Optic Nerve Hypoplasia: An Infant with Poor Fixation and Pituitary Dysfunction

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Abstract

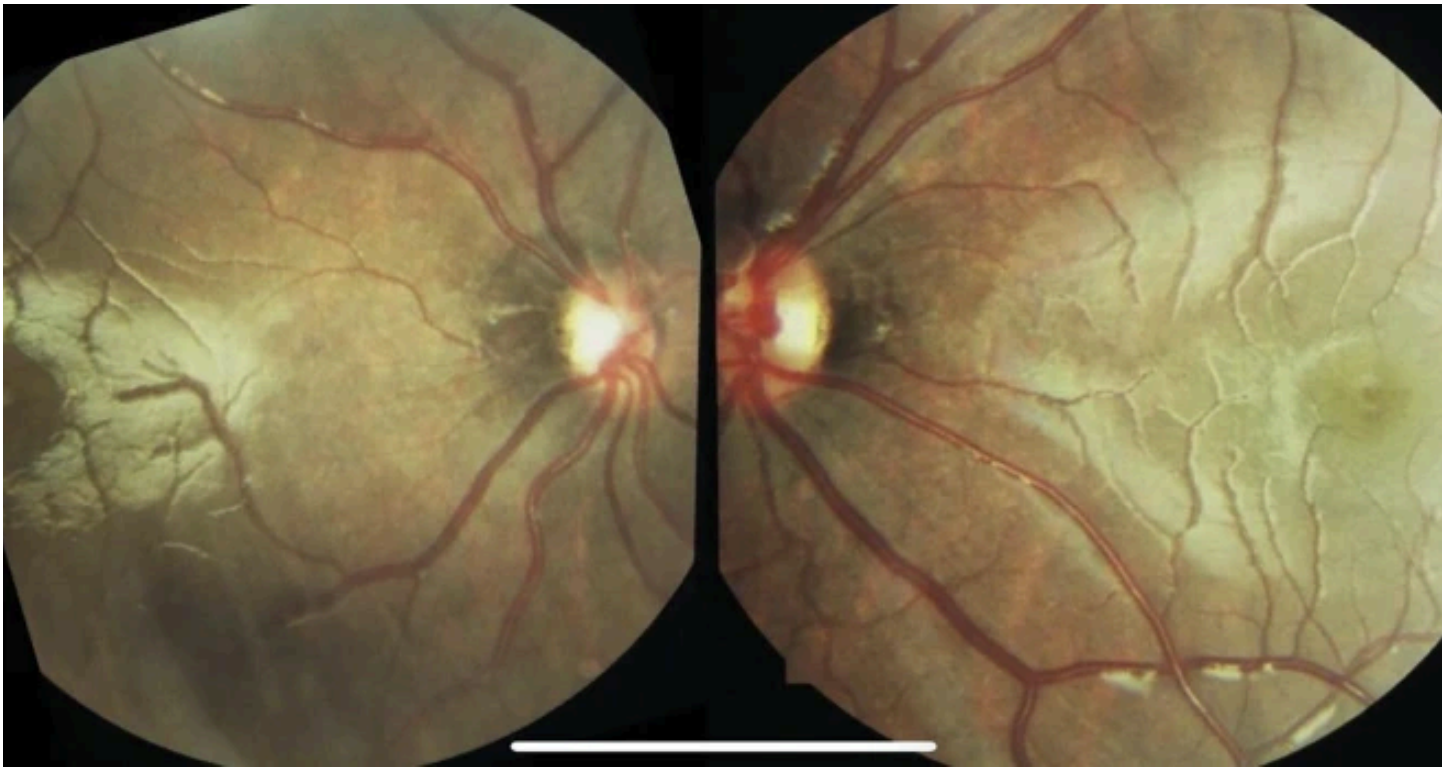
A 5-month-old girl was born full term via C-section for fetal distress and had a prolonged neonatal ICU stay for hypernatremia and hyperbilirubinemia. She was diagnosed with persistent diabetes insipidus. At 5 months of age, ophthalmologic consultation was requested by endocrinology to evaluate the patient for optic nerve hypoplasia. Neuro-ophthalmologic examination showed that the patient had poor fixation, but pursued a 6″ toy at 1 foot and had equally reactive pupils. Her refractive error was –1.00 + 1.75 × 90 right eye and –0.25 + 1.50 × 90 left eye. Ocular motility examination showed full ductions, nystagmus, and an esotropia of 45^{Δ}. The funduscopic exam revealed bilateral optic nerve hypoplasia (ONH). MRI of the brain was normal except for an absent neurohypophysis. She developed adrenal insufficiency and growth hormone deficiency. All young children with ONH need to be monitored for pituitary insufficiency, even when MRI findings may be normal.

