Bowen’s Disease

Robert R. Rickert, M.D.,
Roger H. Brodkin, M.D.
and Robert V. P. Hutter, M.D.

Bowen’s disease, a specific variant of cutaneous intraepidermal squamous cell carcinoma, was originally described in 1912 by Dr. John Bowen. In this report of two patients, each with a chronic solitary lesion, Bowen termed the disease “precancerous dermatosis” and asserted that although no signs of invasive cancer had yet appeared, such an outcome was inevitable. In 1914, Darier reported several additional patients, including some with multiple lesions and evidence of dermal invasion and nodal metastases. Another patient was recorded by Bowen one year later; again there was evidence of invasive squamous cell carcinoma. The special significance of Bowen’s disease, however, derives less from its inherent biologic aggressiveness than from its relationship with the simultaneous or subsequent development of other cutaneous and extracutaneous cancers.

Clinical Features

Bowen’s disease occurs in both sexes and at all ages, but is most common in fair-complexed Caucasian males, usually middle-aged or older, with an average age at diagnosis of 55 years. The lesion is more often solitary than multiple and may develop on exposed or non-exposed skin. The time interval from observed onset to diagnosis is approximately six years in the patient with a typical lesion.

Bowen’s disease appears grossly as a discrete, red plaque, varying from uniformly round to irregular in outline, usually with a scaly and fissured surface. (Fig. 1.) The evolution of the lesion is one of slow, centrifugal growth. Ulceration and thick crusting may occur late in the course of disease, raising the suspicion of invasion, a complication occurring in five to 10 percent of patients. (Fig. 2.) When Bowen’s disease develops on skin exposed to the sun, other lesions indicative of chronic solar damage such as solar keratoses, lentigines, poikiloderma and basal cell carcinoma may also be present. (Fig. 3.) In fact, the differential diagnosis of Bowen’s disease includes superficial basal cell carcinoma, solar keratoses and extramammary Paget’s disease. Bowen’s dis-
Fig. 1. Typical oval plaque of Bowen’s disease with fissured, scaly surface.

Fig. 2. Large ulcerated invasive squamous cell carcinoma arising in Bowen’s disease. The patient subsequently developed oat cell carcinoma of the lung.

ease may also be found in the anogenital area; Abell and Gosling have described 24 women with this disease in the vulva. However, erythroplasia of Queyrat, a lesion of the penile mucosa often considered to be a form of Bowen’s disease, should be regarded as a distinct clinicopathological entity. (See Box, page 162.)

Histopathology
The epidermis exhibits a striking disorganization, with loss of normal cell polarity and disruption of normal progressive maturation of the epidermal cells (keratinocytes). (Fig. 4.) There is often prominent hyperkeratosis and parakeratosis. The atypical cells of the epidermis frequently have large, hyperchromatic nuclei (Fig. 5) and commonly display individual cell keratinization. Multinucleated keratinocytes are also frequently seen. Mitotic figures may be noted at all levels of the epidermis; bizarre forms are common. Vacuolization of cells is often evident, especially in the upper half of the epidermis. (Fig. 6.) The atypical cells in Bowen’s disease characteristically involve the outer root sheath of the hair follicle. (Fig. 7.) This feature differentiates Bowen’s disease from solar keratosis, which although similar in appearance usually lacks involvement of the outer root sheath. Histologic distinction of “true” Bowen’s disease from “Bowenoid” solar keratosis may, however, be very difficult.

A moderate to dense infiltrate of lymphocytes, histiocytes and plasma cells is common in the superficial dermis. (Fig. 4.) The junction between epidermis and dermis is sharply defined, except in those five to 10 percent of lesions in which invasion of the underlying dermis has occurred.

