increased permeability of the intestinal epithelium. A preexisting permeability defect may trigger the expression of celiac sprue by allowing ingested gluten to cross the epithelial barrier and incite a pathologic immune reaction in genetically susceptible individuals.1

Thus, one possible explanation for an association between IJFT and celiac sprue is an underlying systemic permeability defect that is responsible for both increased gluten hypersensitivity in the gut and endothelial decompensation in the retina. As more patients with celiac sprue are identified, future investigations should disclose whether there is a true causal association between celiac sprue and IJFT.

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Figure 3. Optical coherence tomograms of the right (A) and left (B) eyes showing bilateral thinning of the fovea with mild macular thickening.

Infantile Orofacial Hemangioma With Ipsilateral Peripapillary Excavation in Girls: A Variant of the PHACE Syndrome

The PHACE syndrome is a neurocutaneous syndrome that includes the following primary features: posterior fossa malformations of the brain, large facial hemangiomas, arterial anomalies, cardiac anomalies and aortic coarctation, and eye abnormalities.1,2 It occurs almost exclusively in girls. Several recent reports have documented an association between orofacial hemangioma and excavated optic disc anomalies (morning glory disc anomaly and peripapillary staphyloma) in girls. Metry et al3 recently proposed that this association falls within the spectrum of PHACE syndrome. We document ipsilateral intracranial vascular abnormalities in 2 girls with juvenile orofacial hemangioma and excavated optic disc anomalies to provide further evidence that these patients fall within the spectrum of PHACE syndrome.

Report of Cases. Case 1. A 6-year-old girl was referred for evaluation of unilaterally decreased vision in the right eye. She was born full term, and her perinatal course was uneventful. At 2 weeks of age, she developed multiple hemangiomas involving the face, lip, parotid gland, and throat on the right side. At 1 month of age, these hemangiomas began to grow rapidly (Figure 1A). Magnetic resonance imaging confirmed massive hemangiomatous involvement of the right parotid gland and right side of the face. Results of a cardiology evaluation with echocardiography were normal. The hemangiomas continued to enlarge until the patient was 9 months of age. Treatment with oral steroids and multiple laser treatments to the gingival mucosa and the parotid gland produced regression of the tumor. At 1 year of age, she was noted to have an esotropia of the right eye.

Visual acuity was 20/160 OD and 20/20 OS. Both pupils reacted briskly to light, and there was a mild right afferent pupillary defect. Extraocular movements were full. Fixating near, she had 16 prism dipters of esotropia and fixed eccentrically with the right eye. Results of slitlamp examination were normal. Cycloplegic refractive error was +2.00 OD and +2.75 OS. Retinal examination disclosed a morning glory disc anomaly in the right eye with an elevated pigmented area of juxtapapillary scarring temporal to the disc (Figure 1B). Magnetic resonance angiography demonstrated marked tortuosity of the supraclinoi right internal carotid artery and narrowing of the proximal right middle cerebral artery (Figure 1C).

Case 2. A 6-week-old girl was evaluated for right-sided epiphora. Her perinatal course had been complicated by respiratory difficulties requiring temporary resuscitation. External examination disclosed a large capillary hemangioma on the right upper eyelid; tip of the nose; and right cheek, neck, and shoulder. In the ensuing weeks, the patient developed respiratory insufficiency requiring intubation. Results of a cardiology evaluation with echocardiography were normal. Magnetic resonance imaging disclosed several large hemangiomas in the chest, with extension to the upper aorta, displacement of the right upper lobe of the lung, and displacement of the trachea and larynx. The orofacial component of the hemangioma involved the right masseter muscle, parotid gland, orbit, and soft tissues of the tongue and lips on the right side.

Ophthalmologic examination of the patient at age 6 months showed esotropia and dense amblyopia of the right eye. A small con-
A junctival hemangioma was localized to the 3-o’clock position, the pupil was slightly eccentric, the iristroma was moderately atrophic, and a persistent pupillary membrane was noted. Retinal examination showed excavation of the peripapillary retina.

She was treated with oral steroids and interferon, and the hemangioma regressed during the next 2 years. At 7 years of age, orofacial remnants of the hemangioma were still evident (Figure 2A). Visual acuity was 20/80 OD and 20/20 OS. Cycloplegic refraction was –11.75 +2.00 ×95° OD and +3.00 +1.50 ×110° OS. Retinal examination disclosed a large peripapillary staphyloma in the right eye, which enclosed a normal-appearing optic disc (Figure 2B). The macula was situated at the border of the staphyloma. Examination of the left optic disc and retina disclosed no abnormalities. Magnetic resonance angiography disclosed a developmental vascular anomaly of the origin of the right ophthalmic artery (Figure 2C).

