Polymorphous low-grade adenocarcinoma of the palate: a case report and a comparative immunohistochemical study with adenoid cystic carcinoma.

Watcharaporn Thosaporn , Anak Iamaroon* , Nop Porntrakulseri**, Pongsak Mahanupab***, Siriwan Siripalangkanont*****

Abstract

Polymorphous low-grade adenocarcinoma (PLGA) is an uncommon malignant tumor of the salivary glands. Histologically, PLGA may have overlapping features with adenoid cystic carcinoma (ACC), posing difficulty in differentiating one from the other. We, here, presented a case of PLGA and a comparative immunohistochemical study with ACC by the use of a panel of antibodies. The patient was a 52-year-old Thai female who had a painless mass on the right side of the palate. An incisional biopsy revealed characteristic histopathologic features of PLGA. A partial maxillectomy was performed without any complication. On a two-year follow-up, the patient remained healthy and had no evidence of recurrence of the tumor. The results of the comparative immunohistochemical profiles between PLGA and ACC revealed no clear differences between these two tumors. Further studies with different markers may prove to be beneficial in differentiating between PLGA and ACC.

Key words: adenoid cystic carcinoma, immunohistochemistry, polymorphous low-grade adenocarcinoma

Introduction

Polymorphous low-grade adenocarcinoma (PLGA) was recently recognized as a new entity of a malignant tumor of the salivary glands[1]. Although PLGA occurs almost exclusively in the minor salivary glands of the oral cavity[2], an involvement of the extraoral sites including the nasal cavity and nasopharynx have been documented[3]. Most often, PLGA clinically presents as a painless mass with a slow growth. Less frequent symptoms have been reported as otalgia, odynophagia, tinnitus, and airway obstruction. The duration of symptoms varies from 2 weeks to 30 years. PLGA is commonly found in older adults with a peak age of 50-70 years. The most common location of PLGA is the palate, followed by the upper lip and buccal mucosa. Two thirds of PLGA cases occur in females. Predisposing factors associated with PLGA are unknown. Histologically, PLGA can be similar to some other salivary gland tumors, especially ad-

* *Department of Odontology & Oral Pathology Faculty of Dentistry, Chiang Mai University, Chiang Mai*
** *Dental Section, Lamphun Provincial Hospital, Lamphun*
*** *Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai*
**** *Dental Section, Nakornping Hospital, Chiang Mai*

enoid cystic carcinoma (ACC). The differentiation between PLGA and ACC is essential since the prognosis between two tumors is vastly different.

The purpose of the present study was to report a rare case of PLGA with a comparative study between PLGA and ACC by means of immunohistochemical technique.

Case report

The patient was a 52-year-old Thai female who presented to Lamphun Provincial Hospital, Thailand in 1999 with one-day spontaneous bleeding at the gingiva of the maxillary anterior teeth. The medical history included idiopathic thrombocytopenia and thyrotoxicosis. On extraoral examination, the patient was slightly pale and showed facial asymmetry. Cervical lymph nodes were not palpable. Intraoral examination revealed spontaneous bleeding at the marginal gingiva of the maxillary anterior teeth and a smooth, pink, exophytic mass on the right side of the palate, 3.5x3.0x0.5 cm in size (Fig. 1). The mass extended from the right maxillary tuberosity to the midline of the hard palate and from the palatal gingiva of the permanent right second premolar to the anterior part of the soft palate. The patient admitted having the mass for approximately a year. The mass was slowly growing and painless. Incisional biopsy was then performed and the specimen was forwarded to the Department of Odontology and Oral Pathology, Faculty of Dentistry, Chiang Mai University for histopathologic examinations.

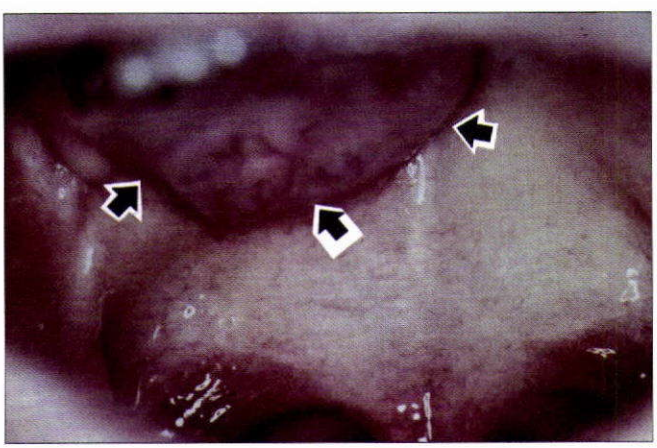

Fig. 1 The clinical feature of PLGA showing a smooth, pink, exophytic mass on the right side of the palate (arrows).

