishments and influence as a clinician, researcher, and educator continue to this day.

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