Volume Two

CANCER *of the* SKIN

Biology-Diagnosis-Management

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W. B. SAUNDERS COMPANY
Philadelphia • London • Toronto

W. B. Saunders Company: West Washington Square
Philadelphia, PA 19105

1 St. Anne's Road
Eastbourne, East Sussex BN21 3UN, England

1 Goldthorne Avenue
Toronto, Ontario M8Z 5T9, Canada

Library of Congress Cataloging in Publication Data

Main entry under title:

Cancer of the skin.

Includes index.

CONTENTS: v. 1. Biology-diagnosis-management.

1. Skin—Cancer. I. Andrade, Rafael. [DNLM: 1. Skin neoplasms. WR500 C215]

RC280.S5C36 616.9'94'77 73-91274

ISBN 0-7216-1245-8 (v. 1)

Cancer of the Skin

ISBN Vol 1: 0-7216-1245-8
ISBN Vol 2: 0-7216-1246-6

Print No.: 9 8 7 6 5 4 3 2

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PART I GENERAL TOPICS

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Basal Cell Epithelioma

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DEFINITION

Basal cell epithelioma (basal cell carcinoma, rodent ulcer, basalioma) is a malignant tumor arising from the epidermis (Lever, 1967) or its appendages (Sanderson, 1968). Usually found in hair-bearing skin (Lever, 1967), the tumor is characterized by slow growth and failure of the cells to mature, keratinize, and desquamate (Van Scott, 1971). It manifests a stromal dependency (Van Scott and Reinertson, 1961; Pinkus, 1965) and very rarely metastasizes. Its potential for localized destructiveness and its tendency to recur after therapy are well known.

ETIOLOGY

Among the predisposing causes, chronic actinic exposure seems to be of great importance—particularly in those individuals with fair skin and blue eyes who sunburn easily (Gellin, et al. 1965). Individuals with more darkly pigmented skin are subject to fewer basal cell epitheliomas (Urbach, et al. 1965; Sanderson, 1968). While there seems to be general agreement about the overall effect of sunlight, some investigators have noted discrepancies in this regard. Urbach et al. (1965), using a special chemical dosimeter system and mannequin heads exposed to sunlight under varying conditions, determined the amount of radiation received by different portions of the head and neck. Comparing these areas with the prevalence and distribution of squamous and basal cell carcinomas in a series of selected hospital and clinic patients, he noted some discrepancies in the location of basal cell epitheliomas.

Squamous cell carcinoma occurred in skin areas most heavily exposed to ultraviolet light. However, about one-third of all the basal cell lesions were found on skin areas receiving less than 20 percent of the maximum possible dose of ultraviolet radiation. Geographic studies cited by Urbach further supported these mannequin chemical dosimeter observations. Brodkin et al. (1969) stated that areas showing dermal elastosis as a criterion for sunlight skin damage do not always correlate with sites of basal cell epitheliomas.

Ingestion of inorganic arsenic in Fowler's solution, insecticide residues, on food, or in drinking water may give rise to skin tumors, including the superficial type of basal cell epithelioma, after a long latent period.

Genetic factors may predispose individuals to the basal cell nevus syndrome (see Chapter 37). Trichoepithelioma (Lever, 1967) and nevus verrucosus rarely become basal cell epithelioma (Sutton, 1956; Litzow and Engel, 1961; Rook, 1968). Basal cell epithelioma develops in nevus sebaceus in adult life in 6 to 50 percent of cases, depending on the series reported (Rook, 1968; Wilson Jones and Heyl, 1970) (Fig. 35–1).

X-ray exposure may predispose the individual to basal cell epithelioma in later life. Formerly it was felt that only squamous cell carcinoma arose in areas of radiodermatitis. Anderson and Anderson (1951) and Traenkle (1964) noted that basal cell carcinoma occurs often in areas of chronic radiodermatitis. Traenkle reported that radiologists have observed carcinomas to occur in roentgen dermatitis resulting from multiple small doses produced over a long period of time, as opposed to large cancericidal doses (4000 to 6000 R.) given over a relatively short period (i. e., a one- to four-week period).

Figure 35–1 Nevus sebaceus with basal cell epithelioma, right temple. (Photograph used by permission, New York University Medical Center, Skin and Cancer Unit.)

