Histopathological and clinical-progressive profile of skin carcinomas: study on 1688 cases

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Abstract
Skin carcinomas represent 90–95% of skin cancers. With the objective of identifying the histopathological and clinical-progressive profile of skin carcinomas, we undertook a retrospective study over a period of seven years, which included a total of 1688 patients with carcinoma of the skin, hospitalized and treated in Craiova Dermatology Clinic between January 1999 and December 2006. Patient data such as identification data, environment, profession, phototype, location of cancer, history of the disease, clinical diagnosis, histopathological diagnosis and response to treatment were included in clinical charts. Basal cell carcinoma (BCC) was diagnosed in a total of 1162 patients, representing 68.84% of cases taken to the study. The most common clinical forms were: pearly BCC (37.95%), nodular BCC (29%), and superficial BCC (22.03%). Regarding the histological type, the most frequent forms were: BCC polymorphic (29.95%), BCC solid (24.96%), and keratinized BCC (19.97%). Epidermoid carcinoma (EC) was encountered in a total of 482 patients, representing 28.55% of all cases. The most frequent forms were: vegetated ulcerated EC (34.03%), nodular EC (31.33%) and keratosic EC (24.27%). Regarding the degree of differentiation, the situation was as follows: well-differentiated EC (64.94%), medium differentiated (29.88%), poorly differentiated (5.18%). Metatypical carcinoma (MC) was found in 44 patients (2.61%). This type of cancer did not presented clinical particular signs, the diagnosis was strictly pathological.

Keywords: skin carcinomas, histopathology, evolution.

Introduction
Cancer is a major public health problem. Cancer related morbidity had an impressive growth in the last decades and, in this context, skin carcinoma incidence increased in the US, Canada, Europe and Australia by 4–8% per year, while the incidence of melanoma is doubling every 10 years in countries with white population [1]. Worldwide 12 million new cases of cancer were in 2007, and approximately 20% of them had skin localization.

In most developed countries, both in Europe and other continents, oncologic diseases are the second cause of death, accounting for 15–25% of all deaths. Incidence was higher in males regardless of age group.

In Romania, since 1978, cancer related mortality was the second leading cause of death after cardiovascular diseases. At the end of 2007, there were more than 370,000 patients registered with cancer. Cancer morbidity was higher when compared to previous years (2001 – 290,000 patients, 2003 – 320,000 patients, 2005 – 354,572 patients). Out of the total number of cancer cases in 2005 (354,572), 10.8% had skin location (5485 patients with melanoma, 32,826 patients with other skin cancers) (National Center for Organization and Information System and Information Assurance in Health, National Cancer Registry).

The most common types of skin malignancies are the skin carcinomas that account for approximately 90–95% of all skin cancers. These carcinomas may develop de novo or on preexisting lesions. The involvement of external carcinogenic factors in their pathogenesis is certain.

Dolj County, with a population of 716,536 in 2006 (Dolj County Demographic Yearbook 1996–2006, National Institute of Statistics, Dolj Regional Direction of Statistics), has a temperate continental climate with average temperatures in excess of about 2°C. The sunny area of the county is in the South, where the sand biotope is described. It is characterized by altitudes of 75 m, with hot and dry summers. We also highlight the existence of a nuclear facility in Bulgaria, located in the vicinity of the Dolj County. The Kozloduy Nuclear Power Plant, an old facility with outdated security systems and frequent leaks of radioactive isotopes into the environment. Natural ecosystems in Southern Dolj County may be affected by radioactive contamination.

Based on these data, we aim at identifying the histopathological and clinical-progressive profile of skin carcinomas. We therefore undertook a retrospective study from January 1, 1999 – December 31, 2006.
The study group included 1688 cases of skin carcinoma, diagnosed and treated at the Dermatology Clinic of Craiova during this period.

**Patients and Methods**

For each of the 1688 cases included in the study group we assessed: identification data (name, surname, sex, age), environment, profession, phototype, location of cancer, history of the disease and clinical diagnosis (clinical typology, lymph-node status groups).

