Glomus tumor: a comprehensive review of the clinical and histopathologic features with report of two intraoral cases

Molly Housley Smith, DMD, a Indranee Bhattacharyya, DDS, MSD, b Donald M. Cohen, DMD, MBA, MS, b Steven R. Hinze, DDS, c and Mohammed N. Islam, DDS, BDS, c

Background. Glomus tumors are benign neoplasms that most commonly present in the subungual region. Their occurrence in the oral cavity is exceedingly rare. Here, we present 2 cases from the oral cavity, detail their clinical and histopathologic features, and review the literature for solitary cases involving the oral regions.

Study Design. The English language literature was queried for cases of benign glomus tumors in/around the oral cavity. Additional citations were cross-referenced from the identified sources.

Results. Thirty-one cases of solitary glomus tumor in the oral and paraoral regions have been described, including the present cases. Patient age ranged from 10 to 85 years, with an average age of 47 years. In 12 of the 31 cases, the tumors occurred in the lips, 5 in the palate, 4 in the tongue, 4 in the buccal mucosa, 3 in the gingiva, and 1 each in the parotid, pterygoid fossa, and oropharynx. Only 18 of these cases had accompanying immunohistochemical stains, with 14 expressing positivity for muscle cell markers.

Conclusions. Although glomus tumors have distinct histopathologic features, diagnostic confusion may exist with regard to extradigital locations. Detailed documentation and discussion of the clinical and histopathologic features of rare tumors like these are vital to understanding them. (Oral Surg Oral Med Oral Pathol Oral Radiol 2019;127:62–70)

Glomus tumors are uncommon, benign, mesenchymal neoplasms, initially described in the literature, in 1812 by Wood, as a painful tubercle about “the size and form of a flattened garden pea” and none “larger than a coffee-bean.” 1 Although Wood has been credited with the earliest well-documented description, earlier literature suggests that these painful growths may have been known in the time of Hippocrates and Galen. 2 In 1924, more than 100 years after Wood’s clinical description, Masson described the histopathologic characteristics and origin of the glomus tumor. 3

The classic presentation of a glomus tumor is a painful nodule that usually occurs in the distal phalanges around the nailbed. They are thought to arise from the glomus apparatus, a specialized arteriovenous (AV) shunt first described by Grosser in 1902. 4, 5 This AV anastomosis is a normal structure that permits blood to pass directly from the veins to the arteries, and vice versa, and is involved in temperature regulation. 6–8 The glomus apparatus is typically found in the stratum reticularis of the skin, most notably in the subungual or digital pad location, but also in lesser known locations, such as the ear pinna, the tip of the nose, sacrococcygeal region (arising from the glomus coccygeum), nasal cavity, and trachea. 6, 7, 9–11 Glomera are made up of complex vascular channels called Sucquet-Hoyer canals and are surrounded by modified smooth muscle cells termed glomus cells. 6 Although structures analogous to the glomus apparatus have been described in the periodontal and temporomandibular regions (the so-called genu vasculosis menisci), 12, 13 for the most part, their occurrence in the oral cavity largely remains undocumented. The etiology of glomus tumors is difficult to explain because these tumors can arise in locations not known to have such a structure. Three theories of origin have been proposed: (1) Glomus tumors are hyperplasias or hamartomas of glomus cells associated with glomera present throughout the body but are scattered so thin that routine biopsy in those areas does not allow discovery 14, 15; (2) they are heterotopic proliferations of glomus cells from the glomus apparatus known to be in other sites 14; or (3) they arise from perivascular cells in the area of the tumor and have undergone glomocytic differentiation. 10, 16 Currently, the third theory seems to be the most accepted

Statement of Clinical Relevance

Oral glomus tumors are extremely rare and demonstrate overlapping features with other neoplasms. Scarcity, inconsistent nomenclature, and perplexing etiology of these tumors contribute to confusion. Documentation with review of the literature is valuable to head and neck pathologists.
one because many investigators believe that myopericytomas, myofibromas, angioleiomyomas, and glomus tumors form a morphologic continuum. Sato et al. demonstrated viral structures on electron microscopy in one intraoral case; however, a viral etiology has not been documented in other reports. Additionally, controversy exists as to whether or not glomus tumors are true neoplasms or, rather, hyperplasias/malformations of the normal glomus body. It is generally accepted, however, that the solid glomus tumors are neoplasms, whereas the other types (glomangioma, glomangiomyoma) may be reactive or malformations.

