A 78 year-old male complained of mild pain at a gingival mass on his anterior mandible, injured and ulcerated by autobicycle accident six months ago. He had suffered from uncontrolled diabetes. The tumor specimens from his chin and gingiva were examined by immunohistochemical method, and their microsections showed poorly differentiated polygonal tumor cells, occasionally formed ductal structures. The tumor cells grew infiltratively into adjacent fibromuscular tissue with frequent atypical mitosis, exhibiting the features of poorly differentiated adenocarcinoma. However, in the computed tomography(CT) view a tumor mass was also found in his lung, and diagnosed lung cancer. In the immunohistochemical observation the tumor cells were strongly positive for thyroid transcription factor 1 (TTF-1), cytokeratin 7, PCNA, p53, and PIM-1, occasionally positive for p63, but sparsely positive for survivin. The tumor cells were almost negative for S-100, cytokeratin 14, and α-SMA, while the vascular structures in the tumor tissue were conspicuously demarcated by the stains of α-SMA. Taken together, the present case was finally diagnosed poorly differentiated adenocarcinoma, metastasized from lung adenocarcinoma. And it was presumed that the metastatic tumor cells tended to be anchored in the traumatized area of anterior mandible, where the wound healing was undergoing with de novo angiogenesis and the activation of different cytokines and growth factors.

Key words: Poorly Differentiated Adenocarcinoma, Metastasis, Lung Cancer, Jaw Trauma
(1) adenocarcinoma, (2) poorly differentiated carcinoma, and (3) squamous cell carcinoma. Informatively, only 6.35% of the patients developed symptoms prior to the diagnosis of primary disease.

While the reports of malignant tumors that have metastasized to the oral regions have been relatively rare, a metastasis to the mandibular gingiva from lung cancers is most unusual. However, in this study a 78 years old male showed a metastatic tumor of poorly differentiated adenocarcinoma was found in the anterior mandible, where he was injured by autobicycle accident six months ago, and then he was asymptomatic and never noticed his lung cancer. After the biopsy examination of oral lesion, which was primarily diagnosed a malignant tumor, he was referred to check his whole body condition to prepare the chemotherapy, and his chest X-ray view clearly disclosed a tumor mass in his lung. However, it was also reported that the primary lesions of two lung carcinomas were late-
diagnosed after the detection of the gingival lesions.

Here, we demonstrated a case of poorly differentiated adenocarcinoma in anterior mandible, metastasized from lung cancer, and also discussed the pathogenetic mechanism of tumor metastasis from lung cancer to the injured mandible.

II. Case report

A 78 years old male visited Gangneung-Wonju National University Dental Hospital with complaining of mild pain at a rapidly growing gingival mass on his anterior mandible, which was injured and ulcerated by autobicycle accident six months ago. He had suffered from uncontrolled diabetes. The panoramic X-ray view showed that the tumor mass involved the whole periapical area of
mandibular incisors extended to the mandibular symphysis, and in the CT view the whole marrow space of mandible became radiolucent, which was also suspicious for the tumor involvement. The cross-sectional view of anterior mandible disclosed the bony destruction in the lingual cortical bone by the tumor involvement.

In the clinical observation the tumor mass was associated with inflamed gingival granuloma and swelled to the whole chin area, at which the traumatic ulceration was still remained. The tumor specimens were examined by immunohistochemical methods. The microsections showed poorly differentiated polygonal tumor cells, occasionally formed ductal structures. The tumor cells grew infiltratively into adjacent fibromuscular tissue with frequent atypical mitosis, and were poorly differentiated mimicking anaplastic adenocarcinoma. However, in the computed tomography (CT) view there found a tumor mass in his lung, subsequently diagnosed lung cancer. In the immunohistochemical (IHC) stainings of thyroid transcription factor-1 (TTF-1, NK2 homeobox 1), cytokeratin 7, cytokeratin 14, proliferating cell nuclear antigen (PCNA), p53, p63, PIM-1, survivin, S-100, and α-smooth muscle actin (α-SMA), the tumor cells were frequently positive for PCNA, p53, diffusely positive for PIM-1, occasionally positive for p63, but sparsely positive for survivin. However, the tumor cells were strongly positive for TTF-1 in their nuclei, and positive for cytokeratin 7 in their cell membranes and cytoplasm. On the other hand, the immunoreactions of S-100, α-SMA, and cytokeratin 14 were not found in the tumor cells, but the S-100 was conspicuously positive in the dendritic histiocytes infiltrated into the tumor tissue, and the α-SMA was positive in the vascular smooth muscle of pericytes, forming the tumor angiogenesis.

