NON-MELANOMA SKIN CARCINOMAS OF THE HEAD AND NECK

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SUMMARY

Background: The aim of this study was to evaluate the incidence and clinical features of non-melanoma tumors of the head and neck, as well as the validity of surgical therapy in their treatment.

Subjects and methods: The study included 530 patients who were operated in the Otorhinolaryngology department of the Livno County Hospital.

Results: In 295 cases (65.1%), it was basal cell carcinoma of the skin and was followed by squamous cell carcinoma of the skin, in 119 cases (29.9%) while the remaining 5% of cases referred to other non-melanoma skin carcinomas. Statistically significant, the most common non-melanoma skin carcinoma was basal cell carcinoma (χ²=625.67; df=4; p<0.01). The most common localization was the skin of the nose (24.2%), which proved to be statistically significant (χ²=290.824; df=5; p=0.00). All patients underwent classic surgery, and in 358 cases (89.5%) the tumor was completely removed, while in 40 cases (10.5%) the tumor was partially removed which proved to be statistically significant (χ²=254.08; df=1; p=0.00).

Conclusions: The results of the study fully confirm the assertion that classical surgery is the method of choice in the treatment of non-melanoma skin cancers and in the vast majority it is proven to be sufficient.

Key words: skin carcinoma – non-melanoma skin carcinoma - baseocellulare skin carcinoma - spinocellulare skin carcinoma - surgical treatment

INTRODUCTION

The incidence of skin carcinomas has been steadily increasing in recent decades and they start to occur at a younger age, and as such they represent an increasingly pronounced health problem. They mostly appear on photoexposed parts of the body, such as the head and neck area, and are directly related to damage caused by prolonged exposure to ultraviolet rays (Apalla et al. 2017, Sandro et al. 2015). Basal cell carcinoma (Carcinoma baseocellulare, BCC) is quite benign in its behavior, slow growth, is not prone to metastasis and represents 50-70 % of all malignant skin tumors (Apalla et al. 2017, Didona et al. 2018, Kraft & Granter 2014). Squamous cell carcinoma (Carcinoma planocellulare, SCC) is much more aggressive, can grow rapidly and metastasize at an early stage (Wong et al. 2003). Incidence rate of non-melanoma skin carcinomas in the population of the City of Belgrade showed significantly increasing trend between 1999 and 2006. The incidence increased with age for both men and women, especially after the age of 60 (Videnovic et al. 2015). The exact incidence rate of non-melanoma skin carcinomas in Bosnia and Herzegovina is still unknown, for the reason that the united National Cancer Register does not exist yet (Simic et al. 2011).

Surgery is the dominant way to treat non-melanoma skin carcinomas, with the highest cure rate. The main goal of surgical treatment is complete tumor removal (pathohistologically negative incision edges), and adequate reconstruction of the defect in aesthetic and functional terms. Because non-melanoma carcinomas of the head and neck rarely metastasize (basal cell less than 1%, planocellular 8-10%), elective neck dissection is rarely performed (Madan et al. 2010). The conventional surgical approach is the most common surgical approach in the treatment of skin carcinoma and constitutes approximately 75% of all surgical procedures for basal cell and squamous cell carcinoma of the skin (Myers et al. 2003). This method is based on excision with predetermined edges, depending on the size, appearance, and location of the tumor (Chen et al. 2013). Resection with this technique is successfull for squamous cell carcinoma of the skin is in 81% of cases for well - differentiated and 46% for poorly differentiated successfull, while for basal cell carcinoma of the skin it is approximately 93% of cases (Connoly et al. 2012, Rowe et al. 1992, Griffiths 1999, Janju & Qureshi 2012). Unlike conventional surgery, in institutions that have the necessary equipment, and in cases of recurrent surgery or advanced skin carcinoma, especially in localities where excision with predicted suitable edges cannot be applied, Mohs, microscopically controlled surgery is used. This type of surgery further improves the results of surgical treatment of carcinoma with a success rate of over 97% (Newlands et al. 2016).
The aim of this study was to evaluate the incidence and clinical features of non-melanoma tumors of the head and neck, as well as the validity of surgical therapy in the treatment of non-melanoma tumors.