In this article, we present 2 new cases of oral glomus tumors, one from the tongue in a 58-year-old female and the other from the lower lip of a 26-year-old male. Additionally, we review the literature for cases of benign glomus tumor in the oral regions and offer data on the clinical and histopathologic features of this rare tumor.

CASE REPORT 1
A 58-year-old white female with no significant medical history presented to her oral surgeon with an asymptomatic nodule on her anterior ventral tongue (Figure 1A). The nodule was approximately 2 × 1 cm and first noted by the patient 2 months prior to excision. The clinical impression was a minor salivary gland tumor. The tumor was excised with no complications (Figure 1B). The patient exhibited normal healing at the 1-month follow-up appointment.

Upon gross sectioning, the tumor appeared as a well-circumscribed, rounded nodule approximately 1 cm in greatest dimension, located subjacent to the overlying epithelium. The cut surface was tan to focally brown in color, homogeneous, and glistened slightly (Figure 1C). Microscopic examination revealed a well-circumscribed, encapsulated tumor (Figure 2A) comprising dense sheets of round to polygonal cells in a mucinous and myxoid stroma (Figure 2B). The cells demonstrated large, uniform, round-to-ovoid nuclei with prominent nucleoli and a fine, open chromatin pattern (Figure 2C). Moderate amounts of pale pink—clear cytoplasm were present around many of the nuclei. Although most areas consisted of densely packed cells, focal areas demonstrated a loose and myxoid background with clumping of the cells around blood vessels (see Figure 2B). Small blood vessels were scattered throughout the tumor. No nuclear pleomorphism or mitotic figures were identified. Focal areas of signet ring—like cells were noted (Figure 2D). Immunohistochemical studies revealed positive reactivity to α-smooth muscle actin (SMA) (Figures 2E and 2F) and muscle-specific actin (MSA, HHF-35) with lack of reactivity to S-100 protein (S100), p63, glial fibrillary acidic protein (GFAP), chromogranin, Sox10, AE 1/3and p63. Vascular markers CD31 and CD34 highlighted the blood vessels.

CASE REPORT 2
A 26-year-old white male presented to an oral surgeon with a painful mass that had been present for months on his lower lip. The clinical impression was a mucocele. Grossly, the tumor was described as a dark tan nodule measuring 1.5 × 0.5 × 0.5 cm. Histopathologic examination demonstrated a well-defined tumor surrounded by a fibrous capsule (Figure 3A). The encapsulated nodule contained large pools of erythrocytes and fibrinous material admixed with islands and clusters of round to ovoid glomus cells. The glomus cells tended to form collars around blood vessels (Figure 3B) and demonstrated distinct cell borders with a fine nuclear chromatin pattern (Figure 3C). They were occasionally arranged in a nodular fashion surrounded by hyalinized and myxoid fibrous connective tissue (Figure 3D). Immunohistochemical staining revealed positive reactivity in the tumor cells for HHF-35 (Figure 3E) and SMA (Figure 3F), although no reaction to AE1/3, STAT-6, CD31, or CD34 was noted. No clinical follow-up data are available for this case.

LITERATURE REVIEW
The English language literature was searched for cases of benign glomus tumor in the oral and paroral regions via PubMed and Web of Science. The following key terms were searched: “glomus tumor,” “glomangioma,” “oral cavity,” and “oral.” Additional citations were cross-referenced from the identified
Fig. 2. A, Microscopic examination of case #1 revealed a well-circumscribed nodule with a thin fibrous capsule (magnification × 1.5). B, The tumor cells are arranged in clusters and collars around blood vessels and set in a loose, myxomatous background (magnification × 10). C, A high-power image demonstrates sheets of monotonous round-ovoid cells with abundant pale eosinophilic-to-clear cytoplasm and distinct cell borders. The nuclei have a fine chromatin pattern with a prominent nucleolus (magnification × 100). D, Occasional foci of signet ring–like cells are seen (magnification × 40). E, Diffuse reactivity to α-smooth muscle actin (α-SMA) is apparent throughout the entire tumor (magnification × 2). F, α-SMA reactivity is intensively positive in the cytoplasm of tumor cells (magnification × 40). A high resolution version of this slide is available as eSlide: VM05172.
sources. We excluded any cases known to have multiple glomus tumors.\textsuperscript{9,23-25} Data from 4 reports in languages other than English (German and Italian) were included in our review because other authors had included them in their reviews.\textsuperscript{26-29}

