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Case Report

A Radiographically Visible Cluster of Mucous Glands Inside the Mandible (Not a Stafne Defect)

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Abstract

Background: Since its first report in 2000, only four additional ectopic salivary glands (choristomas) within the marrow of the jaws have been reported; two were large enough to be radiographically visible, as lobulated radiolucencies. Although rarely reported, such entities are a logical tissue of origin for intraosseous salivary adenomas, carcinomas and cysts. We present the largest such anomaly yet reported, presenting as a cluster of 5 independent mucous glands with no ductal connections to the surface.

Case Report: The lesion was in an 18-year-old male who had his mandibular third molars removed, each associated with small dentigerous cysts. An incidental finding was seen distal to the left third molar: an oval, well-demarcated, multilocular radiolucency with a faint, hazy, reticulated opacity and a thin sclerosis of the borders. The area was asymptomatic, and the cortex was not expanded. Microscopic examination demonstrated a thin, atrophic stratified squamous lining epithelium consistent with a dentigerous cyst, but the adjacent radiolucency, representing most of the biopsy sample, consisted of five independent glandular structures comprised of mucous (mucus) glands virtually identical to minor salivary glands of the mucosa. The largest gland was 1.5 x1.0 x 0.6 cm. in size, and all glands appeared histologically normal and even contained mucus (mucicarmine positive) in some ducts. No large excretory ducts could be identified, and no ducts traversed between glands. The glands were embedded in fibrous stroma, but no true encapsulation was noted, nor was inflammation seen.

Conclusion: We present the largest example yet reported of an unusual, almost never reported jawbone anomaly: intraosseous salivary choristoma (normal tissue in an abnormal location). This is the second reported to contain multiple glands, the fourth to show radiographically, and the only one to show secreted mucus in its ducts. The glands were not encapsulated.

Keywords: Ectopic Salivary Gland; Salivary Choristoma; Heterotopic Salivary Gland; Intraosseous Salivary Gland; Intraosseous Adenocarcinoma; Stafne Defect; Stafne Cyst

Introduction

Hundreds of cases of primary intraosseous salivary gland neoplasms have been reported since the first example was described in 1927 [1,2]. The most common malignancy has been the mucoepidermoid carcinoma, while the most common adenoma has been the pleomorphic adenoma, but a wide variety of different types have been reported [3,4]. All such tumors have, by definition, primary intraosseous origins; they were not metastatic and they did not arise from surface incursion or perforation into the bone.

The cells of origin for such tumors have long been presumed to be from mucus metaplasia of odontogenic cyst linings, or possibly multipotential odontogenic stem cells in embryonic odontogenic epithelial rests [2,4,5]. These source theories were largely based on the not infrequent presence of focal areas of mucus/goblet cells in odontogenic cyst linings, on lesions such as the sialo-odontogic (glandular odontogenic) cyst with numerous goblet cells, even small ductal structures, admixed with odontogenic lining epithelium, and on the occasional presence of salivary neoplasms adjacent to odontogenic tumors or cysts [3-5].

An alternative and rather more logical origin was proposed in 2000, when ectopic salivary glands or choristomas (normal tissue in an abnormal location) were reported within medullary tissues of more than a dozen jaws [6]. These were completely intraosseous salivary glands, not Stafne-type defects, and were found amongst 5,034 consecutive marrow samples from jawbones, providing a relative frequency rate of approximately 3 per 1,000 jawbone biopsies.

The choristomas previously mentioned were located primarily in the mandibular molar/premolar region, but a few were also seen in the maxilla, even within the marrow of the condylar head. All were mucous glands, showing normal acinar structures with cells clearly filled with mucus; they had a minimized but normal fibrous stroma and were histologically normal except that some lacked ductal structures and secreted mucus was not seen in the ducts. One of these 13 choristomas, in the condyle, was not a single gland but, rather, was a cluster of 4 small but individual glands. Additionally, only one mandibular alveolar gland and the cluster of glands in the condylar head were visible radiographically, as well defined radiolucencies with scalloped borders.

It was surprising that such choristomas had not been previously reported in the jaws, since they have been found in so many other locations throughout the body, including the skin of the neck, cervical lymph nodes, lacrimal glands, larynx, pituitary gland, even stomach and prostate (Figure 1) [4].

