

Reflections on a Basal Cell Carcinoma on the Nose of an Adolescent Monozygotic Female Twin

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Key Words

Basal cell carcinoma · Adolescents · Twins · Piercing · Body dysmorphic disorder · Dermatitis artefacta

Summary

The observation of a sporadic basal cell carcinoma (BCC) on the right nostril of a 21-year-old female monozygotic twin gives reason to discuss a possibly relevant pathogenetic factor for this quite frequent and common skin tumour. In addition to scientifically confirmed findings, emotional distress associated with body dysmorphic disorder is considered as a possible co-factor in tumour formation in this case.

Introduction

Dealing with basal cell carcinomas (BCC) is daily routine for a dermatologist. Their pathogenesis therefore receives little attention and interest. If a BCC is observed at an early age or if there is a tendency for multiple BCC's, hereditary predisposing factors like decreased DNA repair (xeroderma pigmentosum), BCC's in the family [Guarneri et al., 2000] or the basal cell naevus syndrome (Gorlin's syndrome) must be excluded. UV-specific mutations of p53 and loss of heterozygosity (LOH) at chromosome 9q22.3 are supposed to be the main pathogenetic steps for tumour formation in hereditary as well as sporadic BCC [Ratner et al., 2001].

Besides scientifically confirmed findings concerning the

Schlüsselwörter

Basalzellkarzinom · Jugendliche · Zwillinge · Piercing · Körperdysmorphie Störung · Dermatitis artefacta

Zusammenfassung

Gedanken zur Entwicklung eines Basalzellkarzinoms auf der Nase eines adoleszenten, weiblichen, eineiigen Zwillinges

Die Beobachtung eines Basalzellkarzinoms auf dem rechten Nasenflügel eines 21-jährigen, eineiigen weiblichen Zwillinges wird zum Anlass genommen, einen möglicherweise relevanten pathogenen Faktor für einen im Prinzip häufigen und somit auch nicht außergewöhnlichen Hauttumor zu diskutieren. Es wird versucht, Hinweise dafür zu finden, dass neben wissenschaftlich anerkannten Faktoren auch psychischer Stress durch eine körperdysmorphe Störung bei der Entwicklung dieses Hautmalignoms eine Rolle spielen könnte.

pathogenesis of skin diseases, dermatologists are aware that psychologic factors may also have an impact on skin diseases. Proposing an epistemology of psychosomatic dermatology, Panconesi and Argentieri [2000] classified dermatoses as 'affectations with high incidence of psychoemotional factors', 'conditions with strong emotional repercussion' or 'psychiatric diseases with cutaneous expressions'. Malignant skin tumours are not included in their lists. The coincidence of body dysmorphic disorders (BDD), the clinical picture and characteristic behaviour patterns of patients with dermatitis artefacta as well as the histopathologically revealed diagnosis of a BCC raises the question: May emotional distress be a co-factor in the development of a sporadic BCC?

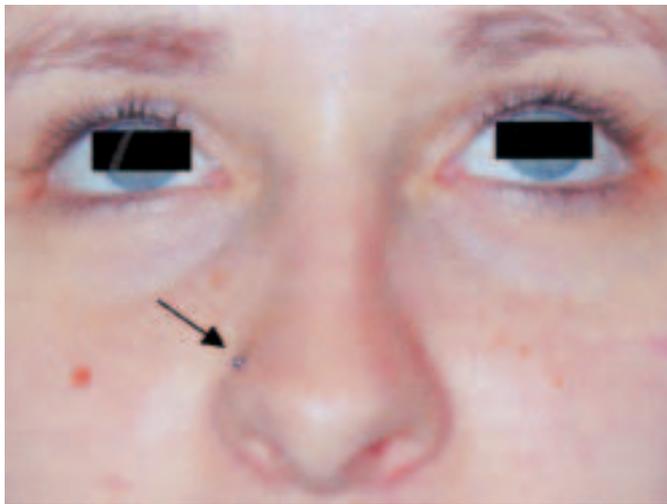


Fig. 1. Pierced right nostril of the patient's monozygotic twin sister.

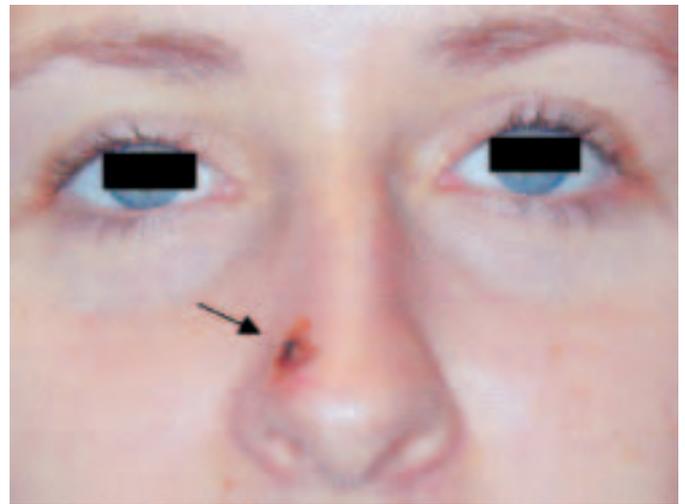


Fig. 2. Crusty lesion on the patient's nose just before the biopsy was done.

