Simultaneous onset of basal cell carcinoma over skin graft and donor site

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INTRODUCTION
Basal cell carcinoma (BCC) is the most common malignant skin tumor among whites. More than 80% of BCCs are found on photo-exposed areas, predominantly on the head and the neck. More uncommonly, BCC may appear on non-sun-exposed areas or on areas with chronic inflammation, scars, burns or skin grafts.

CASE REPORT
We present the case of a white 58-year-old woman with skin phototype III (Fitzpatrick scale) who suffered a second- to third-degree burn in childhood on the external surface of her right arm. A full-thickness skin graft, obtained from the internal surface of her right thigh, was used for the repair. The patient complained of a 3-year history of skin lesions that progressively grew in size located on the graft and the scar of the donor site. She denied having regular sun exposure or previous sunburns. Family history was noncontributory.

A dermatologic examination found 5 pink eroded thin papules and plaques, 5 to 15 mm in size, some with ulcerations, over the donor site of her right thigh (Fig 1, A). On the graft recipient site on the right arm, there was a 10- × 4-mm violaceous papule with a smooth surface (Fig 1, B). Biopsy specimens were taken from both areas. Pathologic examination from both areas found superficial multifocal BCC over foci of actinic keratoses (Fig 2).

Surgical excision of the single lesion on the graft recipient site was performed. The lesions on the donor site were initially treated with 5% imiquimod cream 5 days per week for a total of 16 weeks with partial improvement. Treatment was continued with methyl aminolevulinate under an occlusive dressing for 3 hours and subsequent illumination with noncoherent red light (630 nm at a dose of 37 J/cm²) for 9 minutes, 45 seconds. After 3 monthly sessions, a 50% reduction in the size of the lesions was observed, allowing surgical excision of all lesions. The patient underwent follow-up for 7 years with no evidence of recurrence or new lesions.

DISCUSSION
The appearance of BCC over non-photo-exposed areas is an uncommon form of this tumor with a frequency of less than 15% of all published series. Although exposure to ultraviolet light is the most important factor in the development of BCC in photo-exposed areas, other predisposing factors are involved in the development of BCC in non-photo-exposed areas: immunologic dysregulation, chronic exposure to tar and arsenic, burns, scars, and in areas of vaccination, tattoos, piercings, or chronic ulcers. It has been suggested that a decrease in vascularization and elasticity in skin tissue makes the overlying epithelium more susceptible to repeated trauma-induced carcinogenesis, with a variable latency period from a few weeks to several years.

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The most common tumor found in areas of chronic inflammation is squamous cell carcinoma. BCC may be 3 to 7 times less frequent. Squamous cell carcinoma in these areas has a more aggressive clinical course, whereas BCC has a similar clinical behavior as seen in other areas. From a histologic point of view, the most common pathologic form of BCC found on non-photo-exposed areas is nodular, followed by pigmented, adenoid, invasive, superficial, and basosquamous.3,6,8

In 1984, Cox7 published the first case. Since then, some isolated cases of BCC over graft sites have been reported in the literature (Table I).2-6 The time of BCC development from graft surgery ranged from 1 to 60 years. The graft donor and recipient sites are highly variable as is the thickness of the graft. The most common subtypes of BCC findings are nodular and superficial. Except in the first case, treatment was surgical excision with no evidence of recurrence or onset of new skin tumors. Different etiopathogenic factors have been suggested by these authors: continuous sun exposure with sunburns,2 previous surgical procedures, delay of treatment of cutaneous leishmaniasis,3 transfer of neoplastic cells from the donor site to the grafted site,1 and proliferation of cells from the outer sheath of the hair follicle of the grafted area caused by regular sun exposure.7

Nevertheless, our case is unusual, as the patient showed simultaneous onset of BCC over both the donor and recipient sites, although this occurrence may be a coincidence.

The patient did not have skin tumors in other locations or a family history of them. We believe sun exposure did not significantly influence the etiopathogenesis of these tumors. In addition, the patient did not have any underlying risk factors for the development of BCC such as lymphoproliferative diseases, solid organ transplant, or immunosuppressive treatment.

We considered 2 primary etiopathogenic possibilities: (1) de novo onset of BCC over re-epithelialized areas of skin at the donor site and in the burn site and subsequent graft owing to field cancerization effect and (2) the patient may possess an uncharacterized mutation in a tumor suppressor gene around the graft donor site owing to a mosaic inheritance pattern. This mutated skin was then partially donated to a new area, and basal cell carcinomas subsequently developed in both areas.10

However, we are not able to establish clear etiopathogenic factors.
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## Table I. Description of cases of basal cell carcinoma over graft sites

| Study | Sex | Age, y | Donor site | Recipient site | Graft thickness | Time from surgery to onset, y | BCC over graft site |
|-------|-----|--------|------------|----------------|----------------|-----------------------------|--------------------|
| Cox7  | Female | 80 | Thigh | Presternal area | Partial | 4 | Superficial |
| Martin et al6 | Female | 72 | Forearm | Forearm | Partial | 2 | Nodular Invasive |
| Karri et al5 | Female | 52 | Left thigh | Right thigh | Partial | 30 | Type not specified Nodular |
| Lemierre et al4 | Female | 73 | Left inguinal fold | Right mandibular angle | Partial | 1 | Nodular |
| Yazici et al3 | Female | 75 | Thigh | Upper eyelid | Full | 61 | Nodular |
| Angelos et al2 | Male | 50 | Lateral thigh | Scalp | Partial | 31 | Invasive |