Objective: To establish whether the prognosis of bilateral facial capillary malformation (BFCM) is worse compared with that of unilateral facial port-wine stain.

Design: Retrospective study.

Setting: Paediatric Dermatology Department, Great Ormond Street Hospital for Children NHS Trust, a tertiary referral center for vascular anomalies.

Patients: A cohort of 350 children who presented with facial CM was seen between January 1, 1994, and June 30, 2004. Twenty-seven children with BFCM were identified. A control group of 27 children with unilateral CM was randomly selected from the total cohort.

Main Outcome Measures: Demographic, clinical, and radiographic characteristics were recorded and compared between the 2 groups: age at presentation, sex, distribution, extension, extrafacial lesions, glaucoma, ipsilateral leptomeningeal angiomatosis, and epilepsy. The recorded information was collected from the database of the Paediatric Dermatology Department, the hospital records, and the patients’ photographs.

Results: Compared with the 27 children with unilateral facial CM, the 27 with BFCM showed a higher frequency of association with extrafacial lesions (17 [63%] vs 6 [22%]), glaucoma (21 [78%] vs 2 [7%]), and ipsilateral leptomeningeal angiomatosis (14 [52%] vs 2 [7%]). All patients who had BFCM with bilateral and complete involvement of the ophthalmic area had ipsilateral leptomeningeal angiomatosis.

Conclusion: Patients with BFCM must be considered as a group with a worse prognosis compared with patients with unilateral facial CM.

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Capillary Malformation (CM), also called port-wine stain, is a common vascular anomaly that is present at birth and persists throughout life. Histologically, it is characterized by an increase in the number and diameter of capillaries in the dermis. The cause of CM is thought to be a diminished neural influence on vascular tone. The face and the neck are the most frequently affected sites for CM, but lesions may occur at any site. The distribution of facial CM is traditionally divided into the ophthalmic (V1), maxillary, and mandibular areas (Figure 1). Facial CM can occur either as an isolated cutaneous birthmark or as an association with eye (glaucoma) or brain ipsilateral leptomeningeal angiomatosis (LA) abnormalities, known as Sturge-Weber syndrome. Facial CM is most often, but not invariably, unilateral, with a midline demarcation.

Midline or bilateral lesions do occur, but are much less common. To our knowledge, there has been no specific study on bilateral facial CM (BFCM), and the exact frequency and prognosis of this particular form have not been well documented. This study determines the features of BFCM, aiming to establish whether this presentation has a different prognosis compared with that of unilateral facial CM (UFCM).

Methods

Patients

The medical records from children who were seen in the Paediatric Dermatology Department (a tertiary center for vascular anomalies), Great Ormond Street Hospital for Children NHS Trust, between January 1, 1994, and June 30, 2004, and who presented with facial CM were reviewed for this retrospective study. Individual midline CM was not included in this series.
PROCEDURES

The recorded information was collected from the database of the Paediatric Dermatology Department, hospital records, and patients’ photographs. The hospital ethical committee approved the study. From a cohort of 350 patients with facial CM, we selected patients with BFCM. Bilateral facial CM was defined as CM involving symmetrically or asymmetrically, entirely or partly, both sides of the face. We randomly selected, with a 1:1 ratio, a sample of patients with UFCM from the total cohort of those with facial CM. Unilateral facial CM was defined as CM involving entirely or partly one side of the face. Each lesion was classified according to the distribution of the trigeminal nerve. With regard to the V1 area, complete involvement was defined as an area starting from the lower eyelid, up to the top of the forehead, and into the scalp. In contrast, incomplete involvement was defined as an area starting from the lower eyelid but stopping below the top of the forehead, usually just above the eyebrows. The extension of CM was evaluated by counting the number of branches of the trigeminal nerve involved. For all CMs within the V1 and/or maxillary area, eye and neurological examinations and imaging of the brain (magnetic resonance imaging) were performed. Different characteristics were recorded: age at presentation, sex, distribution, extension, extrafacial lesions, glaucoma, LA, and epilepsy. Comparison between the bilateral and unilateral groups was performed using a t test for unpaired data for age at presentation or a χ² by Mantel-Haenszel test (or a Fisher exact test in case of a few patients) for the rest of the characteristics. Statistical significance was considered at P<.05. The relative risk (RR) was determined if applicable and calculated with a 95% confidence interval (CI). Statistical analysis was performed using computer software (Epi Info 6.0; Centers for Disease Control and Prevention, Atlanta, Ga).