Radiography

The Water's and lateral skull radiographs showed radiopacity at the right maxillary sinus and thickened mucosa at the left maxillary sinus, suggesting a sinusitis. The computerized tomographs with the axial and coronal scans of the paranasal sinuses revealed a mass at the right hard and soft palates with superior extension into the right nasal cavity and the right maxillary sinus (Fig. 2). Bony destruction of the hard palate, lower medial wall of the right maxillary sinus, and the lower right nasal turbinate was evident. The nasopharynx was normal and the base of the skull and the orbits remained intact. The radiograph of the chest area showed a slightly enlarged heart. There was no infiltration or effusion of the lungs.

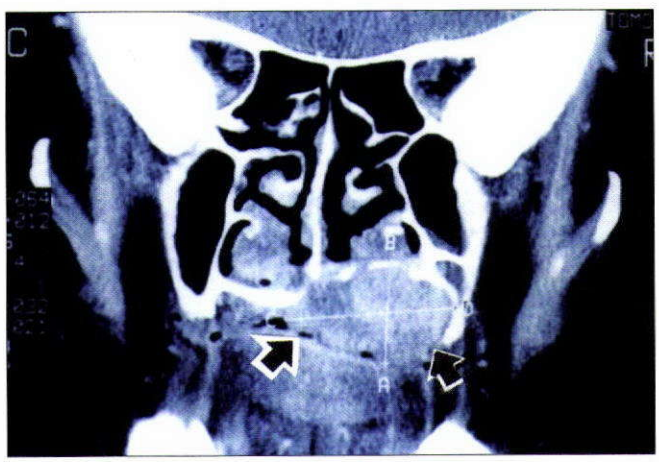

Fig. 2 The computerized tomograph showing the tumor mass (arrows) located at the right side of the palate with superior extension into the nasal cavity and the right maxillary sinus.

Histopathology

Microscopically, the mucosal specimen exhibited non-encapsulated proliferation of spindle-shaped, cuboid or columnar cells with round or ovoid pale basophilic nuclei. The neoplastic cells were arranged in variable patterns including duct-like structures or trabecular, cystic, cribiform or single file patterns at the periphery of the tumor mass (Figs. 3-6). Focally, a papillary growth was observed. Bone invasion by the tumor cells was evident. The connective tissue stroma varied from fibrous, mucoid to hyalinized types. A special stain, alcian blue-periodic acid Schiff (PAS), demonstrated heavy extracellular collection of mucoid material. Collectively, these findings indicated the diagnosis of PLGA.

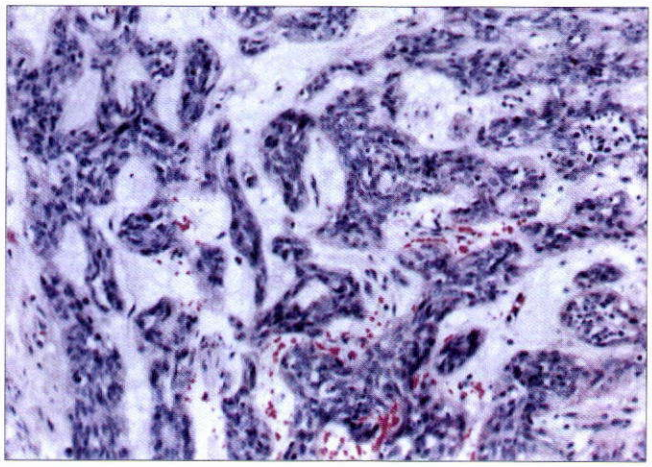

Fig. 3 *The histopathologic feature of PLGA exhibiting a trabecular pattern and mucoid stroma. (hematoxylin & eosin stain, original magnification x100)*

