

However, unspecific bullous or maculopapular rashes, pruritus, cutaneous lupus erythematosus and vitiligo-like lesions have been observed sporadically in the context of CDK4/6i intake.^{2,3} The mode of action how and why CDK4/6i induce skin symptoms is unclear; however, possible explanations include genetic predisposition, drug biotransformation and epigenetic dysregulation of adaptive immune cells. CDK4/6i such as palbociclib may lead to increased T lymphocyte activation by increasing immune checkpoint blockade and thus may trigger the development of immune mediated skin conditions.⁴ On the basis of the WHO Uppsala Monitoring Centre causality assessment criteria, the relationship between palbociclib and the pustular rash is likely in the present case. Of course, AGEP must be differentiated from pustular psoriasis or subcorneal pustular dermatosis.⁵ However, the acute onset of the rash with absence of psoriatic history, the partly flexural skin involvement and the histopathology findings including vacuolar interface changes rather favour a diagnosis of APEG-like rash in the present case. Isom et al.⁵ recently showed that prominent keratinocyte apoptosis along with neutrophilic spongiosis is significantly associated with AGEP when compared to pustular psoriasis.⁵ IgA pemphigus, in particular the subcorneal pustular dermatosis type, must also be considered a differential diagnosis. Clinically, however, IgA pemphigus is characterised by annular circinate plaques.⁶ In conclusion, AGEP-like rashes must be included into the spectrum of cutaneous side effects of CDK4/6i.

Thilo Gambichler  | Lennart Ocker |
Laura Susok | Martin Doerler | Rene Stranzenbach
*Skin Cancer Center, Department of Dermatology, Ruhr-
University Bochum, Bochum, Germany*

REFERENCES

1. Chowdhary M, Sen N, Chowdhary A *et al.* Safety and efficacy of palbociclib and radiation therapy in patients with metastatic breast cancer: initial results of a novel combination. *Adv. Radiat. Oncol.* 2019; 4: 455–7.
2. Russell-Goldman E, Nazarian RM. Subacute cutaneous lupus erythematosus with positive anti-Ro antibodies following palbociclib and letrozole treatment: A case report and literature review. *J. Cutan. Pathol.* 2020; 47: 654–8.
3. Freedman JB, Herskovitz I, Maderal AD. Chronic cutaneous lupus erythematosus (discoid lupus) induced by palbociclib. *Int. J. Dermatol.* 2020; 59: e216–e218.
4. Deng J, Wang ES, Jenkins RW *et al.* CDK4/6 inhibition augments antitumor immunity by enhancing T-cell activation. *Cancer Discov.* 2018; 8: 216–35.
5. Isom J, Braswell DS, Siroy A *et al.* Clinical and histopathologic features differentiating acute generalized exanthematous pustulosis and pustular psoriasis: A retrospective series. *J. Am. Acad. Dermatol.* 2020; 85: 265–7.
6. Kridin K, Patel PM, Jones VA *et al.* IgA pemphigus: A systematic review. *J. Am. Acad. Dermatol.* 2020; 82: 1386–92.

Case Letter

*Pigmented lesions with unusual penile localisation:
Usefulness of reflectance confocal microscopy - Report of 2
cases*

INTRODUCTION

Pigmented skin lesions of the penis include melanocytic and non-melanocytic lesions.¹ Melanocytic lesions on the penis occur in 10–12% of the general population with melanoma accounting for 1.4% of all penile cancers and less than 0.1% of melanoma cases.²

Reed nevus is a deep pigmented melanocytic lesion, commonly located on the lower extremities of young adults and the penile location of this lesion is rarely reported³. The starburst pattern is typical of Reed nevus but it has been also reported in melanoma. Pigmented Bowen disease is an *in situ* squamous cell carcinoma, clinically appearing as a slow-growing, well-defined, hyperpigmented plaque and its location on the genital area is uncommon in white populations.⁴

Reflectance confocal microscopy (RCM) is a non-invasive diagnostic technique that improves the diagnostic accuracy of equivocal pigmented and non-pigmented skin lesions. Only few case reports described RCM features of pigmented genital lesions.⁵

Herein, we report two common pigmented lesions with an unusual penile localisation in which RCM has been useful for diagnosis and management.

CASE 1

A 16-year-old boy presented with a 4 mm brown/black, irregularly shaped macule on the glans penis, that appeared 3 months earlier and changed over time (Fig. 1a). Dermatoscopic examination showed an irregular starburst pattern suggestive of Reed nevus (Fig. 1b). Due to the unusual penile location and differential diagnosis with melanoma, we performed RCM that revealed multiple and diffuse spindle cells in the epidermis with sharp lateral demarcation (Fig. 1c). These features were considered to be characteristic of Spitz nevi and supported the diagnosis

Conflicts of Interest: T.R. reports no conflicts of interests. V.C. reports no conflicts of interests. A.V. received a research fellowship from Sanofi-Genzyme and has served on advisory board and received honoraria from Novartis. M.C.F. has served on advisory board, received honoraria for lectures and research grants from Almirall, Celgene, Eli Lilly, Galderma, Janssen, Leo Pharma, Medac Pharma, Mylan, Novartis, Pfizer, Roche, Sanofi, UCB, Sunpharma, Pierre Fabre, MSD.

