

# Glial Choristoma in the Oral and Maxillofacial Region

## A Clinicopathologic Study of 6 Cases

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• **Context.**—Glial choristoma is an uncommon developmental abnormality typically presenting at birth or in early childhood. The nasal region is most frequently affected. Palate, tongue, cheek, scalp, and orbit can also be affected but these occurrences are relatively rare.

**Objective.**—To report 6 cases of glial choristoma arising in the oral and maxillofacial region and to document the clinical and pathologic features of these lesions.

**Design.**—Histologic and immunocytochemical examinations were performed on 6 cases of glial choristoma. Biologic behavior, prognosis, and pathogenesis were discussed together with a review of the literature.

**Result.**—The patients included 5 boys and 1 girl. They all presented with the lesions at birth or soon after birth. Four lesions occurred on the dorsal side of the tongue, near the foramen caecum. One lesion was present in the infra-

temporal fossa and parapharyngeal space, and the other one was in the submandibular region. All patients received surgical excision, and follow-up data revealed no recurrence for a period of 10 months to 5 years after surgery. Histologically, the lesions showed mature glial cells intermixed with connective tissue. The glial tissue was strongly positive for glial fibrillary acidic protein and S100 but negative for neurofilament.

**Conclusion.**—Glial choristoma should be classified as a developmental malformation that occurs in many sites of the head and neck. In oral cavity, the tongue is the most frequently affected site. Although these lesions are rare, they should be included in the differential diagnosis of congenital masses in the oral and maxillofacial region.

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Glial choristomas are generally considered as brain heterotopias composed of ectopic central nervous tissue arising as a developmental malformation and usually presenting in the head and neck region.<sup>1</sup> The nasal area is mostly affected, and the term *nasal glioma* is especially used to refer to the glial choristoma involving this area.<sup>2,3</sup> The oral and maxillofacial region is a relatively rare site of involvement. Previously reported cases included lesions involving the palate, tongue, oropharynx, upper lip, and submandibular area.<sup>4,5</sup> We present here 6 additional cases of glial choristoma arising in the oral and maxillofacial region and describe the histologic and immunocytochemical findings together with a review of the literature. This article may contribute to the limited clinical knowledge of this condition and assist clinicians in its diagnosis and management.

### MATERIALS AND METHODS

Six cases of glial choristoma were identified from the files of the Department of Oral Pathology, Peking University School of Stomatology, during the years 2001 through 2006. Clinical details of the patients were reviewed, and follow-up data were evaluated

by consulting individual clinical reports and pathology files. The surgical specimens had been fixed routinely in 10% neutral-buffered formalin (18–48 hours), processed, embedded in paraffin, and serially sectioned. In addition to hematoxylin-eosin staining, immunocytochemical staining was also performed using a standard streptavidin-biotin-peroxidase complex method (LAB-SA kits, Zymed Laboratories, San Francisco, Calif). Details of the primary antibodies used are listed in Table 1.

### RESULTS

#### Clinical Findings

The clinical features of patients are summarized in Table 2. They included 5 boys and 1 girl. All of the lesions were present at birth or soon after birth. A total of 4 (cases 1, 3, 5, and 6) of the 6 lesions were present in the midline of the dorsal tongue adjacent to the foramen caecum. The other 2 lesions occurred in the infratemporal fossa (case 2) and the submandibular region (case 4), respectively. One lingual lesion was pedunculated (case 3), but all had intact overlying mucosa. One of the patients with a lingual lesion (case 3) was also accompanied by the presence of soft palate cleft, ventricle septum defect, and patent ductus arteriosus. Case 2 involved a boy 3 years 4 months old who presented with a palatal mass that was noted soon after birth and grew slowly without any discomfort. Physical examination revealed diffuse swelling of right soft palate extending to the lateral pharyngeal wall. There was obvious asymmetry in his face, with the right side being relatively more plump. Computed tomography (CT) scans showed a mass located in the right infratemporal fossa with a bony defect in the middle cranial fossa (Figure 1). The infratemporal side of the greater wing of the right