Taken together, the present case was finally diagnosed poorly differentiated adenocarcinoma metastasized from lung adenocarcinoma to the traumatized area of anterior mandible, where wound healing was undergoing with de novo angiogenesis and activation of different cytokines and growth factors. The usage of the biopsy specimens filed in the Department of Oral Pathology was approved by Life Ethic Committee (KWNUDH-IRB2009-16-3).

III. Discussion

Metastatic tumors of the oral cavity are rare, representing about 1% of oral tumors and affect jaws much more frequently than soft tissues. According to the literature, the major primary sites presenting oral metastasis were the lung, the liver, and the kidney in that decreasing order. Broken down, the prevalent primary sites are the lung, kidney, liver, and prostate for men, breast, female genital organs (FGO), kidney, and colorectum for women. The metastatic lesions that occurred in the mandible were reported more often in the molar regions contrary to the present case, which occurred in the anterior mandible.

The prognosis was better for patients with tumors in the upper 2/3 of the neck than for patients with metastasis in the lower 1/3 of the neck. The prognosis for metastatic adenocarcinoma is poor, but early diagnosis and treatment is essential in order to prevent the pain and discomfort associated with the ulceration, the infection, and the local tissue destruction by the lesions.

Soft tissue oral metastasis from lung adenocarcinoma is extremely rare, and the limited information exists regarding the presentation and work-up of metastatic lung carcinoma into the oral soft tissue. Metastatic lesions from all sources were typically diagnosed in patients in their fifth to seventh decade, with the most common sites of soft tissue metastasis being the gingiva and alveolar mu-
cosa of the mandible. In almost one quarter of patients with a metastatic lesion in the oral cavity was the first indication of an undiscovered primary malignancy.\(^9\) They rapidly grow and tend to bleed and ulcerate.\(^6,10-12\) Histologic and immunohistochemical characteristics can be helpful in identifying the primary tumor.\(^13\) It is essential to distinguish the metastatic tumor from the malignant tumors common in the metastasized region, i.e., squamous cell carcinoma of oral mucosa epithelium, and adenocarcinoma of the minor salivary glands in the oro-facial region.\(^14\)

In the present case the immunohistochemical staining was performed using the different antisera. The tumor cells were strongly positive for PCNA, p53, diffusely positive for PIM-1, occasionally positive for p63, but sparsely positive for survivin. These expressions might imply that the tumor cells were in the transformed processes of abnormal proliferation in antiapoptotic environment. And the tumor cells were strongly positive for TTF-1 in their nuclei, and positive for cytokeratin 7 in their cell membranes and cytoplasms. And more the oncogene of PIM-1, known as frequently positive in lung cancer\(^15,16\), was diffusely expressed in the tumor cells. These findings indicated that the metastatic poorly differentiated adenocarcinoma was originated from lung adenocarcinoma, because TTF-1 and cytokeratin 7 could be used for a biomarker of lung and thyroid tumor cells and for a biomarker of adenocarcinoma, respective.\(^17,20\) However, in this case the patient refused the surgical removal of the lung mass, thus the further pathological examination was not performed.

On the other hand, the immunoreactions of S-100, \(\alpha\)-SMA, and cytokeratin 14 were not found in the tumor cells, but the S-100 was positive in the dendritic histiocytes infiltrated into the tumor tissue, and the \(\alpha\)-SMA was positive in the vascular smooth muscle of pericytes, forming the tumor angiogenesis.\(^21\) The heavy infiltration of dendritic histiocytes detected by S-100 was ascribed to the immune response against the metastatic tumor cells, and more the abundant vasculature detected by \(\alpha\)-SMA was induced by the active \textit{de novo} angiogenesis around the tumor tissue. However, the present case clearly showed that the abundant vasculatures in the granulomatous gingival tissue and chin ulceration were continuous with the vasculatures of the tumor tissue. These findings would be important to explain the processes of tumor metastasis, because the vascular bed is essential to achieve the metastasis of tumor cells, Therefore, in the present case it is presumed that the preceding injury at the anterior mandibular area would be a triggering factor to form the inflammatory granuloma which has abundant vascular bed for tumor seeding, and subsequently recruited the tumor metastasis prior to the other tissues of patient.

The metastatic process is a complex biological process, involving detachment from the surrounding cells, regulation of cell motility and invasion, survival, proliferation and evasion of the immune system.\(^8\) Therefore, the further investigation is needed to elucidate the mechanism of tumor metastasis occurred in the present study. Nevertheless, it could be suggested that the metastatic tumor cells favored to anchor in the granulomatous lesion of mandible, where the wound healing was undergoing with \textit{de novo} angiogenesis and wide activation of different cytokines and growth factors.\(^11\)

### IV. References