Funding: None.

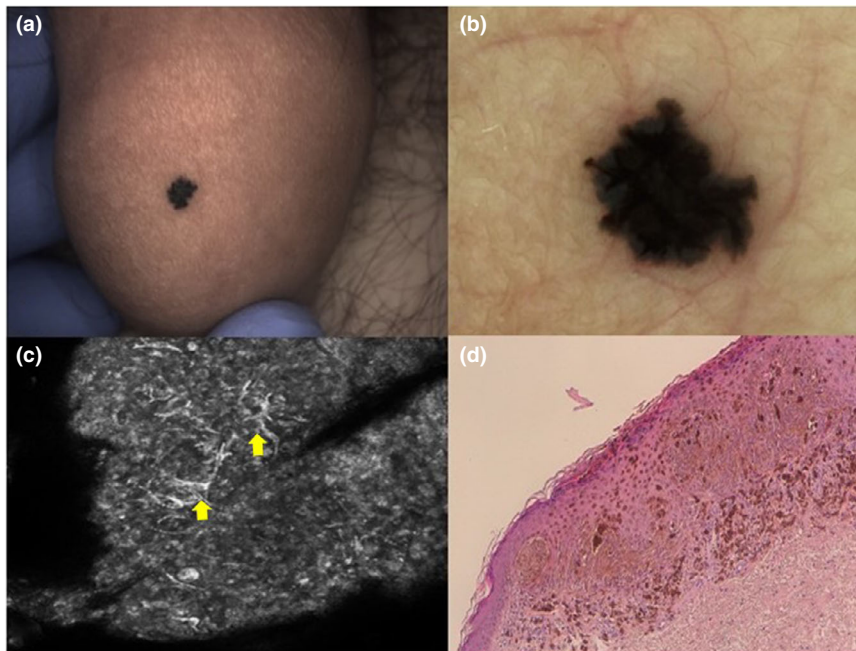


Figure 1 (a) Clinical image: brown/black irregular macule on the glans penis. (b) Dermoscopy shows a starburst pattern with a central blotch of black/dark brown colour and some asymmetric pseudopods at the periphery. (c) RCM image with spindle cells (yellow arrows). Single image = $400 \times 500 \mu\text{m}$. (d) Histopathologic features of Reed nevus with typical spindled melanocytes in interconnected fascicles (H&E staining, 20x magnification). RCM, Reflectance Confocal Microscopy.

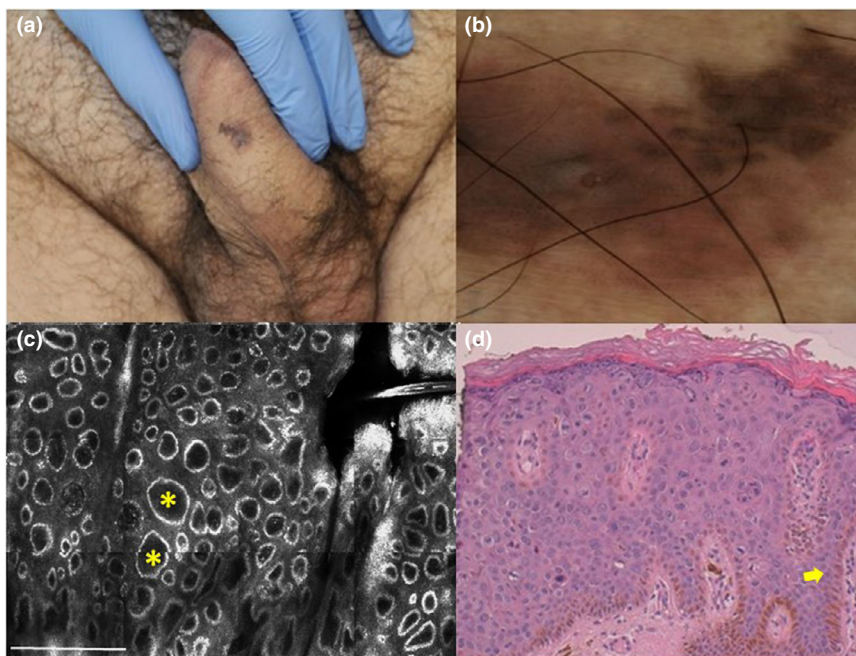


Figure 2 (a) Clinical image: pink/brown macule on the penis shaft. (b) Dermoscopy (x30) shows an eccentric hyperpigmented area and irregularly distributed brown/black globules on a pinkish background (c) High magnification RCM examination at DEJ with edged dermal papillae as bright rings (yellow asterisks). White bar = $500 \mu\text{m}$. (d) Histopathology of pigmented Bowen disease with acanthotic epidermis, thickening of rete ridges and basal pigmented keratinocytes (yellow arrow) (H&E staining, 10x magnification). RCM, Reflectance Confocal Microscopy.

which was histopathologically confirmed after excisional biopsy (Fig. 1d).