Sulzberger et al. (1952), however, reported contradictory results. Dermatologic x-ray therapy (65 to 100 kvp) given in small doses of 37.5 to 75 R. over a period of time up to a total of 1000 R. was unlikely to produce carcinomas. Patients were examined 5 to 23 years after such x-ray exposures. The authors noted that mild x-ray sequelae can be anticipated in 1 out of 87 patients.

Sarkany et al. (1968) noted development of multiple basal cell epitheliomas and fibroepitheliomas of Pinkus over the skin of the back following previous irradiation for lichen planus and spondylitis. The latent period was 11 to 28 years. Dosages varied from 600 R. to 8875 R. The kilovoltage used ranged from 75 to 225 kvp. The treatments ranged in number from 3 to 158 and were given over a 5-month to 16-year period. Meara (1968) added more case material with findings similar to those described by Sarkany.

INCIDENCE

Males show a greater incidence than females (Gellin et al., 1965; Sanderson, 1968). Ten Selden (1963) and Eastcott (1963) found a 2:1 ratio of males to females in Australia and London. However, Miyaji (1963) in Japan and Pantangco et al. (1963) in the Phillippines found the incidence of basal cell epithelioma to be higher in women. The latter noted that women are exposed to actinic rays because of outdoor occupations.

While basal cell epithelioma is less common in the Far East among the indiginous population, Shu (1963) found about an 11 percent incidence in an area of Taiwan with high arsenic levels in the drinking water.

At the University of Texas M. D. Anderson Hospital for the period 1954 to 1961, MacDonald and Bukendorf (1964) noted that nearly one-fourth of 30,000 patients with cancer have had primary cancer of the skin. Of these, 60 percent had basal cell epitheliomas, and 33 percent had squamous cell carcinoma. In the period 1956 to 1960 at the Royal Perth Hospital in Australia, Ten Selden (1963) found that

slightly over half of the histologically verified cases of skin cancer were basal cell carcinomas.

In New Zealand, Eastcott (1963) found that skin cancer was 50.9 percent of all cancers, whereas in London it was only 16.2 percent. In New Zealand basal cell epithelioma showed a yearly incidence of 1130 per million inhabitants (Eastcott, 1963). This was three times as large as the yearly squamous cell carcinoma incidence. Auerbach (1961) showed that skin cancer incidence rates in the United States in the white population doubled for each 3° 48′ of latitude or about 265 miles.

Schreiber et al. (1971), discussing incidence of skin cancer in southern Arizona, cited Belisario's figure of 350 cases of skin cancer per 100,000 population for Queensland in 1960. They showed an incidence in Tucson of 422 per 100,000 cases, of which 75 percent were basal cell epitheliomas, i.e., 315 per 100,000 cases. They ascribed their very high basal cell carcinoma incidence to several factors. Tucson has a very high degree of insolation, low humidity, high temperature (with resultant increase in outdoor activity and fewer protective covering clothes), an altitude of 2410 feet, a latitude of 32° N, and, most important, a low atmosphere ozone.

Blum (1959) pointed out that the atmospheric ozone layer determines the limits of the short wavelengths of sunlight reaching the earth's surface. He also noted that the amount of ozone varies with season of year and latitude. Blum's calculations (for 60° latitude) showed that sunlight at 8 A. M. and 4 P. M. is about 8 percent as effective as at 12 noon. These calculations did not take into account factors such as dust and cloud cover.

Experimental Work and Clinical Observation on Carcinogenesis and Ultraviolet Damage

Wilgrim et al. (1970) noted that, after ultraviolet irradiation of the skin, the keratinosomes decreased at two hours in number in upper malpighian and granular layers. A disappearance of the keratinosomes at three hours is the first sign of epidermal injury following ultraviolet irradiation.

Mitchell (1970), studying premalignant and malignant cells, noted proliferation of basal cells with comparatively large, irregular nuclei, numerous, small mitochondria, and many ribosomes. Fewer desmosomes were noted on the cell surface. He found that premalignant lesions often show thickened or multilayered basement membranes. This latter structure was variably present in invasive cancers, and he felt this finding may indicate the degree of differentiation of cells producing the basement membrane rather than the degree of cancer malignancy. He also noted a similarity of electron microscopic picture of chemically induced experimental skin cancer to the naturally occurring form.

