EPIDEMIOLOGICAL AND PATHOLOGICAL ASPECTS OF SKIN CANCER IN NORTH EAST OF ROMANIA

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EPIDEMIOLOGICAL AND PATHOLOGICAL ASPECTS OF SKIN CANCER IN NORTH EAST OF ROMANIA (Abstract): In the last years skin cancer has become the most frequent cancer in humans, with the majority made up of two tumors: malignant melanoma (MM) and non-melanoma skin cancer (NMSC). Aim: To provide for the first time in the North East region of Romania, descriptive epidemiological data of melanoma and non-melanoma skin cancers. Material and methods: We undertook a retrospective study over a five year period on the most frequent forms of skin cancer, basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and MM, which included a total number of 1231 patients, hospitalized and treated in the Plastic Surgery Department of “St. Spiridon” Emergency Clinical Hospital, Iaşi from 2008 until 2012. Results: BCC was diagnosed in a total of 675 patients, representing 54.9%. SCC was found in 217 patients, representing 17.6% and melanoma was diagnosed in 119 cases, a percent of 9.7% of the total number. The predominance of cutaneous malignancies varied with age, major site distribution was face and neck for BCC and SCC and the trunk for MM. Results: This article describes the most common forms of skin cancer in our region, BCC (almost 55%), SCC (17.6%), and less in number MM (near to 10%); these results are similar to those published abroad in the last years. Conclusions: Future more elaborate interventional studies are necessary to identify the main risk factors in order to design the best preventive methods and, according to the skin cancer trend to specify the needs for dermatology network in our country. Keywords: SKIN CANCER, BASAL CELL CARCINOMA, SQUAMOUS CELL CARCINOMA, MELANOMA.

In the last decades skin cancer has become the most frequent cancer in humans, with the majority made up of two tumors: malignant melanoma (MM) and non-melanoma skin cancer (NMSC) (1). These two are the most common types of cancer encountered in white population, with an increasing incidence rate worldwide, but the epidemiological data regarding this type of cancer are incomplete because of the absence of some cancer registers or simply the lack of information (2). In the battle against cancer we must know all the aspects about the disease with the special features for every country and every region. In the North – East region of Romania, the Cancer registry was recently introduced, and the data were collected and
statistical processing only until 2009, thus
the prevalence and the histological forms
of this type of neoplasm are not very well
known, and there is no national database
for this epidemiological surveillance.

In this retrospective study we have ex-
amined the epidemiological and pathological
features of 1231 skin cancer cases,
made by the Plastic Surgery Department
of “St. Spiridon” Emergency Clinical Hos-
pital, Iași from 2008-2012 with the pur-
pose of documenting the pattern of skin
neoplasia in Iași, the largest city of Mol-
davia.

Non-melanoma skin cancer is the most
common human skin cancer, enclosing
basal cell carcinoma (BCC) and squamous
cell carcinoma (SCC), both derived from
epidermal keratinocytes, and it rarely me-
tastasizes (3). NMSC is the neoplasm of
elderly people, with a predilection for sun
exposed areas, and, in contrast with mel-
noma, rarely metastasize (4). BCC, also
known as “basalioma” was described for
the first time in the 1824, by Arthur Jacob,
as ulcus rodens, and, since then its inci-
dence is continuously rising worldwide.
BCC represents about 65% of the epithelial
skin tumors, it has a maximum incidence in
the 6-th decade of life and a slightly male
predominance. It is a slow-growing, locally
invasive epidermal tumor with a metastatic
rate of <0.1% (4). The majority is found on
the cephalic extremity (head and neck),
almost 80% of the cases respectively; the
distribution but these can vary according to
the histological pattern: superficial BCC is
more often found on the truck (5). Fibro-
epithelioma’s Pinkus is a rare type of BCC
that is usually located above the natal cleft
or on the lower trunk with a pink colored
nodule that may look like seborrheic kera-
tosis. The incidence of NMSC is increas-
ing, while the mortality is decreasing, a
fact that is explained by earliest diagnosis
with efficient therapeutical intervention all
over the world (6). Keratoacanthoma is
relatively common, especially in middle-
aged white people, uncommon in dark-
skinned ones; moreover it is a benign epi-
dermal tumor with a tendency to regression
after a few months that can develop areas
of CSC in approximately 25% of cases (7).
Merkel cell carcinoma is a rare neuroendo-
crine carcinoma of the skin, 40 times less
common than melanoma, but with a higher
mortality (33%) than melanoma (15%) (8).
MM is the most aggressive form of all skin
neoplasms with a reduce survival rate. It
can start either from the existing moles or
from the normal-looking skin. Many stud-
ies have reported at least two important
data about the survival rate: that women
have a longer survival score than men, and
that the anatomic location varies with this
rate. For example, melanomas located on
the trunk were correlated with worse prog-
nostic (8).