CASE 2

A 45-year-old man presented with a 1 cm asymptomatic pink/brown macule on the penis shaft that had appeared one year earlier (Fig. 2a). Dermatoscopy showed non-specific features with a hyperpigmented area and irregularly distributed brown/black globules on a pinkish background (Fig. 2b). RCM showed an atypical honeycomb pattern and edged dermal papillae appearing as bright rings in the absence of junctional and dermal nests of melanocytic cells (Fig. 2c). The cytological atypia of keratinocytes and the absence of diagnostic confocal features of melanocytic lesion supported the diagnosis of keratinocyte carcinoma. Histopathological examination of an incisional biopsy confirmed the diagnosis of pigmented Bowen disease (Fig. 2d).



DISCUSSION

The diagnosis of clinically atypical pigmented lesions on the genitalia can be challenging since differential diagnosis with melanoma might be difficult.

RCM has been recently shown to play a role in the non-invasive diagnosis of vulvar nevi,⁶ providing additional information to the clinical and dermatoscopic examination. In spitzoid lesions, it is not always possible to differentiate a nevus from a melanoma because it is impossible to explore the lesion in significant vertical depth. However, the presence of sharp border cut-offs and spindle cells, as in our case, is more characteristic of a nevus. In our patients, RCM has provided a near-histological morphological accuracy that helped us in the diagnosis of Reed nevus and keratinocyte carcinoma, respectively.

Genital disorders are generally a source of anxiety and a biopsy in this sensitive area is not preferred for the related pain and risk of scarring thus a fast and non-invasive diagnosis is highly desirable. In addition, RCM reduces the risk of infection as well as costs, resources and time.

In conclusion, RCM is an additional tool that can be used in clinical practice to aid clinical diagnosis of pigmented lesions, especially if located in sensitive areas such as genitalia where unnecessary surgery is preferably avoided.

Tea Rocco | Alessandra Ventura  | Valeria Ciciarelli | Maria Concetta Fagnoli 
Dermatology, Department of Biotechnological and Applied
Clinical Science, University of L'Aquila, L'Aquila, Italy

REFERENCES

1. Mahto M, Woolley PD, Ashworth J. Pigmented penile macules. *Int. J. STD AIDS* 2004; 15: 717–9.
2. Sánchez-Ortiz R, Huang SF, Tamboli P *et al.* Melanoma of the penis, scrotum and male urethra: a 40-year single institution experience. *J. Urol.* 2005; 173: 1958–65.

3. Aoyagi S, Sato-Matsumura KC, Akiyama M *et al.* Spitz Naevus of the glans penis: An unusual location. *Acta. Derm. Venereol.* 2004; 84: 524–5.
4. Giuffrida R, Conforti C, Resende FSS *et al.* Clinical and dermoscopic features of genital pigmented Bowen disease. *Clin. Exp. Dermatol.* 2018; 45: 813–6.
5. Collgros H, Vicente A, Díaz AM *et al.* Agminated cellular blue naevi of the penis: dermoscopic, confocal and histopathological correlation of two cases. *Clin. Exp. Dermatol.* 2016; 41: 490–4.
6. Cinotti E, Couzan C, Perrot JL *et al.* Reflectance confocal microscopy for the diagnosis of vulvar naevi: six cases. *J. Eur. Acad. Dermatol. Venereol.* 2016; 30: 30–5.

doi: 10.1111/ajd.13618

Case Letter

Dear Editor,

A rare case report with diffuse ‘sclerodermoid appearance’ due to systemic amyloidosis

Systemic amyloidosis has a wide spectrum of nonspecific manifestations, among which mucocutaneous findings occur in approximately 30–40% of patients.¹ We herein describe a patient with a rare clinical pattern of systemic amyloidosis resembling scleroderma, referred to as a ‘sclerodermoid appearance’.

A 68-year-old man reported with progressive swelling of his forearms and hands for a duration of about two years. A previous presumed diagnosis of systemic scleroderma was based on skin hardness, complaints of fatigue, weakness and mild arthralgias. Further examination revealed an induration as hard as a ‘rock’ and shiny swelling appearance of his forearms, hands, breast, thighs and buttocks. Scattered spontaneous purpura was noted on his arms, chest and legs (Fig. 1).

Results of antinuclear antibody, anti-double-stranded DNA antibodies, C3, C4, rheumatoid factor, serum antibodies against cytomegalovirus, syphilis and human immunodeficiency virus were all negative. Complete blood count results revealed leucocytosis at 19.4 k/ μ L but the serum procalcitonin level was within the normal range. Further laboratory studies revealed an elevated serum immunoglobulin free light chain (FLC) lambda level (46.8 mg/L) (normal range, 8.5–27.0 mg/dL). Laboratory tests for screening for renal involvement were performed. The results were normal including BUN 20.4 mg% (normal range, 07–20 mg%) and creatinine 0.8 mg% (normal range, 0.7–1.3 mg%); complete urinalysis was negative for erythrocytes and white blood cells. The 24-h urinary protein test results were negative. Urine collection for

Conflict of interest: The authors have no conflict of interest to declare.

Funding source: None.