Ann. Ist. Super. Sanità, vol. 32, n. 1 (1996), pp. 29-36

Basal cell and squamous cell carcinomas. Clinico-histological features

Giorgio ANNESSI and Giannandrea BALIVA

Servizio di Istopatologia, Istituto Dermopatico dell'Immacolata, Rome, Italy

Summary. - Basal cell and squamous cell carcinomas are the most common skin cancers, occurring mainly on sun-damaged skin of old persons. Basal cell carcinoma is a neoplasm of follicular germinative cells which may infiltrate and destroy adjacent tissues, but rarely metastasizes. Five clinico-pathologic types of basal cell carcinomas can be recognized, namely, nodulo-ulcerative, superficial, morpheiform, fibroepithelial, and infundibulo-cystic. Actinic keratosis and Bowen's disease are intrepidermal proliferation of atypical keratinocytes that eventually may progress to become overt squamous cell carcinoma. Lesions arising in sites of chronic injury or scarring bear an higher risk of metastases. Keratoacanthoma is a rapidly evolving tumor of keratinocytes that resolves spontaneously. Keratoacanthoma might represent a self-healing type of squamous cell carcinoma.

Key words: basal cell carcinoma, squamous cell carcinoma, keratoacanthoma.

Riassunto *(Carcinoma basocellulare e squamocellulare. Aspettti clinico-istologici).* - Il basalioma e lo spinalioma sono i tumori epiteliali maligni di più frequente riscontro a livello cutaneo. Essi originano prevalentemente nelle aree fotoesposte di persone anziane. Il basalioma è una proliferazione maligna di cellule germinative follicolari che infiltra e distrugge i tessuti circostanti potendo raramente metastatizzare. Sulla base di criteri clinico-patologici, si distinguono cinque forme di basalioma, ovvero, il nodulo-ulcerativo, il superficiale, il morfeiforme, il fibroepiteliale e l'infundibolo-cistico. La cheratosi attinica ed il morbo di Bowen sono proliferazioni intraepidermiche di cheratinociti atipici che nel tempo possono evolvere in uno spinalioma infiltrante. Gli spinaliomi che nascono in aree sottoposte a stimoli infiammatori cronici o in aree cicatriziali hanno maggiore rischio di metastasi. Il cheratoacantoma è un tumore dei cheratinociti che si sviluppa rapidamente e tende a scomparire spontaneamente. Il cheratoacantoma può essere considerato come una forma autorisolvente di spinalioma.

Parole chiave: basalioma, spinalioma, cheratoacantoma.

Introduction

Basal cell carcinomas and squamous cell carcinomas account for approximately 90% of all skin malignancies. Although the vast majority of these tumors occurs on sun-damaged skin of old fair-skinned persons, their occurrence in youngsters may represent a clue for genetic disorders, such as nevoid basal cell carcinoma syndrome [1] or xeroderma pigmentosum [2]. In most instances, the clinico-histological diagnosis of basal cell and squamous cell carcinomas is straightforward. Certain lesions, however, may be difficult to classify histologically because of some apparent overlap with other adnexal tumors or because they display both basaloid and squamous differentiation.

Basal cell carcinoma

Basal-cell carcinoma is a malignant neoplasm of follicular germinative cells that can cause death from local destruction of the tissue, and, rarely, from widespread metastases. Basal-cell carcinomas usually arise from the lowermost layers of the epidermis or of follicular infundibula, although a small percentage may originate from actinic keratoses [3] or seborrheic keratoses. Five types of basal-cell carcinomas can be identified specifically on the basis of clinico-pathologic correlation, namely, nodulo-ulcerative, superficial, morpheiform, fibroepithelial and infundibulo-cystic. The histopathologic patterns of basal-cell carcinoma, however, are numerous, e.g., solid, cystic, adenoid-cystic, adenoid and adamantinoid. These patterns are due in part to features that have no direct bearing on the clinical course of the tumor. All types of basal-cell carcinomas are characterized histopathologically by aggregations of basaloid follicular germinative cells of various sizes and shapes that are focally separated from the surrounding stroma by prominent clefts. Neoplastic cells have slightly elongated nuclei and tend to be aligned in a palisade at the peripheries of some aggregations. Stroma altered by edema, mucin, increased vasculature, infiltrate of lymphocytes and fibroplasia surrounds the neoplastic aggregations. Melanin pigment may be present in various amounts in any type of basal-cell carcinoma. Functional

melanocytes are scattered throughout the tumor islands and there may be numerous melanophages in the stroma [4].

