Correspondence: Dr. F. Prada.
Servicio de Cardiología. Hospital Sant Joan de Déu.
Paseo Sant Joan de Déu, 2. 08950 Esplugues de Llobregat.
Barcelona. Spain
E-mail: fprada@hsjdbcn.org

Received August 18, 2009.
Accepted for publication December 1, 2009.
Patient 1

A female infant with heart failure, failure to thrive, irritability, and respiratory difficulty presented with a facial hemangioma in the left frontal region (Figure 1A). Echocardiographic study showed moderate mitral regurgitation and aortic coarctation with hypoplasia of the aortic arch. Angiography (Figure 2A) depicted the hypoplastic arch with an irregular, 3×4 mm aneurysm. The left subclavian artery was obliterated, but late opacification of the vessel was seen, resulting from retrograde flow from the vertebral artery. The right subclavian artery was aberrant and presented multiple wall irregularities (Figure 2B). At 6 weeks of life, the patient underwent surgical treatment consisting of a left lateral thoracotomy, extended resection, and an end-to-end anastomosis. Microscopic study of the tubular section of the aorta (Figure 3) showed considerable disruption of the arterial wall architecture, which was thickened due to marked fibroblastic proliferation with collagen deposit. There was a pronounced reduction and disorganization of the elastic membranes, with deposits of Alcian blue-positive mucoid material. At 6 months of life, the patient experienced recoarctation and was treated with aortic angioplasty, with good results. At age 1 year, she had no cardiovascular symptoms, but was affected with bilateral amaurosis.

Patient 2

A male infant with aortic coarctation and a right-sided aortic arch underwent surgery at the age of 6 months, consisting of interposition of an 8-mm-diameter Gore-Tex tube graft in the coarcted segment. He presented a hemangioma in the right frontomalar region that completely remitted after the age of 2 years. At age 10 years, while the patient was asymptomatic, he presented clinical signs of aortic recoarctation. Magnetic resonance imaging with gadolinium enhancement showed absence of the right carotid artery and a prominent left carotid artery (Figure 2C). Angiography depicted the right aortic arch (Figure 2D), the left carotid artery emerging before the coarcted segment, practically

---

**TABLE 1. PHACE Syndrome. Clinical Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.5 months</td>
<td>6 months</td>
<td>3.5 months</td>
<td>12 days</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
<td>Female</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>Left frontal</td>
<td>Right frontomalar</td>
<td>Right cervical</td>
<td>Left orbit and nasal ala</td>
</tr>
<tr>
<td>Aortic arch</td>
<td>Left</td>
<td>Right</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>Aortic arch hypoplasia</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Neurologic involvement</td>
<td>Amaurosis</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Arterial anomalies</td>
<td>Aberrant RSA, occluded LSA</td>
<td>Occluded RCCA, aberrant LSA</td>
<td>Stenotic LSA</td>
<td>Aberrant RSA</td>
</tr>
<tr>
<td>Type of surgery</td>
<td>ER+EEA</td>
<td>Graft interposition</td>
<td>Pericardial patch</td>
<td>ER+EEA</td>
</tr>
<tr>
<td>Recoarctation</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

ER+EEA indicates extended resection and end-to-end anastomosis; LSA, left subclavian artery; RCCA, right common carotid artery; RSA, right subclavian artery.

aAt the time of aortic repair.

bArch is hypoplastic when the isthmus-to-ascending aorta ratio is <0.5.
orbit, nose, and lips (Figure 1C). Surgical repair of the coarctation was undertaken 2 weeks after birth, and an aberrant right subclavian artery was found during the procedure. Aortic recoarctation occurred 3 months later and was treated with angioplasty.

**DISCUSSION**

The etiology of PHACE syndrome remains uncertain. The diagnosis is established when the characteristic hemangioma is accompanied by at least 1 concomitant anomaly.6 In our series of 4 patients, there were 3 girls; a larger series has
reported that 83% of affected patients are female.4 It has been noted that there is no difference between sexes in the severity of the condition.2

Hemangiomas can go unnoticed at birth. In the first months of life, they may present a proliferative phase of rapid growth, and later, a phase of involution that can last several years.7 Hemangiomas located in the cervicofacial region and the aortic arch are found on the same side. This isolated configuration is very significant8 and was observed in all our patients.

Patient 3 presented respiratory stridor. In patients with this symptom and a right-sided aortic arch, vascular ring should be ruled out. In some PHACE patients, stridor is caused by a hemangioma located in the subglottic region.5,9 Endoscopic study in our patient revealed signs of tracheomalacia.

Although the association of coarctation and right-sided aortic arch is uncommon,8 it was present in 2 of our 4 patients. Bijulal et al10 reported a case of right-sided aortic arch, coarctation, and tetralogy of Fallot. Intracardiac anomalies are not very common,8,10 although ventricular and atrial septal defects, tetralogy of Fallot, and tricuspid atresia have been observed. Two of our patients had mitral regurgitation, possibly resulting from left ventricular dysfunction due to the coarctation. In both cases, mitral regurgitation remitted following aortic arch surgery. Of note, none of our patients had bicuspid aortic valve, an abnormality commonly associated with aortic coarctation. Around 40% of children with PHACE syndrome have aortic arch anomalies, including coarctation and aortic interruption. Histopathologic study of the diseased aorta shows abnormalities of the intimal and medial layers, likely due to inflammation or dysplasia.8 In the macroscopic study, this is seen as arterial wall irregularities on arteriography (Figure 2B). It may also explain the surgical finding described as “aortitis” in 2 of our patients (Patients 1 and 4), which is characterized by unusual aortic wall thickening.

The vascular damage occurring in this condition can also explain the multiple lesions we observed in the supra-aortic arteries, a finding often reported in the literature. Arterial lesions have also been reported in the intracranial territory.11 This arterial disease places children at a high risk of presenting cerebral thrombotic conditions at an early age12 or later,13 a fact that may be an indication for administration of antiplatelet agents.

With regard to the diagnosis of PHACE, in addition to echocardiography and careful clinical examination of the arterial pulses, we have found that these children need additional tests, such as angiography, magnetic resonance imaging, and multislice computed tomography to adequately assess the aortic arch. Surgical treatment and follow-up of coarctation in a right-sided aortic arch is technically complex. However, the 2 patients with a left-sided aortic arch presented recoarctation that was resolved with angioplasty.

REFERENCES