Thirty-two cases of solitary, oral or paraoral glomus tumors were found in the English language literature, including the cases presented here.\textsuperscript{8,10,15,18-22,26-46} We excluded 1 case that did not provide a thorough histopathologic description or photomicrographs.\textsuperscript{40} Of the 31 total cases (Table I), patient age ranged from 10 to 85 years (average age 47 years; median age 54 years). There was an almost equal ratio of male-to-female patients (16 males, 15 females). The most common site was the lips (8 in the upper lip, 4 in the lower lip). Less common sites included the tongue, palate, buccal mucosa, gingiva, parotid, pterygoid fossa, and oropharynx. Twelve case reports described pain or tenderness as a clinical symptom. Of the 18 reported cases with accompanying immunohistochromical stains, only 14 expressed positivity for muscle markers. Two of the remaining cases did not run actins,\textsuperscript{39, 42} and the other 2 cases were negative for muscle markers,\textsuperscript{21,36} bringing into question the accuracy of the diagnosis.

**DISCUSSION**

Representing less than 2% of all soft tissue tumors,\textsuperscript{16,47,48} glomus tumors are exceptionally rare, and even rarer in the oral regions. We identified 29 cases of benign oral or paraoral glomus tumors from the English language literature and added 2 more cases. Of these, only 14 were confirmed with immunohistochemistry.

