

# Multiple pagetoid Bowen's disease

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A 61-year-old male was presented with oozing crusted erythematous skin lesions on the extensor site of the right forearm, the extensor site of the left forearm, left calf, right shin, and the right portion of the buttock. He was diagnosed as having multiple pagetoid Bowen's disease by H&E staining, special staining and by an electron microscopic examination. He was treated with a topical application of 5-fluorouracil cream and cryosurgery. The skin lesions were mostly healed after 7 months.

We herein report a case of multiple pagetoid Bowen's disease on the sun-protected area that may be caused by arsenic ingestion (*Ann Dermatol* 11(4) 248~251, 1999).

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*Key Words* : Arsenic, Bowen's disease, Pagetoid.

Pagetoid Bowen's disease is the variant of Bowen's disease in which large pale-staining cells are scattered throughout the epidermis<sup>1</sup>. It is essential to rule out the possibility of Paget's disease and malignant melanoma in situ. We did histochemical staining, immunohistochemical staining and an electron microscopic examination. Contrary to Bowen's disease on sun-exposed skin, Bowen's disease on sun-protected skin may be associated with arsenic ingestion<sup>2,3</sup>.

We herein report a case of multiple pagetoid Bowen's disease that may be caused by the ingestion of herbal medications mixed with arsenic.

## CASE REPORT

A 61-year-old male visited this department due to the skin lesions he had for 15 years on the extensor site of the right forearm, the extensor site of the left forearm, left calf, right shin, and the right portion

of the buttock. He had a history of leprosy 50 years ago which was cured about 30 years ago. He had taken some herbal medications mixed with mercury for 1 year and arsenic for 10 days about 40 years ago to treat leprosy. The physical examination showed 5cm~20cm erythematous plaques with a sharp margin, oozing ulcerations, thick scales and crusts accompanied by a foul odor (Fig. 1). H&E staining of the biopsy specimens showed parakeratosis, acanthosis, elongation and a thickening of the rete ridges, disarray and loss of polarity of cells, and the large pale-staining cells were scattered in the epidermis with an intact basal layer (Fig. 2). The biopsy specimens showed a positive reaction to the staining with an anti-pankeratin antibody (Fig. 3) and a negative reaction to PAS/diastase staining and the staining with anti-CEA and HMB-45 antibodies (Table 1). The finding of the electron microscopy showed perinuclear aggregation and condensation of tonofilaments and intracytoplasmic desmosomes (Fig. 4).

Therefore, this patient was diagnosed with multiple pagetoid Bowen's disease and was treated with 5% 5-fluorouracil cream and cryosurgery. The skin lesions were mostly healed after 7 months. To investigate the associated internal malignancy, a series of laboratory tests were done including CBC, SMA, alpha-fetoprotein and carcinoembryogenic antigen, as well as a chest PA, upper GI series, barium enema, and abdominal ultrasonogram. There were no spe-

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Received September 2, 1998.

Accepted for publication January 16, 1999.

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This case was presented at the 10th Japan-Korean Joint Meeting of Dermatology. September 7-8, 1997, Hakone, Japan

**Fig. 1.** Erythematous plaques with crusted oozing ulcerations on (A) the extensor site of the right forearm, (B) left calf and (C) right portion of the buttock.

**Fig. 2.** H&E staining showed parakeratosis, acanthosis and thickening of the rete ridges, disarray and loss of polarity of cells in the epidermis but showed an intact basal layer. there were pagetoid cells in the epidermis.

**Fig. 3.** The biopsy specimen showed a positive reaction to keratin by using an anti-pankeratin antibody.

**Table 1.** Differential diagnosis of pagetoid growth pattern with special staining and immunohistochemistry

Staining immunohistochemical markers	Paget's disease	Squamous cell carcinoma in situ	Melanoma in situ	This case
PAS/diastase(neutral MPS)	V	N	N	N
Colloidal iron(acid MPS)	V	N	N	N.D.
Fontana-Masson(Melanin)	V	V	P	N.D.
immunohistochemistry				
CEA	V	N	N	N
GCDFP-15	V	N	N	N.D.
EMA	P	N	N	N.D.
Keratin	V	P	N	P
S-100	N	N	P	N.D.
HMB-45	N	N	P	N
Vimentin	N	N	P	N.D.