Kligman (1969) observed early onset of sun damage in children in the Philadelphia area. He used elastic fiber changes as his indicator. Onset of this damage was seen as early as the first decade, but the majority of young adults showed evidence of this by 30 years. The histologic evidence preceded clinical changes. The changes correlated with areas of maximum exposure, being greatest in ear rim and cheek.

Jung and Traschsel (1970), using inorganic arsenic, xenon lamp irradiation, and human tissue slices with thymidine uptake studies, showed that the mitotic index was lowered by either irradiation or arsenic. Both arsenic and irradiation concomitantly lowered the mitotic index even more. Apparently arsenic inhibits DNA polymerases and other enzymes.

Daniels (1963) stated that in the white race the effects of skin color, hair color, and eye color on erythema threshold are not consistent. This finding contrasts with the clinical finding and impression that chronic actinic damage and skin cancer depend on the degree of skin pigmentation. He cites Blum to the effect that the process of cancerization begins with ultraviolet doses and continues progressively. There is a great lack of knowledge about events that take place in the skin between first and repeated sunburn and onset of skin cancer.

Knox et al. (1964) cited work to show that sunlight-induced carcinoma in animals is screened out by window glass (wavelengths less than 3200 Å). Ultraviolet penetration into the dermis is diminished 5 percent from untanned to tanned skin.

Norins (1962) showed that ultraviolet irradiation can cause ionization and production of free radicals. He also noted that melanin is a free radical trap and hat sulfhydryl conversion into disulfides takes up free radicals, thereby lessening the pool of free radicals, which in turn lessens the likelihood of skin damage.

Repeated solar insult produces injury first in subpapillary and later in papillary layers of the dermis, resulting in widespread collagen degeneration (Mackie and McGovern, 1958). They felt that damage to these layers caused impaired metabolism with a subsequent effect on overlying epidermis.

From the results of skin transplantation experiments, Orr (1961) showed that dermis damaged by chemical carcinogens is important as a determinant in skin grafts exchanged between normal and diseased skin. Dermis of chemically damaged skin covered with normal undamaged epidermis resulted in formation of skin tumors. Chemically damaged epidermis transplanted to "nondamaged" dermis did not result in formation of tumors if transplantation took place after chemical insult but prior to actual development of skin tumors.

Olson (1971) demonstrated dispersion of pigment throughout the epidermis in well-tanned Caucasian skin. Negro skin showed similar dispersion of melanosomes throughout the epidermis.

The skin of fair individuals who burn easily, freckle, but do not tan showed irregular dispersion of pigment with large melanosome complexes (Olson, 1971). Patients with xeroderma pigmentosum showed deficient transfer of melanin from melanocyte dendrites to keratinocytes, resulting in poor protection from sunlight (Olson, 1971).

Utilizing fibroblasts cultured from actinically damaged skin of patients with xeroderma pigmentosum, Cleaver (1969) and Cleaver and Trosko (1970) demonstrated a failure in these fibroblasts to repair sunlight-damaged DNA strands. His work showed that the fibroblasts lack an endonuclease essential for this repair process. This important work may help to elucidate some of the mechanisms involved in carcinogenesis.

CLINICAL PICTURE

Types of Basal Cell Epithelioma

A common story heard from male patients is that several months prior to their clinic or office visit they nicked themselves with a razor while shaving. Since the original injury, the area has slowly enlarged and formed a persistent crust. This crusted basal cell epithelioma may reveal a telangiectatic, translucent portion or border when the crust has been removed. Such an erythematous lesion 4 to 7 mm. in size is quite common in private dermatologic practice. The slowly growing, translucent papule with or without pigment, displaying a few telangiectatic vessels on its surface, is also a common type of basal cell epithelioma (Fig. 35–2). Both are found on the exposed surfaces of the face, neck (Freeman, and Knox 1967; Baferstedt, 1970), and ears. Rarely basal cell epithelioma lesions will be found on the legs and very rarely on the palms and soles.