Comment. In 1998, Holmstrom and Taylor3 described an association of facial capillary hemangioma with morning glory disc anomaly in 3 girls. Kirath et al4 subsequently reported peripapillary staphyloma in a girl with a large ipsilateral orofacial hemangioma. Our 2 cases demonstrate that these findings may also be associated with ipsilateral cerebral vascular dysgenesis.

The relationship between large facial hemangiomas and cerebrovascular and facial arterial anomalies was recognized by Pascual-Castroviejo5 in 1978. Although cardiac and cerebellar malformations are usually present, it is now believed that PHACE syndrome represents a spectrum of anomalies (Table) that vary considerably from one case to another. In 70% of reported cases, only 1 extracutaneous manifestation of the syndrome has been present, with extracutaneous manifestations biased toward the specialty for which the article was written.2

The orofacial hemangiomas seen in PHACE syndrome are characterized large, segmental, and plaquelike.1,2 The pathogenesis of PHACE syndrome is unknown. The clinical manifestations of PHACE syndrome conform to a developmental field defect, which results from errors within morphoregulatory genes that determine a constellation of developmental anomalies in a spatially coordinated, temporally synchronous manner.2,6 Its confinement to girls raises the possibility of an X-linked lethal mutation.2 To our knowledge, no familial cases of PHACE syndrome have been reported.

Other clinical features of PHACE syndrome are in the Table.2 The most common central nervous system abnormalities have involved the posterior fossa, most notably the Dandy-Walker malformation, characterized by a hypoplastic or absent cerebellar vermis and a posterior fossa cyst continuous with the fourth ventricle.1,7 Cerebellar atrophy and arachnoid cyst with cerebellar hypoplasia have also been reported, as have frequent alterations in the intracranial carotid vasculature.1,8 Pascual-Castroviejo,7 who routinely performs carotid angiography in children with large facial hemangiomas, reports frequent alterations of
the intracranial vasculature, particularly the carotid artery. Burrows et al reported cerebral infarction secondary to progressive occlusive arterial disease in 4 infants who were previously healthy. In addition to a variety of structural cardiac abnormalities and aortic coarctation, ventral developmental defects such as sternal pits, supraumbilical raphe should be sought.\textsuperscript{1,2}

Metry et al\textsuperscript{2} considered the co-occurrence of morning glory disc anomaly and ipsilateral facial hemangioma as falling within the spectrum of PHACE syndrome. The ipsilateral neurovascular abnormalities in the territory of the carotid circulation in our 2 cases supports this contention. The association of a unilateral morning glory disc anomaly or peripapillary staphyloma with ipsilateral facial hemangioma mandates a careful search for associated cardiac, aortic, and cerebrovascular anomalies.

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*Systemic Anomalies Associated With PHACE Syndrome*

<table>
<thead>
<tr>
<th>Anomaly Type</th>
<th>Description</th>
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<tbody>
<tr>
<td>Large plaquelike orofacial hemangiomas, often with subglottic extension and respiratory compromise</td>
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<tr>
<td>Central nervous system malformations—Dandy-Walker malformation, hypoplasia or absence of the cerebellar vermis, posterior fossa cyst</td>
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<tr>
<td>Cerebrovascular anomalies—absence or hypoplasia of the carotid or vertebral arteries, aneurysmal dilatation and anomalous branches of the internal carotid artery, persistent primitive trigeminal artery, dilated cerebral vessels, aberrant subclavian artery</td>
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<tr>
<td>Aortic coarctation or other anomalies—aortic aneurysms, cervical aortic arch, absent right aortic arch, hypoplastic descending aorta, double aortic arch</td>
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<tr>
<td>Cardiac abnormalities—persistent ductus arteriosus, ventricular septal defects, atrial septal defects, pulmonary stenosis, tetralogy of Fallot</td>
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<tr>
<td>Ventral developmental defects—sternal clefts, sternal pits, supraumbilical raphe</td>
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<tr>
<td>Eye abnormalities—morning glory disc anomaly, microphthalmos, Horner syndrome, iris hypoplasia, iris vessel hypertrophy, optic atrophy, optic nerve hypoplasia, congenital cataract</td>
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\textsuperscript{*From Metry et al.\textsuperscript{2}}

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