For histological study, tissue biopsy fragments or whole biopsy specimens were processed by usual paraffin inclusion, and sections were stained with Hematoxylin–Eosin. Depending on the histopathology result, further specific stainings were performed (PAS and Giemsa).

For diagnosis certification of spindle cell epidermoid carcinoma (sarcomatoid) we performed immunohistochemical investigations using LSAB/HRP and several antibodies such as (DakoCytomation): anti-cytokeratins (AE1/AE3 – clone AE1/AE3, dilution 1:50), antivimentine (clone V9, dilution 1:50), anti-protein S100 (polyclonal, dilution 1:500) and anti-alpha actinic (clone 1A4, dilution 1:150). These investigations allowed us EC differentiation of a melanoma and a fibrosarcoma.

Evaluation of histopathological lesions included the following parameters:

- skin carcinoma type: basal cell, epidermoid (squamous), mixed (meta-typical);
- histopathological form of basal cell carcinoma (BCC);
- histopathological variety of epidermoid carcinoma (EC) and the degree of differentiation (well-differentiated, moderately differentiated, poorly differentiated);
- association of cancer with some dysplasia lesions;
- presence of residual malignant cells in the safety margins for cases treated surgically.

We also studied the correlation between clinical and histological diagnosis.

Patients with skin carcinomas in our study group were treated by surgical excision with safety margin (42% of cases) or curettage and electrodessication (68% of cases).

Criteria for selecting therapeutic methods were:

- anatomical location of the tumor;
- tumor diameter and depth of invasion;
- anatomical and clinical type;
- uniqueness or multifocal nature of cancer;
- regional lymph-node invasion;
- biological status of the patient;
- patient choice, after correct information regarding treatment methods.

Treatment was individualized, seeking to satisfy at least two imperatives:

- therapy to be curative;
- treatment to result in only minimal functional and aesthetic repercussions.

The therapeutic results were assessed at the end of epithelisation period and by regular follow-up in the next two years.

**Results**

Of 1688 cases studied, 1162 patients (68.84%) were diagnosed with BCC, 482 patients (28.55%) had EC, while metatypical carcinoma was found in 44 patients (2.61%).

All 1162 cases of BCC had the following distribution:

- by sex: females 55.94%, males 44.06%;
- by environment: rural 83.99%, urban 16.01% (Figure 1);
- by mean age: 67.6 years (27–90 years) (Figure 2);
- by skin phototype: 0.4% phototype I, 49% phototype II, 42% phototype III, 5% phototype IV, 3.6% phototype V (Figure 3).

**Figure 1 – Distribution by environment – BCC.**

**Figure 2 – Distribution by age group – BCC.**

**Figure 3 – Type of skin phototype – BCC.**

Regarding occupation 85.89% were farmers, gardeners, builders, welders. Onset of illness ranged from eight months to nine years. The tumor progression in most cases (69.97%) was 1.5 years to three years. In 88.98% of cases, the tumor was located on photoexposed skin.

In our study, we found all the clinical forms, the most common being:

- pearly BCC (37.95%) (Figures 4 and 5);
- nodular BCC (29%);
- plan scar BCC (22.03%).
Histopathological forms were represented by:
- polymorphic BCC (29.95%) who associated several histopathological forms;
- solid (24.96%): tumoral masses of basaloid cells extend into the dermis in relation to a delicate, specialized, somewhat myxoid tumor stroma (Figure 6);
- keratinized (19.97%): tumoral masses centered on small areas of squamous differentiation, parakeratinized or completely keratinized cells (Figure 7);
- adenoid (13.94%): characterized by the presence of cords composed of 2–3 rows of cells, anastomosis between them, making reticulated appearance (Figure 8);
- pseudocyst (4.04%): solid tumoral masses, some of them showing cystic cavities which may contain necrotic debris;
- superficial (2.58%): showed buds and irregular proliferations of peripherally palisaded basaloid cells attached to the undersurface of the epidermis that is usually atrophic;
- morpheaform (1.72%): tumoral cells arranged in small groups or cords are separated by an appreciable amount of collagen fiber stroma.

