Objective: To compare airway infantile hemangiomas (IHs) and venous malformations (VMs) clinically, radiographically, endoscopically, and histologically.

Design: Retrospective cohort study.

Setting: Tertiary care pediatric hospital.

Patients: The study included patients seen in the Vascular Anomaly Clinic, Seattle Children’s Hospital, Seattle, Washington, between 2001 and 2008.

Methods: All patients with airway vascular anomalies were identified by searching the Vascular Anomaly Quality Improvement Database and hospital discharge data. The data, which were analyzed with descriptive statistics and the Fisher exact test, included presenting age, sex, presenting signs, lesion site, and radiographic, endoscopic, and histologic findings.

Results: Seventeen patients with airway lesions were identified, 6 with VMs and 11 with IHs. Patients with VMs presented at a mean (SD) age of 11.3 (13.7) months (age range, 3-39 months), while those with IHs presented at 3 (1.8) months of age (age range, 1-6 months) (P = .03). The patients with IHs were predominantly female (9 of 11 [81%]), while no sex difference was noted among the patients with VMs (3 of 6 [50%]). All patients with IHs presented with stridor and cutaneous lesions, whereas patients with VMs more often presented with hemoptysis or dysphagia (P = .001). Computed tomographic angiograms demonstrated enhancing endolaryngeal lesions in all IHs, while VMs enhanced poorly. Endoscopically, IHs were transglottic, while VMs were postcricoid or epiglottic (P < .001). Histologically, immunostained lesions showed submucosal lobules of capillaries lined by GLUT-1 (glucose transporter isoform 1)–positive endothelium in IHs, whereas VMs consisted of loosely organized venous channels that lacked GLUT-1 staining.

Conclusion: Patients with airway IHs and VMs differ in presenting age and signs, sex, airway lesion location, enhancement on computed tomographic angiograms, and histologic appearance.


VASCULAR ANOMALIES IN the pediatric airway are uncommon, yet correct diagnosis is crucial to effective management. Different types of vascular anomalies have unique clinical, histologic, and radiologic characteristics, which can be used to obtain the proper diagnosis and to determine appropriate treatments. Vascular anomalies are usually classified as tumors or malformations based on clinical and histologic characteristics. Vascular tumors can demonstrate rapid growth, while vascular malformations do not. The distinction between vascular tumors and malformations is further substantiated by the unique immunohistochemical staining that is present in these lesions. Despite these features, distinguishing airway vascular tumors from malformations can be challenging.

Infantile hemangiomas (IHs) are the most common type of vascular tumor as well as the most common airway vascular lesion. Airway IHs, which were first described in 1864, account for approximately 1.5% of all congenital laryngeal anomalies. Although rare, airway IHs are life-threatening owing to airway obstruction during rapid growth. Venous malformations (VMs) also occur in the airway but are less common than airway IHs. The management and treatment of airway VMs differ from those of airway IHs. The failure of intralesional or systemic corticosteroid treatment for a presumed airway IH should raise suspicion for a possible airway VM. Correct diagnosis of the

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lesion is essential for appropriate medical management and treatment.

Herein, we report our experience using clinical, computed tomographic angiographic (CTA), endoscopic, and histologic findings in pediatric patients with airway vascular anomalies to help distinguish airway IHs from airway VMs. Although the diagnosis of an airway vascular anomaly can usually be made from clinical presentation and endoscopic findings,8,9 the addition of CTA enables high spatial resolution and cross-sectional imaging of enhancing vascular anomalies.9 Along with endoscopy, CTA can be used to further describe these unusual lesions.7 The utility of clinical examination, CTA, endoscopy, and histologic analysis will be examined to provide a guide for the diagnosis and treatment of these challenging lesions.

**METHODS**

Patients with airway vascular anomalies seen in the Vascular Anomalies Clinic, Seattle Children’s Hospital, Seattle, Washington, between 2001 and 2008 were identified from the Vascular Anomaly Quality Improvement Database and Seattle Children’s Hospital discharge data after approval from the institutional review board (No. 12699). The medical records of these patients were evaluated retrospectively by pediatric otolaryngologists (S.C.M., A.F.I., and J.A.P.). Vascular anomalies were classified as either airway IHs or airway VMs based on clinical presentation and endoscopic appearance. The clinical characteristics of airway IHs included rapid onset of respiratory distress in children younger than 1 year. The clinical characteristics, coupled with endoscopic findings of a red vascular lesion in the upper aerodigestive tract, led to the vascular lesion being classified as an airway IH. The clinical characteristics of airway VMs included chronic feeding symptoms without airway compromise or intermittent airway compromise. These symptoms, coupled with a bluish or compressible vascular mass in the upper aerodigestive tract, led to the lesion being classified as an airway VM. Lesions that were predominantly lymphatic malformations and involved the airway were excluded. The following data were collected: patient sex, patient age at presentation and diagnosis, presenting symptoms (eg, stridor, cyanosis, reflux, failure to thrive, dysphagia, hemoptysis), type of treatment (eg, stridor, cyanosis, reflux, failure to thrive, dysphagia, hemoptysis), type of endoscopic evaluation, CTA appearance, endoscopic findings, histologic characteristics, and clinical outcome. Data were analyzed using descriptive statistics (Stata 8.0; Statacorp, College Station, Texas) and the Fisher exact test, as appropriate.

