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# A Case of Kaposiform Hemangioendothelioma of the Pterygopalatine Fossa

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## 익구개와에 발생한 카포시형 혈관내피종 1예

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**= 국문초록 =**

카포시형 혈관내피종은 주로 영유아기에 발생하는 혈관내피세포에서 유래하는 혈관종양이다. 성인에서도 발생할 수 있으나 발생률은 정확히 알려져 있지는 않다. 뼈 또는 연조직을 침범할 수 있으며 경계성 종양으로 알려져 있다. 모세혈관종 또는 카포시형 육종과 유사하게 혈관이 포함된 침습적이고 경계가 불분명한 결절을 형성하며, 보통 사지의 연조직이나 간, 폐에 발생하는 경우가 많다. 문헌상으로 두경부에 발생한 증례가 몇 편 보고되어 있으나, 그 중 익구개와에 발생한 경우를 보고한 경우는 없었다. 저자들은 5개월된 남아에서 익구개와에 발생한 카포시형 혈관내피종을 인터페론 알파와 수술적 절제로 성공적으로 치료하였기에 이를 문헌고찰과 함께 보고하는 바이다.

**중심 단어** : 카포시형 혈관내피종 · 악구개와 · 인터페론 알파 · 영아.

## Introduction

Kaposiform hemangioendothelioma(KHE) is a rare, recently described, locally aggressive, endothelium-derived spindle cell neoplasm that occurs exclusively in infants and children.[1-4] It was previously described as hemangioma with Kaposi-sarcoma-like features, Kaposi-like infantile hemangioendothelioma, locally metastasizing vascular tumor and simply hemangioendothelioma.[1-3] The current term, kaposiform hemangioendo- thelioma, was provide by Zukerburg, Nickoloff, and Weiss[4] due to its focal histologic similarities to Kaposi's sarcoma.

Due to its significant rates of systemic metastases and tumor-related deaths, the classification of the epitheloid hemangioedothelioma as either low-grade malignancy or borderline vascular neoplasm is still in debate.[5] However, recently it has been widely accepted that spindle cell hemangioendothelioma is characterized as a benign, reactive condition or possibly hamartomatous vascular lesion.[6] Thus, to avoid confusion, spindle cell hemangioma may be the correct term for this type of tumor. Furthermore, kaposiform hemangioendothelioma is known to be associated with lymphangimatosis and Kasabach-Merritt Syndrome.[2,4]

This report presents a case of a 5 month-old male infant diagnosed as kaposiform hemangioendothelioma in the pterygopalatine fossa, treated with intramuscular injection of interferon alpha 2a(Intermax alpha®, LG pharmaceutical, Korea) for 7 months, followed by tumor excision via transoral approach.

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## Case Report

The patient was a healthy 5 month-old male infant who presented with right cheek swelling. He was born to healthy par-

ents after an uneventful delivery. Through physical examination, we detected diffuse swelling on the right cheek that caused facial asymmetry. However, no specific findings were noticed in the oral cavity and the results of his laboratory tests were within normal limits. Computed tomography(CT) and magnetic resonance imaging(MRI) image demonstrated a 4×4cm-sized mass with bony destruction of the right mandibular coronoid process in the pterygopalatine fossa(Fig. 1A and 1B). Further evaluation using ultrasonography of the abdomen and pelvis showed non-specific findings. Laboratory tests demonstrated no evidence of coagulopathy. Incisional biopsy via peroral approach was done for pathological verification and initial histology report by H&E and immunostaining for CD34 revealed kaposiform hemangioendothelioma with some aggressive potential. After the treatment with intramuscular injection of interferon alpha 200,000 IU/$m^2$ every other day for 7 months, the mass decreased to 2×2 sized lesion confirmed by CT scan(Fig. 1C and 1D). The residual lesion was completely excised via transoral approach(Fig. 2). Mucosal incision was designed along the posterior alveolar bone and dissection of the soft tissue was done by bovie. After identification of mass contour, mucosa around the tumor was incised, buccal fat pad was dissected using an electrocautery, and destructed coronoid process was resected by bone cutter. Then, the tumor was dissected off the pharyngobasilar fascia through blunt dissection technique. Irregular bloody soft tissue mass along with destructed coronoid process were avulsed.