Of all 1162 patients with BCC, in 53 cases (4.56%) have found basal cell epitheliomatosis, with the following epidemiological aspects: mean age 73 years (33–88 years), sex ratio females/males 29:24, distribution according environment – rural 90.56%, urban 9.44%. In 41 cases, the tumor was located on photo-exposed skin, in five cases on cover skin and the involvement of the two regions was found in seven cases. History of the disease ranged from three years to nine years.

The 482 patients with EC had the following distribution:
- by sex: females 41.91%, males 58.09%;
- by environment: rural 80.91%, urban 19.09% (Figure 9).
- by mean age: 68.7 years (36–89 years);
- by skin phototype: 44.81% phototype II, 41.91% phototype III, 10.58% phototype IV, 2.70% phototype V (Figure 10).
People affected by the EC had occupations involving chronic sun exposure (farmers, mechanical, construction workers, gardeners) or to artificial sources of ultraviolet (welders) – 73.65% of cases.

Onset of illness ranged from five months to four years. Most patients (81.12%) had developed tumors between 1–2 years.

The localization of skin cancer was in 81.74% of cases on photo-exposed skin and in 18.26% on the covered skin. From all cases of EC, 33.40% of patients had the tumor located on the lip.

The most common clinical forms were:
- ulcero-vegetative (34.03%);
- nodular (31.33%) (Figure 11);
- keratotic (24.27%) (Figure 12).

EC distribution was made based on the differentiation degree: well differentiated (64.94%), medium differentiated (29.88%), and poorly differentiated (5.18%) (Figure 13).

**Well-differentiated squamous carcinoma**

We found well-differentiated squamous carcinomas in 313 cases representing 64.94% of all invasive squamous carcinomas. Histopathologically, the tumor consisted in masses and cords of carcinomatous cells similar to the basal layer. Malignant cells had polygonal shape, with rich eosinophilic cytoplasm, and waist and uneven nuclei. Atypical mitosis was common. Tumor stroma connective fiber type was well represented, often with abundant inflammatory infiltrate, predominantly lympho-plasmocytic type or, sometimes, with the presence of foreign body giant cells. In the center of tumor masses, neoplastic cells evolved to maturity and keratinization. Keratinized cells formed concentric lamellar structures, making round-oval formations called keratin pearls (Figure 14).

Particular forms of well-differentiated squamous carcinomas were verrucous carcinoma, adenoid or pseudoglandular squamous cell carcinoma, cancroid.

Verrucous carcinoma was found in 35 cases representing 11.18%. Microscopically, the lesion surface appeared similar to papillomatosis warts, acanthosis, parakeratosis and hyperkeratosis. In the deep wound unicellular keratinization, nuclear atypicals and pearls were missing. Keratinocytes well-differentiated had pale Eosin, colored cytoplasm and small nuclei.

Adenoid or pseudoglandular squamous cell carcinoma was present in 56 cases representing 17.89% of all well-differentiated squamous cell carcinomas. The localization of all these cases were on exposed skin areas.

Microscopically, this type was characterized by the appearance of structures with pseudoglandular or alveolar aspect due tumor acantholisis process. These adenoid changes may be present only in a tumor area or may be included in its entirety. Tubular or alveolar lumina were separated by one or more cell layers. The areas bounded by a single layer of cells, it remember the glandular cells and in areas separated by multi-layer cell lumina cells were squamous cells with partial or total keratinization. Most often these lumina were filled with acantholytic, exfoliated or partial keratinized cell. In some cases, eccrine gland ducts were dilated or proliferated in response to the surrounding inflammatory infiltrate.
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Cancroid is a particular form of squamous cell carcinomas where the keratinization process is particularly sharp. It was present in 14 cases, representing 4.47% of them. Both cases were located on the lip.

