CASE REPORT

Depigmentation of the vulvar area: Is it an alarming sign?

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Abstract
A 34-year-old female patient presented with recurrent bilateral hypopigmented macules on the labia majora. The lesions were treated with topical steroids, which led to mild improvement, but erosive plaques developed after discontinuing the treatment. Histopathological findings were compatible with extramammary Paget disease (EMPD), which was treated with radical vulvectomy with no recurrence in the next months of follow-up.

KEYWORDS
extramammary Paget disease, hypopigmented macule, labia majora, Paget disease, vulvar lesion

1 | INTRODUCTION

Extramammary Paget’s disease is a neoplasm occurring predominantly in women between 50–60 years, and it is often seen in the axillary, perianal, and anogenital areas.1,2 Clinical presentation includes pruritic, erythematous plaques in the anogenital region (most frequently involving the labia majora) described as “strawberries and cream”. Occasionally, it may present with hypopigmented macules, which may lead to misdiagnosis with other diseases like vitiligo or lichen sclerosus.3 Herein, we report an early presentation for extramammary Paget’s disease in a 34-year-old woman who presented early with recurrent bilateral hypopigmented macules. Early biopsy and diagnosis resulted in an excellent prognosis with no involvement of other organs.

2 | CASE PRESENTATION

A 34-year-old female patient presented with mildly pruritic, hypopigmented macules bilaterally involving the labia majora. The problem had commenced two months beforehand, and the patient had used the fluocinolone...
acetonide and zinc oxide creams for about one month. Such therapy led to a mild improvement, but discontinuation was followed by the development of erosive erythematous plaques in the same area (Figure 1). The physical examination was unremarkable. A mucosal biopsy was obtained. Histopathological examination of the specimen revealed focal parakeratosis and mild epidermal acanthosis with diffuse infiltration of large neoplastic epithelial cells in singular form or in small clusters along the basal and supra-basal layers of the epidermis. The tumor cells had large vesicular nuclei and pale eosinophilic cytoplasm with clear perinuclear halo. The underlying dermis revealed mild perivascular lymphocytic infiltrate. No intradermal neoplastic cell infiltrate was identified (Figure 2A). Immunohistochemistry (IHC) staining was carried out according to morphological findings, and the intra-epidermal tumor cells were positive for the Pan Cytokeratin (CK-PAN), cytokeratin (CK7), and carcinomaembryonic antigen (CEA) (Figure 2B). The S100 proteins, Melan-a and HMB45, were detected in the tumor cells. Clinical and histopathological findings were compatible with extramammary Paget disease (EMPD).

3 | DISCUSSION

Extramammary Paget disease is an intra-epidermal neoplasm involving extramammary body areas like the perianal and anogenital regions, less often occurring in the axillary area. It predominantly arises from apocrine glands or keratinocytes as a primary malignant skin neoplasm. It occurs more frequently in women with a predilection for those aged between 50 and 80 years. Clinically, it presents as an erythematous plaque in the anogenital area with an average size of 5 cm. It most frequently involves the labia majora, followed by the labia minora, clitoris, perineum, and perineal area. Pruritus, soreness, and painful erosions are the most associated manifestations. Occasionally, hypopigmentation is evident, which may lead to misdiagnosis.

The histological findings include Paget’s cells distributed along the epidermis, usually with atypical nuclei and a pale cytoplasm. Most often, Paget’s cells are positive for epithelial membrane antigen (EMA), CEA, low molecular weight keratin, periodic acid–Schiff stain (PAS), Alcian blue, and mucicarmine.

Differential diagnoses of EMPD are wide, including contact dermatitis, Bowen disease, lichen sclerosus, lichen simplex chronicus, pemphigus vegetans, and psoriasis. For this reason, detailed history, physical examination in addition to histopathological evaluation are essential for differentiating EMPD from other diseases.

