

ORIGINAL ARTICLE

## Methyl-aminolevulinate photodynamic therapy for the treatment of erythroplasia of Queyrat in 23 patients

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### Abstract

Erythroplasia of Queyrat (EQ) is an intraepithelial squamous cell carcinoma localized on the mucosal or transitional surfaces. Standard therapy usually consists of the surgical removal of the cancer. The use of non-invasive alternative procedures, such as photodynamic therapy (PDT), has been considered for the treatment of EQ, although only a few reports regarding isolated cases or small series exist. We describe our cumulative experience with PDT, using topical methyl-aminolevulinate (MAL), for the management of 23 male patients with EQ of the glans penis and/or prepuce. Patients underwent two consecutive weekly MAL-PDT sessions, with the second session postponed in seven patients because of an excessive local reaction. Nineteen patients obtained a complete clinical remission without any sign of recurrence over an average post-treatment period of 18 months (range, 8–30 months). Cosmetic outcome was excellent in most patients, while dyschromic changes occurred in four cases. All patients experienced transient local adverse reactions and 22 of them reported severe or very severe symptoms during the session.

**Key words:** erythroplasia of Queyrat, genital squamous cell carcinoma *in situ*, methyl-aminolevulinate, penis premalignant lesions, photodynamic therapy

### Introduction

Erythroplasia of Queyrat (EQ) is a squamous cell carcinoma *in situ* localized on the mucosal or transitional surfaces, which can progress into an invasive cancer (1,2). Standard therapy usually consists of the surgical removal of the cancer. Nevertheless, development of effective non-invasive alternative procedures is important and desirable. Topical photodynamic therapy (PDT) might be included among these options, although its use has been limited only to sporadic cases of EQ (3–6). We describe our cumulative experience with topical methyl-aminolevulinate and PDT (MAL-PDT) for the management of EQ.

### Patients and methods

We performed a retrospective analysis of patients who had undergone MAL-PDT for treatment of EQ over a

period of 30 months. The case series included 23 male patients, aged 36–82 years (mean age, 62.5 years) with EQ, which was located on the glans penis and/or the inner surface of the prepuce or the coronal sulcus. In all cases, urethral involvement was absent. Clinical diagnosis was confirmed in each case by histopathology. None of the patients presented any known contraindication to the use of PDT. An informed consent was obtained before PDT treatment. Prior to the cream application, scales and crusts, when present, were gently removed. Subsequently, a thick layer (approximately 1 mm) of MAL 160 mg/g cream (Metvix<sup>®</sup>, Galderma Italy) was applied for 3 h under plastic occlusion. Thereafter, the lesional area was exposed to red light (Aktilite CL 128, PhotoCure ASA, Oslo, Norway) at a fluence of 37 J/cm<sup>2</sup>. Two consecutive weekly MAL-PDT sessions were performed, with the second session postponed in case of excess local reaction. In the post-treatment phase,

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patients were instructed to apply local antiseptics and topical preparations containing antibiotics and corticosteroids for 5–7 days. Clinical assessments were made at monthly intervals after the completion of the PDT cycle for the first trimester, and then every 3–6 months.

## Results

All patients completed the MAL-PDT cycle: 16 patients received one weekly session for two consecutive weeks, whereas in seven the second session was delayed for a week because of persistent local symptoms. Nineteen patients obtained a complete and sustained clearance of their EQ, without any sign of recurrence over a post-treatment period of 8–30 months (mean, 18 months), whereas four patients clinically showed only a partial response within 3 months after PDT cycle. The persistence of EQ was confirmed by histopathology in three cases, whereas only fibrosis was detected on histopathological examination in the fourth patient. Cosmetic outcome was regarded as excellent in 19 patients, who did not have any evident modification of the treated area, while dyschromic changes and especially hyperpigmentation were present in four cases. Local reactions due to the procedure occurred in the whole study population (Table I). In particular, all patients reported discomfort, pain or burning sensation during the session, which was graded as severe or very severe (on a 6-point scale from 0 = absent to 5 = very severe) by 22 subjects. Such symptoms led in six patients to temporary discontinuation of illumination for a few minutes, with application of cold dressings or water spray, and air cooling. Only four patients complained of persistent burning pain lasting 2–4 days, which required the oral administration of nonsteroidal anti-inflammatory drugs.

Table I. Local adverse reactions reported during and after MAL-PDT treatment in 23 patients with EQ.

Adverse reaction	Patients ( <i>n</i> )
Pain/burning	23
Erythema	23
Edema	23
Erosion/ulceration	23
Blistering	4
Dyschromia/hyperpigmentation	4

EQ = Erythroplasia of Queyrat; MAL-PDT = Methyl-aminolevulinic-acid-photodynamic therapy.

## Discussion

EQ is an uncommon premalignant condition that usually develops on the glans penis. EQ may have a worse prognosis and a higher risk of malignant transformation as compared to Bowen disease, despite the histopathological similarities shared by the two conditions (1,2). While they have been regarded as the same disease for a long time, some authors have considered them as two distinct conditions (2), especially because of the different clinical features, and the higher likelihood of EQ progression into invasive forms which might be linked to mucosal involvement. Effective treatment is therefore fundamental in order to minimize such a risk, with standard therapy traditionally consisting of radical surgical excision.

During the past years, there has been increasing scrutiny of non-invasive, tissue-sparing options with efficacy similar to that of surgical procedures for the treatment of nonmelanoma skin cancers, and among these PDT has been considered (7–10).

The literature contains very few reports of treatment of EQ with PDT (3–6), and most of them concern the use of topical aminolaevulinic acid (3,4,6).

Our experience involved 23 patients with EQ on the glans penis and/or prepuce, without urethral involvement, treated with MAL-PDT. In brief, 83% of patients achieved a complete clinical remission, still persisting at a post-treatment average period of 18 months. Therefore, based on these preliminary results, which have shown a high success rate and an overall excellent cosmetic outcome, MAL-PDT can be considered a valid therapeutic approach to penile EQ. However, the use of MAL-PDT for such genital lesions was constantly associated with transient local reactions and discomfort, with most patients complaining of severe or very severe symptoms during the session.

**Declaration of interest:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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