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The value of the histopathologic examination in the diagnosis and management of the actinic keratosis

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Abstract

Actinic keratosis, considered lately as an intraepithelial squamous cell carcinoma in evolution, are powerful predictors of the risk for developing a cutaneous carcinoma and melanoma. The aims of the study were to establish the value of the histopathologic examination as a confirmation method for the actinic keratosis diagnosis, to assess the percentage of these lesions that suffer a malignant transformation, and also the frequency of the association between actinic keratosis and cutaneous carcinomas. This is a retrospective study, performed on 208 patients diagnosed with different types of cutaneous precancers, hospitalized in Dermatology Clinic of Craiova, Romania, between 2006 and 2010. Actinic keratosis represented 37.93% (79 cases) of all cutaneous precancers (the most frequent cutaneous precancer). Patient's age ranged from 17 to 85 years, 54.8% of the patients being from rural environment; 86.07% of the lesions were located on the solar exposed skin (head and face). 72.16% of the actinic keratosis was clinical subdiagnosed. The most frequent form was hypertrophic actinic keratosis (89.06%); in 18.98% of cases, malignant transformation in squamous cell carcinoma was noticed. Actinic keratosis represent 86% of the precancers that associate a carcinoma, basal cell carcinoma being diagnosed the most frequent. In conclusion, actinic keratosis are the most frequent cutaneous precancer, diagnosed in chronic sun-exposed patients, and manifest a tendency to progress into a squamous cell carcinoma without a proper treatment. Pathologic evaluation is mandatory to an accurate assessment of the actinic keratosis prevalence, and for the right management of these lesions.

Keywords: actinic keratosis, histopathology, squamous cell carcinoma, basal cell carcinoma, non-melanoma skin cancer.

Introduction

The concept of a precancerous lesion dates back since the last century, V. Babeş and W. Dubreuilh drawing independently attention about the possibility of malignant transformation of a series of well clinically defined diseases, in 1896. Although actinic keratoses are considered precancerous lesions, there are many controversies related to their nosology, many authors considering these lesions as intraepithelial superficial squamous cell carcinoma in evolution [1, 2]. Nowadays actinic keratosis, Bowen disease, and keratoacanthomas are considered very important lesions, because they are powerful predictors of the risk of the developing of the cutaneous carcinoma and melanoma [2–4].

Ackerman AB and Mones JM consider actinic keratosis as the initial clinical manifestation of a continuous cutaneous disorder, constantly evolving toward an invasive carcinoma. The invasive rate of the derma could be dependent of the immunological status of the patient, the severity of the solar tissue injury, and the lesions age. Hence, the actinic keratosis term will become inadequate, suggesting only a benign solar-induced lesion [5].

The therapeutic expectative attitude, recommended in the presence of some epithelial precancers, and justified by a possible spontaneous regression of the lesions cited in the medical literature, must be avoided due to the risk of the continuous evolution into an invasive carcinoma [5].

Materials and Methods

This retrospective study was performed on 208 patients diagnosed with different types of cutaneous epithelial precancers, hospitalized in Dermatology Clinic of Craiova, Romania, between 2006 and 2010. Dermatological examination, laboratory exams, surgical excision and histopathologic examination were performed in all cases. The biopsy specimens were processed using the classical histopathologic method of paraffin embedding sectioning and Hematoxylin–Eosin (HE) staining method.

All the data were retrospectively included in an Excel 2007 worksheet; the main variables recorded were: the gender, age, living environment, lesion's topography, the clinical diagnosis and the results of the histopathologic examination. Statistical analysis was performed using the add-ins software ExcelStat version 7.5.2; in order to establish the statistical correlation

between different variables, the *chi*-square test was used. The statistical significance was considered for a *p*<0.05 (95% C.I.).

The main purpose of the study was to establish the value of the histopathologic examination in the diagnosis of the actinic keratosis, the assessment of the histopathologic type of the actinic keratosis, and the percentage of the malignant transformation of these lesions. Also, as a second objective, we have assessed the percentage of the actinic keratosis out of all histopathologic diagnosed precancers, and the frequency of the association with the cutaneous carcinomas.

Even though some authors consider cutaneous horn and actinic cheilitis as types of actinic keratosis, these types of lesions were excluded from our study, being used only for comparison reasons.

