The Korean Journal of Pathology 2013; 47: 279-283
http://dx.doi.org/10.4132/KoreanJPathol.2013.47.3.279

■ CASE STUDY ■

Heterotopic Intestinal Cyst of the Submandibular Gland: A Case Study

Mi Jung Kwon · Dong Hoon Kim
Hye-Rim Park · Soo Kee Min
Jinwon Seo · Eun Soo Kim[1]
Si Whan Kim[2] · Bumjung Park[2]

Departments of Pathology, [1]Radiology, and [2]Otorhinolaryngology-Head and Neck Surgery, Hallym University Sacred Heart Hospital, Hallym University College of Medicine, Anyang, Korea

Received: August 1, 2012
Revised: August 29, 2012
Accepted: August 31, 2012

Corresponding Author
Dong Hoon Kim, M.D.
Department of Pathology, Hallym University Sacred Heart Hospital, Hallym University College of Medicine, 22 Gwanpyeong-ro 170beon-gil, Dongan-gu, Anyang 431-796, Korea
Tel: +82-31-380-3939
Fax: +82-31-380-3936
E-mail: homed01@empal.com

Heterotopic gastrointestinal cysts are rarely found in the oral cavity. Most of these cysts are lined with gastric mucosa and involve the tongue. There have been no reported heterotopic intestinal cysts of the submandibular gland that are completely lined with colonic mucosa. An 8-year-old girl presented with an enlarging swelling in the left submandibular area, and a 4-cm unilocular cyst was fully excised. The cyst was completely lined with colonic mucosa that was surrounded by smooth muscle layer, and the lining cells were positive for CDX-2, an intestinal marker, indicating a high degree of differentiation. The pathogenesis remains unclear, but it may be related to the misplacement of embryonic rests within the oral cavity during early fetal development. Although heterotopic intestinal cysts rarely occur in the submandibular gland, they should be considered in the differential diagnosis of facial swellings in the pediatric population.

Key Words: Submandibular gland; Cysts; Heterotopia; Intestines

Heterotopic gastrointestinal cysts lined with gastric or intestinal mucosa are rarely found in the oral cavity.[1] In most cases, these cysts are composed of gastric epithelium alone or together with intestinal mucosa, whereas entirely intestinal mucosa-lined cysts are extremely rare.[1] Since Foderl[2] first introduced the case of an oral heterotopic gastrointestinal cyst in 1895, approximately 45 cases have been reported in the literature.[3-7] Heterotopic gastrointestinal cysts in the oral cavity usually involve the soft tissue of the mouth floor and tongue.[1,7-9] Systematic reviews of the literature revealed that only four published cases of heterotopic gastrointestinal cysts have been described in the submandibular region; three of these cases were exclusively composed of gastric mucosa, and the remaining case's specific mucosa type was not identified.[4,6,10,11] Herein, we report the first case of a heterotopic cyst in the submandibular gland that was entirely lined with intestinal mucosa.

CASE REPORT

An 8-year-old girl suffered from a painless swelling in the left submandibular area that had been progressively enlarging over the previous four months. There was no history of local trauma, surgery or infections on the left side of her face or neck. Her medical and family histories were also unremarkable. Physical examination revealed a soft, mobile, well-circumscribed superficial mass 3 cm in diameter in the left submandibular area. There was no swelling in the floor of the mouth, and the oral mucosa was unremarkable. Computed tomography revealed that a 2.6 cm, cone-shaped, high-density mass with internal microcalcifications was located in the left submandibular gland along the lateral surfaces of the hyoglossus muscle and genioglossus muscle. The mass extended from the anterior aspect of the submandibular gland deep into the mylohyoid, suggesting an ectopic thyroid gland or mucocele likely arising in the deep

pISSN 1738-1843
eISSN 2092-8920

portion of the submandibular gland (Fig. 1A). During the surgical excision, the mass was identified in the surrounding connective tissue of the deep portion of the submandibular gland and was completely excised from the left submandibular gland via an external cervical approach. The gross specimen measured 4×3.5×3 cm and consisted of a unilocular cystic mass that contained grayish brown mucoid material (Fig. 1B). The cyst was serially sectioned and entirely embedded for microscopic examination. Microscopic serial sections of the cystic mass demonstrated structures similar to a large bowel loop. The inner