Nodulo-ulcerative basal cell carcinoma

The nodulo-ulcerative type is, by far the most common clinico-pathologic form of basal-cell carcinoma. It occurs mainly as a single lesion on sun-damaged skin although the occurrence of multiple lesions either simultaneously or subsequently is not infrequent. Around 40% of patients who have had a basal cell carcinoma will develop one or more basal cell carcinomas within ten years. Clinically, early lesions may begin either as small, translucent, round-oval papules partially covered by adherent scales or as small superficial ulcers resembling an excoriation by a finger nail. In time, the neoplasm may take the form of a dome-shaped, translucent, pink or flesh-colored nodule with a smooth and teleangectatic surface or it may appear as a rounded plaque with raised, pearly borders and a slightly depressed center covered by scale-crusts (Fig. 1). Basal cell carcinomas may periodically, erode and crust and the surface contour generally becomes more irregular as the lesions grow. Pigment may be irregularly distributed throughout the tumor in the form of tiny, blue-brownish flecks. Occasionally, the lesion is evenly pigmented (pigmented basal cell carcinoma) mimicking a melanocytic neoplasm. At times, basal cell carcinoma is constituted of an ulcerated plaque with indurated edge and base, in absence of pearly, thread-like margins (rodent ulcer). This lesion may have started as a nodule, but more frequently, it is crusted and eroded from an early stage of its evolution. Rodent ulcer may reach considerable size and may invade deeply causing great destruction especially around the nose, eye or ear. The bones of the face, the skull and the meninges may be infiltrated and this eventually may cause death.

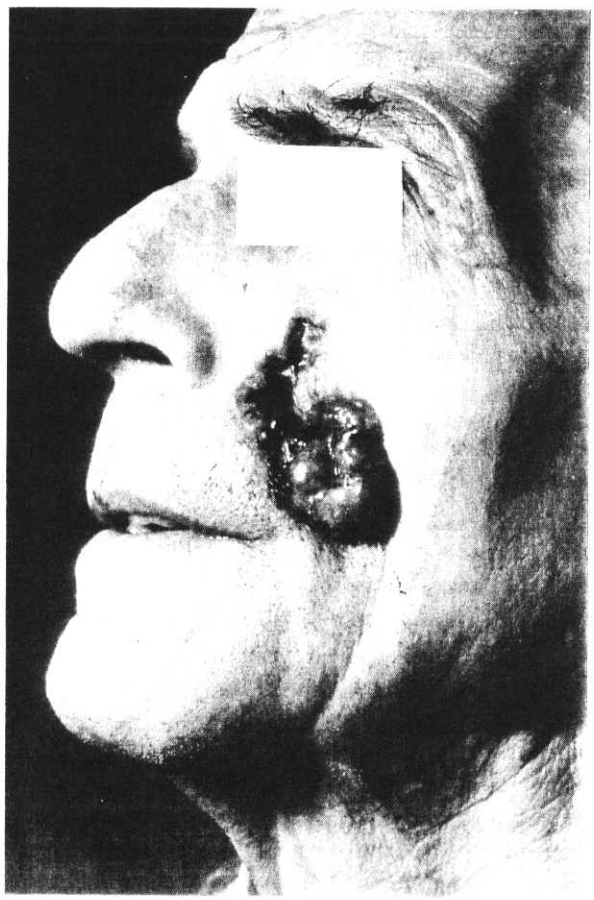

Fig. 1. - Nodulo-ulcerative basal cell carcinoma on the cheek.

Histologically, nodulo-ulcerative basal cell carcinomas mostly consist of small and/or large islands or nests of basaloid cells that are focally connected to the undersurface of the epidermis [5] (Fig. 2). Neoplastic aggregations involve the reticular dermis and may extend into the subcutaneous tissue. Ulceration is frequent in larger lesions and areas of cellular necrosis are frequently seen in the center of the islands. The vast majority of nodulo-ulcerative basal-cell carcinomas is undifferentiated. Neoplastic cells are frequently arranged in a palisade at the periphery of the aggregations and show large, elongated nuclei and relatively little cytoplasm. Although the nuclei have a rather uniform appearance, in rare cases, they appear to be hyperchromatic and pleomorphic with prominent nucleoli. Occasionally, many mitotic figures and necrotic keratinocytes are observed. Nevertheless, the finding of atypical cytological changes does not correlate with an aggressive biologic behavior [6]. In most cases, germinative neoplastic cells form solid masses of various sizes and shapes (solid type) (Fig. 2) whereas in others, one or more cystic spaces develop towards the center of some or all tumor aggregations because of degeneration of neoplastic cells and deposit of mucin (cystic type). The adenoid type of basal-cell carcinoma consists of strands of basaloid cells in a reticulate or lace-like pattern. In contrast, adamantinoid basal-cell carcinoma is constituted by large masses of neoplastic cells with palisade at the periphery inside which the cells have elongated nuclei and stellate cytoplasm stretched as thin, connecting bridges across empty spaces. Rarely, nodulo-ulcerative basal-cell carcinomas may show attributes of follicular differentiation. These may assume the form of limited follicular differentiation, i.e., follicular germs, rudimentary papillae and, sometimes, primitive peri-follicular sheaths, or advanced follicular differentiation i.e., follicular bulbs and papillae, outer root sheath (pale or clear cells, the peripheral ones being arranged in a palisade), inner sheath (trichohyalin granules and blue-gray corneocytes arranged compactly), hair ("shadow" cells), and infundibula or a combination of these. Sebaceous as well as apocrine differentiation is sometimes present within areas of an otherwise undifferentiated