⊟ Results

The distribution of the entire group depending on the histopathological diagnosis

Between 2006 and 2010 there were 208 cases with the following histopathologic diagnosis: actinic keratosis in 64 (30.76%) cases, actinic keratosis with malignant transformation in 15 (7.21%) cases; actinic cheilitis in nine (4.32%) cases, actinic cheilitis with malignant transformation in 11 (5.28%) cases; keratoacanthomas in 28 (13.46%) cases, keratoacanthomas with malignant transformation in 49 (23.55%) cases; cutaneous horn in 20 (9.61%) cases, cutaneous horn with malignant transformation in three (1.44%) cases; Bowen disease in nine (4.32%) cases.
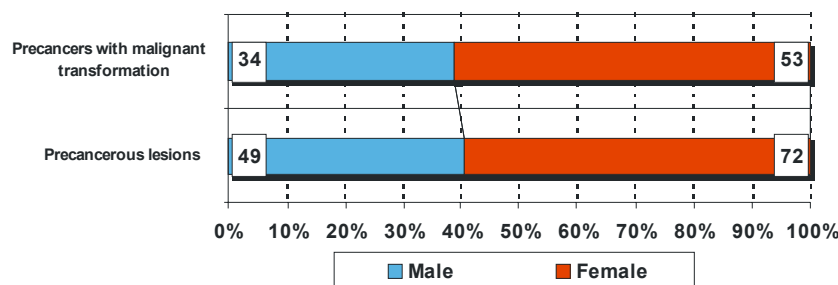
The distribution of cases depending on the environment

Hundred and fourteen (54.8%) patients were from the rural environment and 94 (45.19%) from urban environment.

The distribution of the entire group depending on the gender

The ratio male/female, for all the precancers, precancers with malignant transformation and without malignant lesion is presented in Figure 1; there was a slight dominance in favor of the female gender, for all variables, with no statistical significance (*p*=0.8) (Figure 1).

The distribution depending of the age

For all lesions, patients' age ranged from 17 to 86 years (mean age 67.15±11.75 years); for all epithelial precancers, the average age was 67.61±10.28 years (*p*=0.08). Patients with actinic keratosis had an average age of 66.49±11.82 years; mean age for "benign" actinic keratosis was 66.2±12.45 years, while for actinic keratosis with carcinomas mean age were 67.73±8.51 years (*p*=0.18).

An increase in incidence of the epithelial precancers was noticed starting from the sixth decade; still, the epithelial precancers were diagnosed more often between 71 and 80-year-old. The same tendency in increasing incidence with age is available for the malignant transformation, thus in the eighth decade almost half of the cases present malignant transformation (between 71 and 80-year-old, 44.15% of the cutaneous precancers present malignancy) (Figures 2 and 3).

Figure 1 – *The distribution of the lesions based on the patients' gender.*

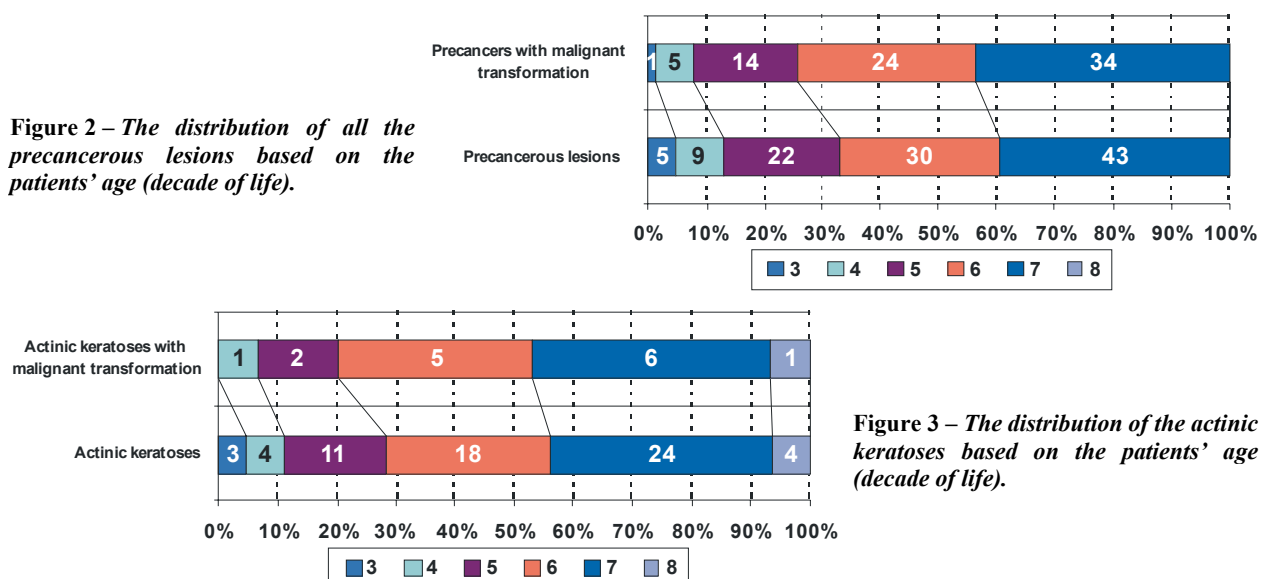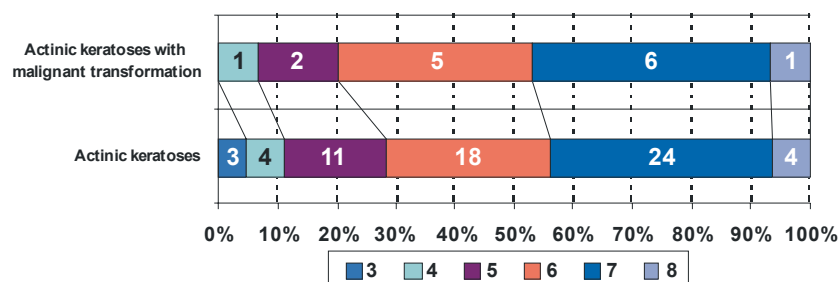Figure 2 – *The distribution of all the precancerous lesions based on the patients' age (decade of life).*