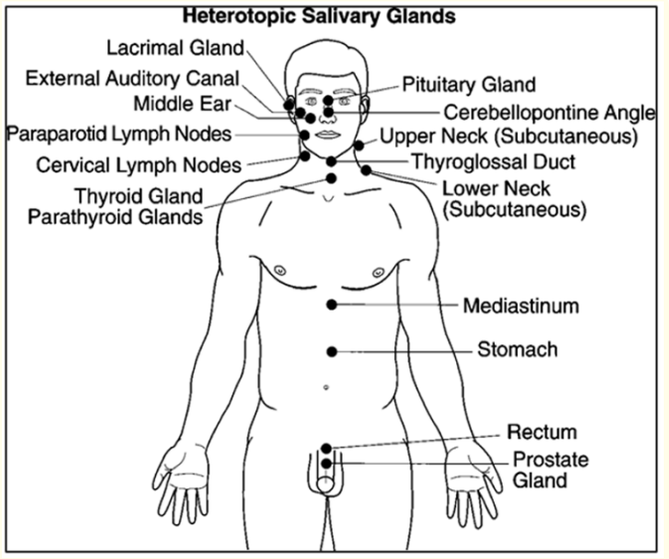

Figure 1: Locations of heterotopic salivary tissue as reported in the literature. Recent TMJ ligament cases are not noted in the drawing, but have been noted in almost 1/3 of posterior ligaments removed for temporomandibular joint dysfunction (figure used with permission) [6].

Additionally, they have been recently reported to be frequently found embedded within and/or attached to ligaments of the temporomandibular joint (TMJ) [5].

Excluding the Stafne defect lesions that have been mistakenly referred to as intraosseous, only 3 additional intraosseous jawbone choristomas have been mentioned in the literature [6-8]. One was comprised only of the choristoma while another was an incidental finding adjacent to a pleomorphic adenoma. The third was condylar head and neck; it was the most radiographically obvious, the largest yet reported (1.3 cm in greatest dimension) and the only one characterized by cone beam CT imaging [7,9]. A point of interest, perhaps significance: the latter choristoma did not expand the overlying cortex, although the cortex was somewhat thinner than normal at that site [7,8]. One can presume from this that such choristomas are not enlarging or expanding, once fully formed.

We present the sixth radiographically visible example of a salivary gland choristoma, located completely within alveolar bone. It represents the largest example yet reported, with the largest number of independent mucous glands, and it is the only one to show mucus in its ducts. This case has previously been presented (poster) to the 2023 meeting of the American Academy of Oral and Maxillofacial Pathology [9].

Materials and Methods

This case represents biopsied tissue submitted to the 3 biopsy services directed by one of the co-investigators (JEB) as routine tissue submissions. These services, combined, include more than 16,000 jawbone marrow samples examined since 1986. A total of 83 salivary gland choristomas have been noted in this group of marrow samples (unpublished data from JEB), including the 17 previously reported; all but 4 were single glands, only 2 were larger than 0.4 cm in greatest dimension, and only 4 were radiographically visible.

All clinical information for this case was taken from the biopsy request forms and submitted radiographs; no additional information was obtained from the surgeon or the subject. The tissue was submitted in buffered formalin, stained with H and E and sectioned in the usual manner, except that, once diagnosed it was completely sectioned through, to determine independent glandular structures and to assure that there was no connection to, or through, the overlying cortex. Mucicarmine staining was performed to confirm the presence of mucus andKi-67 immunostaining was performed in order to generically assess the level of proliferative activity of glandular cells. This case report is exempted from Institutional Board Review because involves too few cases.

Case Results and Discussion

Clinical

An 18-year-old male had his mandibular third molars removed, along with potential pericoronal dentigerous cysts. An incidental radiographic finding was seen distal to the crown of left third molar: an oval radiolucency with a faint, hazy opacity and a well demarcated border with small, uniform “indentations” or scalloping (Figure 3). This lobulated radiolucency appeared to have eroded into, and almost through, the inferior alveolar canal, although the area was, and had always been, completely asymptomatic, nor was the overlying cortex eroded or expanded. There was no paresthesia along the path of the inferior alveolar nerve.

The tooth was removed, and all adjacent soft tissue was curetted out, then submitted for biopsy interpretation. At 9-months post-surgery the area was just as well healed as the opposite normal side of the mandible; there was no radiographic or symptomatic sign of recurrence.

Histopathology

Microscopic examination demonstrated a thin, atrophic stratified squamous lining epithelium with an unremarkable subepithelial fibrous stroma, consistent with a dentigerous cyst. Most of the tissue sample, however, was comprised of 5 completely independent glandular structures identical to minor mucous glands of the oral mucosa, with the largest measuring 1.5 x 1.0 x 0.6 cm (Figures 3-5). All glands were histologically normal and appeared at least somewhat functional, since mucus (mucicarmine positive) could be seen in several ducts and a few areas of surgery-related (presumably) mucus extravasation were seen.