SUBJECTS AND METHODS

This study was conducted in Herzeg-Bosnian County, in a predominantly rural area where the average daily insolation in the last ten years was 6.7 hours / day. The study included 530 patients who underwent surgery at the Otorhinolaringology department of the Livno County Hospital in the period from 2007 to 2017. In all patients, after clinical examination of the skin growth, surgical excision of the skin tumor was performed, followed by pathohistological analysis. The incidence of non-melanoma tumors of the head and neck, clinical and pathohistological characteristics as well as the validity of surgery as the main therapeutic agent in the treatment were assessed. The pathohistological analysis confirmed the final diagnosis as well as the sufficiency of surgical margins in the treatment of non-melanoma skin tumors. Criteria for further investigation, confirmation of non-melanoma skin carcinoma, were confirmed in 398 samples.

Statistical analysis

The collected data were processed by methods of descriptive and inferential statistics. Descriptive data are presented in frequencies and percentages. To determine the existence of statistically significant differences for variables on the nominal measurement scale, $\chi^2$ (Chi-square) test was used. The value of $p<0.05$ was chosen as the level of statistical significance. IBM SPSS Statistics 23 and Microsoft Excel 2016 were used for statistical data analysis.

RESULTS

In a sample of 530 patients, in 398 of them (75%) a diagnosis of non-melanoma skin carcinoma was confirmed. The average age was 67 years, ranging for 53 to 92 years. Of the 398 patients with skin carcinoma, 168 patients (42.2%) were men, while in the sample there were 230 (57.8%) women. Chi-square test confirms the existence of a statistically significant difference in the representation of gender in the number of patients. There are more sick women in the sample than expected according to the equal distribution ($\chi^2=9.658$; df=1; $p<0.01$) (Table 1).

Figure 1 shows the type of skin carcinoma in the sample. In the largest number of cases, 259 of them (65.1%) Carcinoma basocellulare was detected. Carcinoma planocellulare had 119 patients (29.9%), Carcinoma intraepitheliale was detected in 15 patients (3.8%), Carcinoma baseoplanocellulare in 4 patients (1%), while one patient had Merkel cell carcinoma. Chi-square test confirms the existence of a statistically significant difference in the incidence of types of skin carcinoma in the total number of patients (Table 2). There are more cases of Carcinoma basocellulare and Carcinoma planocellulare, while there are fewer cases of Carcinoma intraepitheliale, Carcinoma baseoplanocellulare and Merkel cell carcinoma than expected according to the equal distribution ($\chi^2=625.668$; df=4; $p<0.01$). No statistically significant difference was found in the incidence of skin carcinoma types according to the gender of patients ($\chi^2=7.843$; df=4; $p>0.05$) (Figure 2, Table 3). We also analyzed the incidence of non-melanoma skin carcinomas, by anatomical locations, in the head and neck area. The most common localization was the nasal region, which was proven to be statistically significant ($\chi^2=290.824$; df=5; $p<0.00$) (Table 4).

| Table 1. Examination of gender differences in patients with skin carcinoma (N=398) |
|-----------------|--------|--------|--------|--------|-------|
| fo              | %      | ft     | $\chi^2$ | df    | p     |
| Men             | 168    | 42.2   | 199     | 9.658 | 1     | 0.002 |
| Women           | 230    | 57.8   | 199     |       |       |       |

Figure 1. Distribution of affected patients by type of skin carcinoma (N=398)
Figure 2. Incidence of skin carcinoma type according to gender (N=398)

Table 2. Examination of differences in the incidence of skin carcinoma types in affected patients (N=398)

<table>
<thead>
<tr>
<th>Carcinoma type</th>
<th>fo</th>
<th>%</th>
<th>ft</th>
<th>$\chi^2$</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinoma baseocellulare</td>
<td>259</td>
<td>65.1</td>
<td>79.6</td>
<td>625.668</td>
<td>4</td>
<td>0.000</td>
</tr>
<tr>
<td>Carcinoma planocellulare</td>
<td>119</td>
<td>29.9</td>
<td>79.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma intraepitheliare</td>
<td>15</td>
<td>3.8</td>
<td>79.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma baseoplanocellulare</td>
<td>4</td>
<td>1.0</td>
<td>79.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Merkel cell carcinoma</td>
<td>1</td>
<td>0.3</td>
<td>79.6</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Examination of differences in the incidence of skin carcinoma types according to gender (N=398)