Invasive squamous cell carcinoma in Bowen’s disease usually develops only after many years.
Bowen's Disease and Erythroplasia of Queyrat

A lesion occurring on the penile mucosa that shows a striking histologic resemblance to Bowen's disease is erythroplasia of Queyrat, first described in 1911. Some investigators have regarded erythroplasia as simply Bowen's disease of the penis, but differences do exist, especially regarding the association with internal cancer. A recent detailed study of 100 men with erythroplasia of Queyrat suggests that the disease is a distinct clinicopathological entity, which does not share the close relationship with systemic cancer that has been noted with Bowen's disease. Furthermore, there is no indication that patients with erythroplasia of Queyrat are likely to develop Bowen's disease of the skin. Erythroplasia occurs in uncircumcised males, predominantly Caucasians but occasionally Blacks and Orientals; the disease is essentially unknown in Jews. Some investigators consider that erythroplasia includes similar histologic lesions of sites other than the penile mucosa, such as the glabrous skin, labia minora, interlabial furrow, labia majora, labial fourchette, clitoris, cervix, anus, skin, lip, tongue, buccal mucosa, cheek and tonsils. The natural history of erythroplasia of Queyrat, however, indicates that it is distinct from Bowen's disease.

Clinical Correlates

Associated Cutaneous and Mucocutaneous Lesions

Approximately six to seven years after the onset of Bowen's disease, 40 percent of patients will have developed additional premalignant and malignant cutaneous and mucocutaneous lesions, commonly solar keratosis, basal cell carcinoma and squamous cell carcinoma. Other associated cutaneous lesions include adnexal carcinoma, malignant melanoma and lentigo maligna (melanotic freckle of Hutchinson). More than 10 percent of patients with Bowen's disease will have multiple combinations of both premalignant and malignant lesions. Although Dr. Bowen did not comment on this association, one of his patients also had histologically proven basal cell carcinoma.

Associated Extracutaneous Lesions

In a 1920 report on the further course of two patients, Bowen noted that the patient first detected in 1915, died in 1918 of gastric cancer. The significance of this finding was probably not recognized, however, until 1959 by Graham and Helwig. They studied 35 patients with Bowen's disease who had either been autopsied or had died after surgical and pathological examination. In this group, 28 (80 percent) were found to have one or more primary extracutaneous cancer or a primary cancer of the skin with metastases (24 or 68.7 percent primary internal cancers and four metastasizing cutaneous cancers). The average interval after appearance of Bowen's disease was 8.5 years. Review of an additional 100 patients still living with Bowen's disease revealed that 23 had developed associated internal cancers.

Abell and Gosling stressed the association between Bowen's disease of the vulva and internal cancer, especially squamous cell carcinoma of the uterine cervix and upper vagina. Carcinoma occurred in 37.5 percent of their 24 patients; 25 percent were tumors of the vulva, vagina or uterine cervix, suggesting a regional effect in which the involved anatomical sites might be subjected to similar etiologic factors. Other
sites and types of regional internal cancer in Bowen's disease of the female anogenital region are extramammary Paget's disease and carcinoma of the uterus, ovary, anus, rectum, urethra and urinary bladder.

In descending order of frequency, primary extracutaneous cancers in patients with Bowen's disease may develop in the respiratory, gastrointestinal and genitourinary tracts, the reticuloendothelial system, oral cavity, breast, endocrine system, soft tissues and the mucous membranes of the lip, eye and anus. At least five percent of patients with Bowen's disease have multiple extracutaneous cancers involving more than one anatomic site. An important observation is that five percent of patients harbor occult cancers.

Peterka and co-workers followed 53 patients with histologically documented Bowen's disease; 33 had lesions on non-exposed body surfaces and 20 had lesions on exposed areas. Of the 33 patients with lesions on non-exposed skin, 16 had died at the time of the report. In seven, an associated internal cancer had developed an average of six years after the initial diagnosis of Bowen's disease. Of the remaining 17 patients living at the time of the study, four had internal cancers, also occurring an average of six years after the diagnosis of Bowen's disease. Thus, 11 of 33 patients with Bowen's disease on non-exposed skin surfaces had developed an extracutaneous cancer.