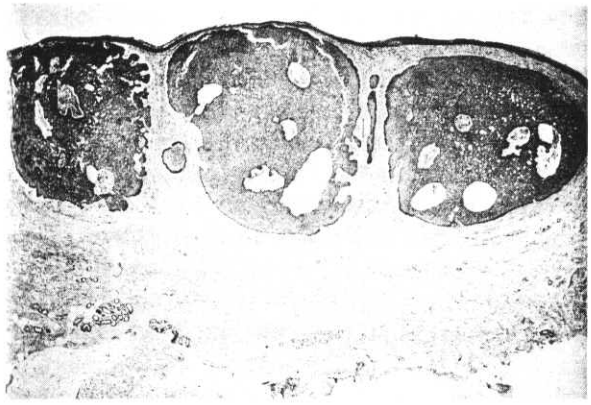

Fig. 2. - Histologically, nodulo-ulcerative basal cell carcinoma shows solid aggregations of basaloid cells that extend into the reticular dermis.

basal-cell carcinoma. Around 5% of nodulo-ulcerative basal-cell carcinomas display a markedly infiltrative pattern of growth with columns and strands of basaloid cells infiltrating between collagen bundles [7]. Often there is a solid pattern superficially with the infiltrating nests at the periphery or base of the lesion. Stroma is scant and neoplastic cells may extend into the subcutaneous fat, skeletal muscle or underlying cartilage in lesions of the nose and ear.

Basosquamous carcinoma. - This term is applied to a basal-cell carcinoma differentiating into a squamous cell carcinoma [8]. Basosquamous carcinoma is mostly constituted of basaloid cells, which are slightly larger and paler than the cells of a solid basal-cell carcinoma and mature into squamoid cells with abundant eosinophilic cytoplasm. Peripheral palisading is less obvious than usual and the stroma is not prominent. "Horn pearls" or complete keratinization may be observed in the centers of some neoplastic aggregations. Recurrent basal-cell carcinomas often exhibit features of basosquamous carcinoma. This histologic variant, moreover, seems to be associated with more aggressive behavior.

Superficial basal cell carcinoma

Superficial basal cell carcinoma accounts for 10-15% of all basal-cell carcinomas. It mostly occurs on the trunk as one or multiple erythematous, scaling, slightly infiltrated plaques that slowly enlarge by peripheral extension (Fig. 3). The lesions often show a thin, thread-like pearly border. The plaques may present small areas of superficial ulceration or crusting and their center may show smooth, atrophic scarring. Superficial basal cell carcinomas are often pigmented and may be mistaken for malignant melanomas.

Histologically, it consists of multiple small islands of basaloid cells emanating from the undersurface of the epidermis and from pre-existing infundibula (Fig. 4). Neoplastic aggregations vaguely resemble follicular germs and are confined to the papillary dermis. A narrow zone of fibrous stroma may surround the nests. The adjective "multifocal" is often applied to superficial basal-cell carcinoma, but it is a misnomer. Studies based on horizontal serial sections have demonstrated that the apparently multifocal aggregations are, in fact, connected. In some instances, superficial basal-cell carcinoma may progress to become a nodulo-ulcerative basal-cell carcinoma. A lymphocytic infiltrate probably plays a role in the focal regression that is seen up to 20% of basal-cell carcinomas especially of the superficial type. Active

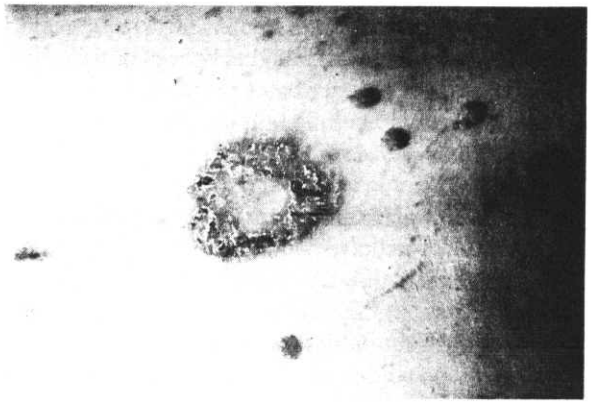

Fig. 3 . - Superficial basal cell carcinoma on the back surrounded by several seborrheic keratoses. Occasionally, superficial basal cell carcinoma may originate from a seborrheic keratosis.