Case Report

In March 1997, two 16-year-old monozygotic twin sisters presented to my practice because their mother was worried about their moles. There were no atypical moles, so no excision was necessary. However, at the age of 19 one of the twins wanted to have 3 moles removed from her trunk because she was revolted by them. Besides that, she also complained about the shape of her nose. Her twin sister had had her right nostril pierced (fig. 1), but she had decided not to have hers pierced as well, because her nose was 'too crooked to be decorated, and a piercing would attract even more attention to it'. Soon after, she noticed a non-healing lesion on her right nostril which persisted for more than 2 years. In February 2002, the patient presented again. An objective disfiguring shape of the nose was not discernible but there was a crusty lesion, about 1 cm in diameter, on her right nostril (fig. 2). The patient denied any preceding injury and refused the proposed biopsy. Various causes for the lesion were considered, including a chronic infectious skin disease (leishmaniosis), lupus erythematosus, a cutaneous malignancy and a neurotrophic ulcer. Dermatitis artefacta was also considered as a plausible cause. In September 2002, the biopsy could finally be done. Histological examination revealed a solid BCC. Direct immunofluorescence was negative and there was no human papilloma virus (HPV) DNA detectable by polymerase chain reaction (PCR). Physical examination of the monozygote twin sister and a thorough inquiry of the medical family history excluded the possibility of hereditary disorders accompanied by the development of BCC's. There were no relevant differences between the environmental factors affecting the twins. There had been some exposure to UV irradiation during a few days skiing in the Alps, yet both sisters denied sunburns. Other predisposing factors for the development of BCC such as arsenic, tar and X-rays were not mentioned.

Discussion

BCC is the most common type of skin cancer. Males are affected twice as often as females. The mean age at diagnosis is 62 years [Roeningk et al., 1986]. 85% of BCC's develop on the face, 25% of them on the nose. UVB irradiation from sunlight produces DNA damage and is supposed to be the main explanation for this condition. Besides, exposure to arsenic, tar and

X-rays are known to be predisposing factors for the development of BCC's.

Sporadic BCC's in children and adolescents under 20 years of age are rare [Baum and Hog, 1994]. If they are observed, hereditary predisposing factors (for which a tendency to develop multiple BCC's at an early age is characteristic) like decreased DNA repair (xeroderma pigmentosum), familial BCC's [Guarneri et al., 2000] or the basal cell naevus syndrome (Gorlin's syndrome) must be excluded. The latter originates from loss of the wild-type allele at chromosome 9q22.3, the human homologue of the *Drosophila* developmental gene patched, which in men represents a tumour suppressor gene [Ratner et al., 2001; Gailani et al., 1996].

Nonsense mutations, deletions and insertions at the same locus, which is equivalent to LOH, can also be found in sporadic BCC [Happle, 1999]. So, besides UV-specific mutations of p53, LOH at chromosome 9q22.3 is supposed to be a main pathogenetic step for tumour formation in BCC [Ratner et al., 2001].

Transforming viruses containing oncogenes like herpesvirus 8 and Epstein-Barr virus are absent in malignant cutaneous epithelial neoplasms [Kohler et al., 1997]. HPV play a significant role in the pathogenesis of squamous cell carcinoma in immunosuppressed patients [Berg and Otley, 2002]. When they are detected in BCC, their pathogenetic role is not yet understood and they 'may be simply a coincidental cutaneous passenger' rather than a real oncogene [Sass et al., 2002].

Interestingly, Milán et al. [1998] showed in a population-based cohort study in twins, that even if there was a slightly elevated risk of BCC for the twin of a diseased patient, there was no difference in risk by zygosity detectable. They therefore concluded that environmental factors played a much more important role in the development of sporadic BCC than hereditary factors.

At the age of 19 the presented patient wanted to have 3 of her moles removed from her trunk because she was revolted by them. Besides, she complained about the shape of her nose. Soon after, she noticed a non-healing lesion on her right nostril which persisted for more than two years until the patient would follow the dermatologist's advice and histopathological examination revealed a solid BCC.