Medium differentiated squamous cell carcinomas

We found in 144 cases representing 29.88%. Histopathologically, masses of tumor cells were poorly demarcated from the surrounding stroma. Keratinization was less obvious than in 1-degree carcinoma. Thus, keratin pearls were rare and had a low keratinized center. Many of the tumoral cells were atypical squamous cells (Figure 15).

Poorly differentiated squamous carcinomas

They were found in 25 cases representing 5.18%. Histopathologically, keratinization was absent on vast areas. Keratin pearls were absent, keratinization being present at small groups of cells that present weak cytoplasm eosinophilia and rare intercellular bridges. We found individual keratinized cells looking dyskeratotic. These cells were round, large, with intense eosinophilic cytoplasm, and dark nuclei. Most nuclei were atypical, showed many mitotic figures that were atypical (Figure 16).

A particular form of poorly differentiated squamous cell carcinomas, found in our study was basaloïd squamous cell carcinoma, a type with high aggression.

Basaloïd squamous cell carcinoma was present in two cases, which represented 8% of poorly differentiated carcinomas. This particular form of squamous cell carcinoma was more commonly found in mucous membranes, thus explaining the low percentage that we found in the skin.

Histologically characterized by the presence of solid tumor masses, which had the appearance of peripheral palisade cell and membranes were bounded by strong base. Some of these masses contain central cystic spaces filled with mucoid material or hyalin, places that remind of adenoid squamous cell carcinoma.

Spindle cell carcinoma (sarcomatoid, metaplastic) was found in 11 cases. Histopathologically, this type was composed of solid masses of elongated tumor cells, without tendency to keratinization with vesicular cytoplasm and atypical nuclei, which had the form of crossed beams. This particular type, most commonly located on the lips, seemed to be associated with an unfavorable prognosis. Its evolution depends on the depth of invasion, however. Shall state that for the establishment of epithelial origin of some of these cases we used immunohistochemical methods using pancytokeratins AE1/AE3 mark as usual color were inconclusive for diagnosis.

For spindle squamous cell carcinomas we investigated immunohistochemical five cases. Study expression of AE1/AE3 revealed a low intensity staining. We noticed that staining was distributed in the periphery of cell masses and on small areas within some of them. (Figures 17 and 18).
For those 44 patients with MC distribution by sex was: 29 females, 15 males, 40 cases having rural origin. The mean age was 69.5 years (30–87 years). Evolution of the disease ranged between one and three years. Localization was found on the photo-exposed skin (79.55%). We observed histopathological aspects of transition, associated or intricate, between BCC and EC.

Regarding the therapeutic results of 1688 cases, through surgical excision (performed for 42%) and electrodessication in addition of curettage (charged for 58%) we obtained 95.02% clinical response. Functional and aesthetic results were very good in 80.04% of cases.

Discussion

Epidemiological aspects

Skin cancers are developed from epithelial tissue, hence the former name of epitheliomas. Skin carcinomas represent the majority of skin cancers (90–95% of cases). The etiopathogenesis of these cancers involves a number of factors: actinic radiation, ionizing radiation, chemical factors, smoking, biological factors (potentially HPV-oncogen), genetic factors, immunodepression [2, 3]. Because the immunodepression of unknown cause, people with organ transplants have increased risk of skin carcinomas, which requires a dermatologic care of their private [4].

There are many arguments that advocates for the role of solar radiation in the production of skin carcinomas. Thus, approximately 80% of these cancers were located in the facies and their incidence increases with as we approach the Equator. In our study, 88.98% of BCC, respectively 81.74% and 79.55% of the EC and MC was located on photo-exposed skin. Most patients came from rural areas, most professions that require prolonged exposure to sunlight (farmers, mechanized, gardeners, fishermen, etc.).

BCC is the most common form of malignant skin tumors, representing 60–80% of skin carcinomas. In our study group, the proportion was 68.84%. This tumor is more common in sunny areas and the white race. The incidence is 1/100 000 in the black population of Africa inhabitants and more than 1500/100 000 in white population in equatorial Australia [5]. In France, the standardized incidence is around 70/100 000 inhabitants, and in some regions of the United States exceeds 200/100 000 inhabitants. Highest prevalence was seen in Queensland (Australia), BCC was currently 4.2% of subjects aged between 20 and 69 years [2].