Contributing to confusion about the entity, the terminology for glomus tumor is inconsistent throughout the literature. The word *glomus* is defined as an anastomosis of arterioles and venuoles; thus, the term *glomus tumor* came about because it is a proliferation of those cells that surround the AV anastomosis of the glomus apparatus. *Glomus tumor*, however, has also been used to describe paragangliomas, which were originally believed to derive from a blood vessel origin. Despite the discovery that paragangliomas actually derive from the nonchromaffin cells of the neural crest, the incorrect terminology has, unfortunately, persisted (e.g., glomus tympanicum, glomus jugulare).\textsuperscript{49} Furthermore, various other names have been used to identify the perivascular glomus tumor, including glomangioma, glomuvenous malformation, glomangio-myoma, neuromyoarterial glomus, angioneuroma, angio-neuromyoma, painful subcutaneous tubercle, Popoff tumor, and subcutaneous glomal tumor.\textsuperscript{16,30}
<table>
<thead>
<tr>
<th>Case</th>
<th>Author</th>
<th>Age</th>
<th>Gender</th>
<th>Race</th>
<th>Duration</th>
<th>Site</th>
<th>Clinical description</th>
<th>Immunohistochemical profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Boros et al., 2010</td>
<td>34 M</td>
<td>H</td>
<td>1 year</td>
<td>Lower lip</td>
<td>Asymptomatic</td>
<td>SMA+, MSA+, S-100+, keratin—, EMA—, CD34—, CD31—, chromogranin—</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Derand et al., 2010</td>
<td>11 F</td>
<td>–</td>
<td>–</td>
<td>Lower lip</td>
<td>Well–defined, painless discoloration</td>
<td>SMA+, vimentin+, factor XIII—</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Ficarra et al., 1986</td>
<td>51 F</td>
<td>C</td>
<td>6 years</td>
<td>Upper Lip</td>
<td>Painless, bluish swelling</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>*Frenkel, 1965</td>
<td>13 M</td>
<td>–</td>
<td>–</td>
<td>Buccal mucosa</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Geraghty et al., 1992</td>
<td>71 M</td>
<td>C</td>
<td>Several years</td>
<td>Palate</td>
<td>Painless, slowly enlarging, cream–colored mass</td>
<td>Actin—, desmin—, chromogranin—, NSE—, PGP9.5—</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>González-Cámpora et al., 1995</td>
<td>72 F</td>
<td>7 years</td>
<td>Oropharynx</td>
<td>Dyspnea, dysphagia, dyslalia, bleeding, tenderness</td>
<td>Vimentin+, SMA and desmin focally +,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>*Grande, D’Angelo, 1962</td>
<td>42 M</td>
<td>–</td>
<td>–</td>
<td>Hard palate</td>
<td>Pain caused by an “antral abscess” of 3 weeks’ duration</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Harris and Griffin, 1965</td>
<td>35 F</td>
<td>–</td>
<td>3 weeks</td>
<td>Periodontium/gingiva</td>
<td>Painful</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Harvey, Walker 1987</td>
<td>15 F</td>
<td>C</td>
<td>2 years</td>
<td>Pterygoid fossa</td>
<td>Painful</td>
<td>Myosin+, vimentin+</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Ide et al., 2008</td>
<td>57 M</td>
<td>–</td>
<td>–</td>
<td>Upper lip</td>
<td>–</td>
<td>SMA+, MSA+</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Ide et al., 2008</td>
<td>54 M</td>
<td>–</td>
<td>–</td>
<td>Upper lip</td>
<td>–</td>
<td>SMA+, MSA+</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Kessaris et al., 2001</td>
<td>46 F</td>
<td>–</td>
<td>10 years</td>
<td>Palate</td>
<td>Painless, bluish swelling increasing in size for 10 years</td>
<td>Vimentin+, S100+, actin—, desmin—, chromogranin—, NSE—, cytokeratin—, EMA—, factor VIII—</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>King, 1954</td>
<td>32 M</td>
<td>–</td>
<td>5 years</td>
<td>Maxillary gingiva</td>
<td>Tender</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>*Kirschner, Strassburg, 1962</td>
<td>56 M</td>
<td>–</td>
<td>–</td>
<td>Gingiva/alveolar mucosa</td>
<td>Tender swelling</td>
<td>Actin+, desmin+, S100+, vimentin+</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Kusama et al., 1995</td>
<td>57 M</td>
<td>A</td>
<td>Several years</td>
<td>Upper lip</td>
<td>Tenderness</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Lanza et al., 2005</td>
<td>65 M</td>
<td>–</td>
<td>4 months</td>
<td>Lower lip</td>
<td>Blue mass, painful on palpation</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Moody et al., 1986</td>
<td>65 F</td>
<td>–</td>
<td>Several years</td>
<td>Upper lip</td>
<td>Asymptomatic swelling</td>
<td>Vimentin+, factor VIII—, CD45—, AbgA—, cytokeratin—</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Rallis et al., 2004</td>
<td>85 F</td>
<td>10 years</td>
<td>Upper lip</td>
<td>Mildly painful (especially at night), brown swelling</td>
<td>SMA+, MSA+, vimentin+, desmin—, S100—, EMA—, NSE—, AE1/3—, leu7—, CD31—, CD34—, CD45—, CD3—, CD20—, Cytokeratins—,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>Sakashita et al., 1995</td>
<td>63 F</td>
<td>–</td>
<td>At least 4 years</td>
<td>Parotid</td>
<td>Pain upon opening</td>
<td>Vimentin +, S100—, keratin—, desmin—, EMA—, chromogranin—, factor VIII—related antigen— for tumor</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Sakashita et al., 1997</td>
<td>54 M</td>
<td>–</td>
<td>5 years</td>
<td>Upper lip</td>
<td>Painless swelling</td>
<td>SMA+, vimentin+, factor VIII—related antigen—</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Saku et al., 1985</td>
<td>45 M</td>
<td>–</td>
<td>6 months</td>
<td>Left buccal mucosa</td>
<td>UNK</td>
<td>SMA+, vimentin+, factor VIII—related antigen—</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Sato et al., 1979</td>
<td>29 M</td>
<td>Japanese</td>
<td>1 year</td>
<td>Tongue</td>
<td>Painless, firm, smooth, slightly reddish, movable nodule</td>
<td>Actin+, smooth muscle myosin+</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Savaci, 1996</td>
<td>55 F</td>
<td>–</td>
<td>&gt;1 year</td>
<td>Left buccal mucosa</td>
<td>Mass; burning pain</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>Sidhu, Subherwal, 1967</td>
<td>10 F</td>
<td>A</td>
<td>6 months</td>
<td>Hard palate</td>
<td>Asymptomatic pink mass, soft</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