Figure 3 – *The distribution of the actinic keratoses based on the patients' age (decade of life).*

The clinical diagnosis accuracy

Out of 85 cases of histologically-diagnosed malignant precancers, only 37 (43.52%) cases were clinically suspected of malignant transformation, while in 123 pathologically diagnosed epithelial precancers were 29 (23.57%) cases of suspected carcinomas (false positive cases). Thus, the clinical diagnostic accuracy for all epithelial precancers was only of 62.98%.

The clinical diagnosis of actinic keratosis

Regarding the actinic keratosis diagnosis there were only 22 clinically suspected actinic keratosis with pathological confirmation, while in the remaining 57 cases the clinical diagnosis was incorrect (pathology established the actinic keratosis diagnosis, in the absence of the clinical suspicion). Thus for the actinic keratosis the percentage of the correct clinically

suspicion was only 27.84%.

Usually diagnosis of actinic keratosis is only clinical, rarely being established histopathologic. The encountered clinical diagnosis were: actinic keratosis in 23 cases (29.11%); basal cell carcinoma in 24 cases (30.37%); squamous cell carcinoma in one case (1.26%); cutaneous horn in four cases (5.06%); seborrheic keratosis in nine cases (11.39%); melanocytic nevi in nine cases (11.39%); filliform warts in six cases (7.59%); keratoacanthomas in two cases (2.53%); lentigo maligna in one case (1.26%).

Actinic keratoses are the most frequent precancerous lesions located on the sun-exposed regions, encountered in our study in 79 cases (37.98%). Most of the patients present multiple lesion of actinic keratosis; out of all cutaneous cancers, the actinic keratoses are associated most often with basal cell carcinoma (Figure 4).

Figure 4 – *(a) Multiple actinic keratosis of the face, severe solar damage in a phototype II patient. (b) Actinic keratosis associated with basal cell carcinoma.*

(a)   (b)

The distribution of actinic keratosis depending of the age and environment

Patients' age ranged from 17 to 85 years (average 66.39±11.86 years); 50.63% (40 cases) of the patients were from the rural environment.

Actinic keratoses' topography

Tumors' topography was face and head skin in 68 (86.07%) cases, thorax in five (6.32%) cases, upper limbs in five (6.32%) cases, and lower limbs in one (1.26%) case.

The histopathologic examination of the actinic keratoses

The histopathologic examination revealed the actinic keratosis aspect in 64 cases. Most of the actinic keratoses (57 cases) were hypertrophic histological type of the actinic keratosis which present atypical keratinocytes and hyper-, ortho- and para-keratosis in various percentage. The pigmented actinic keratosis was diagnosed in four cases, the melanic hyperpigmentation of some cells from profound layers of epidermis noticed. Atrophic actinic keratosis diagnosed in two cases, presents an atrophic Malpighian layer with moderate hyperkeratosis, while dermo-epidermic junction is horizontalized in the most part and epidermic atypically cells buds observed.