BCC is about 1/3 of all cancers in western countries and is probably the most common malignant tumor of the human species [5]. The significant increase of the incidence in the last three decades was characterized by the phrase “silent epidemic of the twentieth century”. Maximum incidence of BCC was the age of 50 years. In our group, the average age of patients with CBC was 67.6 years. Phototype II and III represented over 90% of cases, highlighting important individual predisposition to develop this cancer. In our study, sex ratio M/F was 1.27, close to that recorded in Sweden and Britain (1.1), but lower than the US (2.5).

EC is mostly statistics 20–40% of skin carcinomas. For countries with temperate climate in the northern hemisphere, the proportion is 13–38% of skin carcinomas. In our study, the proportion was 28.55%.

In most European countries, the standardized incidence of EC is 10–20/100 000 inhabitants in men and women 5–10/100 000 inhabitants. In Australia, the incidence is higher (250/100 000 inhabitants). The incidence depends on latitude (doubled when latitude reduces between 8–10 degrees) and increases with age population [2]. EC usually begins after 60-year-old and predominantly in people with light colored skin exposed to sun and weather.

In our study, mean age of patients with EC was 68.7 years, most with phototype II (44.81%) and phototype III (41.91%). Post-combustion scars are risk factors for skin cancers, especially epidermoid, with unclear pathogenesis, with a finding of mutations in p53-gene in cancers developed in post-combustion scar [6]. In most cases, EC was found located on the skin, 50–60% of tumors interesting the head and neck, which showed that exposure to actinic radiations was a risk factor. In our group, EC was located on photo-exposed skin in 81.74% of cases.

We found MC in 44 patients (2.61%), sex ratio (M/F) 0.52 and mean age of 69.5 years. Most patients came from rural areas (90.91%). The proportion of CM in the present study is less than that indicated in the medical literature (5%).
Histopathological aspects

Regarding BCC, our study revealed a polymorphism of such cancer pathology, which is also recorded in the literature [27]. Our patients presented in descending order of frequency following histopathological forms: BCC polymorphic (29.95%), solid (24.96%), keratinized (19.97%), adenoid (13.94%), pseudocyst (4.04%), pigmented (2.84%), superficial (2.58%), morpheaform (1.72%).

Basal cell carcinoma has usually cytological and architectural character quite typical. However, some cases (adenoid differentiation, pseudocyst, sebaceous or as keratinized) raise problems of differential diagnosis. It must be differentiated of:

- Trichoblastoma – when it is not possible to differentiate based on histopathological examination, then is made to immunohistochemical investigations. Thus, Bcl2 is expressed in a diffuse manner in basal cells, whereas expression of this marker is restricted to peripheral strata of trichoblastoma lobules. Also, CD34 is expressed by cells in the stroma of the tumor periphery areas of trichoblastoma, but missing the mark in the BCC. In addition trichoblastoma areas contain Merkel’s cells expressing cytokeratin 20 (CK20), a situation absent in BCC lobules [7].
- Trichoepithelioma – is a benign skin tumor, which resembles clinical and histopathological with BCC. Analysis of elastic fiber content and expression of cytokeratin 15 helps to differentiate the two tumors [8]. It was noted that the BCC contains more elastic fibers than trichoepithelioma, and the cytokeratin location is peripheral, compared to BCC.
- Epidermoid carcinoma – the problem of the differential diagnosis in some cases: keratinized BCC, BCC with pillary differentiation, BCC associated with an epidermal pseudopitheliomatous reaction. Keratinization of BCC keratinized is steep, while in the pearls of the EC, the process is gradual and incomplete. Immunohistochemistry, tumor cells of BCC are positive for the low molecular weight cytokeratins and negative for CEA, EMA and involucrine. Basal membrane surrounding the tumor masses has immunostaining for collagen IV or V, laminin and bullous pemphigoid antigen.
- EC tumor cells are positive for high molecular weight cytokeratins (K903, AE1/AE3, MAK-6) and sometimes average molecular weight cytokeratins, EMA, CEA and involucrine. Adhesion marker CD44 presents intense and diffuse positivity for Ber EP4, unlike EC which is negative.
- Sebaceous tumors – BCC with sebaceous differentiation puts first diagnosis issue and second differential diagnosis problems with sebaceous tumors. The old “sebaceous carcinoma” term is considered by some authors BCC with sebaceous differentiation, while others consider it highly differentiated sebaceous tumor, less aggressive, compared with sebaceous carcinoma. Equally controversial is sebacea, considered by some authors with a basal sebaceous differentiation. However, according to others, individualization of these tumors is important because it is a benign lesion without risk of relapse, contrary to BCC.

