How Airway Venous Malformations Differ From Airway Infantile Hemangiomas

Nooshin Parhizkar, MD; Scott C. Manning, MD; Andrew F. Inglis Jr, MD; Laura S. Finn, MD; Eunice Y. Chen, MD, PhD; Jonathan A. Perkins, DO

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. 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
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

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<th>Table 1. Study Demographics</th>
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<td>Variable</td>
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<tr>
<td>Sex</td>
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<tr>
<td>Male</td>
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<td>Female</td>
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<td>Total</td>
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*There were 3 patients with a syndrome diagnosis in each group.*

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<tr>
<th>Table 2. Lesion Presentation, Location, Cutaneous Findings, and Radiographic Findings</th>
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<tr>
<td>Variable</td>
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<tr>
<td>Presenting sign</td>
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<tr>
<td>Dysphagia, 3/6 (50)</td>
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<td>Hemoptyis, 1/6 (16)</td>
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<td>Snoring, 1/6 (16)</td>
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<td>Endoscopic location</td>
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<td>Epiglottic, 1/6 (17)</td>
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<td>Cutaneous lesion</td>
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<td>Radiographic Findings</td>
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<tr>
<td>Computed tomographic angiography</td>
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<td>Electrocautery, 1/6 (11)</td>
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<td>Observation, 2/6 (30)</td>
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of them (91%) had associated cutaneous IHs. The airway IHs were located in the glottis or subglottis.9 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

Figure 1. Posterior airway infantile hemangioma. A, Endoscopic view of a posterior airway infantile hemangioma. B, Sagittal computed tomographic angiogram demonstrating a localized enhancing mass (arrow). C, Axial computed tomographic angiogram demonstrating an enlarging mass in the posterior laryngeal airway (arrow).

Figure 2. Posterior lateral airway infantile hemangioma. A, Endoscopic view of a posterior lateral airway infantile hemangioma. B, Sagittal computed tomographic angiogram demonstrating an enhancing mass extending from posterior to anterior (arrow). C, Axial computed tomographic angiogram demonstrating an enhancing mass in the posterolateral position (arrow).

Figure 3. Postcricoid venous malformation. A, Endoscopic view of a postcricoid venous malformation. B, Sagittal computed tomographic angiogram demonstrating a nonenhancing mass (arrows). C, Axial computed tomographic angiogram demonstrating postcricoid fullness without enhancement (arrows).
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.

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
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.\(^7\) 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.\(^10\) 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 IH, located in and around the esophageal inlet, can induce symptoms of dysphagia or partial airway obstruction at any age.\(^11\) In older patients, airway VM symptoms can be subtle.\(^14\) At least half of all patients with airway IHs have cutaneous IHs, which regress in childhood.\(^9,15\) Airway VMs do not usually have associated cutaneous lesions, and, if they do, these lesions do not regress.\(^14\) Airway IHs can be associated with PHACES syndrome (posterior fossa anomalies, hemangioma, arterial anomalies, cardiac defect or coarctation of the aorta, eye anomalies, and sternal defect or supraumbilical raphe).\(^9\) In this series and others, airway VMs have been described with CHARGE syndrome (coloboma, heart abnormalities, atresia of the choanae, retardation of growth and development, genitourinary anomalies, and ear abnormalities).\(^14\)

Airway endoscopy allows assessment of airway compromise and provides further diagnostic information.\(^9\) Bedside endoscopy can be safely performed in any patient. Operative endoscopy allows complete airway evaluation and operative treatment, particularly with airway IHs.\(^8\) Bedside endoscopy is valuable, as it enables careful treatment planning and often demonstrates an airway VM that is only enlarged and visible in an awake patient but decompresses during operative endoscopy (Figure 3A).\(^1,13\) In general, postcricoid airway vascular lesions that are first visualized in puberty and adolescence represent vascular malformations rather than IHs, as IHs will have regressed by then.

If necessary, CTA can be performed without endotracheal intubation in 30 to 60 seconds, providing information about lesion arterial phase blood flow and extent of airway involvement, with excellent spatial resolution.\(^8\) Because there is a difference in blood flow rates through IHs and VMs, CTA can be used reliably to distinguish between these entities.\(^7\) With current protocols, magnetic resonance (MR) imaging is not consistent at demonstrating blood flow differences between patients with IHs and VMs and airway lesions owing to slow image acquisition (2-5 minutes per sequence). A complete MR study requires 30 to 45 minutes, necessitating endotracheal intubation. Spatial resolution of the pediatric larynx during the MR examination is limited by endotracheal tube compression of the airway vascular lesion and surrounding tissues, as well as breathing motion artifact. While MR imaging does provide excellent soft-tissue contrast, the limitations due to motion usually outweigh the advantages in this location. Future refinement of MR imaging of these lesions may give MR a larger role in the imaging of airway vascular lesions. In our series, CTA enabled us to differentiate between airway IHs and airway VMs (Figures 1-3).

Airway IHs and VMs have different histologic features.\(^2,5\) Airway IHs are closely compacted lobules of capillary-sized vessels, whereas airway VMs are dysplastic venous channels, irregularly distributed through tissue.\(^1,16\) Immunohistochemical staining that is commonly available can facilitate the categorization of vascular anomalies based on differing endothelial expression.\(^2\) Airway IH endothelium highly expresses GLUT-1, whereas endothelium in other vascular lesions, including VMs, do not. Airway IH tissue expresses GLUT-1, but airway VM tissue does not, as we and others have demonstrated.\(^14,16\) Airway vascular lesions are frequently difficult to biopsy adequately, so immunohistochemical analysis is a useful adjunct to help in differentiating between IHs and VMs.\(^16\) Past reports of “laryngeal hemangioma” lack immunostaining results, so it is impossible to determine if the lesions are truly IHs or some other type of vascular anomaly.\(^13\) In our series, all the vascular anomalies that were analyzed with histologic examination and immunostaining had findings that allowed the diagnosis of either IH or VM. It is possible that in our series an airway IH or VM diagnosed by clinical and endoscopic criteria may actually have had a different diagnosis, since we did not histologically examine all le-

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Figure 6. Decision algorithm for airway vascular anomaly evaluation and diagnosis. CTA indicates computed tomographic angiography; GLUT-1, glucose transporter isoform 1; and IH, infantile hemangioma.

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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 intraliesional 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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Correspondence: Jonathan A. Perkins, DO, Division of Pediatric Otolaryngology, Seattle Children’s Hospital, 4800 Sand Point Way NE, Mail Stop W-7729, Seattle, WA 98105-0371 (jonathan.perkins@seattlechildrens.org).

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