In vivo reflectance confocal microscopy of extramammary Paget disease: Diagnostic evaluation and surgical management

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Background: Extramammary Paget disease (EMPD) is a diagnostic challenge. In vivo reflectance confocal microscopy (RCM) has been reported to be useful for in vivo skin tumor evaluation. It may also assist in the surgical management of EMPD lesions.

Objective: We sought to describe confocal features of EMPD and correlate them with histopathologic findings. The potential of RCM to map the lesions for subsequent surgical management was also investigated.

Methods: A total of 23 lesions from 14 recruited patients were evaluated by RCM and histopathologic examination. RCM was used to delineate preoperative surgical margins in two patients.

Results: Erythematous, hyperpigmented, and hypopigmented lesions were evaluated by RCM and results were confirmed by histopathologic examination. Paget cells were observed throughout the epidermis. Typical Paget cells on RCM were characterized by a mild bright nucleus and dark cytoplasm, frequently twice the size of keratinocytes or larger. At the dermoepidermal junction, tumor nests were seen as dark glandular structures. A high density of dendritic cells was observed in pigmented lesions and a low density in erythematous lesions. Dilated vessels and inflammatory cells were seen in pigmented and erythematous lesions. Paget cells within the epidermis and nest structures at the dermoepidermal junction were seen in most lesions. These two features were useful for delineating the margins. Histologic examination corroborated the surgical margins found by RCM.

Limitations: The sensitivity and specificity of these diagnostic features have not been fully studied, and differential diagnostic features require exploration.

Conclusion: Features correlating well to histopathology are observed on the RCM of EMPD lesions. RCM may be used as an auxiliary diagnostic tool for the diagnosis and management of EMPD. (J Am Acad Dermatol 2012;66:e47-53.)

Key words: extramammary; Paget disease; reflectance confocal microscopy; surgical excision.

Extramammary Paget disease (EMPD) is a rare cutaneous, intraepithelial adenocarcinoma primarily involving the epidermis. EMPD constitutes a diagnostic challenge to clinicians. It may mostly mimic contact or seborrheic dermatitis, superficial fungal infections, Bowen disease,

Abbreviations used:

DEJ:	dermoepidermal junction
EMPD:	extramammary Paget disease
RCM:	reflectance confocal microscopy

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superficial basal cell carcinomas, flexural psoriasis, and lichen sclerosus. Therefore, the diagnosis is often delayed (on average 2 years after disease onset), and is usually made upon the histologic examination performed in the presence of a chronic dermatosis not responding to local treatments.[1]

In vivo reflectance confocal microscopy (RCM) enables the noninvasive, high-resolution imaging of superficial layers of the skin, and provides cellular details. The correspondence of confocal features with dermatoscopy and histopathology has been evaluated.[2,3] RCM has been previously reported to be useful in the in vivo evaluation of skin tumors[2-5] and conditions such as allergic contact dermatitis[6,7] and psoriasis.[8]

The aim of this study was to describe relevant morphologic confocal features of EMPD, and to correlate these features with histopathologic findings. We also investigated the potential of RCM to map the lesions for subsequent surgical management in two patients. This article describes our initial experience using RCM imaging for EMPD, and its potential clinical application.

CAPSULE SUMMARY

- We investigated the reflectance confocal microscopic and histopathologic features of hyperpigmented, hypopigmented, and erythematous areas of extramammary Paget disease.
- Paget cells noted in reflectance confocal laser microscopy imaging, along with characteristic nest structures at the dermoepidermal junction, may contribute to early diagnosis.
- Reflectance confocal laser microscopy also has the potential to delineate surgical margins.

METHODS

Patients

Fourteen patients were recruited from the dermatology department with lesions clinically suggestive of EMPD; these were then biopsy proven. Two of the patients were treated with wide surgical excision in the urology department. This study was conducted according to the Declaration of Helsinki Principles; furthermore, institutional approval and written informed patient consent were obtained.

Reflectance confocal microscopy

Confocal imaging was performed with a commercially available near-infrared reflectance confocal laser scanning microscope (Vivascope 1500, Lucid Technologies, Henrietta, NY), which uses a diode laser with a wavelength of 830 nm and power of less than 15 mW. This system provides high-resolution images (horizontal resolution of 1.0 μm, vertical optical section thickness of 3.0 μm) to a depth of 0 to 250 μm in vivo (from the epidermis down to the papillary dermis). A comprehensive description of this system has been reported previously.[9]

Lesional and adjacent nonlesional skin was examined using RCM. Blocks of 4 × 4 mm mosaics at the level of the superficial epidermis, dermoepidermal junction (DEJ), and dermis were also acquired using software (Vivablock, Lucid Technologies).

Histopathology

At the same sites at which RCM examination took place, biopsies of the lesions were performed for histopathological analysis. The tissue was fixed in formalin, processed routinely, and embedded in paraffin. After routine processing, slides were stained with hematoxylin-eosin; immunohistochemical studies were also performed if necessary.

Surgical excision

Patients 7 and 10 were treated with wide local surgical excision in the urology department. Before the surgery, an experienced urologist inscribed the surgical boundaries of the skin lesion with a marker pen. Then, RCM examinations were performed to delineate the margins of the lesions inside and outside the boundaries inscribed by the urologist. A wide local excision was taken 2 cm beyond the boundaries inscribed by urologist, with deep resection to subcutaneous fat up to the fascia. Intraoperative frozen biopsy was performed to ascertain the surgical margins. After the surgery, the gross skin specimen of patient 6 was further sectioned along the boundaries inscribed by RCM on histologic examination.

RESULTS

A total of 23 lesions from the 14 recruited patients were evaluated by RCM and histopathologic examination. Most of the lesions presented as red or brown plaques or patches. Hypopigmented patches were seen in 4 patients, and black plaques were seen in two patients (Table I). The localized hypopigmentation or hyperpigmentation occurred adjacent to the erythematous plaques of typical EMPD lesions.

RCM and histopathologic findings

The key confocal features of all EMPD lesions and frequency of these features are shown in Table II.