In the acantholytic actinic keratosis diagnosed in our group, in one case the anaplastic cells of the profound layer of the Malpighian seems isolated from the upper epidermic layers through fissures or acantholytic gaps. In 15 cases, the histopathological analysis showed the presence of the malignant transforming of the actinic

keratoses: actinic keratosis with *in situ* carcinoma sites in five cases; actinic keratosis with microcarcinoma sites in six cases; actinic keratosis with moderate differentiated squamous cell carcinoma in four cases (Figure 5).

⊟ Discussion

A peculiar characteristic of the epithelial pre-cancerous lesions is their potential to evolve into squamous cell invasive carcinomas; more and more authors consider actinic keratosis and squamous cell carcinoma as a unique disease, evolving from dysplasia to invasive carcinoma. Out of the epithelial precancers a particular importance presents the keratinocyte lesions, due to their important incidence in the chronic sun exposed population [2, 5].

Out of 208 cases of epithelial precancers histo-pathologically diagnosed, and recognized as a squamous cell carcinoma precursor, actinic keratosis had repre-sented 37.98% of the cases.

The exact estimation of the incidence and the prevalence of the actinic keratosis, in general population, remains the object of the numerous studies, with very different results, influenced by multiple factors: racial differences, age, studied anatomical regions, cases selection method, the skills of the examiners, sun exposure length (professional and recreational), the lack of the histopathologic examination in the majority of the studies [2, 3, 6].

Many studies considers age as the most important risk factor for developing of the actinic keratosis; the prevalence increase from 10% to 80% since the third decade till the seventh decade in the white adults [2, 6].
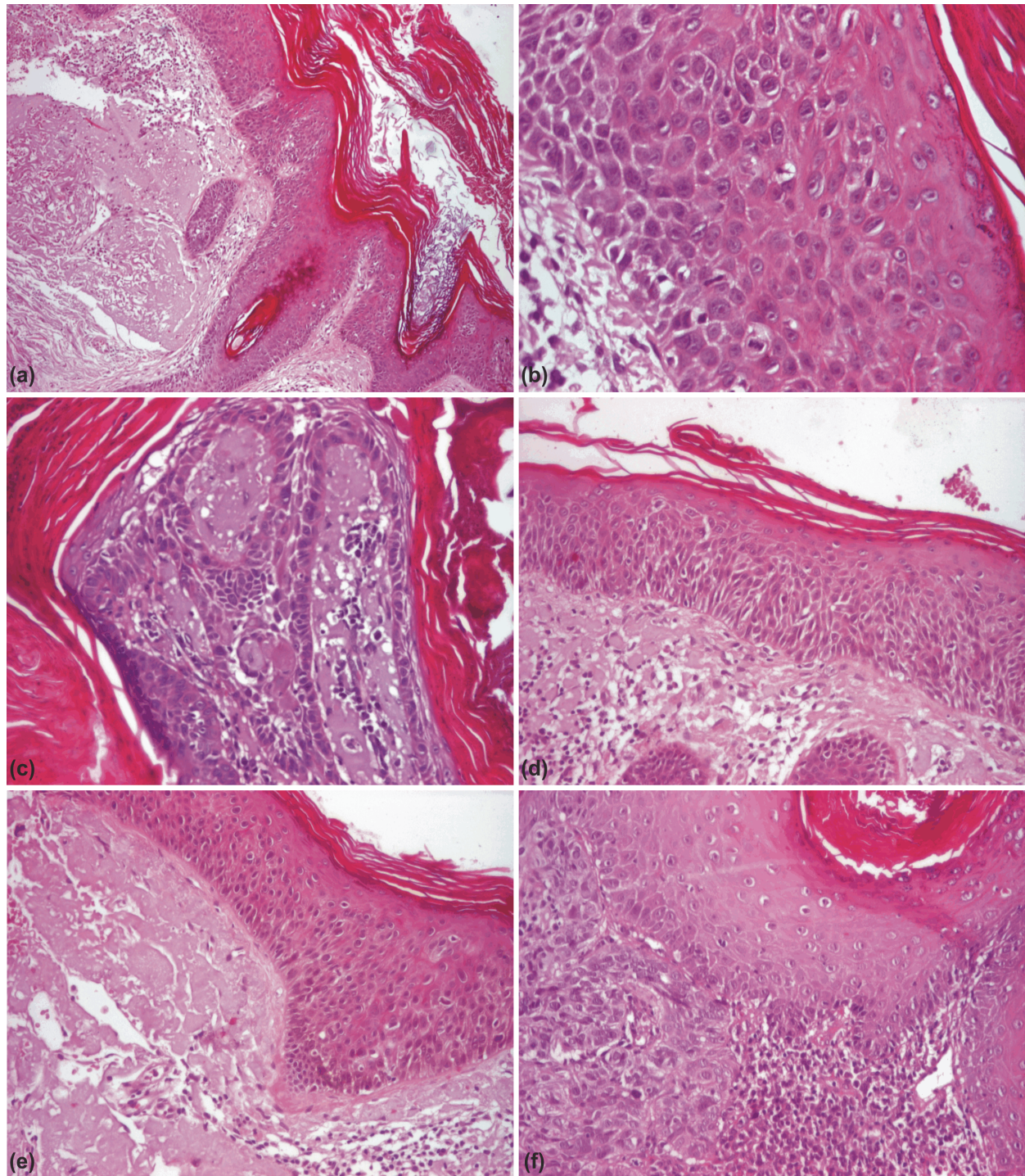
Figure 5 – *(a) Hypertrophic actinic keratosis type: hyper-, ortho- and para-keratosis, mild papillomatosis, Malpighian layer with hyperplasia (HE stain, ×40). (b) Hypertrophic actinic keratosis: parakeratosis, atypical cells (HE stain, ×200). (c) Acantholytic actinic keratosis: widespread keratinocyte acantholysis (HE stain, ×100). (d) Atrophic actinic keratosis: mild hyperkeratosis with parakeratosis, Malpighian layer relatively thin with anaplastic cells that compose the profound Malpighian layer, dermal–epidermal junction is horizontalized with slight buddies into the dermis, in derm is present solar elastosis (HE stain, ×100). (e) Pigmented actinic keratosis: melanic hyperpigmentation of some cells from profound layers of epidermis (HE stain, ×100). (f) Actinic keratosis and squamous cell carcinoma (HE stain, ×100).*