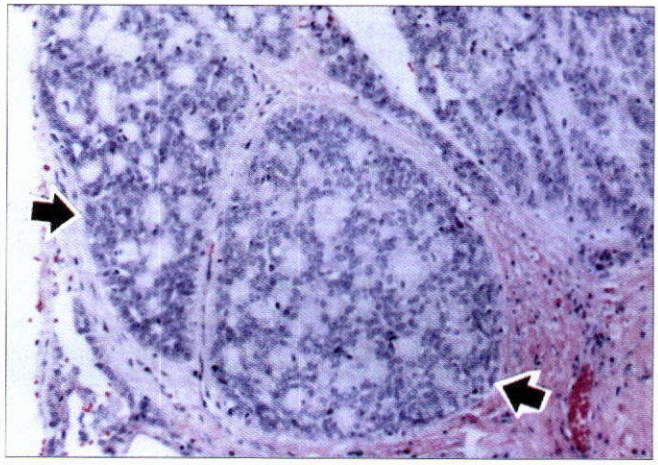

Fig. 4 *The histopathologic feature of PLGA exhibiting a cribiform pattern (arrows). (hematoxylin & eosin stain, original magnification x100)*

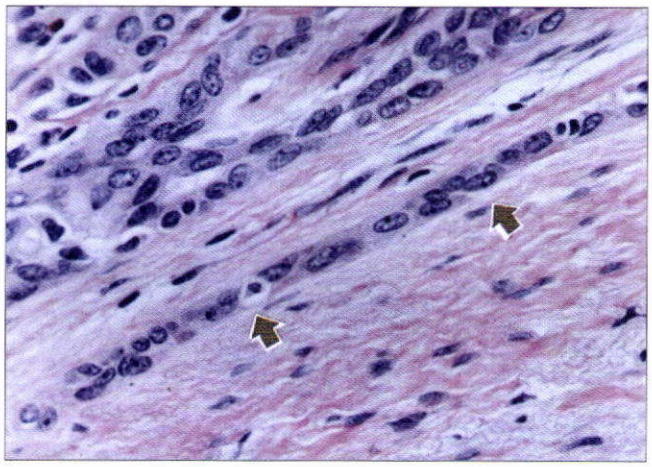

Fig. 5 *At the periphery of the neoplasia, a single-file pattern is shown (arrows). (hematoxylin & eosin stain, original magnification x400)*

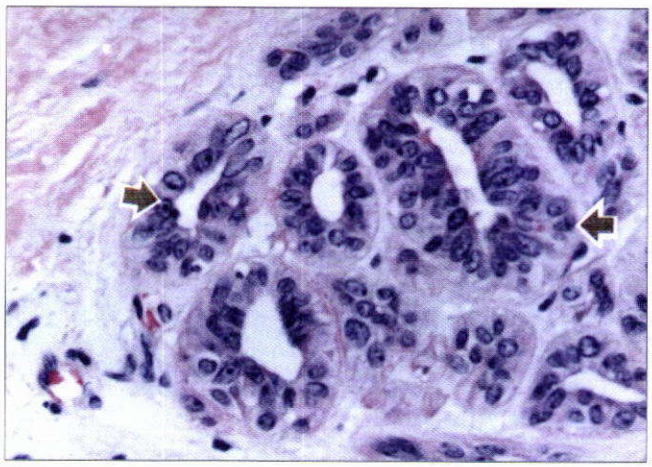

Fig. 6 *The histopathologic feature of PLGA exhibiting duct-like structures (arrows). (hematoxylin & eosin stain, original magnification x400)*

Immunohistochemistry

To compare the profiles of immunostaining of PLGA with ACC, a panel of monoclonal and polyclonal antibodies; including anti-cytokeratin (CK), anti-S-100, anti-muscle-specific actin (MSA), anti-carcinoembryonic antigen (CEA), anti-epithelial membrane antigen (EMA), anti-glial fibrillary acidic protein (GFAP), and anti-vimentin antibodies; was utilized. A case of ACC from the archives of the Department of Pathology, Faculty of Medicine, Chiang Mai University was used to compare with the present case of PLGA. The standard immunoperoxidase staining (biotin-streptavidin, B-SA, technique) was performed. The concentrations and types of the primary antibodies were summarized in Table 1. All antibodies used were purchased from Dako, Denmark. The immunoreactivity of each antibody used was semiquantified with the criteria for interpretation as follows: no staining (-), focal staining if 1-10% of tumor cells were stained (+/-), mild staining if 11-50% of tumor cells were stained (+), moderate staining if 51-90% of tumor cells were stained (2+), generalized staining if 91-100% of tumor cells were stained (3+). The results of the immunoreactivity of each antibody in PLGA and ACC were summarized in Table 2. Of these, PLGA and ACC showed moderate or generalized positive immunoreactivity with anti-CK and anti-S-100 antibodies (Figs. 7-10) while the

other antibodies stained PLGA only focally. MSA and EMA were the only two antibodies that showed different staining patterns between PLGA and ACC.