RESULTS

From the cohort of 350 patients with facial CM, 27 (7.7%) had BFCM. Twenty-seven patients with UFCM were randomly selected. The group of 27 selected patients with UFCM and the total group of patients with UFCM were well matched on age, sex, and affected side.

CHARACTERISTICS OF THE PATIENTS WITH BFCM VS THE PATIENTS WITH UFCM

The age at presentation to the hospital was a mean±SD of 43.5±52.2 months (range, 0-146 months) for the patients with BFCM, compared with 37.5±48.8 months (range, 1-216 months) for the patients with UFCM. The difference between both groups was not statistically significant (P=0.26) (Table 1). Of the 27 patients with BFCM, 19 (70%) were girls and 8 (30%) were boys (ratio, 2.4:1). In the control group, 15 patients (56%) were girls and 12 (44%) were boys (ratio, 1.2:1). The difference in sex distribution between both groups was not statistically significant (P=0.66) (Table 1). Of the 27 patients with BFCM, 17 had extrafacial lesions, compared with 6 patients in the control group (RR, 2.83; 95% CI, 1.32-6.07) (Table 1). Figure 2 shows the extension and distribution of the observed skin lesions in the group with BFCM. The extension and distribution of the CM was compared between the 2 groups (those with BFCM vs those with UFCM) (Table 1). Of the 27 patients with BFCM, 1 presented with involvement of only 1 branch of the trigeminal nerve, compared with 10 patients in the control group (RR, 0.10; 95% CI, 0.01-0.73). Two branches were affected in 7 patients with BFCM compared with 17 patients in the control group (RR, 0.41; 95% CI, 0.20-0.83). Most patients with BFCM had involvement of the

Table 1. Characteristics of Capillary Malformations

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients With BFCM (n = 27)</th>
<th>Patients With UFCM (n = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>19 (70)</td>
<td>15 (56)</td>
</tr>
<tr>
<td>Male</td>
<td>8 (30)</td>
<td>12 (44)</td>
</tr>
<tr>
<td>Extrafacial lesions†</td>
<td>17 (63)</td>
<td>6 (22)</td>
</tr>
<tr>
<td>Extension and distribution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Branch†</td>
<td>1 (4)</td>
<td>10 (37)</td>
</tr>
<tr>
<td>V1 alone</td>
<td>0</td>
<td>3 (11)</td>
</tr>
<tr>
<td>V2 alone</td>
<td>0</td>
<td>4 (15)</td>
</tr>
<tr>
<td>V3 alone</td>
<td>1 (4)</td>
<td>3 (11)</td>
</tr>
<tr>
<td>2 Branches†</td>
<td>7 (26)</td>
<td>17 (63)</td>
</tr>
<tr>
<td>V1 and V2</td>
<td>6 (22)</td>
<td>17 (63)</td>
</tr>
<tr>
<td>V1 and V3</td>
<td>1 (4)</td>
<td>0</td>
</tr>
<tr>
<td>3 Branches†</td>
<td>19 (70)</td>
<td>0</td>
</tr>
<tr>
<td>Leptomeningeal angiomatosis†</td>
<td>14 (52)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Glaucoma†</td>
<td>21 (78)</td>
<td>2 (7)</td>
</tr>
</tbody>
</table>

Abbreviations: BFCM, bilateral facial capillary malformation; UFCM, unilateral facial capillary malformation; V1, ophthalmic branch of the trigeminal nerve; V2, maxillary branch of the trigeminal nerve; V3, mandibular branch of the trigeminal nerve.

*Data are given as number (percentage) of each group.
†The difference between both groups is statistically significant (P<.05).
3 branches of the trigeminal nerve. In contrast, no patient in the control group presented with involvement of all 3 branches ($P < .001$, $\chi^2 = 32.33$).