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Antibodies (Clone)	Pretreatment	Dilution	Company
Glial fibrillary acid protein (ZCG29)	None	1:800	Zymed
Neurofilament (DA2/FNP7)	Citrate HIER	1:150	Zymed
Neuron-specific enolase (E27)	None	1:100	Zymed
S100 (4C4.9)	None	1:300	Zeta

\* HIER indicates heat-induced epitope retrieval; Zeta, Zeta Corp., Sierra Madre, Calif.

sphenoid, both right medial and lateral sphenoid processes, and the petrosal part of the right temporal bone were affected. Although a bony defect was present, the lesion was separated from brain tissue by meninges, and no communication with the brain was found (Figure 1, a). The mass displaced the right temporal lobe upwards. Following the diagnosis established by biopsy, a staged surgical approach was adopted to excise the lesion, first to remove the part located in the infratemporal region, and subsequently, a year later, to remove the parapharyngeal portion. Case 4 involved a 2-year-old boy who presented with a mass in his right submandibular region soon after birth. The mass was excised with a submandibular incision and was found to be located beneath the platysma extending to both medial and lateral sides of the mandible. The mass was multicystic, with clear fluid inside. Thus, all 6 patients were treated surgically at ages ranging from 1 year old to 3 years old, and no recurrence was detected during a follow-up period of 10 months to 5 years.

### Pathologic Findings

All lesions of the present series were poorly demarcated and excised without an obvious capsule. The removed specimens were solid, firm, and dark brown or red, with 1 case also showing obvious cystic components (case 4). Microscopic examination showed mature glial tissue scattered in a background of fibrovascular stroma (Figure 2, a and b). The glial tissue consisted of a delicate eosinophilic fibrillary network containing mainly astrocytes, which were arranged in large clumps or small islands

(Figure 2, b). The cells had round, vesicular nuclei and were sometimes binucleated or multinucleated. Sparse oligodendrocytes or microglia were also seen in all cases (Figure 2, b). Microscopic cystlike spaces lined by papillary formations similar to the choroid plexus were observed in 3 cases (cases 2, 3, and 4). The inner wall of these cystic spaces was lined with a monolayer of flat ependymal cells (Figure 2, c). Neurons were observed in 1 case (case 3; Figure 2, d). Meningeal components were absent. Immunocytochemically, the glial tissue was intensively positive for glial fibrillary acidic protein and S100 in all cases (Figure 2, e and f). The reactions with anti-neuron-specific enolase antibodies showed strong and positive staining in case 3, in which neurons had been found (Figure 2, d, inset) and weak and diffuse staining in other cases. Reaction against antineurofilament antibodies was negative in all cases.