Treatment and follow-up

As the diagnosis of PLGA was established, the tumor was surgically removed. A partial maxillectomy of the right side of the maxilla including the floor of the nose and a skin graft were performed without any complication (Fig. 11). Two units of the whole blood were given during the operation. The surgical specimen was forwarded for histopathologic examinations. Postoperatively, an immediate obturator was placed over the defect. On a three-month follow-up, the patient showed a complete healing of the wound (Fig. 12). The patient could self-feed and speak but with hypernasality sound. On a two-year follow-up, the patient remained healthy and there was no evidence of recurrence of the tumor.

Table 1 *Types and concentrations of antibodies used in the study.*

Primary Antibody	Type	Concentration
CK	Monoclonal	1:500
S-100	Polyclonal	1:200
MSA	Monoclonal	1:50
CEA	Polyclonal	1:300
EMA	Monoclonal	1:100
GFAP	Polyclonal	1:300
Vimentin	Monoclonal	1:100

Table 2 *Immunohistochemical profiles of PLGA and ACC.*

Antibodies	PLGA	ACC
CK	2+	2+
S-100	3+	2+
MSA	+/-	2+
CEA	+/-	+/-
EMA	+/-	2+
GFAP	+/-	-
Vimentin	+/-	+

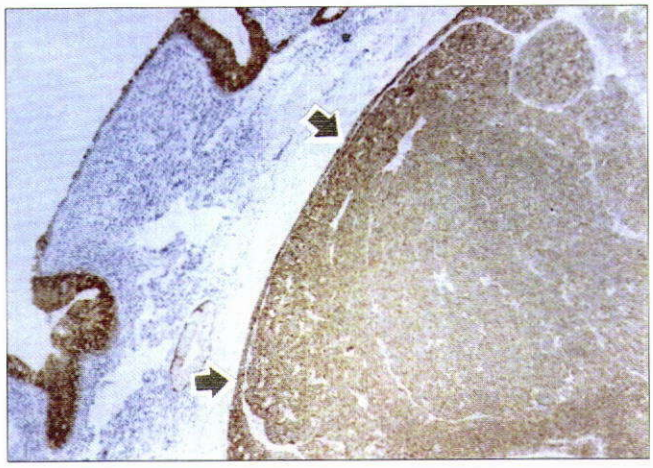

Fig. 7 The tumor cells of PLGA were intensely stained with anti-CK antibody (arrows). Laterally, the mucosal epithelium, as an internal control, was also stained. (B-SA technique, original magnification x40)

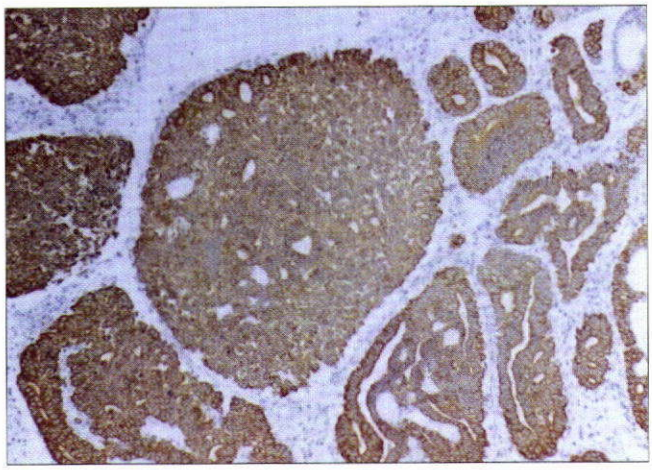

Fig. 8 The tumor cells of ACC showed positive immunoreactivity with anti-CK antibody. (B-SA technique, original magnification x100)