Keywords

Case Presentation

A 5-month-old girl was born full term via C-section for fetal distress and had a prolonged neonatal ICU stay for hypernatremia and hyperbilirubinemia. She was diagnosed with persistent diabetes insipidus. At 5 months of age, ophthalmologic consultation was requested by endocrinology to evaluate the patient for optic nerve hypoplasia. Neuro-ophthalmologic examination showed that the patient had poor fixation, but pursued a 6″ toy at 1 foot and had equally reactive pupils. Her refractive error was –1.00 + 1.75 × 90 right eye and –0.25 + 1.50 × 90 left eye. External examination was unremarkable. Ocular motility examination showed full ductions with an esotropia of 45^{Δ}. Nystagmus was present. The funduscopic exam revealed bilateral optic nerve hypoplasia (ONH, Fig. 1.1).

Fig. 1.1



Fundus photos, which demonstrate bilaterally small optic nerves, worse in the right eye, with temporal disc pallor both eyes and a peripapillary hyperpigmented ring, especially in the right eye. Such “double rings” are typical, but not diagnostic of ONH. The double ring may be hypopigmented, causing confusion with optic atrophy. (Right eye is shown on the left, and left eye is shown on the right).

Full size image

Differential Diagnosis

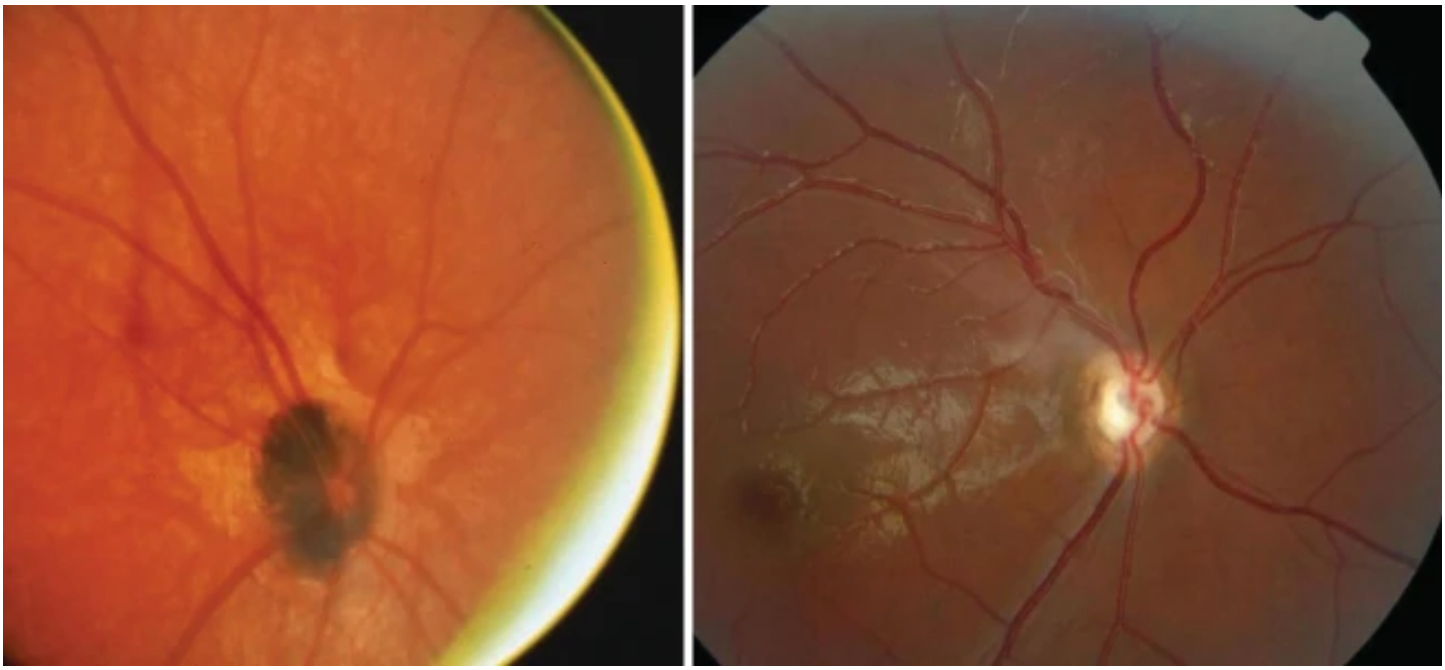
- Optic nerve hypoplasia
- Optic atrophy