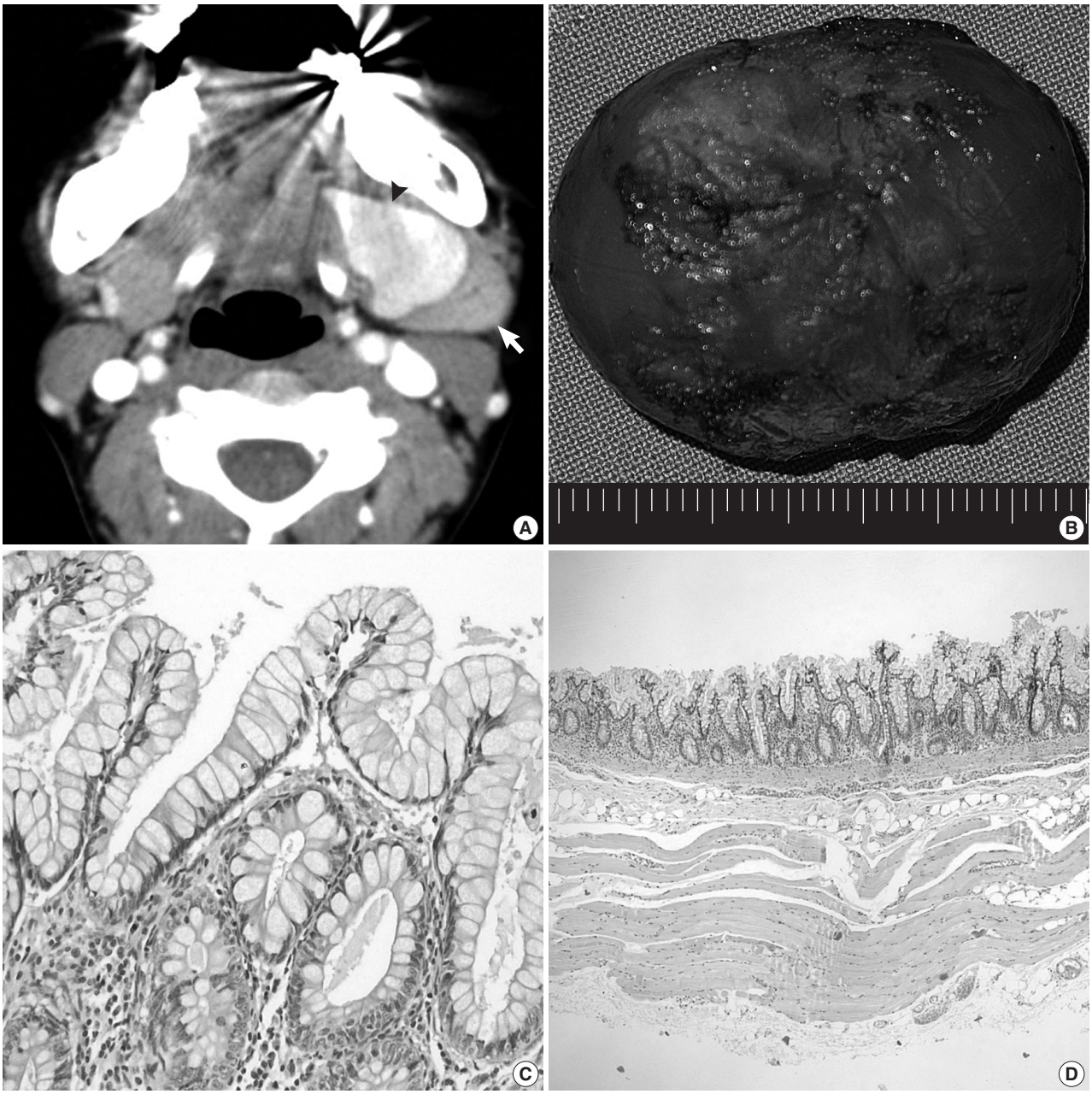

Fig. 1. (A) Computed tomography reveals that a 2.6 cm, cone-shaped, high-density cystic mass (arrowhead) is located at the left submandibular gland, and the mass extended from the anterior aspect of the submandibular gland (arrow) deep to the mylohyoid. (B) The gross specimen, totally excised from the left submandibular gland, is a unilocular cystic mass, measuring 4×3.5×3 cm. (C) The inner cystic space is lined by colonic mucosa with parallel crypts composed of columnar absorptive cells and goblet cells, and the inflammatory cells are in the lamina propria. (D) The cystic wall includes structures similar to a large bowel loop containing muscularis mucosa, submucosa with collagen bundles and capillary vessels, and bundles of smooth muscle mixed with mature adipose tissue.