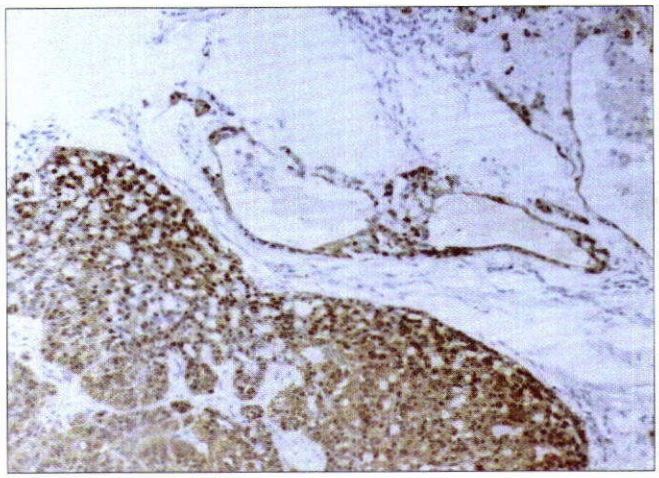

Fig. 9 S-100 was generally stained in the tumor cells of PLGA. (B-SA technique, original magnification x100)

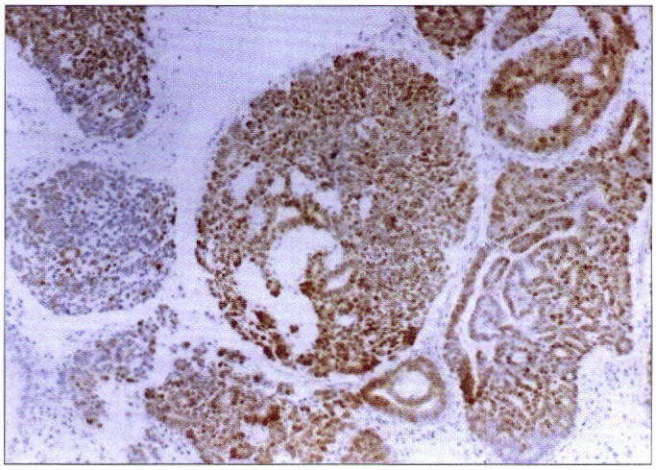

Fig. 10 Most tumor cells of ACC were stained with anti-S-100 antibody. (B-SA technique, original magnification x100)

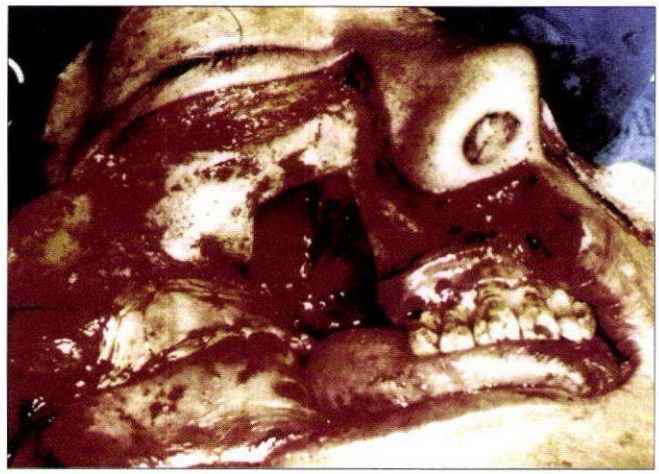

Fig. 11 On operation, the tumor was removed by a partial maxillectomy.

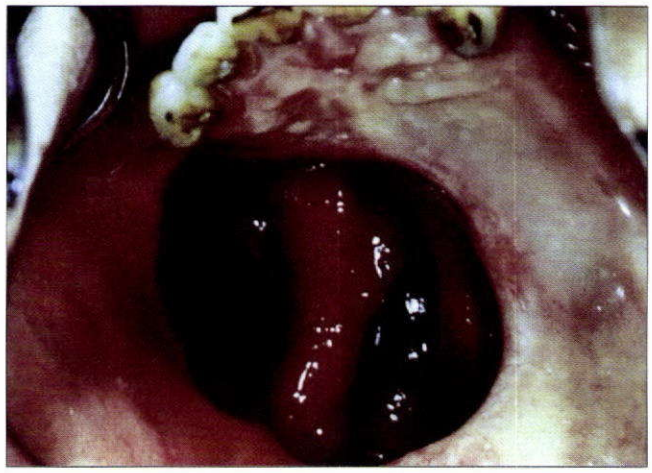

Fig. 12 On three-month follow-up, the wound completely healed with an oro-nasal communication.

