Cutaneous Neoplasms in Myotonic Dystrophy Type 1

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Keywords
Basal cell carcinoma · Myotonic dystrophy · Skin · Steinert disease · Cutaneous neoplasm

Abstract

Background: The most frequent skin features associated with myotonic dystrophy type 1 (DM1) are frontal alopecia and pilomatrixomas. Several reports suggest that the incidence of basal cell carcinoma is increased in DM1. However, two recently published studies examining this topic have contradictory results. Objective: To retrospectively study the incidence of cutaneous tumours in patients with DM1. Methods: The clinical features of 102 Caucasian patients diagnosed with DM1 at Bellvitge Hospital in Barcelona, Spain, were retrospectively analysed. Clinical charts of the patients were reviewed, and cutaneous tumours diagnosed in our hospital were recorded. A group of 103 Caucasian patients matched for age and sex were used as the control group. Results: A total of 56 male and 46 female patients with DM1 were included in the study (mean age 49.07 years, SD 13.02). At least 1 basal cell carcinoma was diagnosed in 6 patients in the DM1 group versus 3 patients in the control group ($p = 0.332$). The mean age at diagnosis of the first basal cell carcinoma was 51 years compared with 66 years in the control group ($p = 0.035$). Five patients with DM1 presented pilomatrixomas versus none in the control group ($p = 0.029$). We did not detect any melanoma in our DM1 patients. Conclusion: Basal cell carcinomas appeared at a significantly younger age in our DM1 patients than in the general population, and this suggests that, at least in some patients, DM1 may predispose to the development of basal cell carcinomas.

Introduction

Myotonic dystrophy type 1 (DM1, Steinert disease) is the most frequent muscular dystrophy in adults. It is an autosomal dominant inherited disorder with multisystemic manifestations including weakness and myotonia, early onset cataracts, heart conduction abnormalities, respiratory insufficiency, insulin resistance, and testicular atrophy. The most frequently reported skin features associated with DM1 are frontal alopecia and pilomatrixomas [1]. Several case reports and one study suggest a possible association with basal cell carcinomas [2–10]. However, two recently published surveys analysing cutaneous neoplasms in patients with DM1 have contradictory results [11, 12].

Our aim was to retrospectively analyse the development of cutaneous tumours in a series of patients with DM1.
**Materials and Methods**

For further details, see the supplementary materials (for all online suppl. material, see www.karger.com/doi/10.1159/000456074) (Fig. 1).

**Results**

DM1 patients included 56 males and 46 females, aged between 20 and 79 years, with a mean age of 49.07 years (SD 13.02). In 6 patients (3 males, 3 females) at least 1 basal cell carcinoma was detected and surgically excised. In 3 patients only 1 basal cell carcinoma lesion was detected, while 3 patients developed more than 5 lesions (Fig. 2). The mean age at diagnosis of the first basal cell carcinoma was 51 years (SD 9.63). Another 5 patients presented pilomatrixomas, and 2 patients developed multiple trichilemmal cysts. In 2 patients a melanocytic nevus was excised, and 2 patients received treatment for actinic keratosis. However, none of our patients developed dysplastic nevi or cutaneous malignant melanoma.

The control group included 57 males and 46 females with a mean age of 51.39 years (SD 17.07). In 3 of these patients (1 male, 2 female) at least 1 basal cell carcinoma was detected (1 lesion in 2 patients and 4 lesions in 1 patient). The mean age at diagnosis of the first basal cell carcinoma was 66 years (SD 1.00). In addition, 4 patients melanocytic nevi were excised, and 4 patients were treated for actinic keratosis. No pilomatrixomas, dysplastic nevi, or cutaneous malignant melanomas were diagnosed in the control group.

The difference in the number of basal cell carcinomas in DM1 patients versus the control group was not statistically significant (Fisher exact test, \( p = 0.332 \)). However, the mean age at diagnosis of the first basal cell carcinoma was significantly lower in the group of DM1 patients (Student t test, \( p = 0.035 \)). The difference in the number of pilomatrixomas was also significant (Fisher exact test, \( p = 0.029 \)) (Table 1).