Diagnostic Workup

Optic nerve hypoplasia may be misdiagnosed as optic atrophy if the examiner does not distinguish the true margins of the optic disc from a hypopigmented peripapillary ring that demarcates the border of the putative scleral canal. This is more easily identified with direct ophthalmoscopy than with indirect ophthalmoscopy. The optic nerve appearance may vary from highly dysplastic (Fig. 1.2) to less dysplastic with the characteristic hypopigmented peripapillary

ring (Fig. 1.2). ONH may also have superimposed optic atrophy with pallor, as in this case.

Fig. 1.2

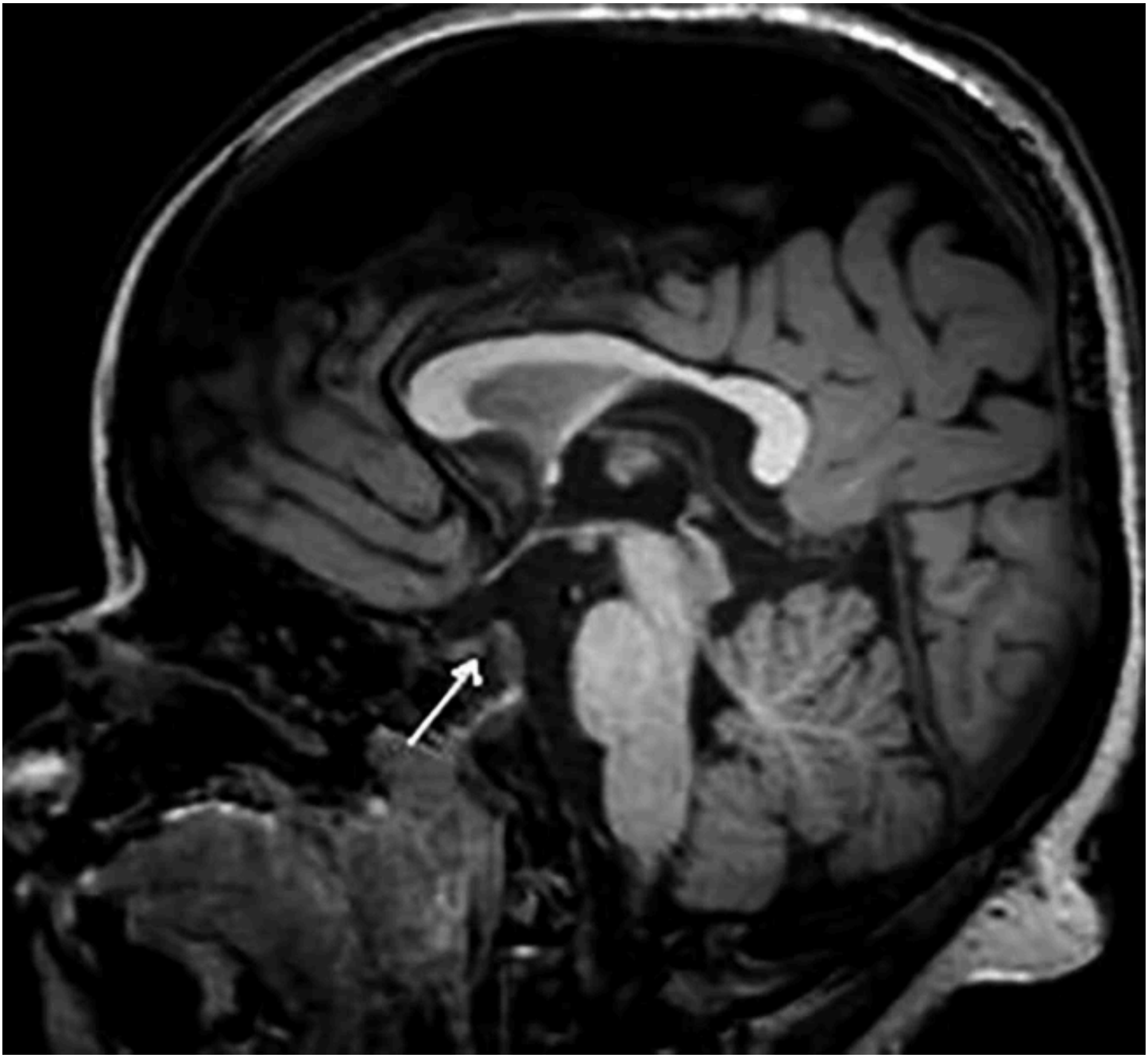


Fundus photos providing examples of the range of optic nerve appearances in optic nerve hypoplasia from severely dysplastic with surrounding peripapillary pigment (shown on the left) to hypoplastic with the characteristic hypopigmented peripapillary ring (shown on the right). (Photos provided courtesy of Paul H. Phillips, MD and Gena Heidary, MD, PhD).

Full size image

Laboratory tests indicated an abnormal IGF-1 at <16 ng/mL and a normal IGFBP-3 at 1.4 mg/L. She had multiple pituitary hormone deficiencies (ADH, TSH, ACTH). Magnetic resonance imaging (MRI) of the brain showed no cerebral abnormalities other than a nonvisualized infundibulum and an absent posterior pituitary bright spot (Fig. 1.3). Cross-sectional diameters of the optic nerves on the MRI were 1.3 mm right eye and 1.6 mm left eye.

Fig. 1.3



Sagittal T1-weighted MRI shows lack of a posterior pituitary bright spot (white arrow) and no visible infundibulum, confirming the absence of the neurohypophysis. Corpus callosum and septum pellucidum are normal, and there are no hemispheric abnormalities.

Full size image

Final Diagnosis

Bilateral optic nerve hypoplasia

Clinical Discussion

Treatment and Prognosis

Children with ONH frequently develop strabismus and refractive error often with astigmatism. Surgical treatment for strabismus should be deferred unless vision is relatively equal and sufficient for binocularity. Patching should not be initiated unless there are risk factors for amblyopia such as anisometropia or strabismus in a child with optic nerves that are similarly affected with mild or moderate ONH and without relative afferent pupillary defects. Vision can spontaneously improve, especially in the first 2 or 3 years of life. This may be due to improved optic nerve function as a consequence of myelination in early years of life. Hypothyroidism decreases the chance of vision improvement [2].