(continued on next page)
The most common clinical presentation of glomus tumors is a subcutaneous nodule, often blue, purple, or red in color and that occurs in the third to fifth decades.\textsuperscript{10,32,51} The majority arises in the subungual location; however, they have been found in all parts of the body, including the stomach, heart, uterus, vagina, penis, mediastinum, lung, bone, trachea, gastrointestinal tract, and kidney.\textsuperscript{16,32,51-53} Although a female predilection has been noted for subungual tumors, no gender predilection (or slight male) exists for glomus tumors in other locations.\textsuperscript{10,22,39,51} In the 31 cases of oral/paraoral tumors in this review, no gender predilection was seen.

A striking clinical symptom associated with glomus tumors is the presence of pain that is disproportionate to the size of the tumor. The pain may vary from slight tenderness upon palpation to excruciating burning, shooting, or stabbing pain that radiates up the limbs and involve the trunk or even half of the body.\textsuperscript{1,5,22} The pain frequently has been described as paroxysmal or associated with changes in temperature or pressure.\textsuperscript{5,10,32} Pain or tenderness was noted in 12 of 31 of the cases evaluated in this review. Investigators have hypothesized that the pain may be associated with the tumor being tightly bound down (e.g., in the nail bed)\textsuperscript{19;} however, the presence of painful tumors in loosely bound tissue argues against that point.\textsuperscript{10,43,45,present case} The high concentration of nerve fibers noted throughout some tumors may explain the pain.\textsuperscript{21,54} Occasional cases have been reported to contain substance P, a pain-related vasoactive peptide, and cyclooxygenase-2, which may contribute to the pain mechanism.\textsuperscript{55,56} Notably, a history of trauma has also been associated with glomus tumors.\textsuperscript{5,22,48,50}

The current World Health Organization classification system lists several types of glomus tumors, including solid glomus tumors, which represent about 75% of cases.\textsuperscript{16} Other variants of the tumor include glomuvenous malformations (also known as glomangiomas), glomangiomyomas, glomangiomatoses, symplastic glomus tumors, malignant glomus tumors, and glomus tumors of uncertain malignant potential. The major distinction between solid glomus tumor, glomangioma, and glomangiomaya lies in the distribution of glomus cells and the amount of vascular and smooth muscle within the lesion; however, no exact percentage for each of these features exists within the classification system.\textsuperscript{16} Histopathologically, solid glomus tumors typically present as encapsulated or well-circumscribed masses of glomus cells arranged in sheets, aggregates, or collars around blood vessels (see Figure 3B). Our first case is most appropriately classified as a solid glomus tumor. The glomus cells are monomorphous and round-to-ovoid in shape with a sharply delineated, round nucleus and