**RESULTS**

Seventeen patients, 6 with airway VMs and 11 with airway IHs, were identified. The age range at presentation for all patients was 2 to 36 months, with a mean of 5.9 months. The demographic data, which showed a younger age at presentation for airway IHs than for airway VMs, are presented in Table 1. The specific characteristics of the lesions are presented in Table 2. Note that all 11 patients with airway IHs presented with stridor, and 10

### Table 1. Study Demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Venous Malformation</th>
<th>Infantile Hemangioma</th>
<th>P Value (Fisher Exact Test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at presentation (range), mo</td>
<td>11.3 (4-36)</td>
<td>3 (1-10)</td>
<td>.03</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3</td>
<td>2</td>
<td>.28</td>
</tr>
<tr>
<td>Female</td>
<td>3</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>11</td>
<td>.34</td>
</tr>
</tbody>
</table>

*a* There were 3 patients with a syndrome diagnosis in each group.

### Table 2. Lesion Presentation, Location, Cutaneous Findings, and Radiographic Findings

<table>
<thead>
<tr>
<th>Variable</th>
<th>Venous Malformation</th>
<th>Infantile Hemangioma</th>
<th>P Value (Fisher Exact Test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presenting sign</td>
<td>Stridor, 1/6 (11)</td>
<td>11/11 (100)</td>
<td>.001</td>
</tr>
<tr>
<td>Dysphagia, 3/6 (50)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoptysis, 1/6 (16)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Snoring, 1/6 (16)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endoscopic location</td>
<td>Postcricoid, 6/6 (83)</td>
<td>Glottic/subglottic, 11/11 (100)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Epiglottic, 1/6 (17)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cutaneous lesion</td>
<td>0/6 (0)</td>
<td>10/11 (91)</td>
<td>.001</td>
</tr>
<tr>
<td>Radiographic Findings</td>
<td>Nonenhancing mass, 0/3 (0)</td>
<td>Enhancing mass, 5/6 (83)</td>
<td>.05</td>
</tr>
<tr>
<td>Computed tomographic angiography</td>
<td>Carbon dioxide laser excision, 2/6 (30)</td>
<td>Carbon dioxide laser excision, 4/11 (36)</td>
<td>.05</td>
</tr>
<tr>
<td>Electrocautery, 1/6 (11)</td>
<td>Steroid injection, 5/11 (45)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observation, 2/6 (30)</td>
<td>Combined steroid injection and laser excision, 3/11 (27)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
of them (91%) had associated cutaneous IHs. The airway IHs were located in the glottis or subglottis. In contrast, patients with airway VMs more commonly presented with subjective complaints of dysphagia and hemoptysis. Airway VMs did not have associated cutaneous vascular lesions and were located in the postcricoid and epiglottic regions. Computed tomographic angiograms of all airway IHs demonstrated enhancing, endolaryngeal, vascular lesions, while CTAs of airway VMs showed poorly enhancing masses in the postcricoid or epiglottic region (Table 2 and Figures 1, 2, and 3). Endoscopy revealed that airway IHs were transglottic and airway VMs were postcricoid or on the epiglottis (P < .001) (Figures 1-3). Tissue was analyzed histologically in 4 of 11 airway IHs and in 3 of 6 airway VMs. Airway IHs consisted of lobules of GLUT-1 (glucose transporter isoform 1)–positive capillaries in the submucosa, while airway VMs were composed of irregular venous channels dissecting through soft tissue (Figure 4).

The management techniques that were used in all 17 patients with airway vascular anomalies were successful in preserving a patent functional airway or producing symptom relief. The treatments used in this series are summarized in Table 2. Differences between surgical techniques used for airway VMs and IHs did not reach statistical significance (P = .05). Fifty percent of airway VMs did not require excision. Indications for the 3 airway VM treatments were hemoptysis, dysphagia, and
unclear clinical diagnosis. All of these lesions were treated or diagnosed with a single operation. The lesion causing hemoptysis and 1 postcricoid lesion posed diagnostic dilemmas (Figure 5). All airway IHs were treated because of airway compromise. Corticosteroid injection of the airway IHs, along with a postinjection corticosteroid taper, was used from 1 to 3 times per patient (mean injections per patient, 1.6). The mean number of laser excisions for airway IHs was 1.25 (range, 1-2). Patients who had a combination of corticosteroid injections and laser excision had 2 to 3 steroid injections before laser excision, with a mean of 1.6 laser excisions (range, 1-2). All 11 airway IH lesions regressed during the study period, whereas the untreated airway VMs did not.