Of the second group of 20 patients with Bowen's disease on exposed surfaces, including the upper neck, face and hands, 10 had died, but internal cancer was detected in only one patient. None of the living patients had evidence of an extracutaneous cancer. These observations indicate that the incidence of associated internal cancers was significantly higher when Bowen's disease occurred on non-solar exposed skin. The rarity of cancer associated with lesions on exposed surfaces probably partly reflects the difficulty in histologically distinguishing Bowen's disease from Bowenoid changes in solar keratosis. These data support the findings of Graham and Helwig and suggest that approximately one-third of patients with Bowen's disease develop extracutaneous cancers at an average of six to 10 years after the initial diagnosis.

Other investigators have also noted a relationship between Bowen's disease and the subsequent development of extracutaneous cancer. The magnitude of the reported risk varies, depending on the number of patients and the length and type of follow-up. Hugo and Conway studied 38 patients, six (15.8 percent) of whom had developed extracutaneous cancer. They found no relationship between the time of appearance of Bowen's disease and the diagnosis of cancer. In one patient, Bowen's disease developed 11 years after treatment for an adenocarcinoma of the rectum. Hugo and Conway compared their findings with the reported "expected" incidence of cancer of all sites and types (1.7 percent) and concluded that patients with Bowen's disease had a nine-times greater risk of developing another, internal cancer.

The widely accepted contention that Bowen's disease predisposes to the simultaneous or subsequent development of non-cutaneous cancer has recently been challenged by Andersen and co-workers in Denmark. They followed 207 patients with Bowen's disease, 23 of whom had neoplasms of other sites. Data were evaluated in relationship to the expected risk of cancer in the Danish population. Of the 23 patients with Bowen's disease who developed extracutaneous cancer, 10 were men and 13, women. According to the Danish Cancer Registry, the expected number in the entire population was 7.7 men and 8.4 women. The differences between observed and expected development of
a cancer were not significant at the five percent confidence level. Furthermore, none of their 22 patients with multiple lesions of Bowen’s disease had extracutaneous cancer. The authors were therefore unable to substantiate the observation that Bowen’s disease is associated with an increased incidence of internal cancer. Nor could they explain the disparity between the American and Danish experience, and suggested the possibility that differences may be due to the method of data collection.

Etiology

The specific etiology of Bowen’s disease is unknown. However, Andersen postulated in 1932 that there might be a correlation between arsenic exposure and Bowen’s disease. It is well documented that the histologic appearance of Bowen’s disease and certain types of arsenical keratosis may be similar or identical. Graham and associates compared the arsenic content in cutaneous lesions of 126 patients and noted that in 82 percent of those with Bowen’s disease there was an increase from two to 40 mg. of arsenic per gram of wet tissue; similar increases were found in 30 percent of patients with other cutaneous lesions. Only about five percent of patients with Bowen’s disease give a history of arsenic intake. However, since arsenic is widely available in the environment from a variety of industrial and agricultural sources including water, soil, tobacco, smoke, soot, tar, insecticides and medicinal agents, it is not surprising that patients are usually unaware of any specific exposure.

Arsenical keratosis and Bowen’s disease may be histologically identical, but the morphologic spectrum of arsenic-related skin lesions is much broader, and includes both benign and malignant.
variants.\textsuperscript{14} A study of a limited geographic area of Taiwan, in which chronic arsenical intoxication resulting from contamination of the water supply is common, revealed that in a population of 160,000 there were 64 arsenical cancers during the period from 1946 to 1961; 39 of these lesions were classified histologically as Bowen’s disease.

Sommers and McManus in 1953 showed that of 27 patients with multiple arsenical cancers of the skin, 10 (37 percent) had an associated internal cancer.\textsuperscript{15} Roth examined vintners with chronic arsenic intoxication and found extracutaneous cancers in 16 of 27 patients.\textsuperscript{16} These studies demonstrate not only a histologic similarity between the cutaneous lesions of arsenic intoxication and Bowen’s disease, but also a similar association with subsequent extracutaneous cancers.

The above data suggest that arsenical
exposure is responsible for at least some cases of Bowen’s disease. However, without specific elemental analyses of the skin lesions of a larger number of patients, it cannot be concluded that all Bowen’s disease is related to arsenic.