This patient, at age 4, continues to be treated for diabetes insipidus and has stable sodium levels with 0.2 mg of SQ DDAVP in the morning and 0.5 mg at night. Thyroid and adrenal functions have been controlled with 75 mcg of levothyroxine daily and 2.5 mg of hydrocortisone in the morning and 5 mg at night. She also receives stress doses of cortisol as needed for illness. She developed growth hormone (GH) deficiency, for which she is on 1.0 mg of GH per day and is tolerating well. She will be monitored for precocious puberty which would limit her response to GH. She is severely obese, requiring a controlled diet to limit milk consumption and increase consumption of fruits and vegetables. Cognitive and developmental support continues to be an important part of her treatment. She receives occupational therapy, physical therapy, and speech therapy. She experiences behavioral issues with head banging.

With respect to visual function, after part time occlusion of her left eye for 6 weeks, she spontaneously fixated on large toys with either eye. She then had strabismus surgery. Her eyes were aligned, but she was unable to cooperate with stereopsis testing. Her postoperative refractive error was –3.00 + 3.00 × 90 right eye and –2.25 + 1.50 × 90 left eye.

This patient has ONH of moderate severity with relatively good vision. Patching appeared to improve fixation with the right eye despite asymmetric optic nerve hypoplasia. She has severe developmental, behavioral, and hormonal abnormalities.

Important Aspects of the Diagnosis

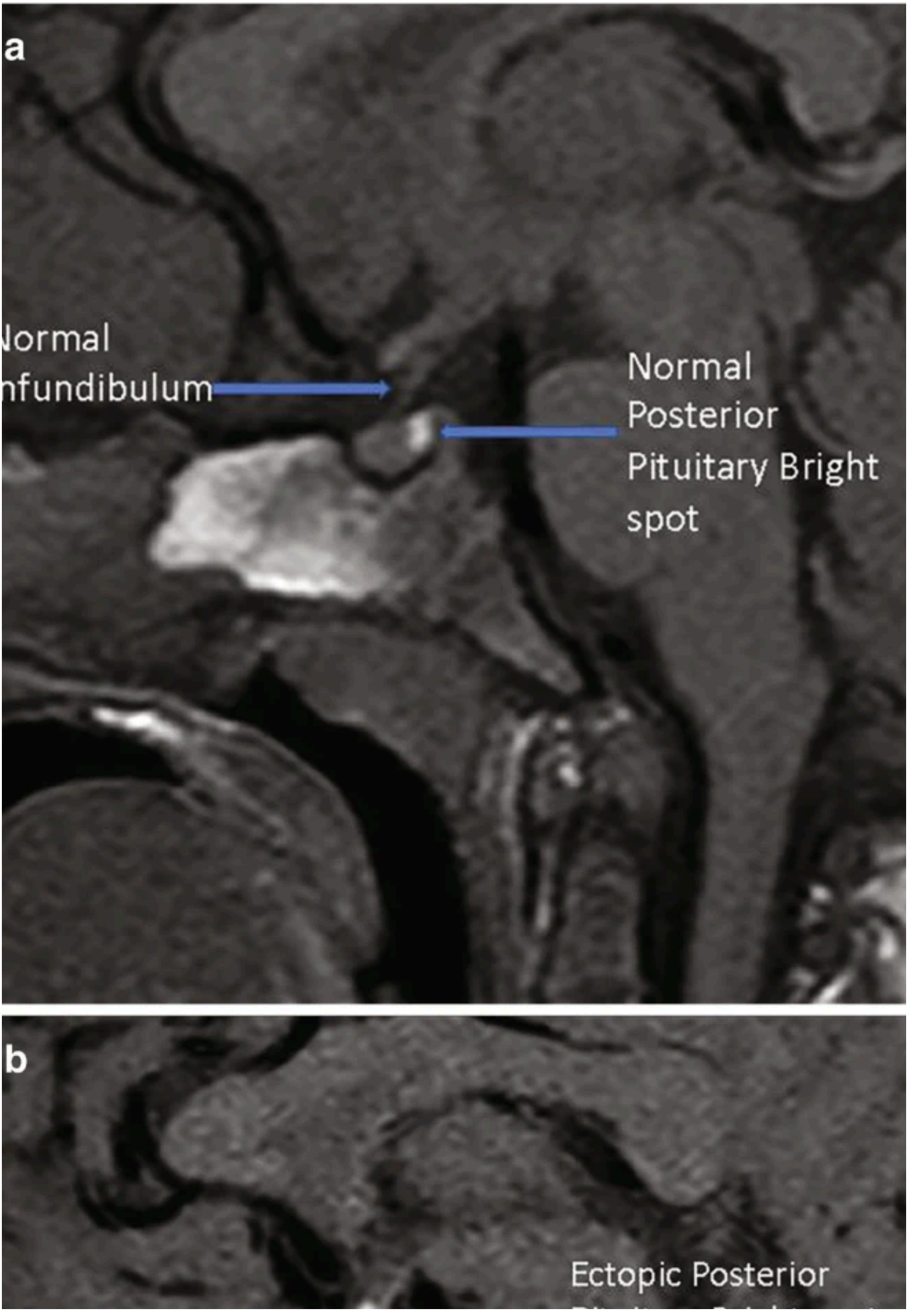
More than 70% of patients with ONH have hypothalamic dysfunction, typically manifested by hypopituitarism [1, 3]. Thus, all infants and toddlers with ONH need endocrinologic evaluation and all infants with panhypopituitarism need