The superficial type of basal cell epithelioma (Fig. 35–3) is usually found on the thorax. In its very early stage it is an erythematous, macular lesion with some

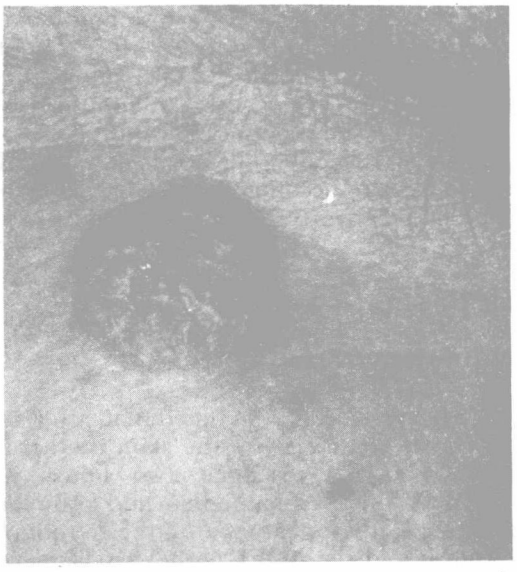

Figure 35–2 Basal cell epithelioma showing fine telangiectasia on surface.

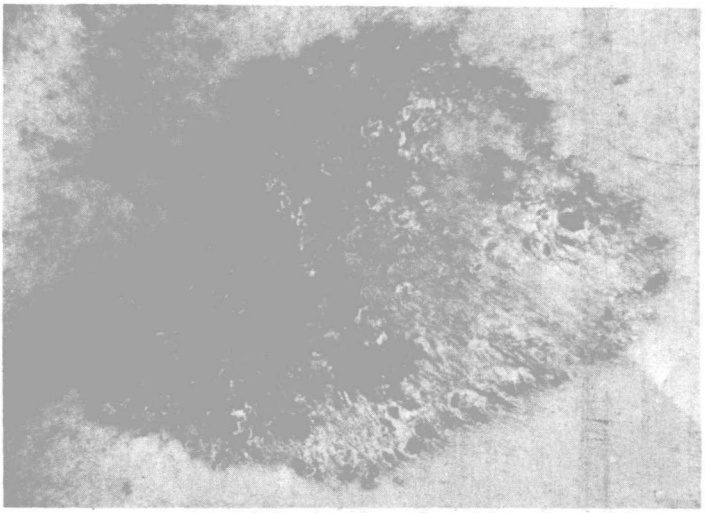

Figure 35–3 Superficial type of basal cell epithelioma.

scaling and may not show the threadlike, rolled edge of the more fully developed lesion. Moreover, it does not show as much scaling and tendency toward central clearing as the older and more well-developed carcinomas. The early lesion can be suspected only if the patient has had one or more superficial basal cell epitheliomas. Superficial basal cell epithelioma lesions tend to be multiple.

Older lesions have an eczematous or psoriasiform picture and frequently a violaceous hue that may be characteristic.

Another clinical type of basal cell epithelioma shows a centrally depressed area with an elevated translucent border. This type is usually seen on the face.

An unusual type of basal cell lesion is the slowly enlarging pore. The patient will note unequivocally that there has been a chicken-pox–like pit on the face. Unlike an ordinary pit, it slowly increases in size. Sometimes the border will show telangiectasia.

The lesions of basal cell nevus syndrome (see Chapter 37) often may be mistaken for small, slightly pigmented, intradermal nevi. However, the multiplicity of lesions in association with the distinctive palmar pits, dentigerous cysts, broadened nasal root, increased interpupillary distance, and other stigmata place the patient into the basal cell nevus syndrome.

Odd locations for basal cell epithelioma lesions have been in vaccination scars (Weary, 1967) and in nevus pigmentosus (Sigal and Saunders, 1967, who also cite Pinkus, Meltzer, and Stegmaier with similar experience).

Lesions may arise in nevus syringocystadenomatosus papilliferus (Zugerman, 1961) and in trichoepithelioma (Lever, 1967). Hyman and Michaelides (1963), Lewis et al. (1965), and Goldberg (1968) reported basal cell epithelioma on the sole. An eccrine gland origin has been postulated for the lesions arising on the sole.

Another clinical variant one sees is the

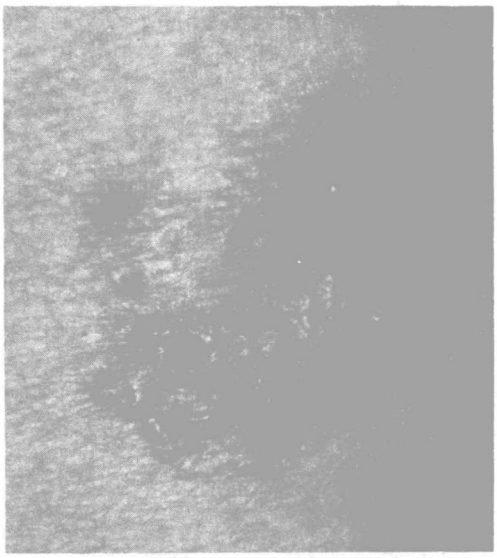

Figure 35–4 Crusted nodular basal cell epithelioma.