In our study the mean age of the patient with actinic keratosis was 67.15±11.75 years; the higher incidence was recorded in the eighth decade (between 71–80-year-old). The incidence of the malignant transformed actinic keratosis increases in the same way, the mean age for actinic keratosis with malignant transformation being 67.73±8.51, with the same higher incidence in the eight decade (40% of the actinic keratosis in this age group were malignant transformed).

Regarding the gender, most of the studies have demonstrated that men are more often affected than women, probably due to an increased exposure to sun [2, 6]. Our study contradicts these results, affected women representing 60.09% of the cases; still the statistical

significance was not reached (p=0.8). At the malignant transformed actinic keratosis, the differences between gender decreases, only 42.4% of the cases affecting women, while in men there was a 40.96% of malignant transformation.

Considering the environmental factors, there were 54.8% of the cases from the rural environment, probably due to an increase exposure to the sun.

Both in women and men, the higher incidence of the lesions was recorded at the face, representing 86.07% of the cases.

The diagnosis of the actinic keratosis is usually clinic, rarely confirmed by pathology, which could explain the shortage of data referring to clinical diagnosis accuracy [2, 7]. Ponsford MW *et al.* have published 94% accuracy for the clinical diagnosis (34 out of 36 clinical suspected lesions of the actinic keratosis being diagnosed histopathological), while Thompson SC *et al.* have demonstrated an 80% accuracy of the clinical diagnosis [8, 9]. In the Venna SS *et al.* study, although the examiners were experimented, there were an important number of patients incorrectly diagnosed, even though the lesions had a classic aspect of the actinic keratosis [4].

At the studied lot, the pathologically assessed actinic keratosis had a clinical diagnosis accuracy of 27.84%, most of the cases having as clinical suspicion the basal cell carcinoma diagnosis (33.76%). Compared to other studies, there was an important percentage of clinically incorrect diagnosed actinic keratosis, probably due to the high clinical variability of these lesions, and also a tendency to be considered as cutaneous cancers.

The importance of the histopathologic examination is determined by the clinical resembles of the actinic keratosis with some cutaneous cancers, and the impossibility of the exact determination of the real actinic keratosis prevalence, when histopathologic diagnosis lack. Moy RL stated that there is no clear way to clinical differentiate between actinic keratosis and squamous cell carcinoma, many lesions considered clinically as actinic keratosis being in fact squamous cell carcinoma, treated as an actinic keratosis [7]. In fact, the differential diagnosis of a typical actinic keratosis includes multiple diseases, demonstrating the lack of clinical specificity of this lesion [2].