### COMMENT

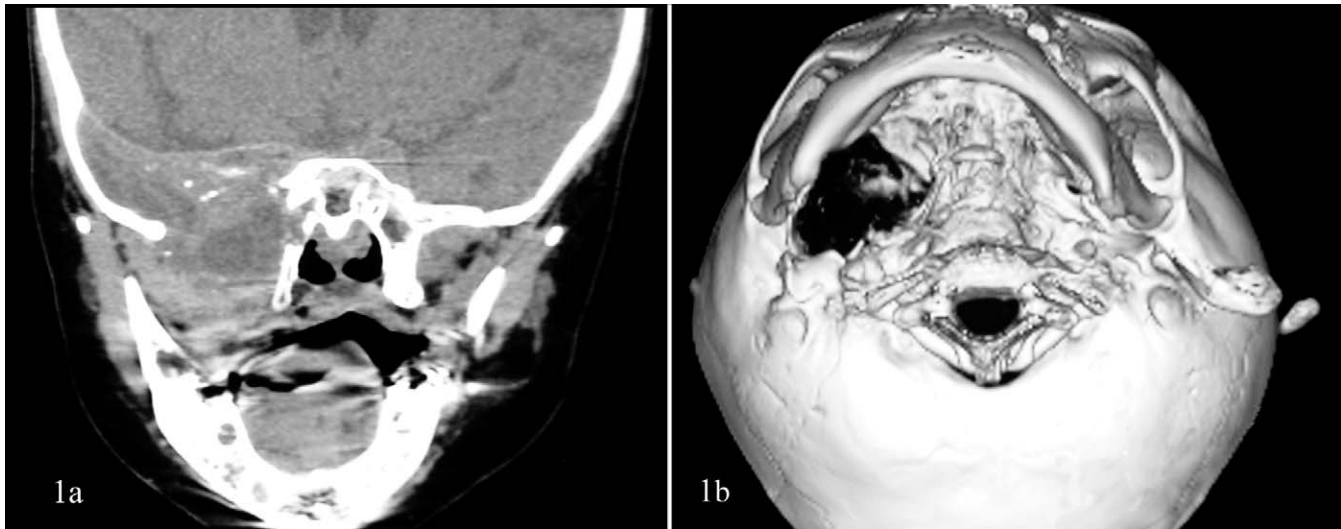
A variety of terms have been used to describe this lesion, which can be categorized into 3 groups. The first group has a tendency to imply the lesion is a neoplasm, such as glioma or nasal glioma. However, the lesion does not manifest any neoplastic behavior, with its growth rate parallel to surrounding tissues. Therefore, the lesion should be classified as a developmental malformation rather than a neoplasm.<sup>6,7</sup> The term *nasal glioma*, referring to those located in the nasal region, remains in use for historic reasons. Another group of terms includes *cerebral heterotopy*, *ectopic brain*, and *heterotopic brain tissue*, with the latter being used most often. We favor the term *glial choristoma*, as it better reflects the lesion's pathologic nature. *Choristoma* is a general term referring to normal tissue found in an abnormal location that may be used synonymously with the term *heterotopia*. The last category of terms, such as *encephalocele* or *meningocele*, has been misused. They all designate the protrusion of cranial tissue through an aperture in the cranium while maintaining communication with the subarachnoid space or the ventricle system. Glial choristomas are usually separated from the cranium and should be differentiated from encephalocele or meningocele.

Glial choristomas generally occur in the head and neck

Case No.	Age 1*	Age 2, y†	Sex	Site	Size, cm†	Solid/Cyst	Symptoms	Accompanied Deformity	Treatment and Follow-up
1	At birth	1.5	Male	Tongue foramen caecum	2.5 × 2.5	Solid	Asymptomatic	None	Excision, no recurrence 5 y after surgery
2	At birth	3	Male	Infratemporal fossa; parapharynx	5 × 5	Solid	Swelling	Bone defect of cranial base	A staged surgical plan involving 2 operations during 1 y, no recurrence 2 y after the second operation
3	At birth	1.5	Female	Tongue foramen caecum	1.5 × 1.0	Solid	Feeding difficulty	Cleft palate; Ventricle septum defect; patent ductus arteriosus	Concurrent excision and palatoplasty, no recurrence 5 y after surgery
4	At birth	2	Male	Submandibular region	3 × 4	Cystic and solid	Swelling	None	Excision, no recurrence 2 y after surgery
5	10 mo	1	Male	Tongue foramen caecum	1.5 × 1.0	Solid	Asymptomatic	None	Excision, no recurrence 1 y after surgery
6	1 mo	1.5	Male	Tongue foramen caecum	1.5 × 1.5	Solid	Asymptomatic	None	Excision, no recurrence 10 mo after surgery

\* The age indicating the time of first discovery of the lesion.

† The age and the size of the lesion identified at the time of treatment.