BCC with sebaceous differentiation may raise problems of differential diagnosis of a sebaceous carcinoma. This cancer has preferential localization eyelid (Meibomius glands starting point), as off-eyelid form is very rare (about 150 cases published). Histopathologically, we can found epithelial malignant proliferation intradermal, non-capsulated, infiltrating, reaching the subcutaneous tissue, muscle, even fascia itself. Architectural aspect is polymorphic. On the immunohistochemical plan, there is a diffuse marker of cells for EMA in sebaceous carcinoma, whereas this marker is restricted to foci of sebaceous cells in sebaceous BCC. Differentiation of the two cancers is necessary because different outcome. With regard to sebaceous carcinoma, local relapses are seen in 29% of cases and metastatic lymph risk is about 15%. Visceral metastases (lung and brain notable) occur in 10% of cases [9]. Others authors considers that the cancer may metastasis in half the cases.

EC histopathological study showed the predominance of well-differentiated forms (64.94% of cases), followed by medium differentiated form (29.88%) and poorly differentiated (5.18%). These data were consistent with those drawn from other studies [10]. What seemed important to point out was that in five patients (three with lip EC-2 with skin EC) with multiple recurrences after surgical treatment, we had witnessed the change of the degree of malignancy in the sense of aggravation.

We found matters in differential diagnosis of EC primary with keratoacanthoma. The difference is slight and the basic rule is that the pathologist should have available the entire tumor or a deep biopsy containing part of the tumor plus a healthy skin [11]. The EC cells and nuclear atypicals were more common and basal membrane presented discontinuities. Another differential diagnosis was made with pseudoepitheliomatous hyperplasia. Absence of cellular and nuclear atypicals, the atypical mitosis and basement membrane integrity advocates pseudoepitheliomatous diagnosis of hyperplasia.

For a nonkeratinized EC, differentiation of an achromic melanoma was mainly immunohistochemistry, as also the differentiation of EC from a spindle cell sarcoma. Cytokeratins expression on tumor cells allowed the differentiation of EC.

We must use immunohistochemistry to distinguish pseudovascular EC from an angiosarcoma. Strong expression of vimentin and positive-expression for cytokeratins, and negativity for vascular factors (CD31, CD34, XIIIa factor) allowed distinguishing the two types of cancers [10].

A special issue of differential diagnosis was a difference of a carcinoma. This was a rare tumor characterized by the presence of two malignant components: epithelial and mesenchimatous, intimately mixed. Locating the skin was extremely rare, with 20 cases reported so far [12]. Carcinomatous component was often epidermoid or basal [13], and rarely type malignant spiradenoma eccrine, malignant pilomatrixoma or eccrine porocarcinoma. Sarcomatous quota may be undifferentiated or differentiated in respect
Cartilage, bone, muscle, etc. The prognosis was reserved, sarcomatous component was itself a testimony to the aggressive nature of this tumor. Lymph nodes or visceral metastases may be of carcinomatous or sarcomatous type or both. They occur in 16–22% of cases, a proportion similar to registering for relapse.