<table>
<thead>
<tr>
<th>Carcinoma type</th>
<th>Men</th>
<th>Women</th>
<th>$\chi^2$</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinoma baseocellulare</td>
<td>118</td>
<td>141</td>
<td>7.843</td>
<td>4</td>
<td>0.062</td>
</tr>
<tr>
<td>Carcinoma planocellulare</td>
<td>40</td>
<td>79</td>
<td>68.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma intraepitheliare</td>
<td>6</td>
<td>9</td>
<td>8.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma baseoplanocellulare</td>
<td>3</td>
<td>1</td>
<td>2.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Merkel cell carcinoma</td>
<td>1</td>
<td>0</td>
<td>0.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Fishers exact test

Table 4. Examination of differences in the frequency of localization of skin carcinoma (N=398)

<table>
<thead>
<tr>
<th>Location</th>
<th>fo</th>
<th>%</th>
<th>ft</th>
<th>$\chi^2$</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nose</td>
<td>96</td>
<td>24.20</td>
<td>66.3</td>
<td>290.824</td>
<td>5</td>
<td>0.000</td>
</tr>
<tr>
<td>Infraorbital region</td>
<td>29</td>
<td>7.16</td>
<td>66.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forehead</td>
<td>32</td>
<td>8.11</td>
<td>66.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower lip</td>
<td>35</td>
<td>8.86</td>
<td>66.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zygomatic region</td>
<td>25</td>
<td>6.30</td>
<td>66.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other regions</td>
<td>181</td>
<td>45.40</td>
<td>66.3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 5. Examination of differences in the frequency of skin carcinoma removal success (N=398)

<table>
<thead>
<tr>
<th>Removal Type</th>
<th>fo</th>
<th>%</th>
<th>ft</th>
<th>$\chi^2$</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Removed</td>
<td>358</td>
<td>89.5</td>
<td>199</td>
<td>254.08</td>
<td>1</td>
<td>0.000</td>
</tr>
<tr>
<td>Partially Removed</td>
<td>40</td>
<td>10.5</td>
<td>199</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Of the 398 operated non-melanoma scalp and neck carcinomas, 358 (89.9 %) of them had complete skin carcinoma removal, while in 40 patients (10.5 %) the incision edges were pathohistologically positive for carcinoma cells (Table 5). Chi - square test confirms the existence of a statistically significant difference in the prevalence of complete and partial cancer removal in the complete number of patients. In a sample of patients, skin cancer was more often completely removed than expected according to an even distribution ($\chi^2=254.08; \text{df}=1; \ p<0.01$). No statistically significant difference was found in the success of skin carcinoma removal according to the type of skin carcinoma ($\chi^2=8.843; \text{df}=4; \ p>0.05$) (Table 6).
DISCUSSION

The results of this study determined the incidence of non-melanoma skin carcinomas over a ten-year follow-up period in Herceg-Bosnian County. In the investigated sample, the incidence of non-melanoma skin cancers (75%) was consistent with the results of similar studies (Apalla et al. 2017, Sandro et al. 2015, Didona et al. 2018) as well as the average age of patients (67 years) (Cigna et al. 2011). We found a significantly higher incidence of non-melanoma carcinomas of the head and neck in women than in men. These results did not confirm most studies showing that basal cell carcinoma is more common in men than women (Didona et al. 2018, Wong et al. 2003, Vučić et al. 2003, Vanscocelos et al. 2014). Results similar to ours were published in a study by Chow et al. (2011). The reasons for such discrepancies can be hidden in the fact that, in our area, women are more exposed to adverse climatic conditions due to the custom of spending much more time working in the field than men. Likewise, women report to the doctor more often because they care more about their health than men who (in these parts) often perceive this as a sign of weakness, which is why they delay and avoid visits to the doctor, often for the fear of diagnosis. In examining the differences in the incidence of types of non-melanoma skin carcinomas according to gender, we did not find a statistically significant difference. Other authors reported mostly inconsistent results - Bartoš et al. (2017) showed a higher incidence of squamous cell carcinoma of the skin in men (68.2% vs. 31.8%), while basal cell carcinoma was equally present in both genders (49.91% vs. 50.09%) (Green & Battistutta 1990). In our study, most non-melanoma carcinomas of the head and neck were localized to the dorsum of the nose and the result was a significant statistical difference. The frequency in this region is understandable in the light of the etiology of non-melanoma skin cancers because this region is the most exposed region to the effects of climatic factors on the skin and, at the same time it is the most rare and the most difficult to be protected from climatic factors. The same results were shown by most recent studies (Chow et al. 2011, Aandani & Gantra 2011). The most common diagnosis was basal cell carcinoma and squamous cell carcinoma.