Classic, actinic keratoses are histological classified in several types. In our study, we have identified the following histologic types of actinic keratosis: 56 (72.73%) cases of hypertrophic actinic keratosis, four cases of pigmented actinic keratosis, two cases of atrophic actinic keratosis, one case of acantholytic keratosis. Similar to the literature data, in our study the most frequent encountered actinic keratosis is the hypertrophic type.

The clinical and histopathologic differential diagnosis is different, depending on the actinic keratosis type. Usually, the histopathologic differential diagnosis must be performed with *in situ* squamous cell carcinoma, superficial basal cell carcinoma, spongiotic dermatosis, bowenoid papulosis.

Unlike the *in situ* squamous cell carcinoma and bowenoid papulosis, characterized by atypia in all the thickness of the epiderma and dyskeratosis, actinic keratosis have atypia limited to the basal layer or to the cells of the lower layers of the Malpighian, and dyskeratosis is rare [1, 2, 10]. While *in situ* squamous cell carcinoma presents positive staining for cytokeratin 10, the bowenoid actinic keratosis did not [11].

Although both, actinic keratosis and superficial basal cell carcinoma may present small buds of atypical cells which enter into the derma, the basal cell carcinoma differentiate by the palisading disposition of the tumoral cells at the tumor's peripheral margins, and also by the stromal retraction and dermal mucin deposits. In the most challenging cases, the immunohistochemical Ber-EP4 staining is used, being positive in basal cell carcinoma and negative in actinic keratosis [12].

The inflamed actinic keratosis may present minimal keratinocytes atypia and medium spongiosis, and must be differentiated by spongiotic dermatosis; the presence of different types of inflammatory cells in the derma may be useful for the differentiation.

The most challenging is the clinical differentiation between a hypertrophic keratosis and squamous cell carcinoma; there are no definite clinical criteria to differentiate between those two diseases, but the presence of induration, pain, a big lesion, marked hyperkeratosis, ulceration, bleeding, fast growth, the recurrence or persistence after the treatment represents alarm signs, suggesting more often a squamous cell carcinoma [2].

Pathologically the hypertrophic actinic keratosis must be differentiated by inflamed seborrheic keratosis, which may also present acanthosis and minimal atypia; the presence of the horn pseudocysts, of the papillomatosis and exocytosis of the inflammatory cells support the seborrheic keratosis diagnosis.

The pigmented actinic keratosis and the extensive pigmented actinic keratosis must be differentiated by the solar lentigo and the seborrheic keratosis at their onset, keratinocyte atypia and the lack of lentiginous proliferation support the diagnosis of actinic keratosis.

Actinic keratosis accompanied by acantholysis and epidermolysis must be differentiated by the achantolytic and epidermolytic acanthomas; these neoplasms does not present keratinocytes atypia, and in most cases does not present the basal layer proliferation.

Lichenoid actinic keratosis must be differentiated by benign lichenoid keratosis and inflamed seborrheic keratosis; due to the nature of the infiltrate, this could be very challenging, the key feature being the atypical keratinocytes: benign lichenoid keratosis presents more dyskeratosic keratinocytes, and colloids bodies in the papillary dermis, and also, they are more expansive than lichenoid actinic keratosis [10].

Alongside with these histopatologic forms there may be encountered combined or intermediate types, some authors describing also a type of inflamed actinic keratosis, clear cells actinic keratosis; also, some authors consider the cutaneous horn and actinic keratosic cheilitis as actinic keratosis variants [2].

In cases in which the clinical aspect suggested a squamous or a basal cell carcinoma, but the histo-pathology reveal the actinic keratosis diagnosis it is

recommended to perform multiple sections, in order to avoid the carcinoma diagnosis omission. Thus, in a study, in which after an initial pathology diagnosis of actinic keratosis over only one pathologic section examined, on seriate examination, in 33% of the initially diagnosed actinic keratosis were subsequently identified in 13% Bowen disease, in 4% a basal cell carcinoma and in 3% an invasive squamous cell carcinoma. Three factors correlated with the malignancy on seriate sections: the ulceration presence, a clinical diagnosis of cutaneous cancer, and a history of cutaneous cancer pathologically confirmed [13].

In a classic manner, actinic keratosis were considered as precancerous lesions with potential to transform into a squamous cell carcinoma; actinic keratosis represents histopathologically an epidermic neoplasia formed by anaplastic keratinocyte and covered by a more or less thickened corneum stratum, as a reaction to chronic exposure on UV radiation [1, 2, 14]. Actinic keratosis could be isolated or in an association with a synchronous squamous cell carcinoma or, seldom, a basal cell carcinoma [15]. In actinic keratosis, an increase in cyclooxygenase-2 and proangiogenetic protein was reported [16, 17].