MATERIAL AND METHODS
In this 5 years (2008-2012) retrospec-
tive and descriptive study a total of 1,231
cases registrated in the Plastic Surgery
Department of “St. Spiridon” Emergency
Clinical Hospital, Iași were investigated.
Detailed description of clinical appearance
of the excision area is previously described
in patients’ clinical records. Surgical exci-
sions and histopathology examinations
were performed in all cases. The biopsy
specimens were processed using paraffin
embedding and hematoxylin-eosin staining
method. Statistical analysis were performed
as case-control analyses, without adjust-
ment for multiple testing, with nominal
significance defined as p<0.05. Intergrupal
qualitative differences were established using the Chi-squared Kruskal-Wallis Test. In this study we included only patients with clinical diagnosis of BCC, SCC and MM. The variables introduced in the current study were: gender, inhabitant population of place of residency (urban/rural), anatomical location of the cancer (face/scalp/neck/trunk/anogenital region/upper limb/lower limb), clinical presentation, histological diagnosis, presence of residual malignant cell in the safety margins (oncologic excision), and risk factors (smoker/non smoker for MM).

RESULTS

Of the total number of patients (1231), 1319 biopsy pieces has been histological analyzed, because of the existing multiple lesions on the same patient. BCC was diagnosed in a total of 675 patients, representing 54.9% of the cases taken to the study, with the nodular form as the most common histological type (40.4%), followed by BCC with adnexal differentiation (21.1%), keratotic (14.8%), superficial (6.8%) and pigmented (6.1%). 81.6% of BCC had a facial localization, 11.4% a trunk localization and 11.1% had the tumor on the scalp. We did not find a male predominance in these forms of carcinoma, but maximum incidence of it was found in the sixth decade of live (4). SCC was found in 217 patients, representing 17.6% with the major histopathological pattern being the keratotic form (81.9%), and MM was 9.7% of the total number with a preponderant level of invasion as Clark III (33.6%). The frequency of BCC, SCC was higher in the rural district versus the urban district (82% vs. 68%) as described in tab. I and on the age group, the variation of skin cancer was significantly statistical: in the group aged 20-29 the MM was the most frequent form, between 50-59 years BCC was the prevalent one and over 90, SCC.

<table>
<thead>
<tr>
<th>Skin cancer</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
<th>Urban</th>
<th>Rural</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>BCC</td>
<td>675</td>
<td>54.9</td>
<td>335</td>
<td>53.9</td>
<td>340</td>
</tr>
<tr>
<td>SCC</td>
<td>217</td>
<td>17.6</td>
<td>123</td>
<td>19.8</td>
<td>94</td>
</tr>
<tr>
<td>MIXT</td>
<td>26</td>
<td>2.1</td>
<td>12</td>
<td>1.9</td>
<td>14</td>
</tr>
<tr>
<td>MM</td>
<td>119</td>
<td>9.7</td>
<td>64</td>
<td>10.3</td>
<td>55</td>
</tr>
<tr>
<td>Other</td>
<td>193</td>
<td>15.7</td>
<td>88</td>
<td>14.1</td>
<td>105</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Kruskal Wallis Test | Chi-square=6.081; df=4; p=0.193 | Chi-square=43.672; df=4; p=0.001

In SCC 76% of the cases had a facial localization and 11, 1% were found on the upper limbs. In MM, the main localization was the trunk (44.5%), followed by the upper limbs with a 28.6% percent as described in table II.

All patients with mixt carcinoma had a facial localization and 26.9% of them were associated with another mixt carcinoma on the scalp or upper limbs.
TABLE II
Site distribution of skin cancer

<table>
<thead>
<tr>
<th>Skin cancer</th>
<th>Face</th>
<th>Scalp</th>
<th>Neck</th>
<th>Trunk</th>
<th>Anogenital region</th>
<th>Upper limb</th>
<th>Lower limb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>BCC (N=675)</td>
<td>551</td>
<td>81.6</td>
<td>75</td>
<td>11.1</td>
<td>14</td>
<td>2.1</td>
<td>77</td>
</tr>
<tr>
<td>SCC (N=217)</td>
<td>165</td>
<td>76.0</td>
<td>11</td>
<td>5.1</td>
<td>1</td>
<td>0.5</td>
<td>12</td>
</tr>
<tr>
<td>MIXT (N=26)</td>
<td>26</td>
<td>100</td>
<td>6</td>
<td>23.1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>MM (N=119)</td>
<td>9</td>
<td>7.6</td>
<td>5</td>
<td>4.2</td>
<td>3</td>
<td>2.5</td>
<td>53</td>
</tr>
<tr>
<td>Other (N=193)</td>
<td>86</td>
<td>44.6</td>
<td>25</td>
<td>13.0</td>
<td>4</td>
<td>2.1</td>
<td>34</td>
</tr>
<tr>
<td>Total (N=1230)</td>
<td>837</td>
<td>68.0</td>
<td>122</td>
<td>9.9</td>
<td>22</td>
<td>1.8</td>
<td>176</td>
</tr>
</tbody>
</table>