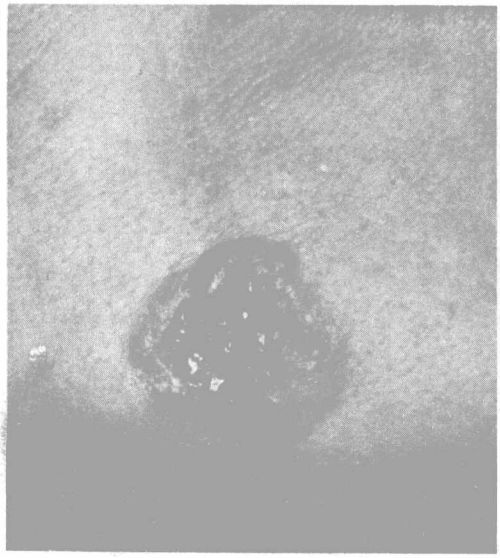

Figure 35–5 Ulceronodular basal cell epithelioma.

so-called "field fire" type of basal cell epithelioma. This shows central scaling and scarring peripheral spread with crusting at the margins (Fig. 35–4). This type is probably a clinical variant of the ulceronodular type (Fig. 35–5) and may become quite destructive.

Another uncommon clinical variant is the morphea type of basal cell epithelioma (Fig. 35–6). Often it presents as a firm, superficially telangiectatic, yellowish white or ivory plaque on the face. At times, the outlines are quite distinct, and at other times the lesion may blend with normal surrounding skin. Histologically, this lesion shows an intimate admixture of fibrous stroma and islets of basal cell epithelioma (Fig. 35–7). Botvinnick (1967) found in one series of 3000 basal cell epitheliomas an incidence of 0.6 percent for the morphea type of lesion.

Another distinct clinical type of basal cell epithelioma is the fibroepithelioma of Pinkus (1965) (Fig. 35–8). It resembles a pink, nonpigmented, seborrheic keratosis. This lesion is most frequently found on the skin of the lower portion of the back and also the abdomen. It may be found in multiples and is either sessile or slightly pedunculated.

Clinical Course

Most basal cell epitheliomas grow very slowly as far as patient and physician can observe. Van Scott (1964) noted that, despite numbers of basal cell epithelioma cells in active mitosis, the growth rate of the lesion is slow. Weinstein and Frost (1970) found a total germinative cycle of 217 hours for basal cell epithelioma. They suggested that a possible explanation for the clinically observed very slow rate of growth, despite the doubling time of nine days, may be that cell death occurs at nearly the same rate as cell division. Jackson (1965) mentioned a growth rate of

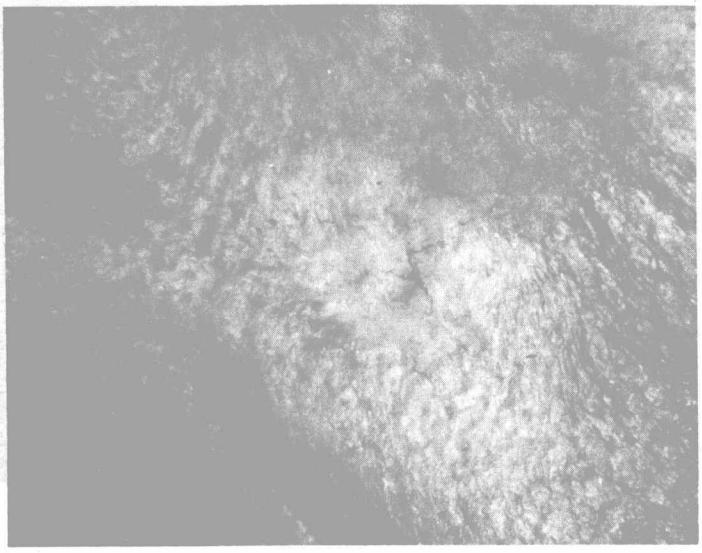

Figure 35–6 Morphea type of basal cell epithelioma. There is a lack of sharply defined margins at some portions of the border.