Solar elastosis is present variably, and some studies suggest that lesions accompanied of the intense solar elastosis have an increased expression of proapoptotic (Bcl-2) and proliferative (Ki-67) markers [18].

Tenascein presence at the dermal level (an extra-cellular matrix protein, expressed around the neoplasic cutaneous lesion) was reported to be associated with the degree of keratinocytes atypia in actinic keratosis, but do not correlate with different histopathologic subtypes [19].

The hypertrophic type has a thick, acanthosic epiderma; the atypia is common over the basal layer, but it could be minimal. Sometimes, a psoriasiform, irregular, hyperplasia may be observed. Papillomatous proliferation is more common in the acral lesions [1, 2]. In this type of actinic keratosis an increased of the p53 expression was reported, which could represent an early and critical event in the development of these lesion [20].

Oncoprotein alteration and an increased in proliferative keratinocytes activity was evident in different types of actinic keratosis and squamous cell carcinoma, suggesting that an important role in the actinic keratosis transformation toward an squamous cell carcinoma belong to the cutaneous immune defense mechanisms [21].

Tomas D *et al.*, in a study referred to the Bcl-2 and Bax correlation in actinic atrophic and hypertrophic keratosis, demonstrated that Bcl-2:Bax ratio was statistically significantly higher in hypertrophic type, which could indicate a better resistance to apoptotic stimuli for keratinocytes in hypertrophic type, which make them more susceptible to progression toward a squamous cell carcinoma [22].

Pigmented actinic keratosis is difficult to be clinically and histologically differentiated of the sun lentigo and sometimes-malignant lentigo; extensive pigmented actinic keratosis must be differentiated of malignant lentigo or a big seborrheic keratosis. In order to differentiate of the lentigo malign, the immunohisto-chemical staining for melanocyte must be performed [23]. An Azure-B counterstain may be useful in order to avoid some diagnostic pitfalls.

The ultrastructural studies have demonstrated that extensive pigmented actinic keratosis has a normal number of melanocyte with types II and IV of melanosome; these melanosomes represents the only characteristic, and may be present in keratinocyte and, also, in Langerhans cells [2, 10].

The skin surrounding the actinic keratosis, which appear to be normally clinic, on histopathologic examination presents atypia, suggesting a graded progression from atypical keratinocytes, without clinical manifestation, toward a squamous cell carcinoma [10].

The untreated, thick, hyperkeratosic and ulcerated lesions have the greatest risk of the malignant transformation, estimated to approximately 1 to 1000 per year [2].

Classic there are described three evolutive possibilities for actinic keratosis: persistence, regression and malignant transformation into an invasive squamous cell carcinoma; still, the spontaneous regression of an actinic keratosis is impossible to be predicted. Marks R *et al.* have reported that up to 25% of the actinic keratosis may regress up to one year, especially if the sun exposure is limited [2, 24]. Other studies have infirmed the clinical regression possibility of the actinic keratosis and drawn attention over a tendency for these lesions to be ignored, and also over the necessity of the treatment of these lesions, due to their potential to evolve into an invasive carcinoma [5].

Although it is impossible to predict the evolutive modality of the actinic keratosis, still it is considered that the risk of the progression toward an invasive carcinoma depends on the lesions age and the actinic keratosis multiplicity; also, the risk to evolve into a squamous cell carcinoma increases with the intensity of the exposure to the UV radiation and with the presence of the immunosuppression.

Several studies have tried to demonstrate the risk of the progression of an actinic keratosis toward a squamous cell carcinoma, but the results seems contradictorily; in the literature this risk varies from less than 1% up to 20% [2]. In a meta-analysis, including five clinical studies over a 10-year period, Glogau RG demonstrated that published results referring to the transformation risk into a squamous cell carcinoma varies from 0.025% to 16% per year; based on these analysis the author suggest a progression rate of the actinic keratosis to the squamous cell carcinoma of 8% [25].

Fuchs A and Marmur E estimate that approximately 20–25% of the actinic keratosis patients will develop finally a squamous cell carcinoma; the progression time is estimated to approximately two years [26].

Berhane T *et al.* consider as clinical markers of progression toward a squamous cell carcinoma the appearance of the pain and actinic keratosis inflammation; hence, a pathologic examination of an actinic keratosis with clinical inflammatory signs reveal the presence of a squamous cell carcinoma in 50% of the cases [27].

