Denouement and Discussion

Lisch Nodules, Ectropion Uveae, and Optic Pathway Glioma (Juvenile Pilocytic Astrocytoma) Due to Neurofibromatosis Type 1

This patient had iris Lisch nodules which, combined with an optic pathway glioma, are diagnostic for neurofibromatosis type 1 (NF1). Ectropion uveae is a rare congenital anomaly of the iris and is associated with NF1 more commonly than other syndromes.[1]

Neurofibromatosis type 1 is inherited in an autosomal dominant pattern, though up to 50% of new diagnoses of NF1 arise from spontaneous mutations. The incidence is as high as 1 in 3000 births; all races and sexes are affected equally.[2] Diagnosis of NF1 is based on well-established criteria that include at least 2 of the following: 6 or more café-au-lait macules that are 0.5 cm or larger (>1.5 cm after puberty), 2 or more Lisch nodules (benign iris hamartomas), 2 or more neurofibromas of any type or 1 or more plexiform neurofibromas, axillary or inguinal freckling, optic pathway glioma, dysplasia or thinning of long bone cortex or dysplasia of the sphenoid bone, or a first-degree relative with NF1.

Lisch nodules are round, elevated, benign hamartomas of the iris that are most frequently located on the inferior portion of the iris.[3] Lisch nodules can be distinguished from normal patches of iris pigmentation and iris nevi owing to their round and raised appearance, which is best appreciated with binocular viewing through a slit-lamp microscope. Most (63%-92%) patients with NF1 are reported to have Lisch nodules.[3,4] They are not immediately present at birth and are found more commonly in postpubertal patients.[3] The number and size of Lisch nodules have no association with the frequency or severity of NF1-associated complications.

Ectropion uveae is a rare anomaly of the iris that causes the pupil to appear misshapen. The eversion of the pigmented posterior epithelium of the iris at the pupillary margin causes this appearance. Though some cases are acquired as a consequence of chronic inflammation, congenital forms are more typically associated with other conditions including Prader-Willi syndrome, facial hemihypertrophy, and, most commonly, NF1.[1,5] Congenital and acquired ectropion uveae are frequently associated with glaucoma and thus require close observation.

Low-grade gliomas (ie, juvenile pilocytic astrocytomas or fibrillary astrocytomas) involving the optic nerve, optic chiasm, optic tract, optic radiation, and hypothalamus are termed optic pathway gliomas and occur in up to 20% of children with NF1.[6,7] Up to half of the children with NF1-related optic pathway gliomas can experience vision loss as a result of their glioma.[6-8] Neurofibromatosis type 1–related optic pathway gliomas rarely cause new vision loss in children older than 8 years.[9] Given that not all children with NF1 will lose vision from their optic pathway gliomas, treatment with chemotherapy is typically deferred until vision loss occurs.

Expert consensus has provided ophthalmologic follow-up and treatment guidelines for children with NF1.[9] All children with NF1 should have a complete ophthalmologic examination by a pediatric ophthalmologist or neuro-ophthalmologist every year until 8 years of age. After 8 years of age, examinations can occur every 2 years. However, if the child is found to have an optic pathway glioma, examinations should occur every 6 months until 8 years of age, then yearly thereafter.[9] All examinations should include a quantitative assessment of visual acuity and color vision. When a reliable visual acuity measurement cannot be obtained in a child with NF1, most commonly owing to lack of cooperation, brain magnetic resonance imaging may be indicated.

Children observed to have Lisch nodules or ectropion uveae should be referred to a pediatric ophthalmologist or neuro-ophthalmologist, preferably with experience in caring for children with NF1. Additionally, children discovered to have a glioma of the optic pathway should be examined for the presence of NF1.

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