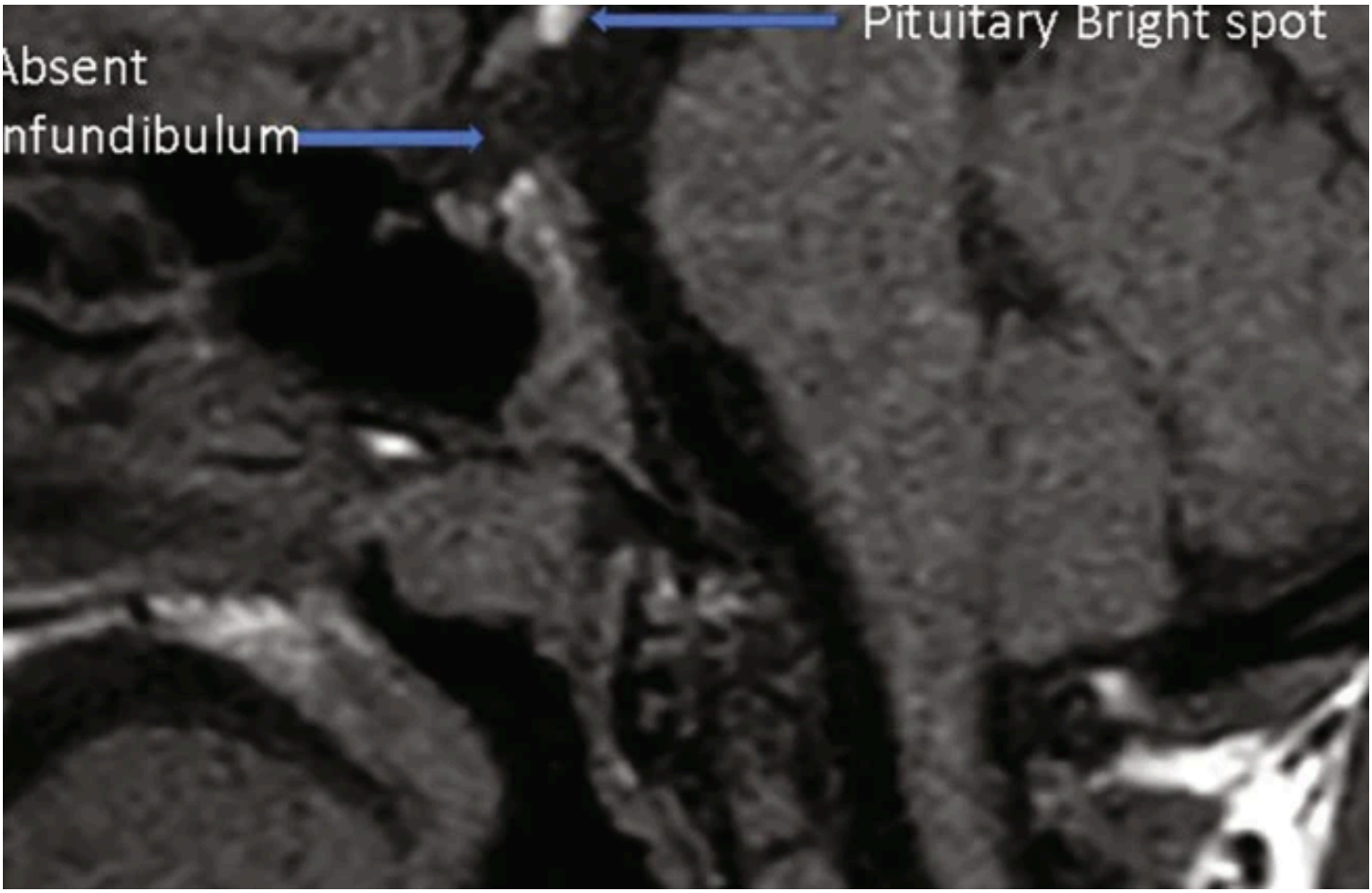
ophthalmologic examination. Hypothyroidism and adrenal insufficiency can evolve over time, so cortisol and free T4 levels need to be checked periodically in the first 5 years of life. Growth hormone stimulation tests should be performed in all cases with growth deceleration or if growth hormone surrogates, IGF1 and IGF-BP3, are low. Hypothalamic dysfunction may also be manifested by abnormal temperature regulation, sleep-wake cycle irregularities, obesity, and precocious or delayed puberty. Poor vision may contribute to sleep-wake irregularities as well.

