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치은의 소아황색육아종

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〈Abstract〉

Gingival Juvenile Xanthogranuloma

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Juvenile xanthogranuloma (JXG) is a benign histiocytosis that occurs in the pediatric population. Cutaneous JXG is the most common form, while extracutaneous lesions, including oral JXG, is extremely rare. Cutaneous JXG can occur as multiple lesions and may have systemic visceral involvement, but this is not seen in oral JXG. In this case, we report a solitary oral JXG at the gingiva in a 3-year old male.

Key words: Juvenile xanthogranuloma, Oral cavity, Histiocytosis

Ⅰ. INTRODUCTION

Juvenile xanthogranuloma (JXG) is a rare non-Langerhans type histiocytosis, that arises in the 1st and 2nd decade[1]. JXG has been earlier referred to as nevoxanthoendothelioma, because this xanthoma complex displayed as circumscribed, colored, chronic skin lesions composed of oval endothelial-like cells with various ranges of vascularity[2,3]. It was later classified as a benign histiocytic disorder most likely of dermal dendritic cell origin, but the specific histiocytic lineage is still controversial[4-6].

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JXG is a pediatric disease with 45~71.0% of the cases diagnosed before the age 1[1,7]. The majority of JXG are cutaneous lesions. It is most common in the head and neck region, closely followed by the extremities and trunk[1,7,8]. Over 80% of the cutaneous JXG cases are solitary with a nearly 1:1 sex ratio, male being slightly more prevalent[1,7]. Whereas in multiple cutaneous lesions, 9 in 10 are male[1]. Extracutaneous lesions, especially those without a concurrent cutaneous lesion are extremely rare and have been seen most commonly in the submucosa and bone of the head and neck. Systemic visceral involvement may accompany the cutaneous lesions and are seen in the central nervous system, eye, lung, liver, pancreas, spleen, kidney, intestines and others[1,7,9,10]. Lesions are well circumscribed, firm nodules

with a yellow to reddish color. In this case, we report a solitary oral JXG at the posterior mandibular gingiva in a 3-year old male.

Ⅱ. CASE REPORT

A 3-year-old male patient was referred from the Department of Pediatric Dentistry for a recently noticed soft tissue mass at the left posterior mandibular gingiva. His mother stated that she had accidentally discovered the mass three days before the initial visit and that her child had not complained of pain or discomfort. She informed us that the patient had a fever about a week before the visit. There were no other known underlying diseases. The lesion was a firm reddish mass surrounding the left primary mandibular second molar (#75) with a smooth surface and bleeding by palpation (Fig. 1A). It had a diameter of 1.5cm at the longest direction. There was no bone erosion on the periapical view or computed tomography (CT) (Fig. 2A, B and C). The clinical impression was pyogenic granuloma, odontogenic fibroma or ossifying fibroma. Excisional biopsy was performed with a supraperiosteal incision, including a portion of normal tissue around the lesion (Fig. 1B).

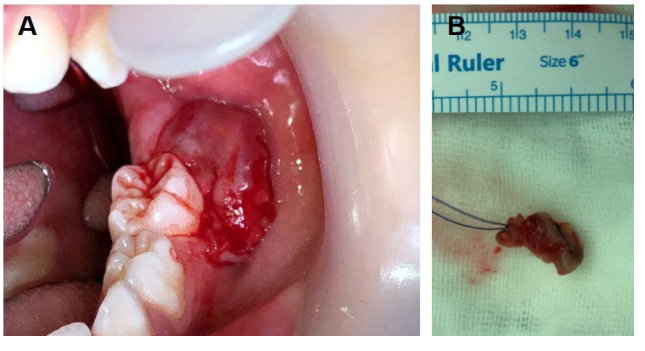

Fig. 1. Clinical image of oral juvenile xanthogranuloma (JXG). A. JXG was a solitary reddish round mass surrounding the primary mandibular second molar. The excessive bleeding was caused by palpation. B. Excised JXG specimen. The size of the specimen appeared smaller than the original lesion, because of tension loss.