The nodules with epitheloid cells were separated by dense hyaline sclerosis where irregular tumor infiltrated skeletal muscle and capillary sized vessels with attenuated lumina were noticed on histologic analysis(Fig. 3). Between these vascular spaces, the proliferation of spindled cells resembled Kaposi sarcoma. In contrast to Kaposi sarcoma, however, occasional rounded and somewhat epithelioid endothelial cells were also recognized simulating epitheloid hemangioendothelioma. These cells formed small nests or larger nodules surrounding the cavernous spaces. Immunohistochemically, epitheloid cells showed positive reaction to kaposiform hemangioendothelioma specific immunostain(CD34) and negative reaction to neuronal immunostain(S-100). The patient was discharged from the hospital on postoperative day 5 without any complications. In his 8 years of follow-up, the patient is free from disease with no residual tumor proven by MRI imaging until present time(Mar. 14, 2013)(Fig. 4).

## Discussion

Kaposiform hemangioendothelioma, a recently delineated disorder that is frequently associated with Kasabach-Merritt syndrome and lymphangiomatosis, is characterized by local aggressive growth. For this reason, the tumor has been classi-

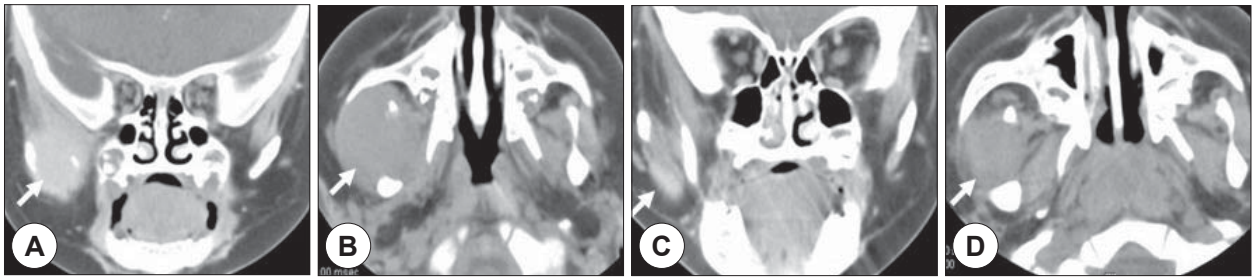


**Fig. 1.** A and B : Temporal bone CT shows a 4×4cm sized mass shadow in right pterygopalatine fossa destructing mandible bone (arrow)(A : Coronal view, B : Axial view). C and D : Temporal bone CT shows decreased mass size(2×2cm) after interferon alpha therapy(arrow)(A : Coronal view, B : Axial view).