 http://dx.doi.org/10.4132/KoreanJPathol.2013.47.3.279

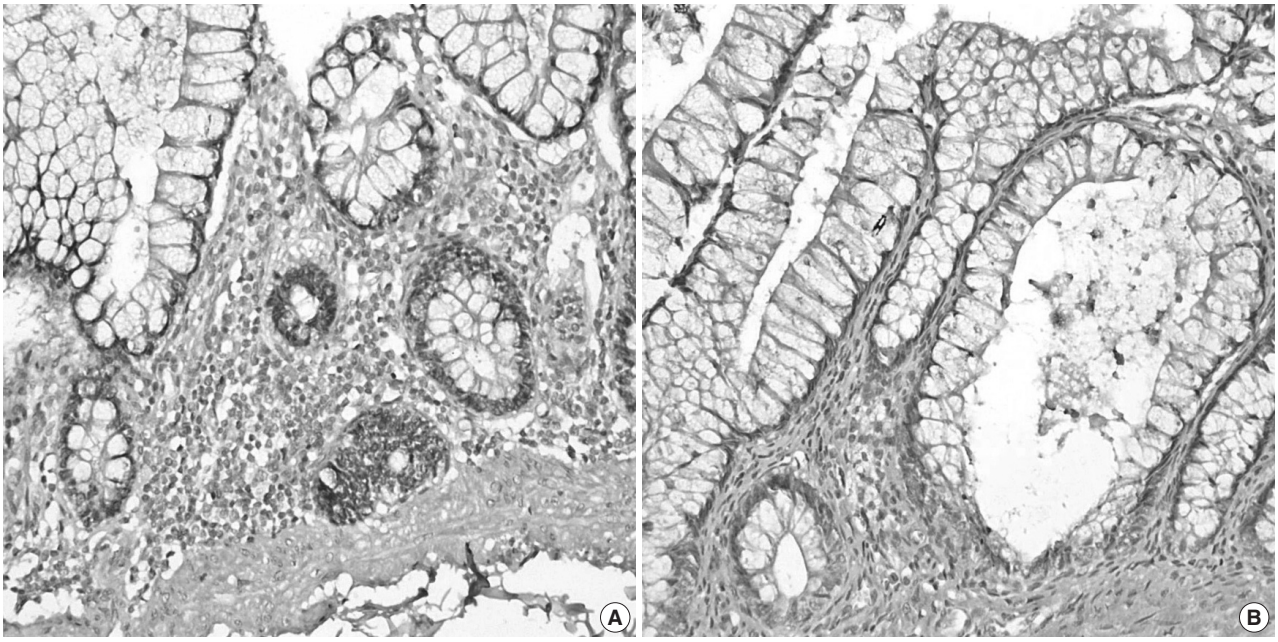

Fig. 2. Immunohistochemical stainings for CDX-2 (A) and CD10 (B). (A) CDX-2 are positive in the mucosal epithelia of the cystic mass. However, CD10 is negative in all parts of the mucosal epithelium.

cystic space was lined by colonic mucosa with parallel crypts composed of columnar absorptive cells and goblet cells, and lymphoid follicles were sometimes scattered in lamina propria-like stroma (Fig. 1C). The cystic surface was composed of colonic mucosa and separated by vague submucosa and muscle layers by the muscularis mucosa (Fig. 1D). The submucosal layer showed loosely cohesive collagen bundles and capillary vessels. The muscle layers consisted of bundles of smooth muscles mixed with mature adipose tissue. The distinction of circular and longitudinal smooth muscle bundles was not prominent in the muscle layers. Some parts of the cyst were completely denuded and were composed of inflamed granulation tissue, inflammatory cells and foamy histiocyte aggregate. The cystic wall did not include salivary gland tissue.

We characterized the cellular lineage of the cystic lining cells by immunostaining with a colonic lineage marker (CDX-2) and a small intestinal marker (CD10). The antibodies used were CDX-2 (1:100, CDX2-88, Biogenex, San Ramon, CA, USA) and CD10 (1:100, 56C6, Novocastra, Newcastle, UK), and the results of the immunohistochemical study are illustrated in Fig. 2. The mucosal epithelia of the present case were positive for CDX-2. However, CD10 was negative in the mucosal epithelium. The final pathologic diagnosis was a heterotopic intestinal cyst occurring in the submandibular gland, and the immunohistochemical results also supported the diagnosis of a heterotopic intestinal lineage. The patient was discharged from the hospital without any complications, and no recurrence was seen during the one-year follow-up period.

