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Three Cases of Mucocutaneous Angiomyolipoma in the Head and Neck Region with Reference to the HMB-45 and Melan-A Immunohistochemistry

Na Rae Kim, MD[1], Dong Young Kim, MD[2], Heung Eog Cha, MD[2], Seung Yeon Ha, MD[1]

Departments of Pathology Surgery[1] and Otolaryngology,[2] Gachon University Gil Hospital, Incheon, Korea

두경부에서 발생한 점막피부 혈관근육지방종 3예 : HMB-45와 Melan-A에 대한 면역화학검사 특징

가천의과학대학교 길병원 병리과,[1] 이비인후과[2]

김나래[1] · 김동영[2] · 차흥억[2] · 하승연[1]

= 국문초록 =

혈관근육지방종은 지방, 평활근, 두꺼운 벽의 혈관이 다양한 비율로 구성된 흔하지 않은 과오종이며, 이는 결정경화증을 동반하거나 산발적으로 발생한다. 저자들은 혈관근육지방종이 드물게 발생하는 두경부에서 발생한 귓바퀴 1예, 구개점막 2예의 혈관근육지방종을 보고하고자 한다. 병리소견상, 3예 모두에서 성숙지방조직, 불규칙한 혈관, 그리고 HMB-45와 Melan-A에 음성을 보이는 평활근육세포로 이루어진 조직소견을 보였으며, 여러군데에서 림프구 침윤이 3예 모두에서 관찰되었다. 점막피부 혈관근육지방종으로 진단하였다. 세증례 모두 결절경화증은 동반되지 않았다. 점막피부 혈관근육지방종에서는 혈관주변세포가 HMB-45와 Melan-A에서 음성을 보였으며, 이는 간이나 신장의 혈관근육지방종에서의 특징적인 양성반응과는 다른 점이었다.

간이나 신장에서 생긴 혈관근육지방종과 다른 임상병리적 특징을 비교 기술하고자 두경부에서 발생한 점막피부 혈관근육지방종 3예를 보고한다.

중심 단어 : 혈관근육지방종 · 점막피부 · 구개 · 귓바퀴 · HMB-45 · Melan-A.

Introduction

Angiomyolipoma is a benign hamartomatous tumor and it shows various proportions of three pathological components: smooth muscle-like cells, thick-walled vessels and mature adipose tissue. Among them, the smooth muscle-like cells are putatively considered to be derived from perivascular epithelioid cell (PEC) and the PEC-derived tumorous lesions have been categorized as PEComas, including hepatorenal angiomyolipomas, lymphangioleiomyomatoses of the lung and sugar cell tumors of the lung. These perivascular cells are generally immunoreactive for premelanosome-related antigens such as HMB-45, Melan-A, tyrosinase and microphthalmia transcription factor (MiTF). These immunohistochemical features provide a valuable clue for diagnosing PEComas. In contrast to hepatorenal angiomyolipomas, the incidence and histopathologic features of mucocutaneous angiomyolipomas are different.[1-12)]

We report here on additional three cases of mucocutaneous angiomyolipomas that arose from an ear auricle and palates of the mouth, and we describe with their immunonegativity for the premelanosome-related antigens.

교신저자 : 하승연, 405-760 인천광역시 남동구 구월1동 1198
가천의과학대학교 길병원 병리과
전화 : (032) 460 3078 · 전송 : (032) 460 3073
E-mail : syha@gilhospital.com

Case Report

1. Case 1

A 51-year-old Korean woman suffered from an oral mass for 4 years, and this mass was accompanied by nasal obstruction and rhinorrhea. Paroxysmal pain was not observed. Physical examination of the oral cavity showed a protruding palatal mass with central ulceration at the left roof of oral cavity. Computed tomography of the neck revealed a 2.0×1.5×1.2cm-sized well marginated low density lesion on the left palate. A laser excision was done under the impression of pleomorphic adenoma. The patient has had uneventful follow-up for 10 years with no recurrence.

2. Case 2

A 51-year-old man presented with a protruding mass in the roof of oral cavity for about 2 years, and the mass measured 0.8×0.8×0.5cm. A laser excision was done under the impression of pleomorphic adenoma. Intraoperatively, a well encapsulated pink-colored, bosselated soft mass was found at the left hard palate. He has been free from recurrence during 9 years of follow up.

3. Case 3

A 56-year-old man presented with a movable polypoid bean sized mass of a purple color at the right ear auricle for 1 year. This was not associated with otalgia or otorrhea. The mass was 0.5×0.4×0.4cm in size. Complete resection was done and the resection margins were free of tumor. She had been free of tumor during 10 years of follow-up. All the patients had no medical history or family history of tuberous sclerosis.

4. Pathologic results

All the resected specimens were fixed in 10% formalin. Grossly, cases 1, 2 and 3 measured 2.0×1.5×1.2cm, 0.8×0.8×0.5cm, and 0.5×0.4×0.4cm, respectively. Pathologically, each tumor of all three cases was composed of various proportions of smooth muscle cells, vessels and mature fat cells (Fig. 1A). The thickened vessels showed occasional hyalinization (Fig. 1B) and foci of mature adipocytes were irregularly scattered over the tumors. No cellular atypism or mitoses was found. Multifocal accumulations of small lymphocytic infiltrations were observed. Immunohistochemically, the perivascular myoid cells were reactive for smooth muscle actin (1A4 ; Dako, Glostrup, Denmark, 1 : 100 dilution) and vimentin (V9 ; Dako, prediluted). Those cells were totally negative for melanoma antigen (HMB-45 ; Dako, 1 : 100 dilution) and Melan-A (A103 ; Dako, 1 : 30 dilution). The thick vessels were positive for vWF (factor VIII-related antigen, Dako, prediluted). All the tumors were diagnosed as angiomyolipoma.