<table>
<thead>
<tr>
<th>Case</th>
<th>Author</th>
<th>Age</th>
<th>Gender</th>
<th>Race</th>
<th>Duration</th>
<th>Site</th>
<th>Clinical description</th>
<th>Immunohistochemical profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>Stojic, Bojic, 1987</td>
<td>65</td>
<td>M</td>
<td></td>
<td>6 months</td>
<td>Tongue</td>
<td>Painless, pink mass, soft</td>
<td>SMA+, CD34+, vimentin+</td>
</tr>
<tr>
<td>26</td>
<td>Tajima et al., 1981</td>
<td>63</td>
<td>F</td>
<td>Caucasian</td>
<td>5 years</td>
<td>Tongue</td>
<td>Asymptomatic nodule</td>
<td>NA</td>
</tr>
<tr>
<td>27</td>
<td>Vasconcelos et al., 2018</td>
<td>67</td>
<td>F</td>
<td>Hispanic</td>
<td>4 years</td>
<td>Hard palate</td>
<td>Mass and tenderness</td>
<td>SMA+, vimentin+, S100, cytokeratin</td>
</tr>
<tr>
<td>28</td>
<td>Present case 1</td>
<td>58</td>
<td>F</td>
<td>Caucasian</td>
<td>2 months</td>
<td>Vental tongue</td>
<td>Asymptomatic nodule</td>
<td>SMA+, vimentin+, S100, cytokeratin</td>
</tr>
<tr>
<td>29</td>
<td>Present case 2</td>
<td>52</td>
<td>M</td>
<td>Caucasian</td>
<td>4 years</td>
<td>Lower lip</td>
<td>Asymptomatic nodule</td>
<td>SMA+, vimentin+, S100, cytokeratin</td>
</tr>
<tr>
<td>30</td>
<td>Present case 3</td>
<td>30</td>
<td>F</td>
<td>Caucasian</td>
<td>6 months</td>
<td>Vental tongue</td>
<td>Asymptomatic nodule</td>
<td>SMA+, vimentin+, S100, cytokeratin</td>
</tr>
<tr>
<td>31</td>
<td>Yoruk et al., 2010</td>
<td>30</td>
<td>F</td>
<td>Caucasian</td>
<td>2 months</td>
<td>Lower lip</td>
<td>Mass and tenderness</td>
<td>SMA+, vimentin+, p53, CD34, CD31, GFAP, NSE, CD117, CD10, STAT6, P63, Sox10, Sox17, CD31, CD34</td>
</tr>
</tbody>
</table>

*Original publication in a non-English language, but included in English language literature reviews.

ASMA, a-smooth muscle actin; C, Caucasian; EMA, epithelial membrane antigen; F, female; GFAP, glial fibrillary acidic protein; H, Hispanic; M, male; MSA, muscle-specific actin; NA, not applicable; NEX, neuron-specific enolase; PGP9.5, protein gene product 9.5; SMA, smooth muscle actin.
pale eosinophilic cytoplasm. The stroma may appear myxoid or hyalinized (as seen in Figure 2B). Occasionally, the glomus cells may demonstrate either an oncocytic or a signet-ring-like appearance (see Figure 2D). Glomangiomias (glomuvenuous malformations) tend to exhibit large, dilated vascular spaces with small collections of glomus cells. This subtype is most commonly associated with multiple lesions. Glomangiomyomas contain more elongated spindle-to-ovoid—shaped cells that are more typical of mature smooth muscle cells. Our second case is difficult to classify because it is a combination of subtypes, containing not only large vascular spaces but also large clusters of glomus cells and spindled cells demonstrating smooth muscle differentiation (shown in Figure 3D at the periphery of the ball-like cluster of glomus cells). Glomangiomatosis is most similar to diffuse angiomatosis; however, clusters of glomus cells are noted around the vessels.

Some glomus tumors demonstrate marked nuclear atypia or nuclear hyperchromatism but do not exhibit other features of malignancy, such as increased mitotic activity, necrosis, large size, or deep location. These tumors are referred to as symplastic glomus tumors. The symplastic nature may best be compared to “ancient” or degenerative features seen in other soft tissue (e.g., Schwannomas). To make a diagnosis of symplastic glomus tumor, it is helpful to find at least focal areas of normal-appearing glomus cells, most commonly found along the periphery of the lesion. Malignant glomus tumors (also referred to as glomangiosarcomas) demonstrate nuclear atypia along with increased and atypical mitotic figures. The World Health Organization classification system breaks malignant tumors down into 2 categories: (1) spindle-cell (resembling fibrosarcoma and leiomyosarcoma) and (2) round-cell. Tumors that lack obvious qualification for malignancy but do demonstrate other worrisome features, such as deep location, infiltrative growth, vascular space involvement, or large size, are classified as “glomus tumors of uncertain malignant potential.”

