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기무라씨 질환, 5예 보고

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=초 록=

기무라씨 질환은 특히 두경부 부위에 피하 종괴를 일으키는 만성염증성, 증식성 질환이다. 저자들은 최근 치험하였던 본 질환 5예를 한국외과 문헌에 처음으로 보고하는 바이다.

기무라씨 질환은 크게는 **ALHE(Angiolymphoide Hyperplasia with Eosinophilia)**의 범주에 속한다. 본 질환의 병리학적 특징은 증식된 **lymphoid follicles, eosinophilic infiltration**과 혈관의 증식성이다.

이 질환은 이하선, 악하선 및 상부 경부 부위등에 흔히 종괴를 일으키며 이들 종괴들은 피하조직뿐만 아니라 타액선과 상부 경부 임파선에까지도 파고 든다. 저자들의 증례 중 한명에서는 서혜부에 종괴가 있었으며 새로이 증식된 혈관과 동상들(Sinusoids)로 인하여 혈관 분포가 매우 풍부하였다.

저자들 증례5명의 평균 연령은 35세이었지만 한명을 제외한 나머지 모두는 38세 이하이었다. 남녀비는 3 : 2이었으며 증상의 평균 기간은 5.2년이었다. 전례에 있어서 말초 혈액 소견상 **Eosinophilia**가 있었다. 전례에서 다발성 종괴들을 보였으며 가끔은 대칭적이기도 하였다.

저자들이 시행한 치료 양상은 수술만 시행한 경우와 수술 및 스테로이드 홀몬요법 시행 경우가 각각 1례씩이었고 수술과 방사선조사 경우가 2례이었으며 나머지 1례에서는 수술, 스테로이드 홀몬요법 및 방사선조사의 복합치료를 실시하였다.

저자들은 기무라씨 질환과 **ALHE** 질환과의 관계를 고찰해 보았으며 기무라씨 질환의 치료 경험을 보고하는 바이다.

REPORT OF EXPERIENCE WITH KIMURA'S DISEASE

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= **Abstract** =

Kimura's Disease is a chronic inflammatory and proliferative condition producing subcutaneous masses especially in the head and neck area. This report of our experience with 5 patients with this disease is the first in the Korean surgical literature.

Kimura's Disease is thought to be part of the larger spectrum of the entity known as angiolymphoid hyperplasia with eosinophilia(ALHE). It is characterized pathologically by hyperplastic lymphoid follicles, eosinophilic infiltration, and vascular proliferation. It produces masses which are most common in the area of the parotid, submandibular gland and upper neck. These masses occupy the subcutaneous tissues but also extend into salivary tissue and into upper neck nodes. One of our patients had masses in the groin. The tumors are extremely vascular due to the presence of new proliferative vessels and sinusoids.

The average age of our 5 patients was 35, but all but one case were younger than 38 years of age. The male : female ratio was 3 : 2, and the average duration of symptoms was 5,2years. All patients had peripheral blood eosinophilia. All had multiple masses, sometimes symmetrical. The management was surgery alone in one case, surgery and steroids in one case, surgery and radiotherapy in two cases, and all three modalities in one case. The relationship of this entity to ALHE and our experience in the management of this disease are presented.

A clinicopathological discrepancy alerted us to the existence of Kimura's Disease. A nineteen-year old male presented with subcutaneous masses over both mastoid areas present for 3 years(Case lll). When biopsy on each side was reported as "eosinophilic granuloma" we submitted the slides to an internationally expert pathologist. Symmetrically occurring tumors in the peri-parotid subcutaneous areas did not fit any category of neoplasm or granuloma known to us. The diagnosis, made by Dr. Gist Farr at the Ochsner Clinic, was Kimura's Disease. We found two additional cases in a review of soft tissue eosinophilic granuloma previously reported at Presbyterian Medical Center, and since then have diagnosed two new cases. These five cases constitute the basis for this, the largest series to be reported in Korea.