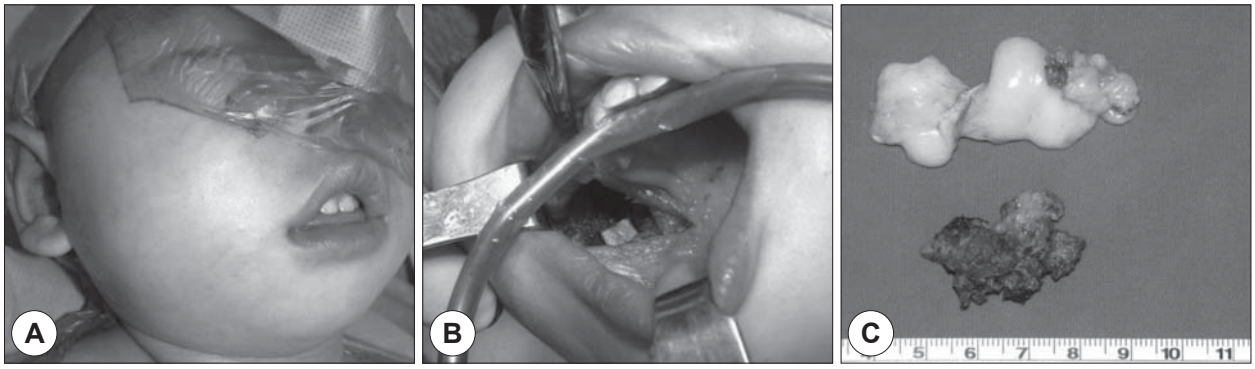


**Fig. 2.** Operative findings. A : Right facial swelling due to mass in pterygopalatine fossa. B : After intraoral mucosal incision, irregular tumor with destruction of coronoid process of mandible was detected. The buccal fat pad, tumor, and coronoid process of mandible were removed. C : Specimen shows buccal fat(upper) and tumor(lower).

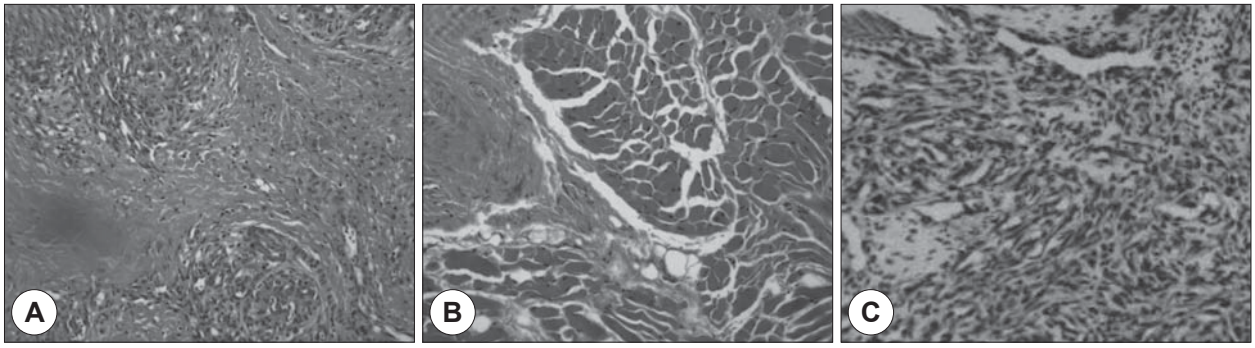


**Fig. 3.** A : The nodules with epitheloid cells are separated by Dense hyaline sclerosis(H&E ×40). B : The irregular tumor nodules infiltrating skeletal muscle with capillary sized vessels with attenuated lumina(H&E ×40). C : Epitheloid cells show positive reaction to kaposiform hemangio- endothelioma specific immunostain(CD34).

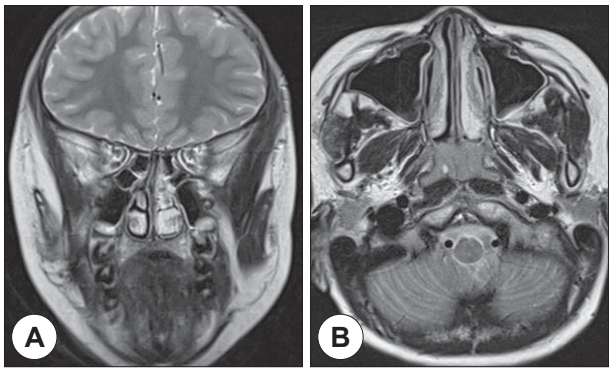


**Fig. 4.** Follow up image of 8-year post operation. Temporal MRI of shows no recurrence or complication such as inflammation or deformity from defect(A : T2 weighted coronal view. B : T2 weighted axial view).

fied as a borderline malignant vascular neoplasm.[2,4] Kaposiform hemangioendothelioma is also known to occur dominantly in infants and young children, with a wide anatomic distribution,[7] possibly occurring in the skin, subcutis, and deep soft tissues, including retroperitoneum. The diagnosis is suspected through clinical manifestation and confirmed by magnetic resonance imaging or pathology. In the case of our patient, we initially suspected other diseases such as lymphoma or sarcoma through diagnostic workup where chemotherapy is the treatment of choice. Thus, incisional biopsy was performed before operation for differential diagnosis and pathology confirmation.

