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Hypopigmentation as a diagnostic clue in primary extramammary Paget disease: Case report and short literature review

Dear Editor,

Primary extramammary Paget disease (EMPD) is a rare malignant tumour occurring in apocrine gland-bearing areas, such as the genitals (mean age at diagnosis 60–70 years).[1] Clinically, EMPD exhibits well-circumscribed, erythematous and scaly patches or plaques often mimicking inflammatory skin disorders, but occasional pigmentary changes such as hypo- or hyperpigmentation are reported.[1,2] Histologically, Paget cells appear as atypical large round cells with prominent nuclei and abundant pale cytoplasm (usually containing mucin), located within the epidermis in a pagetoid pattern. Immunohistochemical staining is useful and, in general, primary EMPD is typically cytokeratin (CK) 7+ and CK20−.[1]

We report the case of a 63-year-old male patient who was referred to our clinic for an asymptomatic hypopigmented patch centred by a pinkish area in the right pubic region (Figure 1a). Dermoscopy showed a diffuse white structureless area (with leukotrichia) at the periphery; in the centre, a pinkish/yellowish area associated with branching white reticular lines and dotted vessels (lava-like areas) was objectified (Figure 1b). A biopsy was performed, and the histology revealed an infiltrating primary EMPD (immunohistochemistry: CK7+, CK20-) (Figure 1c,d). Also, the histological examination of an enlarged right inguinal lymph node showed the presence of tumoral cells (Figure 1e,f); therefore, a diagnosis of metastatic EMPD was made. After a multidisciplinary discussion, the patient was treated with wide surgical excision and systemic therapy (docetaxel + trastuzumab).

An early diagnosis is extremely important for EMPD, because invasive forms lead to a high incidence of metastases and poor prognosis.[1] Recently, new imaging techniques such as Line-field Confocal Optical Coherence Tomography (LC-OCT) have proved to facilitate a prompt diagnosis.[3] Moreover, dermoscopy, a highly available technique, can be very useful and typically shows milky-red areas, vascular patterns (particularly dotted and glomerular vessels), surface scales and ulcers or erosions; less frequently, pigmented or white structures may also be observed.[4] In addition, 'lava-like' structures and 'cloud-like' structureless areas have been recently described as new dermoscopic clues for diagnosing EMPD.[4]

Our paper focuses on an unusual clinical presentation of EMPD, that is the hypopigmented variant. According to the literature (Table 1), this feature can be found both in initial[5–8] and advanced metastatic primary EMPD,[9] and the prevalence of hypopigmentation in primary EMPD can vary from 30% (6/19 patients)[10] to 67.7% (84/124 patients).[2] When associated with the typical erythematous lesions of EMPD, hypopigmentation is usually located around the erythematous plaques.[10] Furthermore, Choi et al. found an association between hypopigmentation and a worse outcome, being hypopigmented lesions related to a higher recurrence rate.[2]

Regarding the possible aetiopathogenesis of hypopigmentation in EMPD, several mechanisms have been proposed, including a tumour-induced dysfunctional melanocyte–keratinocyte interaction,[5] physical replacement of basal keratinocytes or melanocytes by Paget cells[6,7] or decrease in melanocyte growth factors induced by the tumour microenvironment.[11] In addition, according to Choi et al., depigmented EMPD may be a result of the recruitment of CD8+ T cells, which can destroy melanocytes leading to depigmentation, but have a poor tumour cytotoxic effect. This hypothesis could explain the reported association between hypopigmentation and development of an advanced disease, as in our case.[2]

In conclusion, our observations suggest that EMPD should be considered in the differential diagnosis of hypopigmented anogenital lesions. Furthermore, hypopigmentation can be associated with advanced EMPD, leading to a worse outcome, although this hypothesis requires further investigations.

