Malignant Skin Tumors in Patients with Oculocutaneous Albinism

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Abstract

**Background:** Patients with oculocutaneous albinism (OCA) are prone to develop skin cancers.

**Aim and Objectives:** To analyze reports of skin cancers in albinos published in the English and the Japanese literature in order to prepare guidelines for the successful management of skin cancer in albinos.

**Methods and Materials:** We searched on PubMed, Web of Knowledge for English literature, and Ichushi-Web for the Japanese literature.

**Results:** Between 1978 and 2013, 11 malignant melanoma, 4 basal cell carcinoma, and 6 squamous cell carcinoma cases were reported in Japan. The subtypes of the 11 malignant melanomas were nodular in 7 cases, superficial spreading in 3 cases, and metastatic lesions in 1 case. Amelanotic melanomas comprised 7 of the 11 malignant melanoma cases in Japanese patients with OCA. Twenty-five malignant melanoma, 50 basal cell carcinoma, and 151 squamous cell carcinoma cases were reported worldwide in the English literature during the period between 1952 and 2013.

**Conclusion:** Regular skin monitoring by board-certified dermatologists is required for adult OCA patients.

**Keywords:** Oculocutaneous albinism; Skin cancer; Melanoma; Basal cell carcinoma; Squamous cell carcinoma

Introduction

Oculocutaneous albinism (OCA) patients are well known to be susceptible to skin cancer. Among 164 northern Tanzanians with OCA, 127 and 69 exhibited actinic cheilitis and actinic keratosis, respectively, and 14 developed squamous cell carcinoma (SCC) [1]. Malignant melanoma (MM) development has been shown to be strongly associated with sun exposure [2]. Recent sequencing analyses revealed that ultraviolet light induces somatic genome alterations that might lead to MM development [3,4].

A guideline for the management of Japanese albinos is now being prepared, in which, the significance of sunscreens will be stressed. However, data about the development of skin cancers in Japanese albinos is insufficient. Therefore, we conducted a survey on the occurrence of skin cancers in OCA patients in both the Japanese and English literatures.

Materials and Methods

We searched the PubMed and Web of Knowledge (version 5.10) databases for Japanese language reports and the Ichushi-Web (version 5.10) database for Japanese language reports; all publications were available at the end of May 2014.

Results

In the English literature, 25 MM [5-12] (Table 1), 50 BCC [13-17] (Table 2), and 151 SCC [1,12-14] (Table 3) cases were reported between 1952 and 2013. Most of the reported cases were in African subjects, but Caucasians were included and comprised 6 MM cases and 1 BCC case. We found no reported cases of SCC in Caucasian albinos.

In Japan, 11 MM, 4 BCC, and 6 SCC cases were reported (Tables 4, 5) between 1984 and 2013. The 11 reported MM cases included 7 cases of nodular melanoma, 3 cases of superficial spreading melanoma, and 1 case of metastatic lesions. Amelanotic melanomas occurred in 7 cases. No cases of acral lentiginous melanoma were reported, despite this being the most prevalent MM type in Japan. These numbers are depicted in Figure 1; the occurrence of MM in Japanese OCA patients appears to be substantial.

We summarized a case series of malignant skin tumors in non-Asian individuals and in Japanese persons with OCA. In the Japanese OCA patients, BCCs and SCCs were not common, whereas the incidence of MM was substantial.
Among OCA patients, BCC and/or SCC cases were generally reported in Africans, likely due to intense exposure to ultraviolet light, insufficient medical access, and the non-prevalence of sunscreen application. We initially imagined that the numbers of BCC and/or SCC cases would be much higher among Japanese OCA patients because the incidence rates of BCC, SCC, and MM among skin cancer cases in the general Japanese population are 44%, 28%, and 20%, respectively [18-34]. However, we only identified 4 reported BCC cases and 6 reported SCC cases over a period of approximately 3 decades. This might be caused by 3 factors: first, the existence of unreported BCC and SCC cases in OCA patients; second, the under diagnosis of OCA because of skin and hair color compensation during adulthood; and third, the relative rarity of such cancer cases.