These vascular, tumor-like lesions of the skin, subcutaneous areas and subjacent structures of the head and neck have been a variety of names, such as angiolymphoid hyperplasia with eosinophilia, eosinophilic hyperplastic lymphogranuloma, angioblastic lymphoid hyperplasia with eosinophilia, histioid hemangioma, and epithelioid hemangioma. The history of this disease spectrum dates back to 1937 when Kimm and Szeto (1) reported 7 cases of "eosinophilic hyperplastic lymphogranuloma" in the Proceedings of the Chinese Medical Journal. In 1948 Kimura and his associates(2) reported additional cases in Japan under the title "On the unusual granulation combined with hyperplastic changes of lymphatic tissue." From then until 1966 several hundred cases were reported in China and Japan. The first report from the West was by Wells and Whimster(3) in the British Journal of Dermatology, in 1969. These authors coined the term, angiolymphoid hyperplasia with eosinophilia (ALHE). Since that time a debate has ensued as to whether Kimura's Disease and ALHE are distinct

entities, or whether Kimura's is part of the larger spectrum of ALHE, perhaps a later or advanced phase.

From the clinical perspective, surgeons should be aware of the diagnosis of Kimura's Disease not only as part of the differential diagnosis of head and neck tumors but also because these lesions are indolent, and generally require conservative surgical removal as part of the management program.

CASE Ⅰ.

A 37-year-old female company employee presented in August 1982 with submental swelling of 12 years' duration and with inguinal swelling of 7 years' duration. The submental mass measured 5×5cm. and the inguinal mass was 8×4cm. in size. Peripheral eosinophilia varying from 14% to 40% was found. On August 20, 1982, the submental mass was removed and a superficial groin dissection was done. In May 1983 an intraoral lesion of the palate was removed. The patient is free of disease.

CASE Ⅱ.

A 23-year-old unemployed man visited this hospital for the first time in July, 1984, with swelling of the right cheek present for 6 years. The mass was soft and ill-defined but measured 10×20cm. and extended from the submandibular upper neck to the zygomatic arch, and from the mastoid to the cheek, over the parotid gland.
Eosinophilia varying from 27% to 29% was noted in the peripheral blood. On March 21, 1986, the lesion was resected. The procedure comprised an extended superficial parotidectomy from the temporalis fascia to the upper neck. Post-operatively radiotherapy 3000 rad tissue dose was administered using the 6 MeV linear accelerator. The patient remains free of disease.

CASE Ⅲ.

A 19-year-old student came to the clinic with masses over both mastoid areas, present 3 years. On the right there were two adjacent lesions, one over the mastoid, the other in the upper jugular level of the neck. On the left it was a single mass over the mastoid. Eosinophilia varied from 13 to 32% in the peripheral blood, and 11.6% in the bone marrow. Incisional biopsy revealed "eosinophilic granuloma" and a trial of predisolone was employed. The mass increased in size so a small dose of radiation(600 rads) was used, with substantial regression,. The lesion on the left was excised and follwed by 1000 rads radiotherapy. Finally recurrent tumor on the right side was removed on November 5, 1985. The patient remains free of disease.

CASE Ⅳ.

A 29-year-old local merchant had had swelling of both upper necks since childhood. At the time of his first visit on March 17, 1986, the right submandibular mass measured 5×3.5cm. and the right upper neck and parotid tail mass measured 2.5cm. On the left there were masses in the upper neck, the largest of which measured 2.5cm, and of the parotid tail, 2.0cm. in size.(See Fig. 1) Peripheral eosinophilia of 39% was recorded. Left side partial parotidectomy and

resection of the upper neck and subdigstric mases was done on May 2, 1986. The mass involving the right parotid tail and upper neck nodes was removed on Angust 7, 1986. Postoperatively the patient was placed on prednisolone 30 mg. per day. No definite masses are palpable.

CASE V.

A 66-year-old housewife informed us, at the time of her first visit in May, 1986, that she had had multiple neck masses since 10 years ago. On the right side there was a 2.5cm. subcutaneous mass of the upper neck, over the upper jugular chain. On the left there was a 9×4.5cm. mass involving the entire parotid, the post-auricular area and the upper neck. A third mass presented in the submental area and measured 3.5cm. (See Fig. 2) Eosinophilia of 51% was noted in the peripheral blood. partial excision of the left upper neck lesion and complete excision of the submental mass were performed on june 6, 1986. post-operatively she was placed on 20 mg. of prednisolone daily, but when the mass re-grew after two months she was referred to Radiation Therapy for a 2500 rad course of treatment. A barely palpable thickening remains.