The results agree with the results of research conducted by Green et al., who analyzed a ten-year period in Australia (1990) and found that basal cell carcinoma is the most common carcinoma. Similar results, in similar climatic and ecological conditions, were stated by Vučić et al. (2003), and the results are consistent with the results of other authors (Apalla et al. 2017, Didona et al. 2018, Wong et al. 2003).

Surgical therapy is the most common method of treating non-melanoma carcinomas of the head and neck, with the primary aim of removing the tumor entirely, i.e., tumor free excision edges. The other goals of surgical treatment are minimal scarring of the surrounding tissue and preservation of function and an acceptable aesthetic result. In this study, all patients were treated by the classical surgical approach with predetermined excision edges, and it was confirmed that in 89.9% of cases the tumor was removed completely, which is consistent with the results of research conducted by Newland et al., Gulleth et al. and other authors (Chen et al. 2013, Griffiths 1999, Griffiths et al. 2007). These results are consistent across studies according to the available literature, although a few with an extremely high percentage of pathohistologically positive edges (over 50%) have been highlighted (Janju & Qureshi 2012). Such results can probably be justified either by advanced cases, i.e. by delayed check-in with a doctor and the application of an inadequate surgical approach. We did not find a statistically significant difference in the success rate of skin carcinoma removal according to the type of skin carcinoma, although poorer results related to removal of squamous cell carcinoma of the skin have been reported in the literature.

The differences are probably caused by issues of size - prevalence of squamous cell carcinoma and adequate assessment of an appropriate surgical approach. This also confirms the thesis that in the case of a larger, enlarged non-melanoma skin carcinomas, there are indications for the use of Mohs microscopically controlled surgery.

This research should contribute to the validation of excisional surgical techniques in the diagnosis and final treatment of scalp and neck tumors, which will once again indicate the importance of avoiding unnecessary classic skin biopsies that can be extremely harmful by delaying final treatment and by participating in the possible spread of malignant skin tumors.
CONCLUSION

This research confirms the incidence of non-melanoma skin carcinomas is on the rise, especially in photoexposed areas of the skin where the head and neck regions certainly belong. Non-melanoma skin carcinomas are more common in the older population, in the seventh and eighth decade of life, although they are increasingly occurring in the younger age as well. In the observed ten-year period, Basal cell carcinoma was the most common non-melanoma skin carcinoma, accounting for over 65% of all non-melanoma skin carcinomas, followed by squamous cell carcinoma, with a slightly lower incidence, around 30%. The most common localization in the head and neck regions of non-melanoma carcinomas is the dorsum of the nose. That finding is expected, in the light of etiological factors, as it is the most exposed region of the head and neck.

Classical surgical excision is the method of choice in the treatment of non-melanoma skin carcinomas, and in the vast majority of cases, it is sufficient in the treatment. In the case of larger, more widespread non-melanoma skin carcinomas, especially in regions where it is not possible to achieve the predicted excision edges, Mohs microscopically controlled surgery is definitely recommended.

Given that the main risk factor for the development of non-melanoma skin cancer is exposure to ultraviolet radiation, the basis of the prevention strategy in the primary care should be focused on the education of the population. Early detection of skin lesions would lead to reduced need for surgical interventions and it would improve patient health outcomes.

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Contribution of individual authors:
Branko Krišto: design of the study, data collection, literature searches and analyses, interpretation of data, first draft.
Ivana Krželj Vidović: statistical analyses, literature searches and analyses.
Ana Krželj: interpretation of data.
Roberta Perković: design of the study, critical revision of the study.
All authors provided their approval for the final version of the manuscript.

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