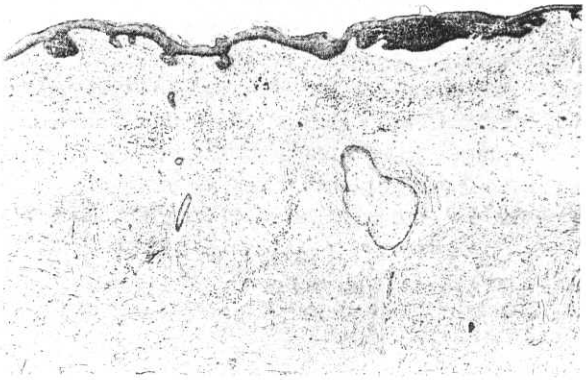

Fig. 4. - Multiple small aggregations of basaloid cells emerging from the basal layer of the epidermis are seen in the superficial type of basal cell carcinoma. Some of those aggregations resemble follicular germs.

regression is characterized by the presence of a lymphocytic infiltrate which surrounds and infiltrates the tumor islands with destruction of the normal palisaded outline and formation of numerous necrotic neoplastic cells [9]. Old regression can be recognized by finding of fibroplasia replacing tumor nests, an increase in small blood vessels, and a variable inflammatory cell infiltrate.

Morpheiform basal-cell carcinoma

Morpheiform basal cell carcinoma is characterized by a solitary, flat or slightly depressed, indurated, yellowish plaque on the face. The surface is smooth and shiny and the borders are ill-defined. The overlying skin remains intact for a long period before ulceration finally occurs. Histological examination shows cords and strands of basaloid undifferentiated cells embedded in a dense fibrous stroma [10]. Necrosis of single neoplastic cells and mitotic figures are common. Clefts are noted between neoplastic cells and stroma. Neoplastic cells frequently infiltrate the lower dermis and subcutaneous fat with, sometimes, involvement of nerves and muscles.

Fibroepithelial basal-cell carcinoma

Fibroepithelial basal cell carcinomas appear as one or several raised, firm, often slightly pedunculated nodules covered by smooth, red or flesh-colored skin. This neoplasm arises mostly on the back and seems to originate from one or more follicular infundibula or in pre-existing seborrheic keratoses. Histologically, fibro-epithelial basal-cell carcinoma consists of long, thin branching, anastomosing cords and columns of neoplastic epithelial cells embedded in an abundant fibromucinous stroma [11]. Many of the cords show connections with the surface of the epidermis. Occasionally, small groups of basaloid cells showing a palisade arrangement of the peripheral cell layer may be seen along the epithelial cords, like buds in a branch. This buds simulate follicular germs and the germ-like structures are contiguous with a zone of mesenchymal cells that resemble primitive papillae. Advanced follicular differentiation may occur episodically in the form of discrete bulbs and papillae that emanate from neoplastic cords. At times, continuous with some fibroepithelial carcinomas is an indubitable nodulo-ulcerative basal-cell carcinoma.

Infundibulo-cystic basal-cell carcinoma

This rare distinctive expression of basal-cell carcinoma presents as a tiny, domed, skin-colored or slightly opalescent papule on the face of an older person. It arises from vellus follicles, displays, in fully developed lesions, numerous infundibular cyst-like structures, and consists of many anastomosing cords of pink "squamous" epithelial cells at the distal ends of which are nubbins of blue basaloid cells that resemble those of follicular germs [12]. Infundibulo-cystic basal-cell carcinoma is devoid usually either of notable stroma or of clefts between neoplastic cells and that scant stroma. Occasionally, infundibulo-cystic basal-cell carcinoma is positioned continuous or contiguous with a nodulo-ulcerative type of basal-cell carcinoma.

Nevoid basal-cell carcinoma syndrome

It is an autosomal dominant disorder in which multiple basal cell carcinomas may be associated with palmoplantar pits and skeletal and central nervous system anomalies, such as, odontogenic cysts of the jaws, anomalies of the ribs, scoliosis, mental retardation and calcification of the falx cerebri. Basal cell carcinomas develop in childhood or adolescence occurring mostly on the face and trunk. The whole spectrum of clinico-histological variants of basal-cell carcinoma can be found in the nevoid basal-cell carcinoma syndrome [13]. However, marked pigmentation, keratinizing cysts and calcification have been reported to occur more frequently in basal-cell carcinomas of the syndrome than in sporadic cases.

Metastases

Metastases of basal-cell carcinoma are rare, occurring in approximately 0.05% of cases. Lesions that give origin to metastases are large, ulcerated and often with basosquamous features. Metastases occur mostly in the regional lymph nodes while bones, lungs and liver are less frequent sites of involvement. The median interval between the diagnosis of the primary lesion and evidence of metastases is around nine years whereas the interval between the appearance of the metastases and the death of the patient is approximately one year [14].

