

CASE REPORT

Multiple basal cell carcinomas in a patient with myotonic dystrophy type 1

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SUMMARY

A man in his early 60s with myotonic dystrophy type 1 (DM1) and an extensive history of non-melanoma skin cancer presented with multiple pearly, erythematous papules on his face, head, trunk and extremities, clinically consistent with basal cell carcinoma (BCC). Due to the numerous BCC and history of multiple and early-onset BCC, examination was concerning for a hereditary BCC syndrome. Subsequent histopathology confirmed BCC. Genetic testing was negative for basal cell nevus syndrome and clinical findings were inconsistent with other known hereditary BCC syndromes. There have been reports of an association between DM1 and BCC, however, it is not well known among clinicians. We hope to raise awareness among clinicians about this association.

BACKGROUND

Myotonic dystrophy type 1 (DM1), or Steinert Disease, is an autosomal dominant disease caused by a cytosine–thymine–guanine (CTG) trinucleotide

repeat mutation in the myotonic dystrophy protein kinase (*DMPK*) gene on chromosome 19, locus 19q13.3.¹ It is the most common muscular dystrophy in adults, characterised by myotonia, progressive muscle wasting and weakness, cardiac conduction abnormalities, cataracts and testicular atrophy.¹ Known associated skin findings include androgenic alopecia and pilomatrixomas.¹ An association with basal cell carcinoma (BCC) has been previously reported, but this is not well recognised by clinicians (table 1).^{2–9}

CASE PRESENTATION

A 60-year-old man with DM1 and a history of numerous BCCs presented for skin cancer evaluation and management. Prior skin cancer history was notable for 28 primary BCCs and four squamous cell carcinomas, with his first skin cancer diagnosed in his early 40s. He denied any systemic or other cutaneous complaints. He reported no family history of skin cancer. He is currently retired and describes his previous occupation as office-based without significant occupation-related sun exposure. He reports a substantial history of recreational sun exposure with multiple sunburns in his youth but denies a history of blistering sunburns or indoor tanning.

Skin exam was notable for Fitzpatrick type I skin, androgenic pattern alopecia (figure 1), and multiple (>20) pearly erythematous papules and plaques distributed on sun-exposed areas of the head and neck, trunk and extremities, all clinically consistent with BCC (figure 2). Sun-protected areas of his buttocks and upper inner arms were spared. There was no frontal bossing, palmar pits or atrophoderma.

INVESTIGATIONS

Biopsy of multiple tumours showed superficial, nodular and infiltrative type BCC (figure 3). Formal genetic evaluation was negative for known hereditary BCC-associated syndromes and there were no mutations or copy number variants in *PTCH1*, *PTCH2* and *SUFU*.

DIFFERENTIAL DIAGNOSIS

This 60-year-old patient with DM1 presented with numerous and early onset BCCs predominantly on sun-exposed skin, raising clinical suspicion for an underlying hereditary BCC syndrome, such as basal cell nevus syndrome, Rombo syndrome and Bazex-Dupré-Christol syndrome. However, clinical exam and genetic testing was negative for basal cell nevus



Figure 1 The patient presents with the characteristic androgenic alopecia of myotonic dystrophy type 1 as well as multiple pearly papules on the face and forehead clinically concerning for basal cell carcinoma.



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Table 1 Summary of published case reports of BCCs associated with myotonic dystrophy type 1

Age	Sex	BCC features (number of tumours, anatomic site)	References
34	Male	Three tumours; nose, neck and back	2
42	Female	Four tumours, nodular subtype; left posterior thigh x2, right upper back and right submammary	3
50	Female	Three tumours; scalp	4
41	Male	Multiple tumours; left upper eyelid x1, left cheek x1, and thorax (multiple, number not specified)	5
42	Female	Multiple tumours, number not specified, nodular subtype; face	6
62	Female	Four tumours, nodular and superficial subtype; face	7
29	Male	Multiple tumours, number not specified; chest	8
18	Female	Three tumours; right parasternal, left breast and abdomen	9

BCC, basal cell carcinoma.

syndrome. Clinical exam was not consistent with other hereditary BCC syndromes, including Rhombo and Bazex-Dupré-Christol, as the patient lacked the characteristic physical exam findings of atrophoderma and milia.