**RISK OF BRAIN OR EYE COMPLICATIONS IN THOSE WITH BFCM VS THOSE WITH UFCM**

Of the 27 patients with BFCM, LA was present in 14, compared with 2 patients in the control group (RR, 7.00; 95% CI, 1.76-27.89) (Table 1). All patients with LA had epilepsy early in life. Also, of the 27 patients with BFCM, glaucoma was present in 21, compared with 2 patients in the control group (RR, 10.50; 95% CI, 2.73-40.45) (Table 1). Leptomeningeal angiomatosis was present on both hemispheres in 6 (22%) of the 27 patients with BFCM. Glaucoma was present in both eyes in 10 (37%) of the 27 patients with BFCM.

**HIGHER-RISK GROUP FOR LA IN PATIENTS WITH CM**

All patients with LA in the group with UFCM ($n = 2$) and the group with BFCM ($n = 14$) had CM with V1 involvement. In patients with V1 involvement, the frequency of LA in the group with BFCM was 14 (54%) of 26, compared with 2 (10%) of 20 in the UFCM group (RR, 5.38; 95% CI, 1.38-21.02; $P = .02$). The risk for LA stratified by complete or incomplete involvement of V1 is reported in Table 2. In the group with UFCM, the risk for LA was statistically higher in those with complete involvement of V1 vs those with incomplete involvement. In the group with BFCM, the risk for LA was 100% in those with complete and bilateral involvement of V1, vs 25% in those with incomplete and bilateral involvement of V1 (RR, 3.00; 95% CI, 1.35-6.68). All patients with complete facial involvement ($n = 8$) had LA. In addition, patients with BFCM who had complete and bilateral involvement of V1 had a higher risk of experiencing LA on both hemispheres compared with patients with incomplete and bilateral involvement of V1 (Table 2).

### Table 2. Risk of Leptomeningeal Angiomatosis in Patients With Capillary Malformation Involving Completely or Incompletely the V1 Area

<table>
<thead>
<tr>
<th>Patients</th>
<th>Leptomeningeal Angiomatosis On One Hemisphere</th>
<th>Leptomeningeal Angiomatosis On Both Hemispheres</th>
</tr>
</thead>
<tbody>
<tr>
<td>Those with UFCM</td>
<td>Complete V1 involvement ($n = 3$) 2 (67)* 0</td>
<td>0</td>
</tr>
<tr>
<td>Incomplete V1 involvement ($n = 17$) 0 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Those with BFCM</td>
<td>Bilateral complete V1 involvement ($n = 9$) 9 (100)* 6 (67)*</td>
<td></td>
</tr>
<tr>
<td>Bilateral incomplete V1 involvement ($n = 12$) 3 (25) 0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: See Table 1.

*The difference between the group with complete vs incomplete V1 involvement is statistically significant ($P < .05$).
HIGHER-RISK GROUP FOR GLAUCOMA IN PATIENTS WITH BFCM

In our series of patients with CM, the presence of eyelid involvement was associated with a higher risk of glaucoma. All patients with glaucoma, in the group with UFCM (n = 2) and in the group with BFCM (n = 21), had superior and inferior ipsilateral eyelid involvement. In patients with inferior and superior eyelid involvement, the risk for glaucoma was 56% (14/25) in the group with BFCM, vs 17% (2/12) in the group with UFCM (RR, 3.36; 95% CI, 0.90-12.48; P = .06). The complete or incomplete involvement of superior and inferior eyelids did not statistically influence the risk for glaucoma in the group with BFCM (9 of 10 vs 6 of 9 patients; P = .21). Furthermore, the risk of glaucoma was not higher (8 of 9 patients) in cases of additional involvement of the complete forehead.

COMMENT

To our knowledge, only 2 studies have previously commented on the specific characteristics of BFCM within facial CM and on the risk of associated eye or brain anomalies. The population of patients referred to our hospital represents a highly selected group. Therefore, the relative proportion of patients with BFCM in our series may not be representative of what is seen in the general population of patients with CM. In the series reported by Bioxeda and Tallman and colleagues, patients with BFCM represented 14% and 11% of the total population of those with CM, respectively. The percentage of extrafacial lesions in our series was significantly higher in the group with BFCM (63%), compared with the control group (22%). Our percentages were similar to those observed by Bioxeda et al (53% vs 10%, respectively). Bilateral facial CMs in our series involved 3 branches of the trigeminal nerve in more than 70% of patients. To a lesser degree, Tallman et al found that BFCMs were usually extensive, involving the 3 branches of the trigeminal nerve in 48.3% of patients.