Nowadays, the treatment of choice for EMPD is surgical resection using Mohs microsurgery or the modified peripheral Mohs technique, which is the preferred treatment to reduce recurrence rates. Treatment options for primary local lesions include wide local excision, or non-surgical options if the patient is not a surgical candidate including topical imiquimod, photodynamic therapy, or radiotherapy. For regional lymph node metastases, the treatment of choice is lymph node dissection, while chemotherapy, anti-HER2 antibody therapy, hormonal therapy, or immune checkpoint therapy are considered for treatment of distant metastases.

In the described case, the patient had an uncommon presentation of EMPD that was confirmed histopathologically and via special IHC staining techniques. Nowadays immunohistochemical staining is used mainly in diagnosis of EMPD and distinguishing it from other diseases. Paget cells are marked with low molecular weight cytokeratins (CK7 or CK20), periodic acid-Schiff (PAS), GCDFP-15, and CEA.

After the diagnosis was established, a complete lymph nodes’ examination, colonoscopy, cystoscopy, and mammography were done and were all normal. All serum tumor markers, including CA 15–3, CEA, and CA 19–9, were also normal. Radical vulvectomy was done, and the tumor involved hair follicles with a size of 4.4 × 4.3 cm and showed stromal invasion 1 mm in depth. There was no lymphovascular invasion.

As mentioned above, the most common presentation of this disease is well-defined, scaly, erythematous plaques, most frequently described as “strawberries and cream,” leading to the typical symptom of pruritus. Our case at first had presented with non-specific lesions (hypopigmented macules) with very mild or even unmentioned pruritus, misdiagnosed as vitiligo and lichen sclerosus et atrophicus. A topical corticosteroid was initiated, and there was a recurrence after it was discontinued. Hence, a biopsy was done, and the definite diagnosis was obtained.
The classical erythematous lesions appeared shortly after confirmation of the diagnosis.

Interestingly, the patient mentioned a family history of malignant melanoma for her aunt. According to a literature review, a history of association between EMPD and malignant melanoma has been reported in a few patients. However, so far, there is no precise explanation of the exact hereditary mechanisms concerning this association. The family history of malignant melanoma and the early presentation of EMPD in our patient may highlight the possibility of a common genetic association between the two neoplasms that needs further studies for confirmation.

According to this uncommon presentation of EMPD in our young patient, we recommend an early biopsy for every suspected recurrent vulvar hypopigmented lesion. An early biopsy can result in a better prognosis. Indeed, our patient had no other organ involvement because of the early diagnosis and definitive treatment.

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CONFLICTS OF INTEREST
The authors have no conflicts of interest to declare.

REFERENCES
1. Kanitakis J. Mammary and extramammary Paget’s disease. J Eur Acad Dermatol Venereol. 2007;21(5):581-590.
2. Flowers RH, Vittitow S, Martin SM, Elston DM. Extramammary Paget Disease. eMedicine. Retrieved 8/19/2021 from https://emedicine.medscape.com/article/1100397-overview
3. Londero AP, Bertozzi S, Salvador S, et al. A review of extramammary Paget’s disease: clinical presentation, diagnosis, management and prognosis. J Med Sci. 2013;4(4):134-148.
4. Rapini RP. Practical Dermatopathology. Saunders, 2nd ed. 2012:267-268.
5. StClaire K, Hoover A, Ashack K, Khachemoune A. Extramammary Paget disease. Dermatol Online J. 2019;25(4):13030.
6. Guerra R, Misra S. Management of extramammary Paget’s disease: a case report and review of the literature. Case Rep Dermatol Med. 2013;2013:436390.
7. Ishizuki S, Nakamura Y. Extramammary Paget’s disease: diagnosis, pathogenesis, and treatment with focus on recent developments. Curr Oncol. 2021;28(4):2969-2986.
8. McDaniel B, Brown F, Extramammary CJS, Disease P. Extramammary Paget Disease. 2021 Aug 9. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021.
9. Lydrup E, Berg JO, Hjorth SV, Holmich LR, Lock-Andersen J, Chakera AH. Extramammary Paget’s disease and melanoma: 2 cases of double cancers. Case Rep Dermatol. 2020;12(2):107-113.

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