Beyond surgical excision, curettage, cautery, cryosurgery, radiotherapy, laser, and photodynamic therapy have been advocated for the treatment of Bowen’s disease, an in situ skin carcinoma that has a 3–5% risk of progression to invasive neoplasm (1, 2). Selection criteria for the different modalities include the size and/or number of the lesions (1–3), localization of the lesion in poor wound-healing regions, such as the legs (3–5), and/or limitations in the availability of certain modalities. There is heterogeneity in the various therapeutic outcomes with cure rates ranging from 47–94% (1, 2, 6–9). In this study, prompted by the need for alternative treatments of Bowen’s disease, we evaluated “immunocryosurgery”, i.e. a combination modality of cryosurgery during continuing topical imiquimod (10) which has been used successfully to treat basal cell carcinoma and lentigo maligna (11,12).

MATERIALS AND METHODS

Eight patients (5 women and 3 men; age range 52–87 years, mean 71.9 years) with 11 biopsy-proven Bowen’s disease lesions (Table I) were recruited between January and December 2007. The study was approved by the local hospital ethics committee according to the principles of the Declaration of Helsinki, and all patients provided informed consent. Treatment consisted of daily application of 5% imiquimod cream (Aldara®; Meda, Athens, Greece) to the lesion and a 5-mm rim of surrounding skin for a total of 5–9 weeks (Table I). At the clinic visit 2–3 weeks after starting imiquimod treatment liquid nitrogen cryosurgery was applied (open spray; two freeze-thaw cycles, 10–20 s freezing time each) to the inflamed skin including a 5-mm rim around the clinical margins of the lesions (Table I). Lesions of area > 1.5 cm² were treated in approximately 1 cm² subsections. Patients were instructed to continue imiquimod after cryosurgery without interruption and were evaluated every 3 weeks until the end of treatment. Persistence of erosion 3 weeks after cessation topical imiquimod was considered as indicative of residual tumour (=partial response) and treatment with an additional cryosurgery course and/or extension of the application of imiquimod for a further 3 weeks was decided (Table I). Fusidic acid 2% cream (Fucidin®, Leo Pharma, Athens, Greece) 2× daily for 1 week and strict sun protection were prescribed after discontinuation of imiquimod. The follow-up period was calculated from cessation of imiquimod application (=endpoint of treatment) and visits were scheduled at 1 month, every 3 months for the following year and at 6-month intervals thereafter (up to 30 June 2009).

RESULTS

All 8 patients completed immunocryosurgery and all 11 lesions cleared completely. For 4/8 patients 5–6 weeks of imiquimod was sufficient, but the remaining 4/8 patients (with one lesion each) required slightly extended periods of post-cryosurgery imiquimod application (1–3 weeks) in order to achieve clearance. Two patients died from unrelated causes after the 6 months follow-up and one was lost to further follow-up. No recurrences were observed after at least 6 months follow-up (median 12 months), including 5 lesions followed for ≥12 months.

DISCUSSION

The rationale underlying the immunocryosurgery protocol is that the combination of imiquimod-immunomodulation during cryosurgery (10) would have an additive or synergistic effect on Bowen’s disease treatment. Eight patients completed the therapeutic regimen and all lesions cleared completely. The response to combined cryosurgery and topical imiquimod was similar to the one seen in the small pilot study of 3 patients (10) and is superior to the cure rate of 47–94% reported in the literature (1, 2, 6–9). The results of this study indicate that immunocryosurgery is a viable therapeutic option for the treatment of Bowen’s disease and should be considered as an alternative to conventional treatments. A large prospective study is needed to confirm these findings.
Corresponding monotherapies. Freezing time each in 10/11 lesions) compared with
and (ii) milder cryosurgery (2 freeze-thaw cycles, 10–15 s freezing time each in 10/11 lesions) compared with
randomized studies generally report significantly lower
clearance rates and concomitantly higher relapse rates
of 10–36% with this modality (7, 8). In the present study
of 10–36% with this modality (7, 8). In the present study
concerning the efficacy of monomodal cryosurgery, an
earlier retrospective study reported a recurrence rate of
only 1/128 Bowen’s disease lesions after two freeze-thaw
cycles with 30 s freezing time each (3), yet subsequent
randomized studies generally report significantly lower
clearance rates and concomitantly higher relapse rates
of 10–36% with this modality (7, 8). In the present study
although, 5 of our patients had therapeutically challeng-
ging facial Bowen’s disease lesions (2), the outcome
of the treatment was excellent (Fig. 1). This can be
attributed to adequate compliance, which was probably facilitated by: (i) shortened total imiquimod application
and (ii) milder cryosurgery (2 freeze-thaw cycles, 10–15
s freezing time each in 10/11 lesions) compared with corresponding monotherapies.

Fig. 1. Immunocryosurgery for Bowen’s disease in patient 1 (Table I). (A) Bowen’s disease on the right mandible. (B) The lesion after 3 weeks treatment with imiquimod, just before the cryosurgery session. (C) The lesion 3 months after the end of treatment. Hypopigmentation without scarring is evident. (D) At 24 months follow-up the treated area is re-pigmented, with a reasonable aesthetic outcome. Note the selective anti-neoplastic nature of immunocryosurgery: the biopsy proven dermal naevus that was initially almost encircled by the Bowen’s disease and was included in the treatment field was not appreciably affected by the treatment.

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