Histologically, kaposiform hemangioendothelioma is a lesion considerably distinct from other childhood vascular tumors. It consists of infiltrating nodules of slit-like or crescentic vessels containing hemosiderin and fragmented erythrocytes, unlike distinct nodules of well-formed capillaries that characterize cellular hemangioma in infancy. The vessels are often shown with poorly canalized structures lacking complete structure of basal lamina and pericytes, and lined by endothelium devoid of Weibel-Palade bodies which are the storage granules of endothelial cells.[4]

Kaposiform hemangioendothelioma must be differentiated from other vascular neoplasms, including Kaposi's sarcoma, cellular hemangiomas(infantile and juvenile hemangioendotheliomas), tufted angioma, spindle cell hemangioendothelima, and angiosarcoma. Kaposiform hemangioendo- thelioma shares distinct similarities to Kaposi's sarcoma. They are both displayed with slit-like vessels, accompanied in some cases by intracellular and extracellular hyaline globules, which presumably are remnants of erythrocytes. The immunophenotypic profile of both tumors express CD34, usually lack factor VIII-AG, and are surrounded by a population of factor XIIIA-positive cells.[8] However, several histologic features of kaposiform hemangioendothelioma contrast to Kaposi's sarcoma. In addition to the spindled endothelial cells, Kaposiform hemangioendothelioma includes a population of more rounded or epitheloid endothelium. More commonly, lesions of Kaposi's sarcoma are surrounded by chronic inflammatory infiltrates, in contrast to the dense hyaline fibrosis that characterizes infiltrating nodules of kaposiform hemangioendothelioma in the skin.

Several treatments for kaposiform hemangioendothelioma have been attempted. Best results are seen in patients that underwent wide surgical excision.[4,9] Unfortunately, many lesions are technically difficult to resect and are prone to recur because of their potential of wide infiltrative growth. Glucocorticoids have been effective in two cases complicated by consumptive coagulopathy, one in combination with cyclophosphamide. Another case was successfully treated with combination of chemotherapy, interferon, and vascular ligation.[4] Increasing evidence demonstrate the effect of interferon for managing kaposiform hemangioendothelioma which does not response to other forms of treatment such as inhibition of proliferation and transformation of fibroblast.[10,11] However, treatment with steroid is successful in only 10% and interferon is known to effective in only 50−60%.[12] A recent report demonstrated a new therapeutic strategy including paclitaxel

for the treatment of KHE, particularly aggressive KHE of the head and neck.[13] Apparently, radiation therapy is ineffective. Prognosis depends on the extent and location of disease. Tumors that are localized to skin are benign, whereas those that invade viscera are fatal. All forms are associated with platelet trapping(Kasabach-Merritt syndrome), however, lymphangiomatosis seems to be limited to cutaneous variants.[4] Despite aggressive treatment, 66% of retroperitoneal and 30% of cutaneous lesions are fatal. In comparison, surgically resectable tumors maintain much lower mortality. Supportive therapy is limited to control coagulopathies and for surgical debulking of tumor masses.

This case demonstrated that intramuscular injection of interferon alpha therapy for 7 months alone was partially effective in controlling tumor progression. The main concern of interferon alpha treatment is the uncertainty of long time effects or occurrence of major complications[14] However, based on the result from this case, we cautiously suggest interferon alpha treatment as an option for nonoperative management or preoperative treatment to decrease the operation risk such as fatal bleeding and patient related morbidity in kaposiform hemangioendothelioma.

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