### Table 1: Twenty-five cases of malignant melanoma with oculocutaneous albinism in the English literature.

| Author(s)       | Year  | No. of Cases | Ethnicity | Ref. No. |
|-----------------|-------|--------------|-----------|----------|
| Bhende          | 1952  | 1            | Indian    | 47       |
| Young           | 1957  | 1            | NR        | 48       |
| Leonardi        | 1958  | 1            | NR        | 49       |
| Higginson       | 1960  | 1            | African   | 41       |
| Kennedy         | 1963  | 1            | NR        | 5        |
| Oettle          | 1963  | 1            | African   | 50       |
| Duron           | 1965  | 1            | NR        | 59       |
| Garrington      | 1967  | 1            | Caucasian | 51       |
| Oluwasanmi      | 1969  | 1            | NR        | 53       |
| Halama          | 1974  | 1            | NR        | 6        |
| Alpert          | 1978  | 1            | Caucasian | 7        |
| Stoll           | 1981  | 1            | African   | 54       |
| Scott           | 1982  | 1            | NR        | 8        |
| Wood            | 1982  | 1            | NR        | 52       |
| Pehamberger     | 1984  | 1            | Caucasian | 55       |
| Luande          | 1985  | 1            | NR        | 9        |
| Kinnee          | 1985  | 1            | NR        | 56       |
| Levine          | 1992  | 1            | Caucasian | 10       |
| Ihn             | 1993  | 1            | Asian     | 11       |
| Casswell        | 1989  | 1            | Caucasian | 57       |
| Schulze         | 1989  | 1            | Caucasian | 58       |
| Perry           | 2001  | 1            | NR        | 12       |
| Asuquo          | 2009  | 1            | African   | 44       |
| Mabula          | 2012  | 1            | African   | 46       |

Note: The report by Ihn H et al. [11] describes a Japanese patient who is likely the same patient in the other report by Ihn H et al. [21].

### Table 2: Fifty cases of basal cell carcinoma with oculocutaneous albinism in the English literature.

| Author(s)       | Year  | No. of cases | Ethnicity | Ref. No. |
|-----------------|-------|--------------|-----------|----------|
| Cohen et al.    | 1952  | 1            | African   | 40       |
| Higginson et al.| 1960  | 2            | African   | 41       |
| Oluwasanmi et al.| 1969 | 6            | NR        | 53       |
| Itayemi et al.  | 1979  | 3            | African   | 42       |
| Kromberg et al. | 1989  | 2            | African   | 39       |
| Yakubu et al.   | 1993  | 3            | African   | 14       |
| Colebunders et al.| 2004 | 1            | African   | 15       |
| Asuquo et al.   | 2007  | 5            | African   | 16       |
| Adegbidi et al. | 2007  | 4            | African   | 43       |
| Asuquo et al.   | 2009  | 1            | African   | 44       |
| Opara et al.    | 2010  | 5            | African   | 45       |
| Baskurt et al.  | 2011  | 2            | Caucasian | 17       |
| Mabula et al.   | 2012  | 15           | African   | 46       |

Discussion

In western Africa, most OCA patients are classified as having OCA type 2 (OCA2), which is caused by the same intragenic P gene deletion mutation as the founder effect [35,36]. Japanese patients with mild OCA2 are frequently undiagnosed and are recognized as having noticeably pale skin and brown hair during infancy and normal pale skin and dark brown hair as adults [37]. We recently identified a polymorphism in the P gene, A481T, that is associated with skin color in the Japanese population.
that many cases of SCC and BCC among Japanese albinos are unreported.

Figure 2: Among 11 malignant melanomas that developed in Japanese albinos, 7 were amelanotic melanomas, and the other 4 were melanotic melanomas.