Regarding MC, in all 44 cases was involved or intricate issues associated with basal cell carcinoma and epidermoid carcinoma. Epidermoid carcinoma was well differentiated in 36 cases, moderately differentiated and six poorly difference in two cases. For three patients with superficial BCC with multiple relapses after electrodessication, initial histological structure (solid BCC) has been replaced in time with metatypical tumor appearance.

Differential diagnosis of MC was made with keratinized BCC, with an EC and pseudoepitheliomatous hyperplasia. In metatypical carcinoma, squamous differentiation areas had cell nuclear atypicals plus atypical mitoses, distinguishing it by pseudoepitheliomatous hyperplasia. As a MC of a CE differentiation, the distinction was purely academic, because the two cancers are similar evolution.

**Clinical and progressive aspects**

On BCC, we found all clinical forms described in medical literature. In our study group were the most numerous cases of pearly BCC (37.95%), nodular BCC (29%) and plan scar BCC (22.03%).

Although interest in histopathology is undeniably, suggestive for BCC were the epitheliomatous pearls on the periphery of the tumor (Figures 1 and 2) and even the presence of a globular tumor with increased consistency, 0.5–2 cm diameter and smooth, glossy, translucent, forming the clinical picture a nodular BCC. Also, the evolution term (of years) and tumor location in the 2/3 upper facies BCC advocates.

Evolution of cancer was assessed by our patients to be between eight months to nine years, over 2/3 of cases with history between 1.5–3 years. In all cases of basal cell carcinoma disease evolved over three years. These data highlight the lack of medical knowledge for awareness, the sick, there account appears cancer.

Regarding EC, vegetated-ulcerated EC prevailed (34.03%), nodular EC (31.33%) and keratotic form (24.27%).

Suggestive of this diagnosis are tumor location in the semimucous or mucous membranes and its appearance on an old scar. Also, history of the disease is short compared to that of BCC. Our patients had tumor progression between five months to four years and at most (81.12%) track is between 1–2 years. In 46.06% of cases, EC developed on precancerous lesions one of the following: keratoses chelitis, actinic keratoses, keratoacanthoma, cutaneous horn, leukoplakia, genital sclerotic lichen, chronic scars, Bowen disease, erythroplasia of Queyrat.

As for MC, diagnosis was strictly histopathological, the clinical examination not leading to diagnosis. Based on the above, especially because of clinical polymorphism of skin carcinomas, come off that histopathology is essential for diagnosis of BCC, EC, MC. It must be supplemented with immunohistochemical investigations in particular cases with histopathological structure (ex., spindle cell EC, pseudovascular EC, etc.).

Regarding the treatment of skin carcinomas, is it in use a wide range of therapeutic methods such as Mohs’ surgery, classical surgery, radiation therapy, cryotherapy, electrodessicication in addition of curettage, photodynamic therapy, 5-fluorouracil, topical immunomod, interferon. The golden standard for nodular BCC treatment of nasal region is surgical excision; in some cases, patients refused this treatment [14]. Imiquimod 5% topical is an effective therapeutic alternative for patients with comorbidities. One year, two years follow showed healing at 89% and 85% in a study on 82 patients [15]. Excellent cosmetic results and efficacy of MAL PDT are one option to treat superficial basal cell carcinomas, actinic keratosis and Bowen’s disease [14, 16, 17]. Identification of HPV in the tumor challenge starting treatment with retinoids in order to prevent recurrences after surgery [18].

Treatment strategy must be preview: patient selection, aesthetic and functional outcome, comorbidities, available techniques and practitioner competence.

Therapy patients in our study group appealed to curettage and electrodessication in 58% of cases and radical excision with oncological safety margin in the remaining 42%. We obtained 95.02% of healings. Moreover, it is recognized that the location “to the view” allow early diagnosis of skin cancers. Direct and indirect costs increased in advanced skin cancers showed the need early diagnosis [19]. These cancers may be curable and, more importantly, they can be prevented. Knowledge of risk factors and their action further limiting diagnosis and early treatment of pre-cancerous lesions are elements of prevention of skin carcinomas.