DISCUSSION

We reported the rare case of an 8-year-old girl with a heterotopic intestinal cyst occurring in the submandibular gland that was entirely lined with colonic mucosa. The most common site of heterotopic gastrointestinal cysts in the oral cavity is the ventral surface of the tongue extending to the floor of the mouth, and these cysts present as asymptomatic swellings. The cysts exert mass effects, including feeding difficulty and breathing problems depending on their sizes, which can range from 0.7 to 9 cm.[7] The cysts predominate in male infants or young children with an average age of 10 years, although they have been reported to occur in patients from newborns to adults of 35 years.[7] The cysts are usually lined with gastric or intestinal mucosa, sometimes with stratified squamous, simple or ciliated columnar epithelium.[6] To the best of our knowledge, there have been no reports of heterotopic intestinal cysts entirely lined with colonic mucosa in the submandibular gland.

Heterotopic gastrointestinal cysts are believed to be congenital.[7-9] The pathogenesis of these lesions remains controversial. Several theories have been proposed, but they cannot explain all types of heterotopic tissues.[7] According to the most recent theory, the cysts arise from islands of endoderm that originate from

the lining of the primitive stomodeum and become entrapped at the embryonic age of 4-5 weeks when the entire gastrointestinal endoderm remains undifferentiated.[12] Another theory is that the cysts develop from salivary retention cysts, where the salivary gland tissue is dedifferentiated and subsequently differentiated into gastrointestinal tissue.[13] In the present case, the cellular lineage of the cystic lining cells was evaluated to confirm the presence of heterotopic colonic mucosa. The mucin phenotype of the gastrointestinal tract can be used to trace back to the cell of origin.[14] CDX-2 is a marker for differentiation of intestinal-type epithelium with a goblet cell-type mucin that is predominantly expressed in the colon.[14] CD10 is an intestinal marker for the striated border on the luminal surface of small intestinal absorptive cells.[14] The cystic lining cells were positive for CDX-2, whereas they were negative for CD10. These results are consistent with the colonic lineage mucosa and indicate a high degree of differentiation. Coric *et al.*[7] evaluated the histochemical and immunohistochemical studies and also supported the hypothesis of misplacement of embryonic rests.

Preoperative differential diagnoses of cystic lesions in the submandibular gland should include swellings in the submandibular gland, such as submandibular sialoadenitis, dermoid and epidermoid cysts, branchial cleft cysts, thyroid cysts, cystic hygroma, laryngoceles, lymphomas, hydatid cysts, nonspecific cervical lymphadenopathies, and other malignancies involving the submandibular salivary gland.[15] Our case was surgically resected under a clinical diagnosis of ectopic thyroid or mucocele. Because cystic lesions in the submandibular gland are extremely rare, their definitive diagnoses often await histologic examination after surgical excision.

Histologically, differential diagnoses of cystic lesions lined with intestinal epithelium in the submandibular gland include extravasated type mucoceles,[16] dermoid cysts,[17] and enteric duplication cysts.[18] The extravasated type mucocele consists of a central cystic space containing mucin and a pseudocyst wall composed of loose vascularized connective tissue.[15] An important feature of extravasated type mucoceles is the absence of epithelial tissue in the pseudo cyst wall.[15] Dermoid cysts are usually lined with stratified squamous epithelium, and their cyst walls contain sebaceous glands and fibrocollagenous tissue.[19] The diagnostic features of enteric duplication cysts include attachment to some parts of the alimentary tract and the presence of smooth muscle layers.[7] Our case was lined with colonic epithelium and goblet cells, and the cyst wall contained no sebaceous glands. Smooth muscle fibers were noted, but the cyst did not attach to the alimentary tract.

Conservative surgical excision is the treatment of choice, and long-term follow-up is also recommended.[6,8] Recurrences are uncommon, but there is a report of local recurrence of the lesion that occurred after a period of 13 years.[20] No evidence of atypia or malignancy has been documented in heterotopic intestinal cysts.

