症例報告

A CASE OF FATAL CONJUNCTIVAL MELANOMA FOLLOWING MULTIPLE TREATMENTS OF PAM (PRIMARY ACQUIRED MELANOSIS)

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Abstract : This study reports a rare Japanese case of malignant melanoma of the conjunctiva initially diagnosed as primary acquired melanosis (PAM) with atypia.

A 59-year-old Japanese woman presented with black-brown lesions in the conjunctiva. The patient was initially treated with resection of the lesion and cryopexy of the adjacent areas. The pathological diagnosis was PAM with atypia. Despite treatment, the patient died of systemic metastasis after multiple local recurrences.

Racial pigmentation that masks recurrences, possible existence of PAM sine pigmento, and some unknown factors, may be causes of the reported poor prognosis of Japanese patients.

Key words : conjunctival melanoma, primary acquired melanosis, cryopexy

INTRODUCTION

Primary acquired melanosis (PAM) of the conjunctiva is usually a unilateral, flat, brown pigmentation in middle-aged and older patients caused by the proliferation of atypical melanocytes in the epithelium that do not invade the subepithelial tissue until malignant transformation has occurred. It tends to progress slowly but may wax and wane. It may involve any part of the conjunctiva[1-4].

Conjunctival melanoma is rare in Japan, with only 61 cases reported in a 38-year period[5], which seems much less than the annual average age-adjusted incidence rate of 0.012 per 100,000 population in middle-aged whites[6]. Furthermore, Japanese case reports of conjunctival melanoma associated with PAM are few[7-10].

We report a Japanese patient with an initial diagnosis of PAM with atypia, resulting in lethal melanoma after multiple recurrences.

PATIENTS AND METHODS

A 59-year-old Japanese woman first presented at Nara Medical University on March 7, 1991, with a recently apparent black lesion in the medial bulbar conjunctiva. The vision was 20/16 OD and 20/12 OS, with intraocular pressures 12 mmHg OD and 8 mmHg OS. The right eye had a zone of flat black area in the upper bulbar conjunctiva extending medially to the caruncle. Foci of black lesion were also present in the upper tarsal conjunctiva (Fig. 1, 2). The ocular media and fundus were unremarkable.

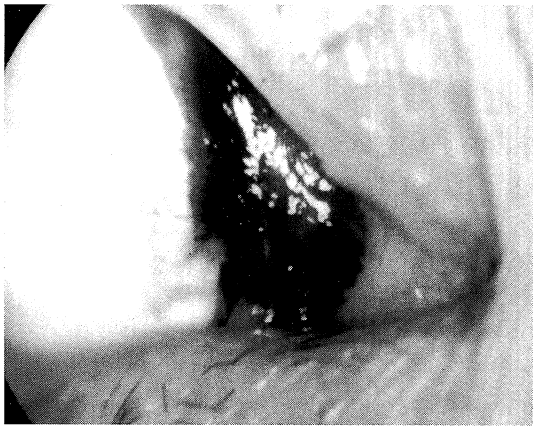

Fig. 1. An anterior segment photograph. A zone of black lesion is present in the bulbar conjunctiva, involving the caruncle.

Fig. 2. An illustration of the distribution of the pigmented lesion. The upper bulbar conjunctiva had a zone of black area,extending medially to the caruncle, superiorly to the fornicial and tarsal conjunctiva. An island of black area was present in the tarsal conjunctiva.

The clinical diagnosis was primary acquired melanosis (PAM) or malignant melanoma. On April 5, 1991, a complete resection of the black areas and cryopexy of the adjacent areas were performed. Pathological examination of step-sections of the black areas revealed intraepithelial atypical pigmented cells that did not invade the basement membrane (Fig. 3, 4, 5). Foci of junctional nevus were present in some areas (Fig. 6). A diagnosis of PAM with atypia was made. The patient was periodically followed, and multiple recurrences were found. Multiple treatments with cryopexy for recurrent flat pigmented areas were done on

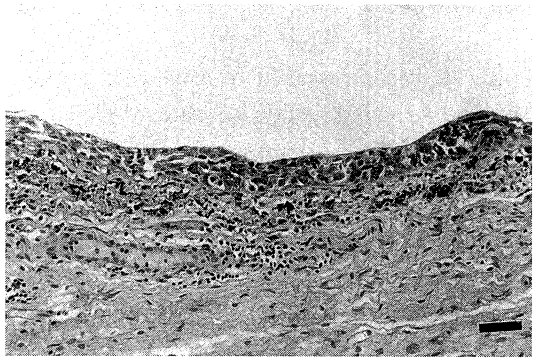

Fig. 3. A pathological section of the tumor. The conjunctival epithelium is mostly occupied by atypical pigmented cells, which do not invade the basement membrane. Hematoxilin & Eosin, Bar=50 μm

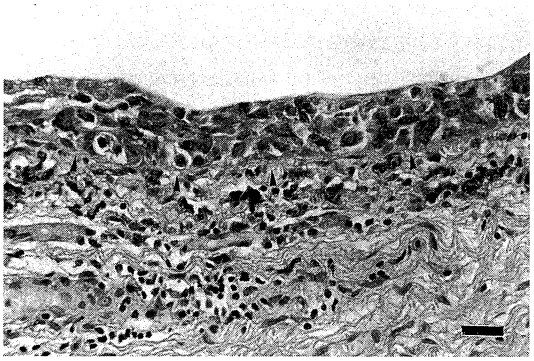

Fig. 4. A higher power photograph of the tumor. The tumor cells are large and have atypical features. The tumor cells are confined to the epithelium and do not invade the basement membrane (arrowheads). In the subepithelial layer, lymphocytes and melanophages are present. Hematoxilin & Eosin, Bar=25 μm