Summary of Clinical Experience

In this small series the average age was 35, but with the exception of the 66-year-old lady all of the patients were relatively young, averaging 27. The male : female ratio was 3 : 2. The average duration of symptoms was 5.2years. All of our patients had peripheral blood eosinophilia. All had multiple masses. The location of the lesions is shown in Table 1. Sixteen of the 17 masses occurred in the head and neck, 14 were in the subcutaneous tissues, and 13 were in the peri-parotid or peri-submandibular salivary gland areas.

All were extremely vascular at the time of surgery, although the bleeding was never massive. The rubbery subcutaeous tissue or dermis appeared to ooze blood freely with little natural hemostasis. The process extended into lymph nodes and salivary tissue in a diffuse, poorly demarcated manner. When it extended to the nerve sheath of the seventh nerve or its branches the nerve became extremely difficult to dissect, as a consequence of which conservatism was employed rather than sacrifice nerve function for a benign lesion.

Surgery alone was employed in one case and was successful in controlling the disease despite the presence of three masses. Surgery was supplemented by steroid therapy in one patient. Three patients had post-operative radiotherapy, and one of these three had steroids. At this writing the disease is controlled in all 5 patients.

Discussion

The relationship between kimura's Disease and angiolymphoid hyperplasia with eosinophilia has become a matter of some controversy. Kung, Gibson and Bannatyne,[4] in Hong Kong, have recently described the clinical and pathological differences between Kimura's and ALHE based upon their

experience with 21 cases. They mention several points of contrast between these two entities(Table Ⅱ), particularly the fact that ALHE commonly involves the superficial subcutis and creates smaller nodules averaging 1 cm., whereas Kimura's involves the deep subcutis and has masses averaging 3cm. In addition, mast cells are unusual in Kimura's, common in ALHE ; and the swollen endothelial cells form uncanalized masses in ALHE whereas in Kimura's the endothelial cells may line sinusoids or clefts but always appear in canalized pattern.

On the other hand, Olsen and Helwig[5] at the Armed Forces Institute of Pathology, after reviewing 116 pathology specimens from patients with ALHE, are unconvinced that this and Kimura's are different diseases. "We prefer to retain the entity of Kimura's Disease as part of the specturn of ALHE until more definitive evidence becomes available," "they state.

Our tabulation of the three principal histological features of Kimura's demonstrates the variation in degree of lymphoid and eosinophilic infiltration, and in the severity of the vascular changes(Table Ⅲ). It provides support for the diagnosis of Kimura's Disease in the five cases presented, but does not help in the controversy as to the relationship of this entity and angiolymphoid hyperplasia with eosinophilia. Studies of DNA content and chromosome ploidy were also normal.

Five cases have been previously reported in Korea : one by Kim , M.L. et al in 1975[6] ; two cases by Song, K.S. and Kang, D.Y., in 1983[7] ; one case by Choi, S. W., et al in 1985[8] ; and one case by Mok, H.S. et al, in 1985[9]. All but Song and Kang's case were reported in the Korean Journal of Dermatology. Without a review of the pathological material the distinction between Kimura's Disease and ALHE cannot be made in these cases, but the photographs in Choi's and Mok's cases suggest that their lesions arose in the subcutis and were generally smaller than those reported here. This suggests that the lesions they described may be closer to ALHE than to Kimura's Disease if the pathological criteria of kung, Gibson, and Bannatyne are accepted.

Conclusions

1. Kimura's Disease, an uncommon entity involving subcutaneous tissuies espe cially in the head and neck, occurs in Korea as well as in Japan and China and must be suspected when chronic soft tissue swelling, especiall around major salivary glands, is associated with eosinophilia in the peripheral blood.