Squamous cell carcinoma

Squamous cell carcinoma is a malignant neoplasm of keratinocytes that mostly arises in areas of direct sun exposure [15] or at sites of chronic inflammatory or scarring processes [16], such as those caused by thermal burns, tar exposure, x-irradiation, discoid lupus erythematosus, lichen sclerosus et atrophicus and chronic draining sinuses. Squamous cell carcinoma can present with three clinico-pathologic patterns, namely, actinic keratosis, Bowen's disease and overt squamous cell carcinoma. All of these are characterized, histologically, by proliferation of atypical keratinocytes, dyskeratotic cells, crowded nuclei of keratinocytes and ortho-parakeratosis. Actinic keratosis and Bowen's disease, however, represent squamous cell carcinomas confined to the epidermis (carcinomas *in situ*). In other terms, they are early, evolving squamous cell carcinomas that may

remain embryonic for the lifetime of a patient or may grow to become mature squamous cell carcinomas. Since actinic keratosis and Bowen's disease on one hand and squamous cell carcinoma on the other are a continuum, there is no clear-cut boundary that enables an histopathologist to separate these conditions. However, for purposes of communication with clinicians, the terms actinic keratosis and Bowen's disease may be arbitrarily applied to lesions whose atypical keratinocytes are confined to the papillary dermis. If the same lesion, at a later time, is present within the reticular dermis the diagnosis will be squamous cell carcinoma

Actinic keratosis

Actinic keratoses are generally seen as single or multiple lesions on sun-damaged skin of persons who have fair complexions and who have been exposed for long periods of time to the rays of the sun. They appear as irregular erythematous patches covered by a rough, yellow-brownish adherent scale. This may be detached with difficulty revealing a reddened base with bleeding points. Occasionally, lesions exhibit marked hyperkeratosis and then have the clinical aspect of a cutaneous horn. A lesion analogous to actinic keratosis develops on the vermilion border of the lower lip as actinic cheilitis and present with areas of erosion and hyperkeratosis. Histologically, an actinic keratosis is constituted of atypical keratinocytes that form buds in the lower part of an epidermis that is topped by alternating columns of ortho and parakeratosis (Fig. 5). Atypical keratinocytes characteristically spare intra-epidermal epithelial structures of adnexa (acrosyringia and acrotrichia) and mature to become parakeratotic corneocytes. Epidermis of actinic keratoses may be atrophic, digitated or hypertrophic. In hypertrophic lesions (Fig. 5), buds of atypical keratinocytes extend throughout the papillary dermis to about the level of the reticular dermis and a "cutaneous horn" often overlies the thickened epidermis. In other cases, atypical keratinocytes may extend throughout the entire thickness of the epidermis ("Bowenoid" actinic keratosis). Occasionally, buds of atypical keratinocytes are marked by suprabasal clefts above which are assembled acantholytic dyskeratotic cells that produce a "pseudoglandular" or "acantholytic" pattern. The dermal changes include severe solar elastosis and a mild lymphocytic infiltrate. At times, a band-like lymphocytic infiltrate is present at the base of an actinic keratosis with necrotic keratinocytes in the basal layer and some basal vacuolar changes ("lichenoid" actinic keratosis).

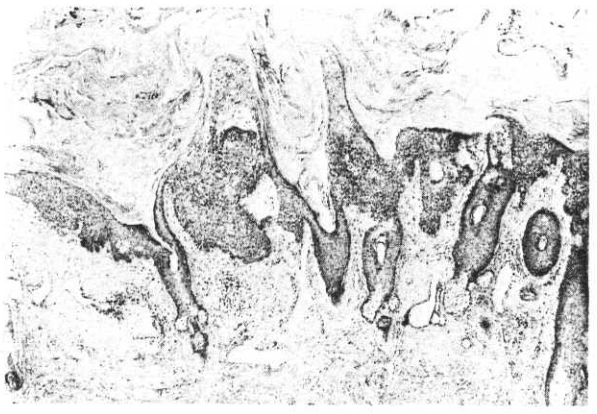

Fig. 5. - This actinic keratosis (squamous cell carcinoma in situ) consists histologically of atypical keratinocytes that form buds in the lower part of an "hypertrophic" epidermis. Neoplastic keratinocytes mature to become parakeratotic corneocytes. Severe solar elastosis is seen in the papillary dermis.

Bowen's disease

Bowen's disease may occur anywhere on the skin surface. It consists of an asymptomatic, erythematous patch of sharp but irregular outline, showing little or no infiltration. Within the lesion are usually areas of scaling and crusting. The patch gradually enlarges and, at times, the surface may become hyperkeratotic, verrucous or ulcerated. Histologically, Bowen's disease consists of a proliferation of atypical keratinocytes throughout the entire thickness of the epidermis. This is associated with disorderly maturation of epidermal keratinocytes, dyskeratotic cells, multinucleated keratinocytes and mitotic figures. In contrast to bowenoid actinic keratosis, atypical keratinocytes involve acrosyringia and acrotrichia in Bowen's disease. The epidermis is usually thickened with loss of the granular layer and overlying parakeratosis. Occasionally, neoplastic cells may be arranged in pagetoid pattern, i.e., pale atypical cells are scattered as solitary units and in nests throughout a thickened epidermis, and the basal layer gives the appearance of being spared by the process (pagetoid variant).