Discussion

Diagnosis of PLGA on a histopathologic basis can be quite challenging since PLGA may mimic several other benign and malignant tumors of the salivary glands such as; benign mixed tumor (pleomorphic adenoma), monomorphic adenomas, and ACC, as also observed in the present case. Of these, ACC is perhaps the most difficult tumor to differentiate histologically from PLGA[3]. The clinical behavior of ACC is much more aggressive than that of PLGA, making differentiation between these two tumors important for therapeutic and prognostic purposes[4]. Based on clinical and histologic examinations, PLGA may be distinguished from ACC by the following criteria[2,3]. 1) Characteristically, ACC clinically presents as a painful mass, while PLGA is usually asymptomatic. 2) Histologically, PLGA shows various growth patterns; solid, glandular, cribiform, ductular, tubular, trabecular, cystic, single-file, and papillary patterns, so-called polymorphous low-grade adenocarcinoma, whereas ACC has only three prominent morphologic patterns; cribiform, tubular, and solid

patterns. 3) The nuclei of PLGA are usually paler than those of ACC. 4) PLGA commonly has a single-file pattern that is often located at the periphery of the tumor. According to the above criteria, the clinical and histologic profiles of our case were consistent with PLGA.

Several attempts have been made to characterize these two tumors by means of immunohistochemical studies. The results showed that PLGA consistently yielded positive immunoreactivity to anti-CK, anti-EMA, anti-S-100, and anti-vimentin antibodies[3-8]. CEA and MSA were variably stained and GFAP was not stained or focally stained in PLGA[3,5,7,8]. ACC showed positive immunoreactivity with anti-CEA, anti-EMA, anti-CK, anti-MSA, and anti-S-100[3,8]. In ACC, vimentin was variably stained[4,9,10] and GFAP showed no staining[8]. These findings were essentially similar to those of our study except that EMA and vimentin were stained only focally in PLGA and CEA was focally stained in ACC. Taken together, we agreed with the conclusion made by Simpson et al[4] that the staining profiles of the two tumors were not sufficiently dissimilar to be of practical value. Therefore, the histopathologic features remain the most reliable criteria to distinguish between these two tumors.

The prognosis of PLGA is relatively good. Although recurrence of PLGA can occur, distant metastases appear rare[2]. In the cases with adequate follow-up ranging from a few months to 25 years after treatment, 80% of patients were alive and well[3]. Likewise, we, here, reported a case of PLGA with a successful treatment with two-year follow-up, confirming an indolent nature of PLGA.

In conclusion, a rare case of PLGA of the oral cavity was reported. The immunohistochemical staining with several markers appeared unable to differentiate PLGA from ACC. Further studies with a larger sample size and different types of markers will be needed to distinguish between these two tumors.

Acknowledgements

The authors are thankful to Mrs. R. Kitikamthon and the staff of the Department of Pathology, Faculty of Medicine, Chiang Mai University for the technical assistance.

References

1. Evans HL, Batsakis JG. Polymorphous low-grade adenocarcinoma of minor salivary glands. A study of 14 cases of a distinctive neoplasm. ***Cancer*** 1984; 53:935-42.
2. Neville BW, Damm DD, Allen CM, Bouquot JE. Oral and maxillofacial pathology. Philadelphia: WB Saunders; 1995. p. 355-8.
3. Wenig BM, Gnepp DR. Polymorphous low-grade adenocarcinoma of the salivary glands. In: Ellis GL, Auclair PL, Gnepp DR, editors. Surgical pathology of the salivary glands. Philadelphia: WB Saunders; 1991. p. 390-411.
4. Simpson RH, Clarke TJ, Sarsfield PTL, Gluckman PGC, Babajews AV. Polymorphous low-grade adenocarcinoma of the salivary glands: a clinicopathological comparison with adenoid cystic carcinoma. ***Histopathol*** 1991; 19:121-9.
5. Anderson C, Krutchkoff D, Pedersen C, Cartun R, Berman M. Polymorphous low grade adenocarcinoma of minor salivary gland: a clinicopathologic and comparative immunohistochemical study. ***Mod Pathol*** 1990;3:76-82.
6. Araujo V, Sousa S, Jaeger M, Jaeger R, Loyola A, Crivelini M, et al. Characterization of the cellular component of polymorphous low-grade adenocarcinoma by immunohistochemistry and electron microscopy. ***Oral Oncol*** 1999;35:164-72.
7. Perez-Ordonez B, Linkov I, Huvos AG. Polymorphous low-grade adenocarcinoma of minor salivary glands: a study of 17 cases with emphasis on cell differentiation. ***Histopathol*** 1998;32:521-9.
8. Regezi JA, Zarbo RJ, Stewart JCB, Courtney RM. Polymorphous low-grade adenocarcinoma of minor salivary gland. ***Oral Surg Oral Med Oral Pathol*** 1991; 71:469-75.
9. Bergman R, Lichtig C, Moscona RA, Friedman-Birnbaum R. A comparative immunohistochemical study of adenoid cystic carcinoma of the skin and salivary glands. ***Am J Dermatopathol*** 1991;13:162-8.
10. Takahashi H, Tsuda N, Fujita S, Tezuka F, Okabe H. Immunohistochemical investigation of vimentin, neuron-specific enolase, alpha 1-antichymotrypsin and alpha 1-antitrypsin in adenoid cystic carcinoma of the salivary gland. ***Acta Pathol Jpn*** 1990;40:655-64.

