



In vivo identification of tumor cells of the basal layer of the epidermis in an early lesion of extramammary Paget disease: A reflectance confocal microscopic analysis

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INTRODUCTION

Extramammary Paget disease (EMPD) is a cutaneous adenocarcinoma.¹ In early lesions, tumor cells (Paget cells) are often arranged sporadically in the basal regions of the epidermis.¹ Evaluating the extension of EMPD is challenging, because it can mimic eczema.² Additionally, Paget cells are often detected beyond clinically suspected margins.² At present, invasive biopsies are conducted to precisely evaluate the extent of the disease.

Reflectance confocal microscopy (RCM) is a noninvasive modality for visualizing the epidermal and papillary dermal areas in high-resolution images.² RCM has been used for detecting advanced or recurrent lesions of EMPD²⁻⁵; however, its usefulness in detecting early lesions of EMPD has not been well evaluated. Here, we demonstrated that RCM images depicted the presence of tumor cells on a per-cell basis in the epidermal basal layers in an early lesion of EMPD.

CASE REPORT

A 72-year-old man presented with pruritic ill-defined erythema on the right side of the scrotum (Fig 1, A). A biopsy from the erythema revealed

Abbreviations used:

EMPD: extramammary Paget disease
RCM: reflectance confocal microscopy

Paget cells, 10-25 μ m in diameter, located sporadically in the basal layer of the epidermis (Fig 1, B and C), leading to the diagnosis of an early lesion of EMPD. To assess the lesion extent noninvasively, we performed RCM for the patch as well as the surrounding, macroscopically uninvolved, skin. RCM of the macroscopically uninvolved skin revealed dark, oval areas corresponding to dermal papillae, separated from the epidermis by high signal lines corresponding to the basal layers of the epidermis, at a depth of 90 μ m below the stratum corneum (Fig 1, D). RCM of the erythema revealed low-signal spots located sporadically in the high signal lines of the basal layer (Fig 1, E and F). The low-signal spots, 10-25 μ m in diameter, were approximately the same size as Paget cells in the biopsy specimen. We screened for Pagetoid cells with CK7 (a marker for Paget cells), human leukocyte antigen DR-1 (Langerhans cells and other leukocytes), Melan A (melanocytes), and

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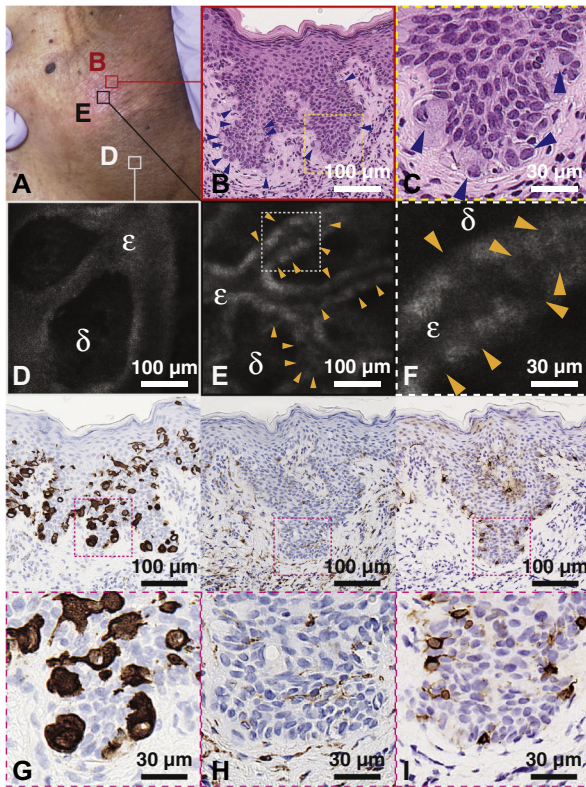


Fig 1. Clinical, histopathologic, and reflectance confocal microscopic findings. **A**, Erythema on the right scrotum. **B**, **C**, Hematoxylin-eosin-staining of a biopsy specimen. Blue arrowheads indicate tumor cells. **D**, **E**, **F**, Reflectance confocal microscopic visualization of the macroscopically uninvolved skin (**D**) and erythema (**E**, **F**) at a 90- μ m depth. Dark oval areas are dermal papillae (indicated with δ) circumscribed by the epidermis (ϵ). Orange arrowheads indicate dark spots of 10-25- μ m diameter spreading sporadically along the basal layer in the erythematous lesion. **G**, **H**, **I**, Immunohistochemical analysis for CK7 (**G**), HLA-DR (**H**), and Melan A (**I**).

S100. All of the Pagetoid cells were positive for CK7 (Fig 1, *G*). Human leukocyte antigen DR-1 was stained on polymorphic small cells with a diameter less than 10 μ m (Fig 1, *H*). Melan A-positive cells were located in the basal layer with a diameter of 10 μ m (Fig 1, *I*). The patient underwent surgical resection, and no recurrence occurred during the follow-up period.

DISCUSSION

In this study, we succeeded in visualizing Paget cells as 10-25 μ m-sized low-signal spots spreading sporadically along the basal layer in an early lesion of

EMPD. In previous studies, the detection of Paget cells using RCM was limited to advanced lesions, in which RCM revealed intraepidermal dark cells, nested structures, or large nested structures at the dermo-epidermal junction.²⁻⁵ The present study indicates the potential of RCM for depicting each Paget cell.

This study has several limitations. Our validation on the authenticity of the low-signal area as Paget cells was based on the cell size, although the size of cells may differ between in vivo and formalin-fixed, paraffin-embedded specimens. We did not analyze the contralateral normal scrotal skin as a control. Further validation is required to determine whether our findings can be applied to defining the margins of any stage of EMPD.

Although the sensitivity and specificity of confocal features in EMPD are yet to be determined through studies like ours, the near-histologic quality of images is advantageous than that from other noninvasive modalities such as dermoscopy, photodynamic diagnosis, and optical confocal tomography.⁶ By combining it with other noninvasive modalities, RCM can make invasive mapping biopsy more efficient and reduce the burden on the patients with EMPD.

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Conflicts of interest

None disclosed.

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