Immunohistochemically, glomus tumors should demonstrate positivity to vimentin, SMA, MSA, and h-caldesmon. Distinct cell borders may be highlighted by a periodic acid—Schiff (PAS) stain or toluidine blue. Cytokeratins, S100 protein, and factor VIII—related antigen are reportedly negative. Desmin is usually negative, although occasional cases have been reported to demonstrate weak positivity. Although most authors agree that S100 protein should be negative, occasional cases have reported positive reactivity. The case reported by Kessaris et al. demonstrated uniformly round cells but was negative for actin and positive for S100, questioning a diagnosis of glomus tumor being appropriate. Additionally, a case published by Geraghty et al. demonstrated no reactivity to α-actin, desmin, chromogranin, neuron-specific enolase or protein gene product, but electron microscopy disclosed filamentous material within the glomus cells, compatible with smooth muscle myofibrils. Furthermore, the case presented by Geraghty et al. showed a classic hematoxylin and eosin presentation of uniformly round glomoid cells cuffing blood vessels. In certain locations (e.g., the digits), the diagnosis of glomus tumor often is easily made; however, in extradigital sites, diagnostic difficulty may exist. When the nodules occur under the skin, adnexal tumors (e.g., eccrine spiradenoma, nodular hidradenoma) may be considered but are usually excluded with cytokeratin markers. Salivary gland tumors (e.g., myoepitheliomas) may also be excluded by discovery of negative cytokeratin markers. Neuroendocrine markers frequently are performed, likely because of the fine chromatin pattern of the glomus nuclei. Because of occasional signet ring—like cells, cells with abundant pale cytoplasm, and the mucinous background in case 1 presented here, we considered a myoepithelioma or a signet-ring cell (mucin-producing) adenoma of minor salivary glands (the benign counterpart to the adenocarcinoma first described by Ghannoum and Freedman in 2004). Negative reactivity to cytokeratins and myoepithelial markers (Sox10, S100, p63), as well as lack of mucicarmine staining within the cytoplasm of the cells, ruled out those diagnostic considerations. For the most part, glomus tumors are diagnostic on hematoxylin and eosin staining and confirmatory immunohistochemical reactivity with SMA. Categorizing the type of glomus tumor often is the more difficult challenge. Like other tumors in the perivascular/myoid category (e.g., myofibroma), glomus tumors have a tendency to be multiple and/or familial. Generally, glomus tumors are multiple in less than 10% of cases. At least 3 cases of multiple glomus tumors (glomuvenuous malformations) affecting the oral regions have been described. Notably, multiple glomus tumors have been associated with neurofibromatosis type 1. Multiple occurrences have been linked to chromosome 1p21Y22 (the glomulin gene) and demonstrate an autosomal dominant inheritance pattern with variable expressivity and incomplete (approximately 90%) penetrance.

The treatment for glomus tumors is excision. The recurrence rate varies from 2% to 50%, depending on the tumor site (e.g., the nailbed may pose a more difficult challenge in excising the entire tumor) or atypical features. Of the 16 cases in this review that had the follow-up period specified, no recurrences were reported. The average follow-up time was 2.6 years (of 1 month
to 7 years). In a review of glomus tumors (not specifically oral) by Mravic et al., only 3 of 137 tumors recurred (median follow-up period of 2 years). Malignant cases demonstrate a higher rate of recurrence and metastasis compared with benign tumors. When pain is associated with the tumor, removal often provides immediate relief, although hypersensitivity may persist for weeks after the surgery.

CONCLUSIONS

Glomus tumors are rare and even rarer in the oral cavity. We presented here 2 cases with benign intraoral tumors and a comprehensive review of the clinical and histopathologic features common to this entity. Although the histopathologic diagnosis often is not difficult to make, unfamiliarity with this tumor may lead to diagnostic challenges. Therefore, oral and maxillofacial pathologists and head and neck pathologists should be knowledgeable about and cognizant of this entity when dealing with perplexing soft tissue lesions in the oral regions.

REFERENCES

50. Stout A. Tumors of the neuromyoarterial glomus. Tumors of the neuromyoarterial glomus. 2012:20;301-301.

Reprint requests:
Molly Housley Smith, Division of Oral and Maxillofacial Pathology, University of Kentucky College of Dentistry, 800 Rose Street, Rm. 530, Lexington, KY 40536, USA.
molly.housley.smith@gmail.com