บทวิทยาการ

โพลิมอร์ฟัสโลว์เกรดอะดิโนคาร์ซิโนมาของเพดานช่องปาก : รายงานผู้ป่วย 1 ราย และการศึกษาเปรียบเทียบกับอะดินอยด์ซิสติกคาร์ซิโนมาโดยเทคนิคอิมมูโนฮิสโตเคมี

วัชราภรณ์ ทศพร, อะนัฆ เอี่ยมอรุณ*, นพ พรตระกูลเสรี**, พงษ์ศักดิ์ มหานุภาพ***, ศิริวรรณ สิริพลังคานนท์*****

บทคัดย่อ

โพลิมอร์ฟัสโลว์เกรดอะดิโนคาร์ซิโนมา (PLGA) เป็นเนื้องอกชนิดร้ายแรงของต่อมน้ำลายที่พบได้ไม่บ่อย ซึ่งอาจมีลักษณะทางจุลพยาธิวิทยาใกล้เคียงกับเนื้องอกชนิดอะดินอยด์ซิสติกคาร์ซิโนมา (ACC) ดังนั้นการให้การวินิจฉัยแยกโรคระหว่างเนื้องอกทั้งสองชนิดจึงทำได้ค่อนข้างยาก ในการศึกษาครั้งนี้เป็นการรายงานผู้ป่วยหนึ่งรายที่เป็น PLGA และได้มีการศึกษาเปรียบเทียบลักษณะการติดสีระหว่าง PLGA กับ ACC โดยเทคนิคอิมมูโนฮิสโตเคมี ผู้ป่วยเป็นหญิงไทยอายุ 52 ปี มาพบทันตแพทย์ด้วยอาการมีก้อนที่บริเวณเพดานปากข้างขวาซึ่งไม่มีอาการเจ็บปวด จากการตรวจชิ้นเนื้อพบว่าเนื้องอกดังกล่าวมีลักษณะสำคัญทางจุลพยาธิวิทยาตรงกับ PLGA ต่อมาผู้ป่วยได้รับการรักษาโดยการตัดกระดูกขากรรไกรบนออกไปเป็นบางส่วนโดยไม่มีอาการแทรกซ้อน และจากการเฝ้าติดตามผู้ป่วยเป็นระยะเวลา 2 ปี ผู้ป่วยแข็งแรงดีและไม่พบว่ามีการกลับเป็นซ้ำใหม่ของ PLGA ผลของการศึกษาเปรียบเทียบลักษณะการติดสีระหว่าง PLGA กับ ACC โดยใช้เทคนิคอิมมูโนฮิสโตเคมี พบว่าไม่มีความแตกต่างกันอย่างชัดเจนระหว่างเนื้องอกทั้งสองชนิดนี้ การศึกษาเพิ่มเติมในอนาคตโดยการใช้แอนติบอดีชนิดอื่นที่เหมาะสมอาจมีประโยชน์ในการแยกเนื้องอกทั้งสองชนิดออกจากกันได้

** ภาควิชาทันตวิทยา-พยาธิวิทยาช่องปาก คณะทันตแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่,*

*** แผนกทันตกรรม โรงพยาบาลลำพูน,*

**** ภาควิชาพยาธิวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่,*

***** แผนกทันตกรรม โรงพยาบาลนครพิงค์ จ.เชียงใหม่*