Squamous cell carcinoma

Overt squamous cell carcinoma may occur anywhere on the skin even though it mainly arises in sun-damaged skin, either as such or from an actinic keratosis or Bowen's disease. Squamous cell carcinomas may present as asymptomatic or tender, infiltrated plaques or nodules with firm consistency. The limits of the neoplasms are ill-defined and usually extend beyond the visible margin of the lesions. The edge of the nodules or plaques is indurated and red-yellowish in color. The center may be covered by an hyperkeratotic crust or may show a shallow ulcer that conceals a red, granular base (Fig. 6). At times, squamous cell carcinoma manifests itself as a fungoid or

Fig. 6. - Squamous cell carcinoma appears as a plaque with raised borders and central ulceration on sun-damaged skin.

verrucous lesion without ulceration. Histologically, the neoplasm consists of nests and islands of atypical keratinocytes that emanate from the undersurface of the epidermis or from epithelial structures of adnexa and extend into the reticular dermis for a variable distance (Fig. 7). The cells have abundant eosinophilic cytoplasm and a large vesicular nucleus with prominent nucleoli. There is variable central keratinization and "horn pearl" formation depending on the differentiation of the tumor (Fig. 7). Numerous dyskeratotic cells and mitotic figures are usually present. Squamous cell carcinoma may occasionally infiltrate along nerves, blood vessels, lymphatics and fascial planes and may induce a stromal desmoplastic response. Numerous squamous cell carcinomas show features of actinic keratosis at the periphery of the lesions. Around 2% of all squamous cell carcinomas consist of nests of squamous cells with central acantholysis leading to an impression of gland formation. A mild to moderate chronic inflammatory cell infiltrate, at times with eosinophils, is generally observed at the periphery of the neoplasm. In some cases squamous cell carcinoma is almost entirely constituted of clear cells [17] with abundant cytoplasm containing glycogen (clear cell variant) while in others the neoplastic cells are spindled-shaped (spindle cell variant) [18]. The spindle cells have a large vesicular nucleus and scanty eosinophilic cytoplasm, often with indistinct cell borders. There is variable pleomorphism, usually with many mitoses.

Recurrence and metastases

Recurrence is more frequent in squamous cell carcinomas with deep infiltration [19], perineural involvement, poor differentiation and acantholytic features [20, 21]. The risk of metastases depends upon the clinical setting in which the lesion arises [22]. The lowest risk is for squamous cell carcinomas originating on sun damaged skin [23]. In contrast, squamous cell carcinomas with acantholytic changes, those emanating from Bowen's disease [24], and squamous cell carcinomas arising in skin not exposed to the sun [25] seem to bear an higher risk of metastases. The incidence of metastases increases in lesions occurring in sites of chronic injury and scarring [26]. Metastases usually develop in the regional lymph nodes to extend subsequently to other organs.

Keratoacanthoma

Keratoacanthoma consists of a firm, dome-shaped, nodule with a keratin-filled crater in its center (Fig. 8). The lesion has a pink-red color and a smooth surface with teleangectases. Keratoacanthomas reach their full size within 8 weeks and then resolve spontaneously in less than 6 months leaving a depressed scar. In most cases the neoplasm presents as a solitary lesion on sun-damaged skin, although multiple lesions may occur in patients who have been exposed to tar. Occasionally, solitary lesions may attain a large size (giant keratoacanthoma) or may extend peripherally with a raised, rolled border and central atrophy (keratoacanthoma centrifugum marginatum). Rarely, a widespread eruption of hundreds of keratoacanthomas may occur (generalized eruptive keratocanthoma) or multiple keratoacantomas may develop in familiar settings (familiar primary self-healing epithelioma of the skin). All clinical types of keratoacanthomas, however, display the same histological features. Keratoacanthoma begins at the base of infundibula with proliferation of atypical keratinocytes. The infundibula then become dilated because of accumulation of cornified cells within them. At this stage the lesion takes on a crateriform appearance, with bowing

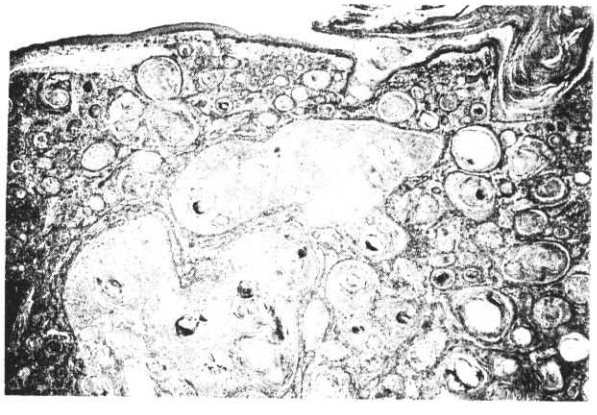

Fig. 7. - Aggregations of atypical keratinocytes that arise from the epidermis and extend into the reticular dermis are diagnostic features of overt squamous cell carcinoma. "Horn pearls" formation is seen in more differentiated types of squamous cell carcinoma.