Histopathological evaluation of the lesion revealed a submucosal mass composed of oval to polygonal cells intermixed with giant cells, inflammatory cells and minimal stromal tissue (Fig. 3A, B). The lesion cells had a round, bland nucleus and homogenous eosinophilic cytoplasm. Among those, some of the lesion cells had a finely vacuolated, foamy cytoplasm. The lesion cells lacked cohesiveness and did not show cellular atypia. The lesion cells had an epithelioid morphology, so immunohistochemistry was performed to distinguish the origin of the lesion cells. Antibody staining of cytokeratin AE1/AE3 (for epithelial tumors), CD45 (for lymphocytic tumor), desmin (for muscle origin tumor), CD68, CD1a, S-100 (for histiocytosis, Fig. 3C,

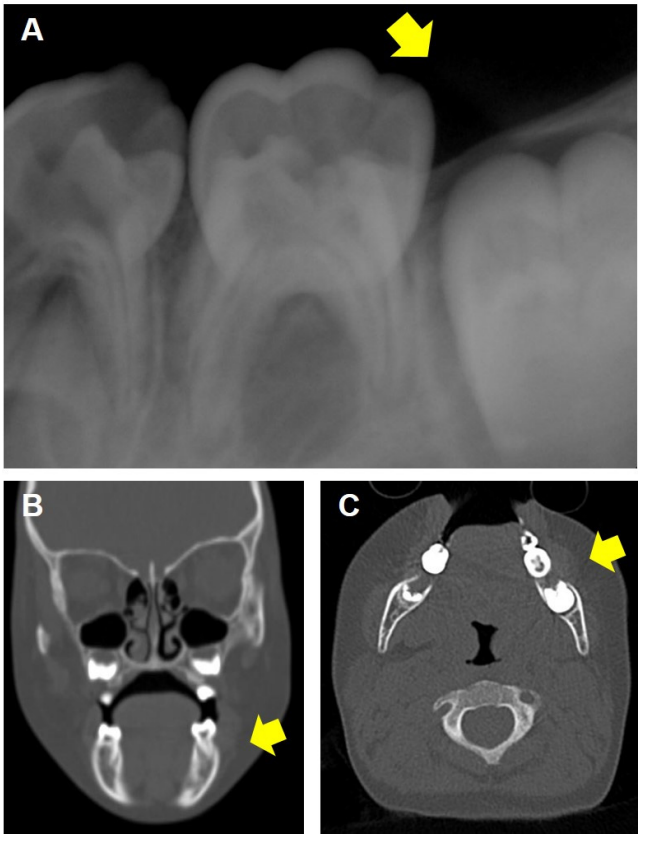

Fig. 2. Radiologic image of the lesion (yellow arrow). A. Periapical view of lesion located at the posterior of the primary mandibular second molar. B. Computed tomography (CT) coronal view. C. CT axial view. The cortical bone near the lesion does not show signs of erosion or resorption.

3D, and 3E, respectively) and CD31 (for vascular tumors, Fig. 3F) were done. Epithelial tumors and muscle origin tumors were ruled out due to the cytokeratin and desmin-negative pattern, respectively in lesion cells. CD31 stain patterns were focally positive and patchy, so we considered the possibility of epithelioid hemangioendothelioma, but zonal patterns were not definite and stain patterns were weak. The lesion cells were CD68-positive and CD1a-negative which indicated a histiocytic origin but excluded Langerhans cell histiocytosis (LCH). They were focally S-100 positive and CD45-negative (which was positive in reactive lymphocytes). Comprehensive judgement of the clinical and pathological findings concluded the final diagnosis as juvenile xanthogranuloma (JXG). The associated giant cells were Touton type, which supported the diagnosis. The JXG lesion was proved anaplastic lymphoma kinase (ALK)-negative and BRAF wild type by additional immunohistochemistry.

The patient was evaluated at a systemic basis, particularly the ocular region. The mother of the patient informed the staff that the child had been treated for a skin disease right after birth until he was 6-month old. The ophthalmologist confirmed no signs of JXG in the ocular region. Positron Emission Tomography (PET)/CT results were of normal range. Healing status was normal 2 months after operation and additional surgical procedures were not proceeded (Fig. 4).