Discussion

Angiomyolipoma is a mesenchymal tumor that is frequently associated with tuberous sclerosis complex, and this tumor also occurs sporadically. Its diagnosis depends on observing the presence of vessels, smooth muscle and mature adipose tissue under light microscopy. Besides those findings, the tumor's immunoreactivity for several premelanosome-related markers is an ancillary method for making the proper diagnosis. Angiomyolipoma commonly occurs in the kidney and liver, but the head and neck regions are rare sites for this tumor. To date, there have been only twelve reported cases of intraoral angiomyolipoma[1-7] ; Six cases overall have occurred in the hard palate, three cases in the lips, two cases in buccal mucosa and one case in the tongue. All the reported intraoral angiomyolipomas presented clinically as

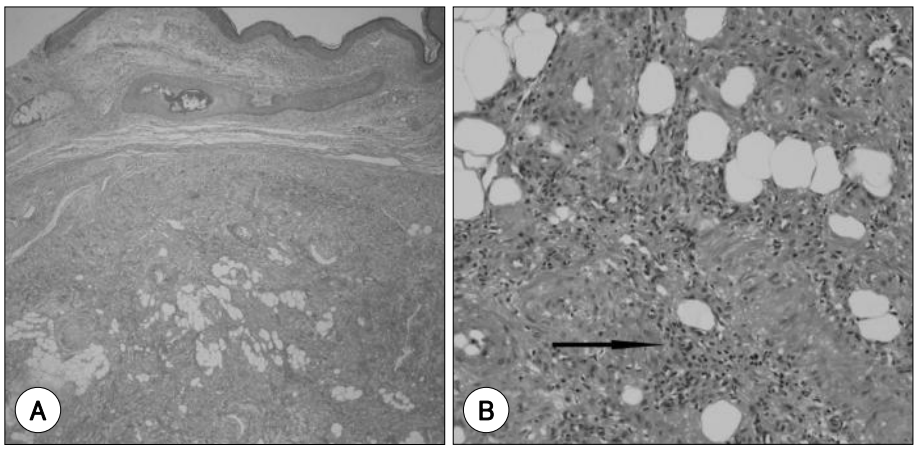

Fig. 1. A : Thick-walled vessels, smooth muscle tissue and mature adipocytes are seen (hematoxylin and eosin stain, ×100). B : Hyalinized blood vessels and mature adipose tissue are irregularly mixed over the tumors (hematoxylin and eosin stain, ×100). Note the mature lymphocytic infiltrations (arrows).

slow growing painless masses, and they developed in adults between the fourth and eighth decades, with no gender predilection. The microscopic appearance and clinical behavior of the intraoral angiomyolipoma are identical to those of the lesions in the skin and nasal cavity of the head and neck region and these tumors are usually grouped together as mucocutaneous angiomyolipoma. Mucocutaneous angiomyolipomas in the head and neck region can rarely occur in the skin, nasal cavity and oral mucosa,[1-11] even in the larynx[12,13] and their histologic features resemble those of hepatorenal angiomyolipoma. However, some differences exist between their clinicopathologic and immunohistochemical features.[1,2,14-17] From the clinical viewpoint, the former preferentially occurs in older males with a small tumor size (less than 4.0cm), while the hepatorenal counterpart predominate in females. None of the previously reported mucocutaneous angiomyolipomas were associated with tuberous sclerosis. The pathologic differential diagnosis of angiomyolipoma includes angiolipoma, angioleiomyolma, hemangioma with partial involution and fatty replacement and other reactive processes, such as fibrolipomatous hyperplasia. Among them, distinguishing mucocutaneous angiomyolipoma from angioleiomyoma is challenging because both these lesions' pathologic and immunohistochemical features overlap. The pathology of fat tissues may be found in angioleiomyoma, but only a small proportion of the angioleiomyomas contain fat and all these have occurred in the head and neck region. There is controversy as to whether or not mucocutaneous angiomyolipoma may be a variant of angiomyolipoma. However, lymphocytic aggregation is commonly found and the pleomorphic variant is rarely seen in the nonhepatorenal mucocutaneous angiomyolipomas, and these features are not seen in the angioleiomyoma. From the immunopathological viewpoint, it is intriguing that the PECs of mucocutaneous angiomyolipoma are immunonegative for the monoclonal antibodies against premelanosome-related markers, conversely to the usual immunopositivity shown in angiomyolipomas from other sites.[18] These different histopathologic and immunohistochemical features suggest that mucocutaneous angiomyolipomas may be distinct from hepatorenal angiomyolipomas. Clinically, the lower extremities of female are affected by angioleiomyoma, whereas the acral portions of body, head and neck region of older males are affected by mucocutaneous angiomyolipoma. Based on these different clinicopathologic characteristics, we can suggest that mucocutaneous angiomyolipoma may be distinct from hepatorenal angiomyolipoma. Not much is currently known about intraoral and cutaneous angiomyolipomas in the head and neck region and these additional cases will contribute to understanding the clinical and histopathologic features of this rare tumor.

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