The risk of the malignant transformation was assessed, also, by determining the percentage of the squamous cell carcinomas aroused on preexistent actinic keratosis; there are many studies, which using the pathologic evaluation of an invasive squamous cell carcinoma specimen, have tried to determine the percentage of cases in which a contiguous or associated actinic keratosis was identified, the results varying from 60% to 82.4%, 97% or even 100% [28–30].

Czarnecki D *et al.*, in a prospective study using pathologic examination of the squamous cell carcinomas treated over a year period, in order to determine the presence of an actinic keratosis, demonstrated on the examined specimen a contiguous actinic keratosis in 72% of the cases [31].

Out of 79 actinic keratosis cases pathologically confirmed, in 15 (18.98%) cases was demonstrated the malignant transformation: five cases of actinic keratosis with *in situ* carcinoma sites, six cases of actinic keratosis with microcarcinoma sites, and four cases of actinic keratosis with moderate differentiated squamous cell carcinoma sites. Related to the all-malignant transformed precancers in the studied group (85 cases – 40.86%), transformed actinic keratosis represents 17.64% of the cases.

Considering the type of the carcinoma developed from actinic keratosis, there is no unanimous consent; some authors report a majority or even exclusivity of the squamous cell carcinoma, while others find out a dominance of the basal cell carcinoma [1, 2, 5, 6].

In our study, we could identify only the squamous cell carcinoma transformation of the actinic keratosis.

Besides their evolutive peculiarities, actinic keratosis are important because they are significant clinical markers in the development of a non-melanoma skin cancer: the presence of an actinic keratosis indicate a long solar injury and allow the clinician to identify a high risk group for development of a squamous cell carcinoma, basal cell carcinoma or melanoma [32].

Many studies concentrate over the association between the actinic keratosis and the skin carcinomas, insisting on the risk of the development of a cutaneous cancer at workers with daily, chronic exposure to ultraviolet radiation; Budhwar R *et al.*, in study on 46 bricklayer Indians, with 8–10 hours of sun exposure daily, have found a statistically significant increase of the DNA-protein cross-links, as possible marker of the sun exposure [33].

In 50% of the studied epithelial precancers association with cutaneous cancer was detected, basal cell carcinoma representing 86% of the cases; multiple actinic keratoses at the same individual were most often associated, basal cell carcinoma being present at 86% of the cases associating a carcinoma.

In the recent years there were made many efforts in order to re-define the actinic keratosis as a malignant neoplasia, as they represent in evolution intra-epithelial squamous cell carcinomas. Even though accepted, that not all of the actinic keratosis become a squamous cell carcinoma, they are considered the initial lesion of a continuous disease that may progress toward a squamous cell carcinoma; as an argument for this concept is the analogy with the carcinoma of the cervix, in which the cervix intra-epithelial neoplasia represents the initial precancerous lesion [34].

Many authors have proposed for a better classification of actinic keratosis terms as intra-epithelial keratinocytes neoplasia (KIN), developed by Cockerell, while Goldberg proposed the concept of proliferative actinic keratosis, and Berhane the concept of inflamed actinic keratosis [5].

Ackerman AB and Mones JM, based on extensive studies and clinico-histological arguments, consider that it is not possible to draw a line in order to establish where actinic keratosis ends, and where the squamous cell carcinoma begins, mainly due to the fact that actinic keratosis represents a superficial squamous cell carcinoma [5].

Even avoiding the controversies regarding the nosology of the actinic keratosis as precancers, and the relation with the squamous cell carcinoma, actinic keratosis represent important clinical lesions, being one of the most powerful predictors for a melanoma or non-melanoma skin cancer development [32].

⊞ Conclusions

There are many controversies regarding the nosology of actinic keratoses, many authors considering these lesions as superficial squamous cell carcinoma.

The malignant transformation risk of the actinic keratosis must not be underestimated, especially taking into consideration the increasing incidence of cutaneous carcinomas in our geographic area.

The histopathologic examination emphasized that the percentage of the malignant transformed actinic keratosis is the same as the medical literature.

The correlation between clinical and histopathologic examination allowed an accurate diagnosis of the actinic keratosis and may surprise the malignant transformation of these lesions.

Knowing that ultraviolet radiation represents the main environmental factor implied in carcinogenesis and epithelial precancerous lesions induce, it has become clear that a reduce in cutaneous cancer incidence may be obtained only through prophylactic measures, especially populational education to photoprotection, and also, the early diagnosis and treatment of the cutaneous precancers.

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