Advances in Pediatrics 63 (2016) 127–146

ADVANCES IN PEDIATRICS

The Optic Nerve Hypoplasia Spectrum

Review of the Literature and Clinical Guidelines

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Keywords

• Optic nerve hypoplasia • Septo-optic dysplasia • Epidemiology • Hypopituitarism • Hypothalamic-pituitary dysfunction • Clinical presentation • Diagnosis • Management

Key points

- Optic nerve hypoplasia (ONH) is a complex congenital disorder of unknown etiology and is the leading cause of permanent, congenital visual impairment in children in the western world.
- The causes of ONH are complex and multifactorial, with most cases being sporadic. Further studies are necessary to elucidate the causes of ONH.
- ONH is frequently associated with congenital brain malformations, hypothalamic-pituitary dysfunction, neurocognitive disability, obesity, and autism spectrum disorders.
- Hypothalamic-pituitary dysfunction in ONH occurs independently of brain malformations and may evolve over time, necessitating long-term evaluation and follow-up.

Financial Disclosures: M.E. Geffner is a clinical trial consultant for Daiichi-Sankyo; is on the data safety monitoring board for Tolmar; has research contracts from Novo Nordisk and Versartis; serves on advisory boards for Ipsen, Pfizer, Inc, and Sandoz; is a lecturer for Sandoz; and receives royalties from McGraw-Hill and UpToDate. The other authors have no disclosures to report.

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0065-3101/16/$ – see front matter
http://dx.doi.org/10.1016/j.yapd.2016.04.009

INTRODUCTION

Optic nerve hypoplasia (ONH) is a common complex congenital disorder of unknown cause, involving a spectrum of anatomic malformations and clinical manifestations ranging from isolated hypoplasia of 1 or both optic nerves, with a variable degree of visual impairment, to extensive brain malformations, hypothalamic-pituitary dysfunction, neurocognitive disability, and/or autism spectrum disorders (ASDs) [1,2]. ONH is the second leading cause of congenital visual impairment, superseded only by cortical visual impairment [3,4]. According to the United States (US) Babies Count registry for children with visual impairment from birth to age 3 years, ONH carries a worse visual prognosis compared with cortical visual impairment, retinopathy of prematurity, and albinism [5]. It is the single leading cause of permanent legal blindness in children in the western world [3].

Owing to early observations of co-occurrence with agenesis of the septum pellucidum and hypopituitarism [6,7], ONH has long been recognized as part of the septo-optic dysplasia (SOD) syndrome, a clinically inaccurate term that attributes prognostic importance of the hypothalamic-pituitary dysfunction development to the absent septum pellucidum and/or other midline brain malformations. More recent, larger studies have demonstrated ONH to be an independent risk factor for hypothalamic-pituitary dysfunction, with abnormalities of the septum pellucidum having no prognostic value [1,8–11].

Currently, there are no consensus or clinical practice guidelines available for evaluation and management of children with ONH. This article focuses on the current state of knowledge about the prevalence, causes, and associated clinical features of the ONH spectrum, including their presentation, diagnosis, and management. The authors recommend a family-centered, multidisciplinary approach to caring for all children with ONH. Herein, are presented comprehensive guidelines for clinical evaluation and management based on an extensive literature review and the authors' clinical experience.

EPIDEMIOLOGY

The prevalence of ONH has increased substantially since the 1980s. The Swedish Register of Visually Impaired Children reported a fourfold increase in prevalence between 1980 and 1999 [12]. In an epidemiologic study conducted between 1944 and 1974, the prevalence of ONH in British Columbia, Canada, was reported to be 1.8 per 100,000 [13]. In 1997, Blohme and Tornqvist [4] reported that 7.1 per 100,000 children younger than 20 years of age with visual impairment or blindness in Sweden had ONH. The most recent estimates from the United Kingdom reported a prevalence of 10.9 per 100,000 in children younger than 16 years of age [14] and, from Stockholm, Sweden, 17.3 per 100,000 children younger than 18 years of age [2]. In another 2014 report using data derived from a registry of children with severe visual impairment in New Zealand, ONH was found in 6.3% of cases of children younger than 16 years of age [9]. This finding most likely underestimates the true prevalence because mild and/or unilateral cases are not consistently enrolled in the registry.