**Summary**

The lesion described by John Bowen as “precancerous dermatosis” remains, we believe, a specific clinicopathological entity. Bowen felt that the precancerous nature of this disease related to its ultimate conversion to an invasive cutaneous lesion. The observations of Graham and Helwig greatly expanded the concept of precancer in Bowen’s disease. These and other studies have identified the most significant feature of Bowen’s disease, that is, its relationship with the simultaneous or subsequent development of additional cutaneous and extracutaneous cancers. While the magnitude of the risk cannot be accurately estimated, it seems justified at this time to regard Bowen’s disease as a cutaneous sign of a predisposition to cancer. Although a recent report from Denmark fails to confirm this association, it is unlikely that the relationship is purely a statistical artifact. We therefore believe that the term Bowen’s disease should be restricted to those lesions that fulfill certain clinical and histological criteria and should not be used as a synonym for all types of intraepithelial squamous cell carcinoma of cutaneous and mucocutaneous surfaces or for solar keratoses with Bowenoid features. The therapeutic management of Bowen’s disease presents no special problem. The patient, however, should have continuous clinical surveillance because of the possibility that another, more serious neoplasm may either co-exist or subsequently develop.

---

**References**

1. Bowen, J.T.: Precancerous dermatoses: a study of two cases of chronic atypical epithelial proliferation. J. Cut. Dis. 30:241-255, 1912.
2. Darier, J.: La Dermatose precancereuse de Bowen, dyskratose lenticulaire et en disques. Ann. Dermat. et Syph. 5:449-471, 1914.
3. Bowen, J.T.: Precancerous dermatoses: a sixth case of a type recently described. J. Cut. Dis. 33:787-802, 1915.
4. Abell, M.R.; and Gosling, J.R.G.: Intercellular and infiltrative carcinoma of vulva: Bowen’s type. Cancer 14:318-329, 1961.
5. Graham, J.H., and Helwig, E.B.: Erythroplasia of Queyrat: a clinicopathologic and histochemical study. Cancer 32:1396-1414, 1973.
6. Graham, J.H., and Helwig, E.B.: Premalignant cutaneous and mucocutaneous diseases. In: Graham, J.H.; Johnson, W.C., and Helwig, E.B. (eds.), Dermal Pathology. Hagerstown, Md., Harper and Row, 1972, Chapter 24, Pp. 561-624.
7. Bowen, J.T.: Precancerous dermatoses: the further course of two cases previously reported. Arch. Derm. and Syph. 1:23-24, 1920.
8. Graham, J.H., and Helwig, E.B.: Bowen’s disease and its relationship to systemic cancer. Arch. Derm. 83:738-758, 1961.
9. Peterka, E.S.; Lynch, F.W., and Goltz, R.W.: An association between Bowen’s disease and internal cancer. Arch. Derm. 84:623-629, 1961.
10. Hugo, N.E., and Conway, H.: Bowen’s disease: its malignant potential and relationship to systemic cancer. Plast. Reconstr. Surg. 39:190-194, 1967.
11. Andersen, S.L.C.; Nielsen, A., and Reymann, F.: Relationship between Bowen’s disease and internal malignant tumors. Arch. Derm. 108:367-370, 1973.
12. Anderson, N.P.: Bowen’s precancerous dermatosis and multiple benign superficial epithelioma: evidence of arsenic as an etiologic agent. Arch. Derm. and Syph. 26:1052-1064, 1932.
13. Graham, J.H.; Mazzanti, G.R., and Helwig, E.B.: Chemistry of Bowen’s disease: relationship to arsenic. J. Invest. Derm. 37:317-332, 1961.
14. Yeh, S.; How, S.W., and Lin, C.S.: Arsenical cancer of skin. Histologic study with special reference to Bowen’s disease. Cancer 21:312-339, 1968.
15. Sommers, S.C., and McManus, R.G.: Multiple arsenical cancers of skin and internal organs. Cancer 6:347-359, 1953.
16. Roth, R.: The sequelae of chronic arsenic poisoning in Moselle vintners. German M. Month. 2:172-175, 1959.