**Discussion**

Patients with DM1 are at increased risk of developing cancer. Specifically, there is an increased risk of developing brain, ovarian, and colon cancer, endometrial thyroid tumours, and choroidal melanoma [13, 14]. Concerning benign skin tumours, the association with pilomatrixomas is well known. However, there are contradictory data about the association with malignant cutaneous tumours (Table 2). A possible association with basal cell carcinomas is supported by several case reports [2–9]. In addition, in a study analysing 911 patients with DM1, 10 basal cell carcinomas and 6 melanomas were detected. However, the incidence of cutaneous tumours was not
compared with a control group [10]. In recent years two studies analysing cutaneous lesions in DM1 have been published, with 55 and 90 patients, respectively. In one of these surveys several dermatological diseases were significantly more frequent in patients with DM1 compared with controls (focal hyperhidrosis, follicular hyperkeratosis, early androgenic alopecia, nail pitting, pedunculus fibromas, twisted hair, seborrheic dermatitis, and macules of hyperpigmentation) [11]. However, the authors did not detect any increase in the prevalence of preneoplastic or neoplastic skin lesions in DM1 [11]. In contrast, the other study detected significantly higher numbers of nevi, dysplastic nevi, and melanomas in the group of patients with DM1 (3 patients with DM1 presented cutaneous melanoma vs. none in the control group) [12]. However, the number of basal cell carcinomas diagnosed in DM1 patients was not increased in this study (only 1 patient with DM1 had undergone excision of a basal cell carcinoma compared with 12 patients in the control group) [12]. In summary, while some studies suggest an association with basal cell carcinomas, others have detected an increased incidence of melanomas. This may indicate that these possible associations are not very strong.

In our study we detected 6 patients with DM1 and at least 1 basal cell carcinoma (a single lesion in 3 patients and more than 5 lesions in the other 3 patients). Although differences with the control group in the number of basal cell carcinomas were not significant, the mean age at diagnosis of the first basal cell carcinoma was significantly lower in DM1 patients. This suggests that some patients

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**Table 1.** Comparison of results between the DM1 group and the control group

<table>
<thead>
<tr>
<th></th>
<th>DM1</th>
<th>Control group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>56/46</td>
<td>57/46</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>49.07 ± 13.02</td>
<td>51.39 ± 17.07</td>
<td></td>
</tr>
<tr>
<td>Patients with BCC</td>
<td>6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Patients with multiple BCC</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Age at first BCC</td>
<td>51.00 ± 9.63</td>
<td>66.00 ± 1.00</td>
<td>0.035</td>
</tr>
<tr>
<td>Pilomatrixomas</td>
<td>5</td>
<td>–</td>
<td>0.029</td>
</tr>
</tbody>
</table>

Data are presented as numbers or means ± SD. DM1, myotonic dystrophy (Steinert disease); BCC, basal cell carcinoma.

**Table 2.** Case series reported on cutaneous malignant tumours in patients with DM1

<table>
<thead>
<tr>
<th></th>
<th>DM1 patients</th>
<th>BCC patients</th>
<th>Melanoma patients</th>
<th>Control group</th>
<th>BCC patients</th>
<th>Melanoma patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Das et al. [10]</td>
<td>911</td>
<td>10</td>
<td>6</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Campanati et al. [11]</td>
<td>55</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Zampetti et al. [12]</td>
<td>90</td>
<td>1</td>
<td>3</td>
<td>103</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Present series</td>
<td>102</td>
<td>6</td>
<td>0</td>
<td>103</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are presented as numbers. DM1, myotonic dystrophy (Steinert disease); BCC, basal cell carcinoma.

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**Fig. 2.** Multiple basal cell carcinomas in a patient with DM1.

(a) Right eyebrow. (b) Left eyebrow. (c) Right arm.
with DM1 have a tendency to develop basal cell carcinomas, frequently multiple.

DM1 is caused by an unstable trinucleotide CTG expansion in the 3′ non-coding region of the DM1 protein kinase gene on chromosome 19q13.3 [1]. There is a wide variation in the number of CTG repeats in this gene, and in general a higher number of CTG repeats is associated with a more severe clinical phenotype [1]. The pathogenesis of DM1 is due to intranuclear sequestration of important splicing proteins with toxic RNA leading to a wide array of protein mutations [1]. At least two dozen transcripts are altered; many of these individual transcripts can be traced to specific findings in DM1 [1]. It is not known how this abnormal RNA splicing induces skin tumorigenesis. One explanation is that the accumulation of abnormal nuclear RNA interferes with normal DNA repair including repair of ultraviolet-induced DNA damage, causing eventual malignant transformation of keratinocytes [8].

It has been proposed that DM1 patients, due to their muscular disease, are less exposed to sunlight [12]. Therefore, DM1 patients might be less likely to develop basal cell carcinomas than the general population. This might explain why the difference in the incidence of basal cell carcinomas in our study between DM1 patients and the control group is not significant.

In the present study pilomatrixomas were statistically associated with DM1. Concerning malignant tumours, the differences in the incidence of basal cell carcinoma between DM1 patients and the control group were not significant. However, patients with DM1 developed basal cell carcinomas at a significantly younger age, and the lesions were frequently multiple. We did not detect any melanoma in our DM1 patients.

Although it cannot be affirmed that basal cell carcinomas are more frequent in DM1 patients than in the general population, it seems that, at least in some patients, DM1 predisposes to the development of multiple basal cell carcinomas at an early age.

Key Message

Myotonic dystrophy predisposes to the development of basal cell carcinomas at a young age.

Statement of Ethics

The study protocol was approved by the institute’s committee on human research.

Disclosure Statement

The authors declare that there is no conflict of interest. The authors received no financial support for the research, authorship, and/or publication of the article.

References


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