N.D. : Not done.

V : Variable

P : Positive

N : Negative

Fig. 4. Electron microscopic findings showed perinuclear aggregation, condensation of tonofilaments and intracytoplasmic desmosomes( $\times 23,000$ ).

cific findings except abdominal ultrasonogram and barium enema. A cyst was found in the pancreas by abdominal ultrasonogram and a polyp was found in the rectum by barium enema. Abdominal CT fouding showed no demonstrable mass in the pancreas.

## DISCUSSION

Pagetoid Bowen's disease is the variant of Bowen's disease which is characterized by the large pale staining cells(pagetoid cell) throughout the epidermis in a pagetoid growth pattern. The dis-

eases requiring histologic differential diagnosis include Paget's disease(mammary and extramammary), squamous cell carcinoma in situ(Bowen's disease) and melanoma in situ<sup>1</sup>. In addition to this finding, all may clinically appear as pruritic, scaly and erythematous to brown plaques. The distinction between these diseases is important because of the differences in prognosis and associated diseases. Bowen's disease is squamous cell carcinoma in situ and rarely causes a serious danger to the patient, but mammary Paget's disease is broadly associated with the underlying carcinoma of the breast requiring prompt therapy<sup>4,5</sup>. The distinction between these diseases sometimes seems to be very difficult. Rosen et al. reported a case which was most consistent with Bowen's disease by H&E staining but was diagnosed as Paget's disease by immunohistochemical staining<sup>6</sup>. Reed et al. reported a case which was misdiagnosed as superficial spreading melanoma by routine staining, but the original diagnosis was changed into Paget's disease by immunohistochemical staining<sup>7</sup>. The histochemical and immunoperoxidase markers most useful in distinguishing the group of neoplasms are summarized in Table 1. In this case, the finding of H&E staining was mist consistent with Bowen's disease with the area of the pagetoid growth pattern. Therefore, this case was suspected as multiple pagetoid Bowen's diseases and was conformed by immunohistochemical stainings(Fig. 3, Table 1) and electronmicroscopy(Fig. 4).

Numbers of etiologic factors<sup>2</sup> have been impli-

cated in the formation of Bowen's disease. The important implicated factors are ultraviolet light, arsenics and the human papilloma virus. This patient had taken herbal medications mixed with arsenic for 10 days about 40 years ago and the lesions occurred on the non-exposed area. We could speculate that Bowen's disease in this patient might be associated with the history of arsenic intake. Norquest et al<sup>10</sup> demonstrated that the granules, which resembled the virus in the epidermal cells of the lesion of Bowen's disease, were not shown in the patients with Bowen's disease that was caused by arsenic. In our case, the granules were not shown by the electron microscopy. Kim et al. reported that Bowen's disease caused by arsenic mainly occurred on the trunk and have thick scales on the lesions<sup>11</sup>. In our case, the lesions were similarly on the trunk and had thick scales. In the patient of arsenic carcinoma, the arsenic content of the normal skin as well as the lesional skin was high and was not related to the dose of ingestion and the duration after stopping the ingestion of arsenic<sup>12</sup>. Because only a few people experience high arsenic content in the skin and the carcinoma can occur by ingestion of extremely small amounts of arsenic that were present in the nature, it is suggested that individual variation of the occurrence of Bowen's disease may be due to the difference in arsenic metabolism<sup>13</sup>. The mean duration of carcinogenesis by arsenic is generally long, which is about 24 years<sup>14</sup>.

Although there were many reports of the pagetoid growth pattern of Bowen's disease, which was initially described by Blobstein et al<sup>15</sup>. as pagetoid Bowen's disease, there was no report that occurred in the leprosy patient, who had taken herbal medication containing arsenic to treat leprosy. We reported a case of multiple pagetoid Bowen's disease that may be caused by arsenic ingestion and was successfully treated with a topical application of 5-fluorouracil cream and cryosurgery.

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