**Figure 1.** Computed tomography of case 2. *a*, A frontal slice showing the lesion located in the infratemporal fossa and partly protruding into the cranium through the bony defect of the middle cranial fossa. It is separated from the brain by meninges. *b*, A 3-dimensional image of cranial base bony defect from an inferior view.

region. The most frequently affected site is the nasal area,<sup>6</sup> followed by the tongue,<sup>3,5</sup> palatopharyngeal complex,<sup>8,9</sup> orbit,<sup>10,11</sup> scalp,<sup>12-14</sup> and ear.<sup>15</sup> These lesions are more likely to affect the midline craniofacial structures. They can also develop in normal tissue spaces, like the infratemporal space<sup>1,16</sup> and the submandibular space.<sup>17</sup> In the present series, tongue was the most frequently affected site, and these lingual lesions had a notable propensity to arise near the foramen caecum. Other congenital abnormalities, such as lingual thyroid, teratoma, or thyroglossal duct cyst, may also be associated with the foramen caecum of the tongue,<sup>18</sup> which suggests that glial choristoma is likely to be congenital in nature. In the present series, the infratemporal space and the submandibular region were also affected, which indicates that glial choristoma may occur at various anatomic locations near the skull.

Glial choristomas are generally present at birth or become manifest within the first few years of life.<sup>3,6</sup> Most of the glial choristomas grow slowly with a rate parallel to the surrounding tissue in an expansive fashion. Although a bony defect may be present, especially in those located near the cranium, it is not a sign of destruction due to aggressive behavior, but a disturbance of the normal development of bone structures.<sup>1</sup>

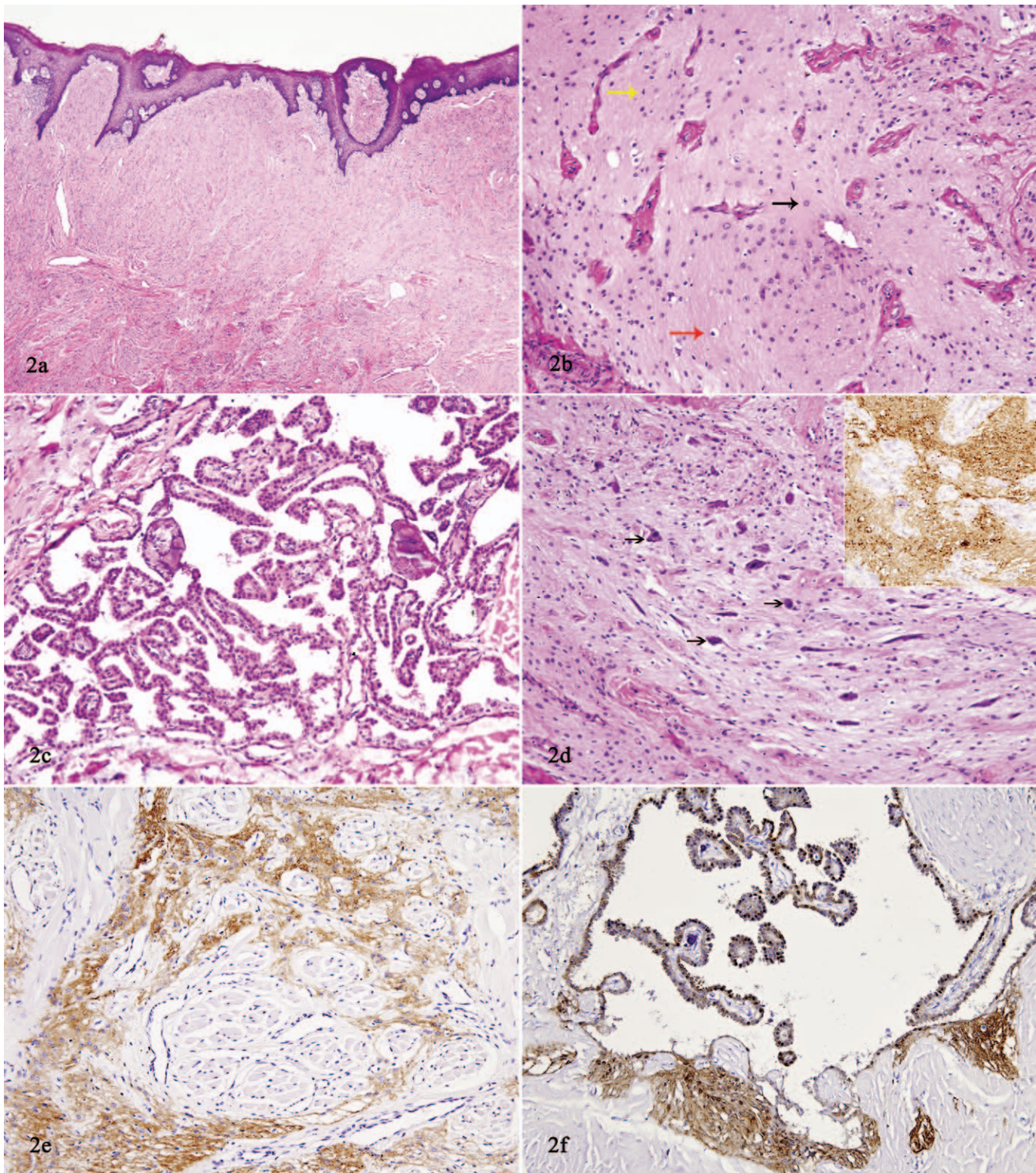
Two patients in the current series presented with swelling and a third patient had feeding difficulties. The remaining 3 patients in the current series were asymptomatic. Previous reports documenting severe complications caused by glial choristomas of the palatopharyngeal area were not uncommon.<sup>7,9,19-22</sup> Dyspnea and dysphagia were the most predominant presenting symptoms. Mechanical obstruction of the airway in newborns may be life threatening, and immediate endotracheal intubation or tracheostomy is needed.<sup>1</sup> Anatomic site and the size of the lesions accounted for the possible symptoms. Most of the lesions of the tongue do not cause any complications.<sup>3,5</sup>