This large series allows the precise description of the pattern of BFCMs. We found that the distribution of the lesions was variable and did not follow the 3 sensory trigeminal area demarcations. We noted in 74% (20/27) of the BFCMs the presence of a spared area of skin in a midline distribution (Figure 2 and Figure 3). This was often seen as a V-shaped area in the midline of the forehead, which could extend down to the nose and the upper lip. This pattern does not fit properly to any of the developmental units of the face (nerve, vessels, and embryologic facial prominences). Nevertheless, the presence of a midline-spared area suggests that BFCM is an addition of 2 unilateral lesions rather than only 1 bilateral lesion. This hypothesis is further supported by the fact that 67% (18/27) of patients presented with non-symmetrical lesions. Finally, involvement of the chin was always bilateral.

An important aspect of our study was to establish the fact that BFCM carries a higher risk of eye or brain anomalies compared with UFCM. Regarding the brain, we found in our series that BFCM carried a higher risk for LA, compared with UFCM: 52% vs 7%. Our results were comparable to those found in the literature, but we found higher percentages of complications. Tallman et al showed that 24% of patients with BFCM had LA with seizures, compared with 6% of those with unilateral lesions. In the same manner, Bioxeda et al reported that 26% of the patients with BFCM had LA with seizures, compared with 14% of those with unilateral lesions. The fact that BFCM is associated with a higher percentage of LA may account for the higher percentage of BFCMs observed in series of patients with Sturge-Weber syndrome: between 25% and 41% according to Fritsch et al, Pascual-Castroviejo et al, and Uram and Zubillaga. In our series, the frequency of brain anomalies on both hemispheres was 22%, which is similar to the frequency of 23% reported by Pascual-Castroviejo et al in 40 patients with Sturge-Weber syndrome who had BFCM. To our knowledge, no relationship has been established in the literature between unilateral or bilateral location of the CM and clinical neurological impairment. Conversely, a direct relationship has been established be-
within CM, categories of children with a higher risk for worse.

Another important aspect of our study was to define, within CM, categories of children with a higher risk for brain complications. According to the literature on UFCM, patients with V1 involvement have a high risk for LA, the highest risk being observed in patients with complete V1 involvement. In our series of patients with BFCM, we found that the risk for LA was higher in cases of complete, compared with incomplete, bilateral involvement of V1 (100% vs 33%). Notably, all patients with complete facial involvement had associated LA. Finally, we observed that the risk for brain complications on both hemispheres was higher in cases of complete, compared with incomplete, bilateral involvement of V1 (67% vs 0%).

Regarding ocular complications, we demonstrated in our series that the risk for glaucoma was higher in those with BFCM compared with UFCM (78% vs 7%). Tallman and Bioxeda and colleagues found a higher frequency of glaucoma in those with BFCM vs UFCM: 24% vs 6% and 47.3% vs 17%, respectively. The risk of glaucoma in those with UFCM is dependent on the involvement of the eyelids and is higher if inferior and superior eyelids are covered by CM. Our results were in accordance with the literature, because all patients with glaucoma had CM on superior and inferior eyelids. In contrast to brain complications, the risk for glaucoma was not dependent on complete or incomplete involvement of superior and inferior eyelids. To our knowledge, the frequency of bilateral glaucoma has not been previously investigated. In our series of BFCMs, this frequency was 37%.

In conclusion, this series shows that BFCM is often present with a nonsymmetrical extensive distribution, with a midline-spared area of skin. Bilateral facial CM is often associated with extrafacial lesions and eye and brain complications. The reason why is unknown, but this could be related to the fact that BFCM is more extensive. The bilaterality could also be relevant to the occurrence of extrafacial lesions. When examining a child with CM, clinicians must be aware of the fact that patients with BFCM have a higher risk of ocular or brain anomalies, which can be bilateral. To evaluate the risk for glaucoma, the involvement of superior and inferior eyelids must be noted because it is associated with a high risk of glaucoma. To properly evaluate the risk for LA, clinicians must determine whether V1 is involved and if this involvement is bilateral and complete; bilateral and complete involvement of V1 is associated with the highest risk of LA (100% in our series), often affecting both sides of the brain. Recognizing these groups of patients at high risk is crucial in relation to management and counseling of parents. Early referral to a specialist pediatric neurological center is essential for brain magnetic resonance imaging and eye examination with pressure measurements.

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