In this study, we identified a trend in which the incidence of MM was higher in Japanese OCA patients than in African or Caucasian patients. The number of diagnosed Japanese OCA patients is approximately 5000, and MM occurred in 11 of these patients during a 35-year period. Therefore, the annual ratio of MM development in OCA patients is estimated to be approximately 1/16,000, whereas that in the general population is estimated to be 1/100,000 [38]. In fact, we recently identified an association between another decrease-of-function polymorphism in the P gene and the occurrence of MM [39-60].

Figure 3: Among 11 malignant melanomas in Japanese albinos, 7 were nodular melanomas; 3, superficial spreading melanomas; and 1, metastatic melanoma.

In this report, it was first suggested that the incidence of amelanotic melanomas in Japanese albinos was 64% (7 out of 11; Figure 2). It is conceivable that amelanotic melanomas develop in patients with severe forms of albinism, for example, those with OCA type 1A. However, reports about the development of skin cancers in albinos usually do not have information about genetic analysis. The diagnosis of amelanotic melanoma is generally difficult via macroscopic examination. Therefore, any small skin tumor occurring in albinos should be carefully examined by board-certified dermatologists.

Table 3: One-hundred fifty-one cases of squamous cell carcinoma with oculocutaneous albinism in the English literature.

| Author           | Year | MM | BCC | SCC | No. of Cases | Ref. No. |
|------------------|------|----|-----|-----|--------------|----------|
| Yoshioka J       | 1978 | +  | -   | -   | 1            | 18       |
| Ikeda S          | 1981 | +  | -   | -   | 1            | 19       |
| Nagao H          | 1991 | -  | +   | +   | 2            | 20       |
| Ihn H            | 1992 | +  | -   | -   | 1            | 21       |
| Inaba Y          | 1992 | +  | -   | -   | 1            | 22       |
| Yuasa T          | 1996 | +  | -   | -   | 1            | 23       |
| Hirose I         | 1999 | -  | +   | +   | 1            | 24       |
| Hozumi H         | 2002 | -  | +   | +   | 1            | 25       |
| Sakurane J       | 2003 | +  | -   | -   | 1            | 26       |
| Sakai H          | 2005 | +  | -   | -   | 1            | 27       |
| Obata M          | 2005 | -  | -   | +   | 1            | 28       |
| Tsuji T          | 2011 | +  | +   | Bowen | 1          | 29       |
| Inazuka Y        | 2012 | +  | -   | -   | 1            | 30       |
| Minagawa T       | 2012 | -  | -   | +   | 1            | 31       |
| Fukai T          | 2013 | +  | -   | -   | 1            | 32       |
| Aizawa A         | 2013 | +  | -   | -   | 1            | 33       |

Table 4: Malignant skin tumors in patients with oculocutaneous albinism in the Japanese literature.

According to statistical reports of MM in Japan, the frequencies of acral lentiginous melanoma (ALM), superficial spreading melanoma (SSM), nodular melanoma (NM), and lentigo maligna melanoma
The prevalence of NM among Japanese albinos might also be related to a frequency of the above MM types among Japanese albinos were 0%, 30%, 70%, and 0%, respectively.

It is noteworthy that ALM, the most common MM type in the general Japanese population, has not been reported. The frequency of SSM, which is associated with chronic sun-exposure, was not observed. The most striking finding was that as many as 70% of albino MM cases were classified as NMs (Figure 3). The cause of the high prevalence of NM among Japanese albinos might also be related to intermittent severe sun-damage and the consequent oxidative stress; however, this remains to be examined in the future.

It is important to note that MM occurred on the upper arms in 3 patients with OCA patients and on the thighs in 2 patients because these regions are considered somewhat “blind” areas when applying sunscreen agents (Figure 4). Patients with OCA are advised to apply sunscreen agents to all sun-exposed areas, including the upper arms and thighs. Gene mutation analyses were not performed in any of the reports of albino MMs. The accumulation of such data is certain to be useful with respect to sun-protection protocols for albinos.

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