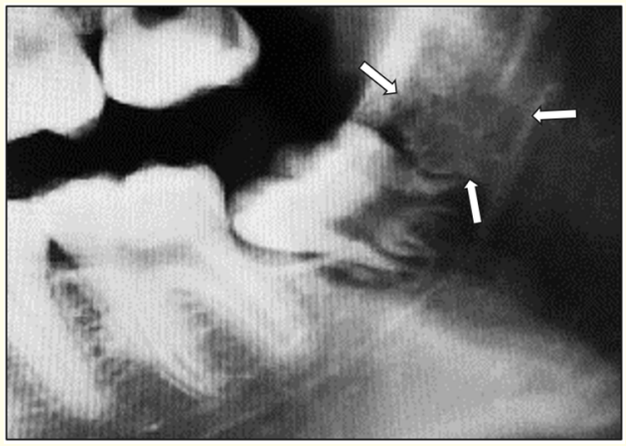

Figure 2: A honeycombed radiolucency (arrows) is seen just distal to the impacted left mandibular third molar. It is slightly more radiodense than the eruption/dentigerous cyst around the crown of the molar, and appears to have produced destruction of the superior aspect of the inferior alveolar canal wall, presumably via pressure resorption.

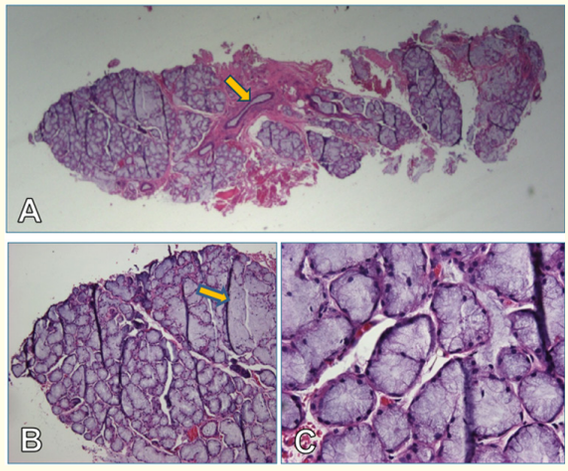

Figure 3: One of the largest of the 5 salivary glands; A) Entire gland show several lobules on right and a few large ducts (arrow); B) Higher power shos extravasation of mucus (arrow); C) Higher power show normal mucus-filled acinar cells identical to a minor mucus gland from the surface mucosa.

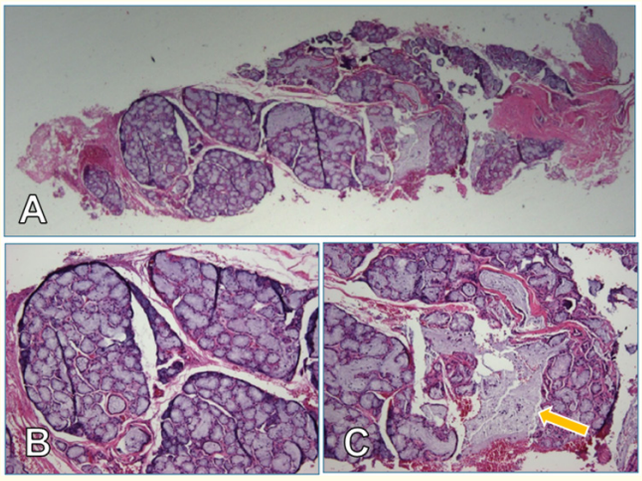

Figure 4: Second large mucous gland in the lesion. A) Elongated gland comprised of multiple lobules, with minimal fibrous stroma; B) Higher power showing fibrous stroma surrounding salivary lobules; C) Higher power showing mucus extravasation.

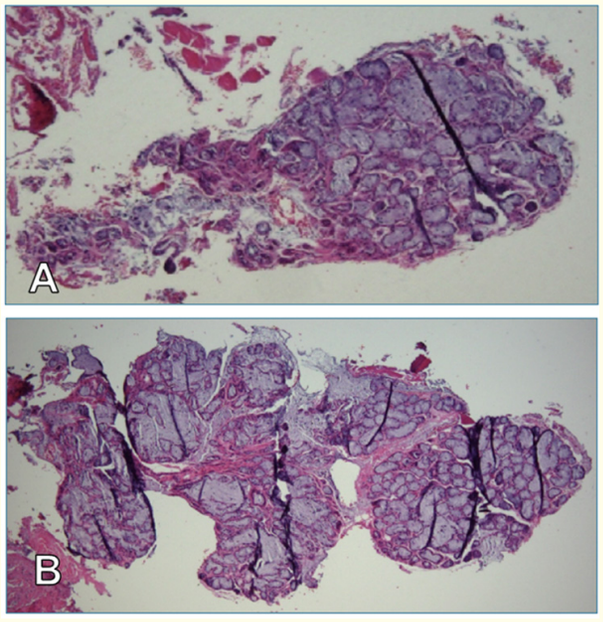

Figure 5: Two smaller mucous glands. A) Triangular shaped gland, with extravasated mucus and focal degenerative changes on left; B) Another gland with mure mucus extravasation and more fibrous stroma.