Fig. 5. An area of pagetoid (superficial spreading) growth pattern of tumor. Nests of tumor cells (arrows) extend along the basement membrane of the epithelium. Hematoxilin & Eosin, Bar=50 μm

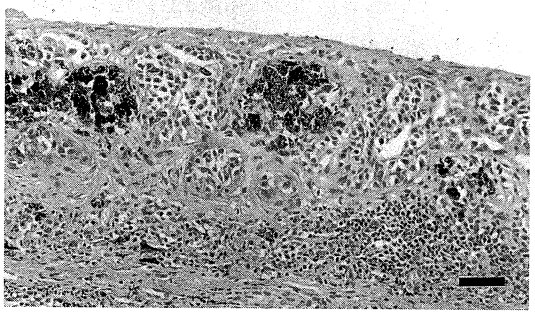

Fig. 6. Foci of junctional nevus are present in some areas. Hematoxilin & Eosin, Bar=50 μm

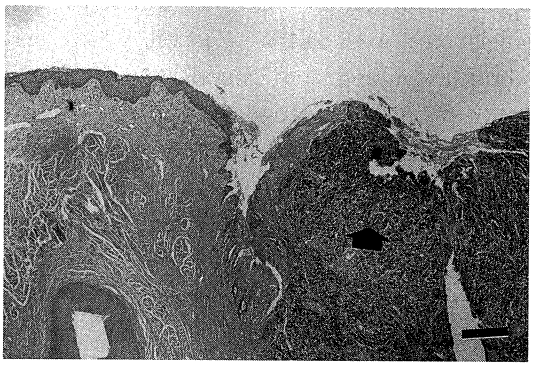

Fig. 7. Melanoma after multiple recurrences. The tumor is present in the lid (arrow). Hematoxilin & Eosin, Bar=250 μm

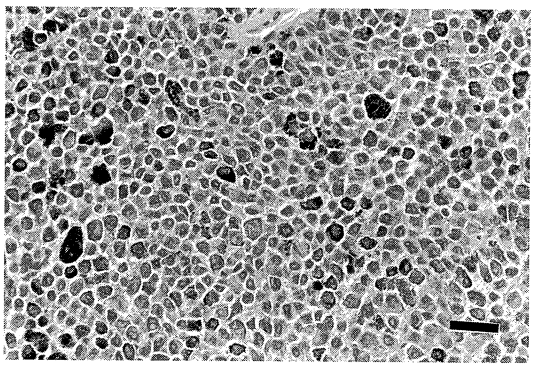

Fig. 8. A high power photograph of the tumor. The tumor cells are large, atypical, and have epithelioid appearance. Hematoxilin & Eosin, Bar=25 μm

2/12/92, 3/4/92, 6/26/92, 9/11/92, 5/19/93, and 11/10/93, 5/18/94. There were no signs of swelling of regional lymph nodes or systemic metastasis during the period. After the last treatment, a mass of pigmented tumor appeared in the right upper eyelid, which was resected on 11/16/94. The pathological diagnosis was malignant melanoma (Fig. 7, 8). A 60 Gy of radiation therapy was done in 1/95. On 3/23/95, chemotherapy with DAV and interferon, followed by an orbital exenteration were performed. The patient died of systemic metastasis on 7/1/95.

DISCUSSION

In an American study, careful slit-lamp examination revealed that the prevalence of PAM in 146 consecutive patients who were outpatients at a corneal and external diseases service, who had no known non-European ancestry, and who were older than 10 years of age, was 36%[2].

The frequency of PAM of the conjunctiva in Japan is not well recognized. In a Chinese

report of excised pigmented lesion of the conjunctiva[3], among eighteen pigmented lesions, no PAM was present. The pattern was very different from that of Caucasian series. It appears that the appearance of PAM may be infrequent in Asians.

To establish diagnosis of conjunctival pigmented, biopsies of such lesions are often be taken before more extensive therapy is planned[1]. However, complete resection should done simultaneously when malignancy is clinically suspected, since biopsy alone may disseminate tumor cells[11]. In the present case, we took the latter strategy.

Regarding the cause of the conjunctival melanoma, approximately 75% of conjunctival melanomas arise from an area of primary acquired melanosis[1]. The rest arise from the junctional component of nevi or without a detectable antecedent lesion[1]. In the present case, we could not determine the cause because both components coexisted.

The mortality for both those with and without primary acquired melanosis is approximately 25%[2]; but one subtype, those with a pagetoid (superficial spreading) growth pattern in the primary acquired melanosis, has a 44% mortality rate[2]. In the present study, pagetoid pattern was observed. This may be one reason for the poor outcame in this case.

The five-year survival rate of conjunctival melanoma was 53.4% in Japan, which was relatively low compared with those reported in Europe and the United States[5]. Racial differences of prognosis may be present. However, differences of prognosis between various pathological pattern have not been clear in Japan, since pathological reports have been rare. Accumulation of clinical reports may olarify this point in the future.

Treatment of primary acquired melanosis with atypia is usually surgical excision supplemented with cryotherapy [12-15] or laser therapy. The entire conjunctiva of these eyes should be carefully inspected at regular intervals since recurrences are common.

Not all PAM with atypia and conjunctival melanomas are pigmented. This may be one reason that the range of tumor invasion is masked, leading to multiple recurrences in some cases[16,17]. We suspect that this may be one reason for the multiple recurrences in this patient.

Some may argue that more early exenteration might have been more appropriate. Exenteration of the orbit is sometimes necessary for large melanomas that have invaded the orbit, but this procedure does not always improve the prognosis[1]. In the present case, whether an orbital exenteration much earlier in the course of the disease could have extended survival of the patient is not clear.

We discussed it with the patient, but with no sign of systemic metastasis and with useful vision, we could not choose it.

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