In summary, although heterotopic intestinal cysts are very rare lesions, they should be included in the differential diagnosis of swelling in the submandibular region in the pediatric population.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Kinoshita Y, Honma Y, Otuka T, Shimura K. Gastrointestinal mucosal cyst of the oral cavity: report of case and review of literature. J Oral Maxillofac Surg 1994; 52: 1203-5.
2. Foderl O. Uber einen fall von congenitaler ranula glandulae nuhni. Arch Klin Chir 1895; 49: 530-40.
3. Kim S, Kil TJ, Hahm TH, Kim HS, Yi CK, Cha IH. Heterotopic gastrointestinal cyst of the tongue: case report. J Korean Assoc Maxillofac Plast Reconstr Surg 2011; 33: 73-6.
4. Eom JW, Hwang MS, Kang MS. A case of concurrent mature teratoma and heterotopic gastrointestinal cyst in head and neck. Korean J Otolaryngol-Head Neck Surg 2003; 46: 536-9.
5. Said-Al-Naief N, Fantasia JE, Sciubba JJ, Ruggiero S, Sachs S. Heterotopic oral gastrointestinal cyst: report of 2 cases and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1999; 88: 80-6.
6. Crivelini MM, Soubhia AM, Biazolla ER, Neto SC. Heterotopic gastrointestinal cyst partially lined with dermoid cyst epithelium. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001; 91: 686-8.
7. Corić M, Seiwerth S, Bumber Z. Congenital oral gastrointestinal cyst: an immunohistochemical analysis. Eur Arch Otorhinolaryngol 2000; 257: 459-61.
8. Eppley BL, Bell MJ, Sclaroff A. Simultaneous occurrence of dermoid and heterotopic intestinal cysts in the floor of the mouth of a newborn. J Oral Maxillofac Surg 1985; 43: 880-3.
9. Lalwani AK, Lalwani RB, Bartlett PC. Heterotopic gastric mucosal cyst of the tongue. Otolaryngol Head Neck Surg 1993; 108: 204-5.
10. Gosain AK, Wildes TO. Lateral cervical cyst containing gastric epithelium. Arch Pathol Lab Med 1988; 112: 96-8.
11. Kauffman SL, Stout AP. Tumors of the major salivary glands in children. Cancer 1963; 16: 1317-31.

 http://dx.doi.org/10.4132/KoreanJPathol.2013.47.3.279

12. Morgan WE, Jones JK, Flaitz CM, Hicks MJ. Congenital heterotopic gastrointestinal cyst of the oral cavity in a neonate: case report and review of literature. Int J Pediatr Otorhinolaryngol 1996; 36: 69-77.
13. Woolgar JA, Smith AJ. Heterotopic gastrointestinal cyst of oral cavity: a developmental lesion? Oral Surg Oral Med Oral Pathol 1988; 66: 223-5.
14. Shiroshita H, Watanabe H, Ajioka Y, Watanabe G, Nishikura K, Kitano S. Re-evaluation of mucin phenotypes of gastric minute well-differentiated-type adenocarcinomas using a series of HGM, MUC5AC, MUC6, M-GGMC, MUC2 and CD10 stains. Pathol Int 2004; 54: 311-21.
15. Ozturk K, Yaman H, Arbag H, Koroglu D, Toy H. Submandibular gland mucocele: report of two cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005; 100: 732-5.
16. Hze-Khoong EP, Xu L, Shen S, Yin X, Wang L, Zhang C. Submandibular gland mucocele associated with a mixed ranula. Oral Surg Oral Med Oral Pathol Oral Radiol 2012; 113: e6-9.
17. Gattia KV, Kacouchia NB, Kouassi YM, Kouassi-Ndjeundo J, Vroh Bi TS, Abouna AD. Submandibular dermoid cyst extended to the cervical region. Rev Stomatol Chir Maxillofac 2012; 113: 173-5.
18. Tucker R, Maddalozzo J, Chou P. Sublingual enteric duplication cyst. Arch Pathol Lab Med 2000; 124: 614-5.
19. Tas A, Yagiz R, Altaner S, Karasalihoğlu AR. Dermoid cyst of the parotid gland: first pediatric case. Int J Pediatr Otorhinolaryngol 2010; 74: 216-7.
20. Daley TD, Wysocki GP, Lovas GL, Smout MS. Heterotopic gastric cyst of the oral cavity. Head Neck Surg 1984; 7: 168-71.