Novel Insights

Multiple congenital CNS malformations occur with ONH including corpus callosum hypoplasia (54%), absent septum pellucidum (38%), pituitary malformations (10–30%), and hemispheric and gyral malformations (22%). MRI is recommended to evaluate the risk of developmental delay or seizures that are associated with hemispheric malformations and corpus callosum hypoplasia [1, 3]. Patients with pituitary malformations such as posterior pituitary ectopia, an absent bright spot, or an absent infundibulum are at increased risk of hypopituitarism with a positive predictive value of 82–100% (Fig. 1.4) [1, 4]. However, hypopituitarism may occur with normal pituitary findings on MRI. Therefore, all children with optic nerve hypoplasia require endocrinologic evaluation. Cases of unilateral ONH have half the risk for hypopituitarism and developmental delay compared to bilateral cases. MRI scans are not reliable for diagnosing ONH since atrophic, or even normal, optic nerves may appear small in young children [5].

Fig. 1.4


a
Normal
Infundibulum
Normal
Posterior
Pituitary Bright
spot
b
Ectopic Posterior



(**a**) Sagittal T1-weighted MRI of a patient with normal pituitary function shows a normal infundibulum and orthotopic posterior pituitary bright spot in the correct location in the sella. (**b**) Sagittal T1-weighted MRI of a patient with hypopituitarism shows an absent infundibulum and an ectopic posterior pituitary bright spot. Patients with pituitary malformations such as posterior pituitary ectopia, an absent bright spot, or an absent infundibulum are at increased risk of hypopituitarism [1, 4]. (Images provided courtesy of Paul H. Phillips, MD).

Full size image

Clinical Pearls

- All infants and young children with optic nerve hypoplasia require vigilance in monitoring pituitary function regardless of MRI findings or laterality.
- Optic nerve hypoplasia is an ophthalmoscopic diagnosis, not a neuroimaging diagnosis.
- Developmental delay and behavioral problems are common in patients with optic nerve hypoplasia regardless of endocrine function.

- Treatment with patching for superimposed amblyopia may improve visual function in children with ONH.

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