The histopathological pattern of SCC revealed approximatively 82% of them as SCC with keratinisation and 3.7% in situ SCC. Precancerous keratinocytic lesions found in our study were: actinic Keratosis (AK), Bowen’s disease, Bowenoid papulosis and Erythoplasia of Queyrat (9). Regarding the safety margins of the excision of the tumor, there were differences between the three types of cancer: 87.6% for the BCC, 85.3% for SCC and only 72.3% for the MM.

DISCUSSION

Although skin tumors registries have been established for several European countries, in Romania only since 2007 regional registries were created in order to collect and to analyze data regarding all cancers that were diagnosed in our oncology clinical units. Specific data regarding evolution and tendency of skin cancer will be available probably in the next years. Although non-invasive therapeutic ways of screening a skin lesion are increased, such as dermartercospy, the most frequent way of treating such lesion remains the surgery. Unlike BCC, SCC has some premalignant lesions, such as actinic keratoses or Bowen disease, lesions that may benefit from a non-invasive treatment, first-rate for the patient and less expensive for the health insurance companies. In the studied period the major forms of skin cancer was homogenous (p=0.927) (fig. 1).

Related to the histopathological forms of skin cancer, we found some statistically semnificative differences between BCC, SCC and MM. The majority of NMSC lesions were encountered on the head and neck area, a visible site that affects the quality of live score on these patients (10). 81.6% of BCC had a facial localization and 76% our cases of SCC were in this site. The major histopathological form of BCC was the nodular one, in accordance with other data (11). According with another international data, the BCC and SCC localization was predominantly in the same area- head and neck (limit: 74 - 84% - Plesko et all. 2009, Jung G.W et all. 2010, Dacosta Byfield et all. 2013). The clinical presentation of BCC is quite variable: nodular lesion, ulcerated lesion, erythematous plaque or nodule like lesion and tends to occur in elderly people (12). Due to the good prognosis and high inci-
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dence of this type of NMSC, BCC is not considered an aggressive cancer, but the local destruction potential may bring some intricate methods of treatment (13). Related to the histo-pathological forms of skin cancer, we found some statistically significantly differences between BCC, SCC and MM. Our findings are similar to one of the largest systematic review of worldwide incidence of nonmelanoma skin cancer, made by Bath-Hextall et al (2012): the most frequent skin cancer was BCC (54.9%) while a smaller percentage is represented by SCC (17.6%) and melanoma (9.7%) (6, 14). The frequency of BCC, SCC was higher in the rural district versus the urban district (82% vs. 68%), but the frequency of MM was significantly higher in the urban area (12.3% vs. 5.9%) (p=0.001). On the age group, the variation of skin cancer was significantly statistical: in the group aged 20-29, the MM was the most frequent form, between 50-59 years BCC was the most prevalent one and, over 90, SCC. MM was predominant in men and, in comparison with other adult cancers, more common in young people. We did not find the increasing incidence of MM in this period of study, probably due to the short duration of it. More than 25% of MM occurs in persons less than 45 years old with an incidence that has increased significantly worldwide, especially in lightely pigmented Caucasians (7). In our study the majority of MM cases were in 20-29 group of age. In order to improve the chance of an early diagnosis, the histopathological exam remains the golden standard in the all forms of skin cancer and the way to a proper staging (15).

![Graph](image)

**Fig 1.** Years distribution of major forms of skin cancer by year of study.
Other: trichoepithelioma, leiomyosarcoma, hemangioma, papilloma.

**CONCLUSIONS**

This study has investigated the prevalence of skin cancer and the histopathological pattern of BCC, SCC, MM in North-East Romania, with the aiming at bringing an overview to the exact incidence of skin cancer in our country. To our knowledge these data are provided for the first time in this region and our findings are similar to other international data.

In a five years retrospective study, the most frequent skin cancer was BCC (54.9%) and less in number SCC (17.6%) and melanoma (9.7%). Future more elaborate interventional studies are necessary to identify the main risk factors in order to design the best preventive methods and, according to the skin cancer trend to specify the needs for dermatology network in our country.
REFERENCES