Photodynamic Therapy by Topical Aminolevulinic Acid, Dimethylsulphoxide and Curettage in Nodular Basal Cell Carcinoma: a One-year Follow-up Study

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Fifty-eight patients with 119 nodular (2 mm or more in thickness) basal cell carcinomas successfully treated with photodynamic therapy were included in this 1-year follow-up study. The initial cure rate at 3–6 months was 92% after photodynamic therapy, which included an initial debulking procedure and topical application of dimethylsulphoxide in order to enhance penetration of 5-aminolevulinic acid (20% in cream) to which the lesions were exposed for 3 h prior to exposure to light. At examination 12–26 months (mean 17 months) after treatment 113 lesions (95%) were still in complete response. Six lesions (5%) had recurred, located on the face, scalp and ear. The cosmetic outcome was evaluated as excellent to good in 91%. Microscopic examination of biopsies taken from healed areas in 7 patients did not reveal any sign of damage in 5 and only minor alterations in 2. Key words: photodynamic therapy; nodular basal cell carcinoma; 5-aminolevulinic acid; curettage; dimethylsulphoxide.

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Photodynamic therapy (PDT) is a treatment method based on the use of a photosensitizer and light to induce cell and tissue damage. PDT has been used experimentally for the treatment of multiple cancers for decades. During the past few years a haematoporphyrin derivative has been approved for certain indications. The drug is administered systemically causing a prolonged period of skin photosensitization (1, 2).

The compound 5-aminolevulinic acid (ALA) is a precursor in haem synthesis, and when given in excess, induces production and accumulation of protoporphyrin IX (PpIX), a highly photosensitive substance. In 1990 Kennedy et al. (3) showed that ALA administered topically induces a strong fluorescence in superficial basal cell carcinomas (BCCs) and, when subsequent red light is applied, the lesions show a complete remission rate of about 90% after a single treatment session. For nodular BCCs a much lower response rate has been reported (4–6), even if repeated treatment sessions have been shown to improve the results (4). In deep tumour lobules of nodular BCCs, little or no fluorescence is induced by ALA applied topically (7).

Peng et al. (8) have demonstrated that both the depth of penetration and the fluorescence intensity were increased by the use of dimethylsulphoxide (DMSO), either as a pre-treatment or as an adjunct to the ALA-containing cream. In clinical application, the addition of DMSO improved the remission rate of thin nodular BCCs (9). By adding curettage as a debulk-
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Several methods have been used in the treatment of nodular BCC. Mohs’ micrographic surgery is the most successful, with a 5-year recurrence rate of 1–5.6% (11). Radiotherapy in the treatment of nodular BCC has a reported cure rate of 89–95% (12). Curettage with electrodesiccation and cryosurgery reports 5-year cure rates of 92% (13).

A major advantage of ALA-based PDT is that the cosmetic outcome scored excellent or good in 91% of cases. Such a favourable result is advantageous for lesions on the face. The main stigma seen was scarring after an eventual diagnostic biopsy, which also made the clinical evaluation of treatment response more difficult. Skin scrapings from suspicious tumour recurrences did not affect the cosmetic results. By scraping the lesions, the consistency of the lesion was revealed. Cystic nodular tumours were easy to shave, whereas infiltrative or sclerotic lesions were more difficult to debulk completely. However, morphea type elements in a mixed ulcero-nodular BCC may be verified only by histology.

No residual deep tumour was detected in the 7 biopsies investigated. An increased number of biopsies would have strengthened the study. However, most patients eligible for punch biopsies refused. In our experience over more than 5 years of using PDT with large nodular tumours, an incomplete cure often arises in small separate spots within cured areas, and a punch biopsy would not be representative for the entire lesion area treated. Due to the limited malignant potential of the tumours an awaiting attitude concerning deep residual tumour may be adopted. Clinical evaluation and cytology might be adequate for safe follow-up.

Certain areas of tumour localization, i.e. on the nose, ear and hairy scalp, are found to be difficult to treat with our therapeutic method, as with alternative treatments. Here, repeated treatment sessions may be necessary.

Using curettage and DMSO as pre-treatment improves the penetration of ALA and thereby the possibility of PpIX production in the deeper layer of the nodular lesion. ALA is a molecule of low lipid solubility and certain ALA-derivatives (esters, ethers) have shown improved properties of penetration and induction of PpIX due to their more lipophilic molecular structure (14, 15). Ongoing studies may reveal whether the improved properties of these ALA derivatives will prevail or whether mechanical and chemical pre-treatment may nevertheless be necessary.

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The current report shows that topical ALA-based PDT offers a therapeutic option even for nodular BCCs when the lesions are pre-treated by curettage and DMSO. Therapy may be repeated successfully in cases of non-cure or recurrence without cosmetic impairment or deterioration of skin structure. The challenge is to determine which BCC lesions are suited to various treatment methods as a primary treatment.

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REFERENCES