There was no evidence of serous or oncocytic glandular structures. The glands were embedded in a minimal stroma of moderately dense and mature fibrous tissue, with no inflammatory cells present. There was no obvious encapsulation, but there was a sharp demarcation between the fibrous stroma and the surrounding fatty marrow. The surrounding marrow was unremarkable. Ki-67 immunostaining was not reactive outside the nuclei, indicating that these glands were not actively enlarging or proliferating.

Discussion

We report the largest ever aggregate of mature, normal salivary tissue (mucous gland choristomas) within the marrow spaces of the jaws. It had produced no obvious difficulties for the patient, although it was easily visible radiographically and appeared to "erode" the underlying wall of the inferior alveolar canal. Our assumption is that this "pressure erosion" of the canal was actually a developmental inability of the canal to form properly in the presence of such a large mass, but we have no proof of this.

This choristoma (multiple choristomas?) is not only the largest yet reported, it is the most mature, contains the largest number of individual glands, and is the only one with intraductal mucus present. The latter suggests that the glands were more maturely functional than previously reported 17 cases, or the 83 unreported examples mention previously, perhaps because of the larger size involved. It must be said, however, that all previously reported and unreported (observed by JEB) examples appeared perfectly normal and "healthy," albeit nonfunctional [6,9].

We do not suggest that this is the only acceptable histogenetic explanation for the many intraosseous salivary neoplasms reported in the literature. Certainly, mucus-filled goblet cells are occasionally seen in the walls of dentigerous cysts, and such cells are seen, rarely, in islands of benign odontogenic epithelium within the marrow tissues. However, for these cells to become neoplastic they must not only undergo the initial metaplasia from squamous to mucus cells but must further undergo transformation into neoplastic cells. Embryonic glandular rests, moreover, have a further potential influence: the largely unknown inductive effects of the marrow itself on embryonic and developing epithelial cells, perhaps occurring before the bony cortex is even formed or matured. It is presumed that ectopic tissues within the jawbones arise from primitive stem or progenitor cells capable of becoming a variety of relative mature epithelia, and just like similar cells of the surface epithelium, they are influenced by their surrounding stroma and structures and a single cell can develop into such complicated structures as teeth and salivary glands [10,11].

It is also important to point out that the submandibular gland, and to a much lesser extent the sublingual gland, are so close to the early embryonic edge of the future mandible that missed tim-

ing or chemical cues could possibly cause incorporation of salivary tissue into the bone prior to the creation and maturation of the cortex. This is one theory for development of a Stafne cyst/defect, although with that defect the salivary tissue is a lobule of the submandibular gland and is seen to "push into" the lingual aspect of the mandible, it is not enclosed within that bone. Moreover, intraosseous glandular choristomas, at least those reported, have all been purely mucus producers, while the submandibular gland is more complex than that. Of course, the sublingual gland is pure mucus-producing, so its embryonic rests would look similar to those in the present case, but no salivary choristomas have yet been seen within the anterior mandible.

A comment should address the ability of a choristoma to become an adenocarcinoma or adenoma. A recent mandibular salivary choristoma has been seen in intimate contact with a pleomorphic adenoma, so this seems reasonably proven, but more interesting is the fact that several extragnathic choristomas have been in close contact with salivary neoplasms [8].

We do not believe that we have merely found degenerative mucosal gland remnants implanted years earlier during an extraction or other surgical procedure, or that our sample represents salivary gland anlage tumors. There was, in fact, a decided lack of degenerative changes in all cases observed by the authors, and very few, including the present case, had a history of previous surgery at the biopsy site.

A final comment should be made about the lack of choristomas in the literature. The authors believe that the large number of identified intraosseous salivary choristomas in our experience is very much related to the highly unusual presence of a massive number of jawbone marrow samples in our biopsy services. Marrow biopsies are not common in the normal practice of an oral pathology biopsy service, so one would not expect to see such uncommon phenomena. If one excluded the marrow samples from the services of one of us (JEB), there would be no salivary choristomas amongst an estimated total of more than 61,000 other bone biopsy samples reviewed in a half-century career.

Conclusion

We present the largest example yet found of a rarely reported phenomenon: 5 intraosseous salivary choristomas in one radiographically obvious mandibular cluster. It is also the most functional choristoma yet reported, and the only one to apparently prevent proper formation of the underlying inferior alveolar canal. As with previously reported examples, this provides a logical tissue of origin for the development of intraosseous salivary neoplasms. It was found adjacent to a dentigerous cyst but was not microscopically attached to the cyst.

Conflict of Interest

None of the authors have any conflict of interest, financial or otherwise, relative to this case.

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