The patient's complaints about her flaws on the face and on the trunk could be interpreted as a symptom of BDD [Cotterill, 1996]. BDD is defined as 'a preoccupation with an imagined defect in appearance. If a slight physical anomaly is present, the person's concern is marked excessively. The preoccupation causes clinically significant distress or impairment in social, occupational, or other important areas of functioning' [Stangier, 2000]. It is also possible that the young woman 'misused' her crooked nose as an excuse to reject the piercing and to demonstrate difference from her monozygotic twin sister. Possibly, this forced separation from her twin sister caused feelings of guilt. The fact that the patient could wait more than 2 years before seeking treatment for her disfigured nose, during which time she exposed the visible lesion relatively comfortably to everyone in her environment, also reflects a characteristic behaviour pattern of patients with dermatitis artefacta [Koblentz, 2000]. As she refused referral to a psychiatrist or psychologist, we do not know if the BCC developed by itself or rather as a result of a self-inflicted injury [Alcolado et al., 1993]. Furthermore, it was not possible to explore in depth whether the patient really suffered from BDD according to its definition. However, the patient's decision not to have her nose pierced was followed by an enormous degree of emotional distress as a result of the discrepancy between her preoccupation with her crooked nose (to which she did not want to draw attention by a piercing) and the delay in seeking treatment for her ulcerated nose, thus living with it for more than two years!

Emotional distress as a co-factor in tumour induction has been discussed for many years, but has not been proven yet [Bahson, 1986]. On the contrary, Schwarz [1993] points out that social and psychological differences between cancer and non-cancer patients are rather the result than the cause of the disease. Furthermore, Graham et al. [2002] could demonstrate in a prospective study that women with breast cancer need not worry that stressful experiences might precipitate relapse of their disease. Similarly, Petticrew et al. [2002] concluded in a recent systematic review that survival from or recurrence of cancer is not influenced by psychological factors. On the other hand, there is evidence that emotional repression is associated with some aspects of host virus interaction. Esterling et al. [1990] asked students to write an essay about a stressful event of their life. Immediately after writing, blood was collected from each subject to measure changes in the level of antibody titer to Epstein-Barr viral capsid antigen (EBV-VCA). Students who abstained from disclosing emotional material and subjects with psychometrically derived repressive interpersonal styles showed high antibody titers to EBV-VCA. Thus diffi-

culties in expressing stressful events were found to be associated with impaired control of a latent EBV infection (an infection with known oncogenetic potential!).

Only few cases have been reported of BCC's arising within chronic scars, venous insufficiency or as a result of dermatitis artefacta [Alcolado et al., 1993]. The unique observation of a BCC on an earlobe after auricular acupuncture lets Brouard et al. [2002] suggest that local trauma like acupuncture or ear piercing may play a putative role in the pathogenesis of BCC. But acupuncture is a frequent treatment option and piercing is practiced throughout the world. Considering these innumerable artificial injuries of the skin it is astonishing that tumour formation related to this kind of skin injury is not reported more often. Furthermore, every dermatologist knows that even after incomplete excision of a BCC complete tumour regression is possible. In other words: tumour *regression* induced by skin injury is without doubt observed more frequently than tumour *induction*. Hayashi et al. [2002] offer an explanation for this observation: Mechanical injury induces cell necrosis, surrounding keratinocytes become activated (undergoing early apoptosis) and produce different cytokines and growth factors which trigger the inflammatory response and finally induce wound healing. However, the contrary may happen, too: 'Disruption of this regulatory mechanism may contribute to the development of malignant tumours in chronically inflamed regions' [Hayashi et al., 2002]. So, besides presuming that skin injury may in unique cases induce a BCC [Alcolado et al., 1993; Brouard et al., 2002], we can presume with even more justification that acupuncture or piercing may protect from developing a BCC!

Here, a 19-year-old female monozygotic twin observed a non-healing lesion on her right nostril while at the same time her twin sister decorated the same part of her body with a piercing. Two years later a sporadic BCC was diagnosed.

What would have happened if the patient had decided to have her right nostril pierced, as well? We could then either report about the first case of a piercing-induced BCC on the right nostril of an adolescent monozygotic female twin, or we would never have met the patient because she would not have developed a BCC on her nose.

Considering the pathogenesis of the presented BCC there remain two possibilities: It was either pure coincidence that this woman with UV-specific mutations of p53 and LOH at chromosome 9q22.3 developed a BCC just at the same part of the body and at the same time her twin sister had her piercing; or a BDD and its accompanying emotional distress have impaired the function of a suppressor gene and kept the patient from a nose piercing and its potentially self-healing inflammatory reaction.

While the first possibility seems to be an almost unbelievable coincidence, the second possibility seems to be sheer speculation. However, a sporadic BCC on the nose of an adolescent female monozygotic twin remains rare. Reflections on its pathogenesis confront *knowing* (with certainty) with *believing*

(without certainty), the two competing epistemological orientations of *rationalism* and *empiricism* [Panconesi and Argentieri, 2000]. In other words: *Knowing* that UV-specific mutations of p53 and LOH at chromosome 9q22.3 were the main

pathogenetic steps [Ratner et al., 2001] should not exclude *considering* that in the given case, BDD may have been an important co-factor in the development of the BCC.

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