**COMMENT**

We have demonstrated that airway IHs have readily identifiable clinical, endoscopic, CTA, and histologic findings that can be used to distinguish them from airway VMs. Airway IHs present at a younger age, always with stridor and often with cutaneous lesions. Airway VMs can present at a much older age and have a variety of symptoms besides stridor. Endoscopically, airway IHs are visualized in the subglottis or glottis, whereas VMs are most

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**Figure 4.** Histologic features of an airway infantile hemangioma (A and C) and a venous malformation (B and D). A, Infantile hemangioma demonstrating a submucosal collection of proliferating capillaries (hematoxylin-eosin, original magnification ×100). B, Venous malformation demonstrating irregular venous channels permeating soft tissue (hematoxylin-eosin, original magnification ×40). C, Immunohistochemical staining for GLUT-1 (glucose transporter isoform 1) is positive in the endothelium of an infantile hemangioma (diaminobenzadine, original magnification ×100). D, Immunohistochemical staining is negative for GLUT-1 in the endothelium of a venous malformation; erythrocytes and perineurium (upper left) serve as a positive internal control (diaminobenzadine, original magnification ×40).

**Figure 5.** Histologically proved epiglottic venous malformation causing hemoptysis and posing a diagnostic dilemma.
often found in the postcricoid region. Bright enhancement on CTA imaging reveals the arterial nature of airway IHs. Airway VMs do not readily enhance on CTA, demonstrating venous characteristics. Histologically, airway IH endothelium stains positively for GLUT-1 and is much more cellular than VM endothelium, which is GLUT-1 negative.

Initial clinical evaluation provides clues to the diagnosis of an airway vascular anomaly. Airway IHs commonly present with stridor in infants because the IHs are located in and around the narrowest portion of the pediatric airway (glottis and subglottis). Rapid growth of the IH, which is seen during the proliferative stage, precipitates worsening stridor. Once the patient enters childhood, airway IHs become asymptomatic. Airway VMs are present at birth, grow at the same rate as the child, and increase in size with dependency or Valsalva maneuvers, inducing clinical symptoms. Intermittent swelling of the malformation, located in and around the esophageal inlet, can induce symptoms of dysphagia or partial airway obstruction at any age. In older patients, airway VM symptoms can be subtle. At least half of all patients with airway IHs have cutaneous IHs, which regress in childhood. Airway VMs do not usually have associated cutaneous lesions, and, if they do, these lesions do not regress.

Airway IHs can be associated with PHACES syndrome (posterior fossa abnormalities, hemangioma, arterial anomalies, cardiac defect or coarctation of the aorta, eye anomalies, and sternal defect or supraumbilical raphe). In this series and others, airway VMs have been described with CHARGE syndrome (coloboma, heart abnormalities, atresia of the choanae, retar-
sions. However, this theory is unlikely given the clinical history of lesions in the airway IH category. In summary, immunostaining for GLUT-1 can be used to further differentiate airway IHs from other vascular malformations when there is a diagnostic or treatment dilemma and tissue biopsy is necessary.\(^3,16\)

It is beyond the scope of this article to discuss all aspects of airway vascular anomaly management. Traditional medical therapy for enlarging airway IHs has been treatment with systemic and intraleisional corticosteroids. Propranolol therapy has now been reported to be effective in reducing airway IH in a dramatic fashion.\(^17\)

Surgical excision, endoscopic or open, has been used for airway IHs. Airway VMs, however, do not respond to therapy and, in some cases, require no treatment. In airway VMs that require therapy, serial sclerotherapy treatments and/or surgical excision, via endoscopic or open approaches, can be performed.\(^14\) Distinguishing between airway IHs and airway VMs is important for optimizing the medical management of airway IHs and for avoiding unnecessary interventions.

Our study was limited by its small sample size and retrospective data analysis as well as by the fact that histologic analysis was not performed on all airway vascular anomalies in this series. Therefore, it is impossible to make recommendations for the most appropriate evaluation of these lesions. Despite this, differentiating between these anomalies using the described measures is important, as medical treatment for IHs and VMs is different. A treatment decision diagram is presented in Figure 6, which demonstrates how this battery of tests can be applied to the evaluation of airway vascular anomalies.

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Author Contributions: Drs Parhizkar, Manning, Chen, and Perkins had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Parhizkar and Perkins. Acquisition of data: Parhizkar, Manning, Inglis, Chen, and Perkins. Analysis and interpretation of data: Parhizkar, Manning, Finn, Chen, and Perkins. Drafting of the manuscript: Parhizkar and Perkins. Critical revision of the manuscript for important intellectual content: Manning, Inglis, Finn, Chen, and Perkins. Statistical analysis: Perkins. Administrative, technical, and material support: Parhizkar, Manning, Inglis, and Finn.

Study supervision: Chen.

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Additional Contributions: Randolph Otto, MD, critically reviewed the radiologic aspects of the manuscript; Stacy Russ prepared the manuscript; and Eden Palmer prepared the figures.

REFERENCES


