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

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 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...
portion of the submandibular gland (Fig. 1A). During the sur-
gical excision, the mass was identified in the surrounding con-
nective 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

![Image](http://www.koreanjpathol.org)

**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.
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. 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. The cysts are usually lined with gastric or intestinal mucosa, sometimes with stratified squamous, simple or ciliated columnar epithelium. 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. The pathogenesis of these lesions remains controversial. Several theories have been proposed, but they cannot explain all types of heterotopic tissues. 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. Another theory is that the cysts develop from salivary retention cysts, where the salivary gland tissue is dedifferentiated and subsequently differentiated into gastrointestinal tissue. 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. CDX-2 is a marker for differentiation of intestinal-type epithelium with a goblet cell-type mucin that is predominantly expressed in the colon. CD10 is an intestinal marker for the striated border on the luminal surface of small intestinal absorptive cells. 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 al. 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, laryngoeles, lymphomas, hydatid cysts, nonspecific cervical lymphadenopathies, and other malignancies involving the submandibular salivary gland. 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 mucocysts, dermoid cysts, and enteric duplication cysts. The extravasated type mucocyst consists of a central cystic space containing mucin and a pseudocyst wall composed of loose vascularized connective tissue. An important feature of extravasated type mucocysts is the absence of epithelial tissue in the pseudo cyst wall. Dermoid cysts are usually lined with stratified squamous epithelium, and their cyst walls contain sebaceous glands and fibrocollagenous tissue. The diagnostic features of enteric duplication cysts include attachment to some parts of the alimentary tract and the presence of smooth muscle layers. 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. Recurrences are uncommon, but there is a report of local recurrence of the lesion that occurred after a period of 13 years. 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.

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