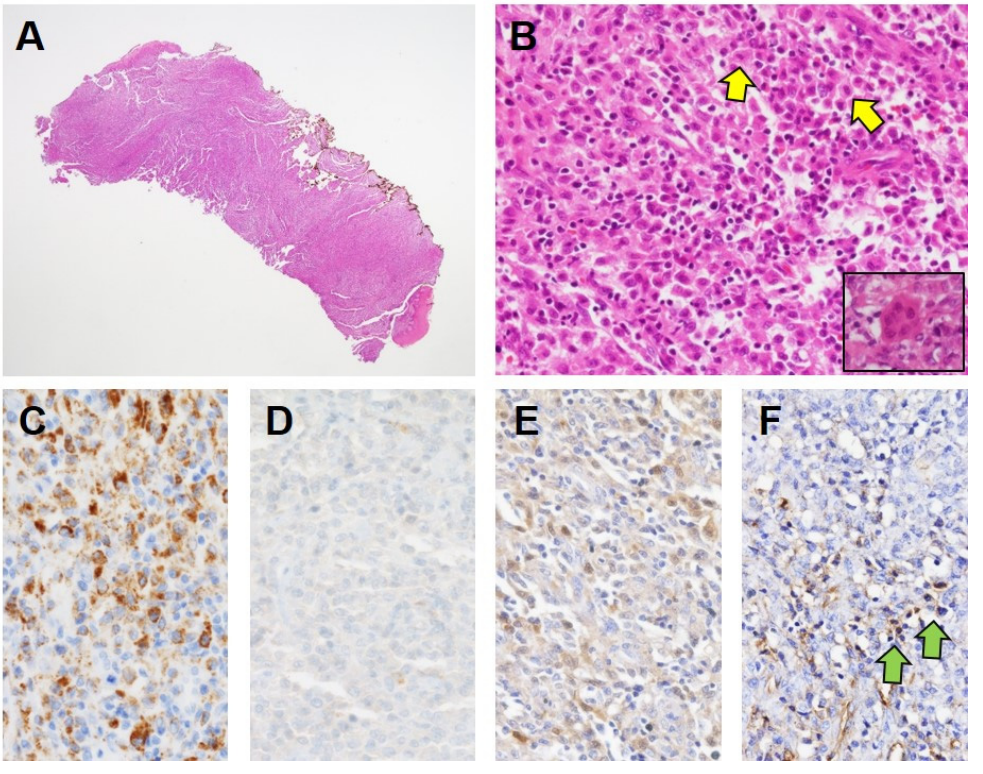

Fig. 3. Histopathologic examination and molecular pathology results of the surgical specimen.
A. Submucosal infiltrate of lesion cells (Hematoxylin and eosin [HE], original magnification x12.5). B. Oval to polygonal histiocytes with eosinophilic cytoplasm, Touton giant cells (inset) and mixed inflammatory cells, mainly lymphocytes. A portion of the histiocytes have pale and foamy cytoplasm (yellow arrow) (HE, original magnification x400, inset x400). C. The infiltrated lesion cells were CD68-positive, indicating a histiocyte origin (Immunohistochemistry [IHC], CD68, original magnification x400). D. The histiocytes were CD1a-negative (IHC, CD1a, original magnification x400) E. Focal areas of the histiocytes were S-100-positive (IHC, S-100, original magnification x400). F. A few histiocytes were weak CD31-positive (green arrow) (IHC, CD31, original magnification x400).

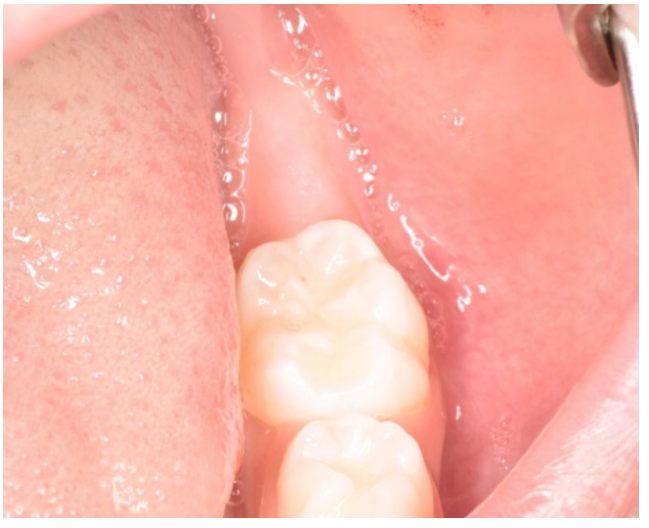

Fig. 4. Clinical image of the oral cavity 2 months after the previous excision. Healing was favorable and there were no signs of recurrence.