TREATMENT

The patient was treated with multiple modalities including field therapy using fluorouracil 5% cream and photodynamic therapy, electrodesiccation and curettage, excision and Mohs surgery. Systemic treatment with nicotinamide was initiated. Acitretin and SUBA-itraconazole were discussed and declined by the patient.

OUTCOME AND FOLLOW-UP

The patient had an excellent response to field therapy. He is closely followed with complete skin examinations and referrals for excisions and Mohs surgery as needed.

DISCUSSION

To our knowledge, this is the ninth reported case of an association between DM1 and multiple, early-onset BCCs (table 1).²⁻⁹ A population-based nested case-control study found a significantly higher BCC risk among DM1 patients than age- and sex-matched controls (HR=5.78, 95% CI 3.36 to 9.92, $p < 0.0001$).¹⁰ Another



Figure 2 Numerous well-demarcated, erythematous, pearly crusted papules and plaques on the patient's chest, clinically concerning for basal cell carcinoma.

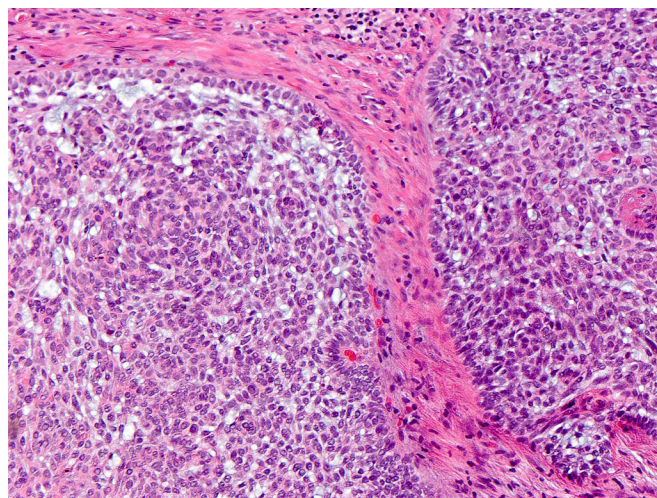


Figure 3 A biopsy of the patient's right anterior shoulder showing basal cell carcinoma, nodular subtype.

study found that, BCCs developed at a significantly younger age in patients with DM1 as compared with the general population (51 years vs 66 years, $p = 0.035$).¹¹ There may also be an association between DM1 other forms of skin cancer. A recent study found higher numbers of nevi, dysplastic nevi and cutaneous melanoma in DM1 patients when compared with controls, despite a greater proportion of the control subjects reporting a history sunburn.¹²

The mechanism of action for increased BCC risk may involve the mutated *DMPK* gene, which creates abnormally spliced mRNA that may interfere with protein production, DNA repair (including ultraviolet-induced damage) and cell death.¹⁷ Defects in the 19q chromosomal locus near the *DMPK* gene are associated with an increased risk of BCC.¹³ Mutations to this region may affect the nuclear genome or disrupt the normal function of tumour suppressors or DNA repair mechanisms. Further evidence of the role of the *DMPK* gene in BCC carcinogenesis comes from analysis of tumour-normal pairs where BCCs from a DM1 patient contained a larger trinucleotide repeat expansion than the patient's healthy skin.⁹ Additional case reports of patients with DM1 have found markedly longer CTG expansions in tumours (endometroid carcinoma, insulinoma, gastric adenocarcinoma and adenocarcinoma of the colon) as compared with healthy tissue of the same organ.^{14 15} However, it has also been reported that the trinucleotide expansion in the oligodendrogloma of a patient with DM1 was shorter than surrounding healthy brain tissue.¹⁶ Thus, alterations (consisting of both expansions and contractions) in CTG repeat length appear to be implicated in tumourigenesis in DM1 patients.

Learning points

- ▶ There have been multiple reports of numerous and early basal cell carcinomas (BCCs) in patients with myotonic dystrophy type 1 (DM1).
- ▶ Future research is needed to elucidate the exact molecular mechanism underlying the increased BCC risk in DM1.
- ▶ Sun protection and skin cancer surveillance should be emphasised with DM1 patients
- ▶ Dermatologists should be involved in the interdisciplinary approach for the care of patients with DM1.

Multiple BCCs in DM1 patients may suggest a link between the *DMPK* gene and keratinocyte carcinomas, possibly highlighting a novel pathway for BCC carcinogenesis.

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