If positive edges excision, increase the risk of relapse, especially in aggressive histological types [20]. Recurrence rate depends on the type of treatment. For superficial BCC is 1% recurrence rate after Mohs’ surgery, 5–10% after conventional excision, radiotherapy, cryosurgery, 7–13% after curettage and electrodessication [21]. After treatment should avoid factors that increase the risk of recurrence. The patient should be examined regularly for capturing any relapse; self-examination is also important [22].

Unfortunately, we encountered 15 cases with T3 and T4 (nine patients with skin carcinoma and six patients with lip cancer). Analyzing the causes and consequences of “historical cancers”, we noticed the following:

- Long history of disease (dependent on lack of medical education), the reactivity of the body (particularly the immunological factor) and presence of empirical treatment explained the most cases of T3 and T4;
- The EC over 4 cm was correlated with frequency of metastases in regional lymph nodes, but remote;
- Oncologic and aesthetic results were satisfactory in such situations and the cost of treatment was high.

Comparative analysis of cases cured and those followed by treatment failure, and collate these data with data drawn from several studies in the field allow us to affirm the following:
BCC prognosis was good in most cases because the cancer spread to exceptionally rare. In literature was reported about 200 cases of metastatic BCC. Metastasis occurred after an interval of between 1.5 and 14 years from initial treatment of primary tumor and lymph nodes were interested and/or visera [23, 24]. The prognosis depended on established cancer, as clinical and tumor size. Thus, cancers with the location in the ditches perinasal in nasopharyngeal–orbit angles and retroauricular offend more frequently. For large tumors, relapses were also more numerous, due to insufficient excision. Clinical morphoeform forms had medium malignancy, while ulcerated forms, invasive have the highest risk of relapse. Best therapeutic results were obtained by superficial and nodular BCC.

EC prognosis was in relation to a number of factors [2, 10, 25], which outlines the major risk profile tumor: histological differentiation grade, carcinoma relapse, perineural invasion, depth of invasion, location of cancer. Tumors larger than 2 cm, poorly differentiated, with depth invasion and perineural infiltration had unfavorable prognosis because the increased risk of metastasis. The frequency of metastasis was also higher for the EC in the mucosa, compared with EC of the skin. Other prognostic factors were the quality of surgical excision respecting the oncological safety margins (margins free of cancer cells) and ground patient (whether or not immunosupression). Kyzas PA et al. [26], investigating the role of immunohistochemical expression of vascular endothelial growth factor (VEGF), had found a significant association of high expression of this factor and increased incidence of local recurrence. Also, Somma P et al. [27] had investigated the immunohistochemistry expression of FAS/FASL in cancer cells and inflammatory infiltrate in the EC. They found that patients with supra-expression FAS/FASL and FAS in cancer cells “+” in the T-cells had cancers with an aggressive clinical behavior. MC prognosis was similar to the EC.

### Conclusions

The increased incidence of skin carcinomas in Dolj County was due to climatic particularities of the region, to the share of population with significant concerns involving prolonged exposure to sunlight and deficiences of factor.

BCC represented 68.84% of skin carcinomas. The most common clinical forms were pearly BCC, nodular BCC and superficial BCC. Subject matter pathology prevailed polymorphic, solid and keratinized forms.

EC was found in 28.55% of cases. The most common clinical forms were: vegetated-ulcerated, nodular, keratinized. Most have been well-differentiated (64.94%), followed by medium differentiated forms (29.88%) and low differentiated (5.18%). In cases with multiple recurrences, the degree of histological differentiation may get worse over time.

MC, like other skin carcinomas, was located mainly on photo-exposed skin. It takes particular clinical aspects and prognosis was similar to the EC. Most times, in a MC, epidermoid carcinoma developed from the BCC.

Long history of disease (dependent on lack of medical education), the reactivity of the body (particularly the immunological factor) and empirical treatment explained most cases of T3, T4.

Option for surgical treatment of skin carcinomas was warranted by the oncological, functional and aesthetic results, very good in most cases.

Is required public education for awareness of risk factors and to detect mucous and muco-cutaneous carcinomas in early stages.


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