Ⅲ. DISCUSSION

Histiocytoses are a wide spectrum of disorders with accumulation of histiocyte-derived cells. The included subtypes range from an indolent reactive form to an aggressive, malignant tumor. The initial classification of histiocytic disorders in children was given in 1987 by the Working Group of the Histiocyte Society[11]. The disorders were categorized into 3 groups (LCH, mononuclear phagocytes other than LC, and malignancies). In 2016, Emile et al. proposed a revised classification for histiocytic disorders modified with newly recognized entities by molecular pathology that categorized them into 5 groups (LC-derived, cutaneous and mucocutaneous, malignancies, Rosai-Dorfman disease, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome)[12]. By their criteria, JXG belongs to the xanthogranuloma family in the cutaneous and mucocutaneous histiocytosis group along with adult xanthogranuloma (AXG), solitary reticulohistiocytoma, benign cephalic histiocytosis, generalized eruptive histiocytosis and progressive nodular histiocytosis, with JXG being the most common one. In previous literatures, JXG and AXG have not been well distinguished and the term "Juvenile" has been used regardless of age[13].

The diverse origin of histiocytic disorders can be confirmed by immunohistochemical stain pattern combination. Bone marrow-derived tissue macrophages commonly express CD14 and CD68. LCs are CD1a, langerin (CD207)-positive and CD14-negative[14]. Factor XIIIa is expressed in dermal dendritic cells and activated macrophages[4,15]. In addition to factor XIIIa, dermal dendritic cells are CD68-positive and CD1a, langerin-negative[14]. JXG belongs to the non-LC group and is believed to be derived from macrophages, dermal dendritic cells, or plasmacytoid monocytes[4-6]. We used a combination of CD68, CD1a and S-100 to prove the histiocytic lineage of our lesion and distinguish it from other histiocytic lesions, such as LCH. The CD68-positive and CD1a-negative expression pattern was consistent with JXG. S-100 is known to show various levels of expression in histiocytic disorders, and is generally negative or weak in JXG[4,14,16]. In our lesion, we observed a focal positive pattern in the lesion cells. Recently, it has been known that CD31 is possible of positive stain in certain macrophages and the results have misinterpreted histiocytic lesions or intratumoral macrophages as vascular origin[17]. In a few studies, CD31-positive patterns have been observed in about 45% of solitary JXG cases and exhibit a weaker and granular stain compared to endothelial cells or vascular tumors[4]. Our case was focal and weak CD31-positive, with most of the stained cells positioned near the endothelial cells at the blood vessels which gave confusion as a vascular tumor at first sight.

Cutaneous JXG is the predominant type, so the clinical manifestations mentioned in our introduction are relevant to cutaneous cases. Although there were not sufficient numbers of oral cases, several differences of oral and cutaneous JXG has been reviewed. Compared to the majority of cutaneous JXG cases occurring before the age 1, only 14% of the oral JXG cases were diagnosed in the 1st decade[1,7,18]. Oral JXG has been observed at the tongue, gingiva, palate, lips, and

buccal mucosa[13,18]. Near to 90% of oral JXG cases are solitary, and systemic JXG has not been reported in oral JXG[18]. Our patient was examined of the entire body and particularly the eye, in case of systemic lesions. Visceral involvement results in complications and poor prognosis. Furthermore, ocular JXG can lead to glaucoma and other severe vision problems[10]. In previous literature, oral lesions have only been accompanied with cutaneous lesions. Importantly, cutaneous JXG is known to progress with indolent clinical behavior and result in spontaneous regression. Unfortunately, this is not the case for extracutaneous JXG. Surgical excision is required, and incomplete removal can lead to recurrence[13]. Oral JXG has been reported to have a recurrence rate of 14%[18]. A periodic follow up is recommended, as there have been cases that have recurred after 1 to 7 months after surgical excision[13].

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