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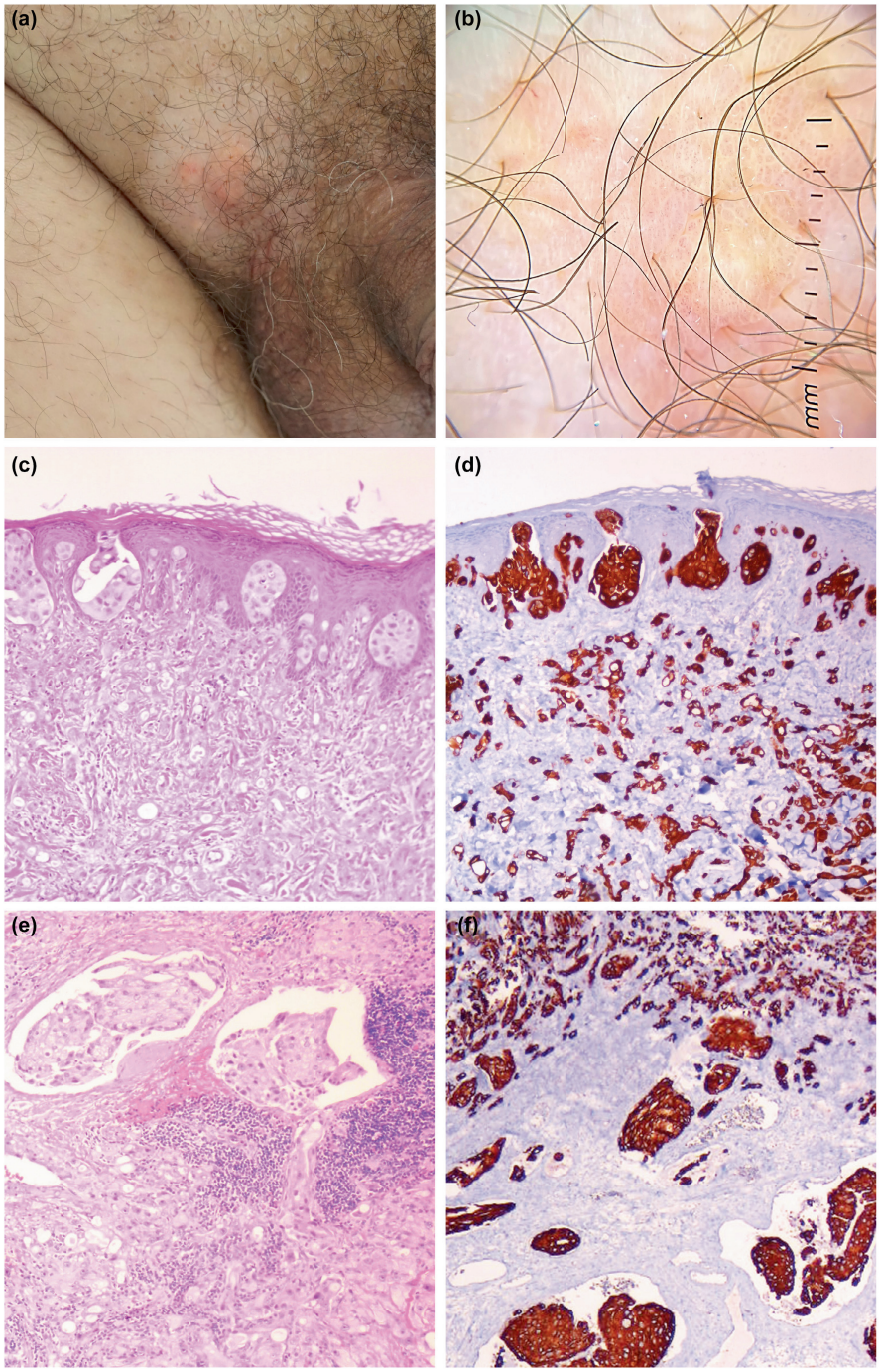

FIGURE 1 (a) Clinical presentation of extramammary Paget disease: hypopigmented patch in the right pubic region. (b) Peripheral white structureless area and central pinkish/yellowish area with white reticular lines and dotted vessels (lava-like areas) at the dermoscopic examination. (c, d) Paget cells infiltrating epidermis and dermis in skin biopsy specimen; (c) H&E staining, 10×; (d) CK7 immunohistochemistry staining, 10×. (e, f) Lymph node specimen consistent with EMPD metastasis; (e) H&E staining, 10×; (f) CK7 immunohistochemistry staining, 10×.

TABLE 1 Clinical features of hypopigmented extramammary Paget disease cases reported in the literature.

Authors (Year)	Number of patients	Age (years)	Gender	Body region	Hypopigmentation as initial presentation or as recurrent disease	Lymph node metastasis
Kakinuma H et al. (1994)[5]	1	76	M	Penile root + left groin + right groin	I	No
Sawamura D et al. (1996)[6]	1	60	M	Right groin + scrotum	I	No
Chen YH et al. (2001)[7]	1	69	M	Penile root	R	No
Yang CC et al. (2004)[10]	6	66	F	Pubic area	I	Not reported
		72	M	Penile root + scrotum	I + R	
		73	M	Penile root	R	
		74	M	Scrotum	R	
		78	M	Right groin	R	
		83	F	Vulva	R	
Iwamoto K et al. (2018)[9]	1	74	M	Scrotum	I	Left inguinal + external iliac
Choi S et al. (2021)[2]	84	65.91 (mean)	75% M 25% F	Penile shaft Scrotum Pubis Labia majora Perineum and anus	I	Not reported
Diab R et al. (2022)[8]	1	34	F	Vulva	I	No

Note: F, female; I, initial presentation; M, male; R, recurrent disease.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The research conforms to the ethical standards described by the Declaration of Helsinki.

INFORMED CONSENT

The patient in this manuscript has given written informed consent to publication of their case details and clinical photographs.

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