of the lateral aspects of infundibula at the periphery of the lesion that tend to embrace the keratin-filled crater partially (Fig. 9). By the time apogee of keratoacanthoma is reached, the lesion may extend deep into the dermis and, at times, into the subcutaneous tissue with perineural infiltration. The cells have a large eosinophilic cytoplasm and nuclei may vary from very small and monomorphous to large and pleomorphic. Mitotic figures may be few or many. Fully developed keratoacanthomas show a dense infiltrate of lymphocytes, eosinophils and neutrophils at the base of the lesion. Neutrophils may extend into the epithelial nests to form small microabscesses. The combined effect of inflammatory cells on neoplastic epithelium is extensive necrosis. In time, histiocytes and giant cells ingest necrotic debris of neoplastic keratinocytes. Regressing keratoacanthoma is characterized by fibroplasia at the base of the lesion. The effects of inflammatory cells together with fibrosis push the crater containing cornified cells beyond the bounds of the skin. At the end stage, the only residuum of keratoacanthoma is a scar.

The observation that keratoacanthoma spontaneously regresses in the vast majority of cases have led most colleagues to conclude that the neoplasm is not a carcinoma, but an acanthoma as the name denotes. At times, however, it may be difficult to distinguish keratoacanthoma from squamous cell carcinoma on histologic ground alone. In fact, both the neoplasms may exhibit an infiltrative pattern of growth, marked nuclear atypia and numerous mitotic figures. In the last years, moreover, there are reports of what seem to be be clinically (history of rapid growth of a crateriform nodule) and histologically authentic keratoacanthomas that have metastasized to lymph nodes [27, 28]. On these bases, some authors consider keratoacanthoma as an authentic squamous cell carcinoma of a particular type, that is, the type that usually undergoes spontaneous regression but that rarely demonstrates capability of metastasis.

Fig. 9. - Histologically, keratoacanthoma shows a central crater formed of dilated follicular infundibula containing ortho- and parakeratotic cells. Aggregations of atypical keratinocytes extend from the bases of infundibula into the reticular dermis.

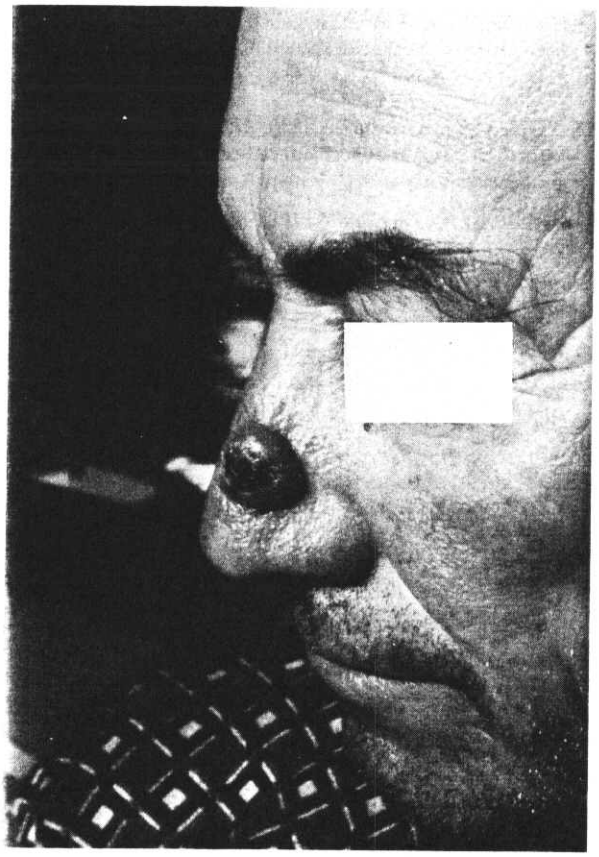

Fig. 8. - Keratoacanthoma presents as a dome-shaped nodule with a keratin-filled crater in its center.

Submitted on invitation.
Accepted on 30 November 1995.

REFERENCES

1. GUTIERREZ, M.M. & MORA, R.G. 1986. Naevoid basal cell carcinoma syndrome. *J. Am. Acad. Dermatol.* **15**: 1023-1030.

2. JUNG, E.G. 1986. Xeroderma pigmentosum. *Int. J. Dermatol.* **2**: 629-233.

3. LAMBERT, W.C. & SCHWARZ, R.A. 1988. Evidence for origin of basal cell carcinomas in solar (actinic) keratoses. *J. Cutan. Pathol.* **15**: 322 (abstract).