2. This entity responds best to a combination of appropriate surgical removal, steroids, and radiation therapy.

3. The relationship of this disease and angiolymphoid hyperplasia with eosinophilia requires further study.

TABLE Ⅰ. Location of Lesions

Parotid and Mastoid Integument	7
Palate	1
Cheek	1
Submandibular	1
Submental	2
Upper neck	4
Inguinal	1
Total	17

TABLE Ⅱ. Clinical and Pathological Distinctions between Kimura's Disease and ALHE

	Kimura's Disease	ALHE
Location	Deep subcutis, common salivary gland involvement	Superficial subcutis, common dermal involvement
Size	Average 3cm. diameter	Average 1cm. diameter
Lymphocytic infiltrate	Mild to marked	Marked
Lymphoid follicles	Always	Sometimes, especially in deeper and older lesions
Tissue eosinophilia	Always ; may include abscesses	Always
Mastcells	Unusual	Common
Vascular changes	Capillary proliferation, swollen endothelial cells, no uncanalized masses	Exuberant angiomatoid proliferation. Uncanalized masses of endothelial cells often present
Fibrosis	Prominent	Often absent

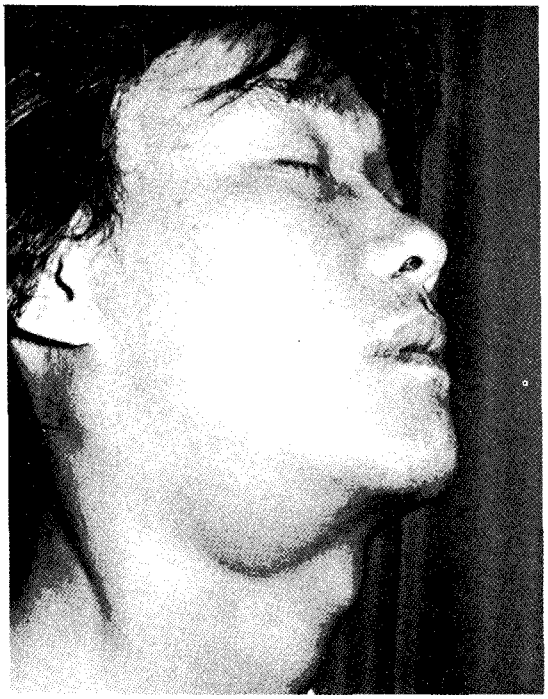

Fig. 1. Case Ⅳ : Right submandibular and parotid tail masses in a 29-year-old man.

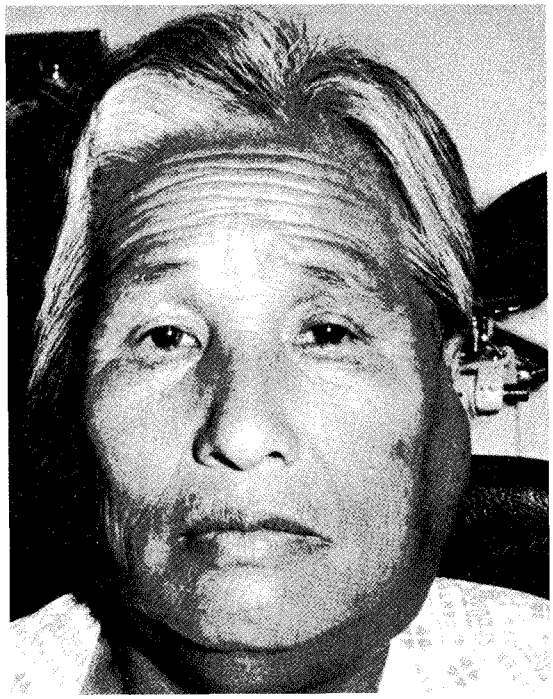

Fig. s. Case Ⅴ : Left parotid area and submental masses in a 66-year-old housewife.

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TABLE Ⅲ. Tabulation of Histologic Features in 5 Cases of Kimura's Disease

	Case Ⅰ	Case Ⅱ	Case Ⅲ	Case Ⅳ	Case Ⅴ
1. Hyperplastic lymphoid follicles in subcutaneous tissue primarily	++++	+++	++	+	+
2. Size of masses	5−8cm	10−20cm	2.5−3cm	2.5−3cm	2.5−9cm
3. Eosinophilic infiltration					
Focal	++	++++	+	++	++
Abscesses	+−	−	+	+	++
4. Vascular Proliferation					
Endothelial cells	++	+	+	+	+
Intimal fibrosis	+−	−	+−	−	+
Hyperplasia of Muscularis	+	+	+	−	+−
Endothelial aggregates with clefts and sinusoids	++	++	+	+−	+−
5. Mast cells	5−10 / hpf	> 20 / hpf	5−1- / hpf	10−15 / hpf	5−10 / hpf