Computed tomography and magnetic resonance imaging are complementary in determining the location and extent of the lesion for diagnosis and treatment planning. Axial and coronal CT images of the head are helpful in delineating the location of the tumor and its relationship

to the skull base,<sup>22</sup> especially for those located around the cranium. The lesions generally present as a soft tissue density isodense to brain and with a possible bony defect.<sup>2,6</sup> On magnetic resonance imaging, the lesions show isointense signal on T1 and a slight hyperintense signal on T2-weighted image,<sup>6,23</sup> which resemble the normal brain tissue. These attributes might be helpful in differentiating glial choristomas from other more common congenital lesions. If a bony defect of the skull base is detected, magnetic resonance imaging will be helpful in discerning whether an intracranial connection exists.<sup>6</sup> Like in our case 2, most of the lesions around the cranium are reportedly totally extradural, with no direct communication with the brain.<sup>1,13</sup>

An interesting fact is the high percentage of the oropharyngeal glial choristomas occurring concurrently with cleft palate. Uemura et al<sup>19</sup> reviewed 17 glial choristomas of the oropharynx and found that up to 6 cases were accompanied by cleft palate. Thus, they speculated that the presence of heterotopic brain tissue in this area could have disturbed the normal fusion process of palatal shelves.<sup>19</sup> We noticed that the case in the present series and the reported cases of glial choristoma concurrent with cleft palates were all with incomplete cleft palate.<sup>9,19,20,24-31</sup> This phenomenon indicates that the occurrence of glial tissue in the dorsum of tongue or the palatopharyngeal region might have disturbed only the posterior portion of palatal processes fusion. The presence of cleft palate, therefore, might be the result rather than the cause of ectopic glial tissue.