4. BLEEHEN, S.S. 1975. Pigmented basal cell epithelioma. *Br. J. Dermatol.* **93**: 361-370.

5. McGIBBON, D.H. 1985. Malignant epidermal tumours. *J. Cutan. Pathol.* **12**: 224-238.

6. OKUN, M.R. & BLUMENTAL, G. 1964. Basal cell epithelioma with giant cells and nuclear atipicality. *Arch. Dermatol.* **89**: 598-600.

7. SIEGLE, R.J., MACMILLAN, J. & POLLACK, S.V. 1986. Infiltrative basal cell carcinoma: a nonsclerosing subtype. *J. Dermatol. Surg. Oncol.* **12**: 830-836.

8. LOPES DE FARIA, J. & NUNES, P.H.F. 1988. Basosquamous cell carcinoma of the skin with metastases. *Histopathology* **12**: 85-94.

9. CURSON, C. & WEEDON, D. 1979. Spontaneous regression in basal cell carcinoma. *J. Cutan. Pathol.* **6**: 432-437.

10. RICHMAN, T. & PENNEYS, N.S. 1988. Analysis of morpheiform basal cell carcinoma. *J. Cutan. Pathol.* **15**: 359-362.

11. PINKUS, H. 1953. Premalignant fibroepithelial tumors of the skin. *Arch. Dermatol.* **67**: 598-615.

12. TOZAWA, T. & ACKERMAN, A.B. 1987. Basal cell carcinoma with follicular differentiation. *Am. J. Dermatopathol.* **9**: 474-482.

13. LINDBERG, H. & JEPSEN, F.L. 1983. The nevoid basal cell carcinoma syndrome. Histopathology of the basal cell tumors. *J. Cutan. Pathol.* **10**: 68-73.

14. DOMARUS, H. & STEVENS, P.J. 1984. Metastatic basal cell carcinoma. Report of five cases and review of 170 cases in the literature. *J. Am. Acad. Dermatol.* **10**: 1043-1060.

15. EPSTEIN, J.H. 1983. Photocarcinogenesis, skin cancer and ageing. *J. Am. Acad. Dermatol.* **9**: 487-502.

16. CRUICKSHANK, A.H., McCONNELL, E.M. & MILLER, D.G. 1963. Malignancy in scar, chronic ulcers, and sinuses. *J. Clin. Pathol.* **16**: 573-580.

17. KUO, T. 1980. Clear cell carcinoma of the skin. A variant of the squamous cell carcinoma that simulates sebaceous carcinoma. *Am. J. Surg. Pathol.* **4**: 573-583.

18. EVANS, H.L. & SMITH, J.L. 1980. Spindle cell squamous carcinoma and sarcoma-like tumors of the skin. A comparative study of 38 cases. *Cancer* **45**: 2687-2697.

19. FRIEDMAN, H.I., COOPER, P.H. & WANEBO, H.J. 1985. Prognostic and therapeutic use of microstaging of cutaneous squamous ell carcinoma of the trunk and extremities. *Cancer* **56**: 1099-1105.

20. IMMERMAN, S.C., SCANLON, E.F., CHRIST M. & KNOX, K.L. 1983. Recurrent squamous cell carcinoma of the skin. *Cancer* **51**: 1537-1540.

21. FREEMAN, R.G. & DUNCAN, W.C. 1973. Recurrent skin cancer. *Arch. Dermatol.* **107**: 395-399.

22. WILKINSON, J.D. 1982. Current treatment of epitheliomas of the skin. *Clin. Exp. Dermatol.* 7: 75-88.

23. LUND, H.Z. 1984. Metastasis from sun-induced squamous cell carcinoma of the skin: an uncommon event. *J. Dermatol. Surg. Oncol.* **10**: 169-170.

24. KAO, G.F. 1986. Carcinoma arising in Bowen's disease. *Arch. Dermatol.* **122**: 1124-1126.

25. CHUANG, T-Y., POPESCU, N.A., SU, W.P.D. & CHUTE, C.G. 1990. Squamous cell carcinoma. A population-based incidence study in Rochester, Minnesota. *Arch. Dermatol.* **126**: 185-188.

26. MOLLER, R., RAYMANN, F. & HOU-JENSEN, K. 1979. Metastases in dermatological patients with squamous cell carcinoma. *Arch. Dermatol.* **115**: 703-705.

27. PISCIOLI, F., ZUMIANI, G., BOI, G. & CRISTOFOLINI, M. 1984. A gigantic, metastatizing keratoacanthoma. Report of a case and discussion on classification. *Am. J. Dermatopathol.* **6**: 123-129.

28. POLLACK, E. & ACKERMAN, A.B. 1993. Solitary keratoacanthoma is a squamous cell carcinoma: three examples with metastases. *Am. J. Dermatopathol.* **15** (4): 332-342.