Histologically, the lesions were composed of mature glial tissue intermixed with fibrous or muscle tissues. The glial tissue was formed primarily by astrocytes, with round to oval one or more basophilic nuclei, and eosinophilic fibrillar cytoplasm. Oligodendrocytes could also be found in rows and clusters. Glial choristomas may be solid or partially cystic. The cystic lesions usually encapsulate fluid, which is similar to the cerebrospinal fluid.<sup>20</sup> Cyst formation might result from the cerebrospinal fluid production by functioning choroid plexus. In the present series, cystic changes and papillary formation of choroid



**Figure 2.** a, Poorly circumscribed submucosal mass of glial tissue that was intermixed with muscle or fibrous tissue. The overlying mucosa is intact in this lingual lesion (hematoxylin-eosin, original magnification  $\times 40$ ). b, Higher-power view showing that the lesion is made up of mature glial tissue containing mainly astrocytes (black arrow), as well as oligodendrocytes (red arrow) and spindle-shaped microglia (yellow arrow) (hematoxylin-eosin, original magnification  $\times 200$ ). c, Choroid plexus-like areas showing cystic appearance with papillary formation inside (hematoxylin-eosin, original magnification  $\times 200$ ). d, Neurons were seen in 1 case (case 3) characterized by large cell bodies (arrows) with Nissl substance (hematoxylin-eosin, original magnification  $\times 200$ ). Note strong neuron-specific enolase reactivity in this case (inset). e, The glial cells showing intensive reactivity for glial fibrillary acidic protein (original magnification  $\times 200$ ). f, The glial cells and the cuboidal cells of choroid plexus-like areas all show positive staining for S100 (original magnification  $\times 200$ ).

plexus with ependymal-type lining cells were found in 3 cases. Immunocytochemically, our results as well as those in previous reports indicate that the glial tissue in the lesions are intensively positive for S100 and glial fibrillary acidic protein but weakly positive for neuron-specific enolase.<sup>3,15,32</sup>

Among the hypotheses regarding the pathogenesis of glial choristoma, two have been most widely accepted. One concerns protrusion of the neural glial tissue from the developing cerebral tissue that becomes isolated from the brain in later development.<sup>4,14,20</sup> This theory is strongly supported by the observation that some nasal glial choristomas may have a fibrous stalk connecting with the intracranial contents. Glial choristomas around the skull, such as nasal, orbital, scalp, and palatopharyngeal lesions, might develop in this way. The other theory speculates that the displacement of neuroectodermal cells, occurring at an early stage of embryogenesis, may subsequently differentiate into a variety of cells of neuroglial tissue.<sup>4,21</sup> The glial choristoma of the tongue may have developed in this manner. According to this theory, the tongue musculature is derived embryologically from occipital myotomes that differentiate into myofibroblasts and migrate to the stomatodeum. Lingual glial choristomas might develop from a nest of pluripotent cells, which become separated before complete fusion of the neural tube and integrate with those migrating myoblasts to finally reach the tongue.<sup>3,7,21</sup>

Glial choristoma should be included in the differential diagnosis of congenital developmental malformations of infants. For lingual lesions, especially those near the foramen caecum, the differential diagnosis should include lingual thyroid, vascular or lymphatic malformations, and teratoma. A thyroid scan should be carried out to ascertain the presence of thyroid gland so that excision can be performed safely. Glial choristomas occurring in the infratemporal fossa or parapharyngeal space should also be differentiated from encephalocele or meningocele, as a bony defect may exist in all of these lesions. Computed tomography can be helpful in differentiating lesions with or without intracranial connection. Glial choristoma occurring concurrently with an encephalocele has also been reported.<sup>33</sup>

Conservative excision is adequate for glial choristoma, and rare recurrences are due to incomplete excision.<sup>3,9</sup> For those patients with cleft palate, simultaneous excision of the lesion and palatoplasty of the cleft palate is a good option for treatment.<sup>19,31</sup> In conclusion, glial choristoma is a rare but distinct clinical entity. In the oral and maxillofacial region, the tongue and the palatopharyngeal region are the most frequently affected sites. Tissue spaces like the infratemporal fossa and the submandibular region may also be affected. The prognosis of glial choristoma is good, and excision is usually curative. However, the possibility of encephalocele or ectopic thyroid should be excluded by postoperative CT or thyroid scan examination.

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