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LETTER TO THE EDITOR

Re: Erythematous Plaque in the Left Axillary Region

A diagnostic challenge where dermoscopy can help

Dear Editor,

We read with interest, the article by Pegalajar-García *et al*. published in the November 2023 issue of SQUMJ.[1] The authors reported a 70-year-old man, who was diagnosed with extramammary Paget's disease (EMPD).[1] At first, the main clinical hypothesis considered for differential diagnosis included Langerhans cell histiocytosis, Bowen's disease, amelanotic melanoma and mycosis fungoides. However, a dermoscopy evaluation revealed whitish and dotted vessels suggestive of the EMPD diagnosis, which was further confirmed by the gross cystic disease fluid protein 15 (GCDFP-15), mammaglobin and CK7 positive, and HMB 45 and S-100 protein negative. Imaging and complementary laboratory determinations discarded concomitant malignancies, a major prognostic factor, which can occur in contiguous (23%) or distant (8–46%) locations. He underwent the excision of the plaque; however, there are also non-surgical procedures which include management utilising imiquimod, photodynamic therapy or radiotherapy. The authors emphasised the common genital or perianal and rare axillary sites, the prevalence from 35–80 years of age, the high recurrence rate and the long follow-up.[1] Considering the importance of this case report to increase the suspicion index of non-specialists about the EMPD, which may evolve unsuspected or misdiagnosed, the objective of the current writing is to present a short review of additional literature from 2022 and 2023.[2–6] Besides, the classical dermoscopic patterns of EMPD, as the milky-red and white structureless areas, polymorphous vascular patterns and glomerular vessel patterns, surface scales, ulcers, shiny white lines, and pigmentary structures must be highlighted; this resource is useful to assess and detect recurrent EMPD and improve the outcomes.[1,3]

Caruso *et al*. reviewed 96 studies (5 prospective, 24 retrospective, 30 case series and 37 case reports) about vaginal Paget's disease (VPD); 5,617 patients were aged between 29 and 100 years with the average at 71 years of age at diagnosis.[2] The majority of VPD lesions were erythematous, eczematoid and pruriginous. The median follow-up varied from 1 month to 9 years, with 23–73% of recurrences managed by new surgical excision or imiquimod, 5-fluorouracil or radiotherapy.[2] The authors stressed the need for the creation of databases to better understand this challenging disease. Fang *et al*. reported the use of dermoscopy to monitor recurrences of EMPD in 4 patients with histopathological diagnosis of EMPD in the axilla (n = 1) and in genital area (n = 3); 3 patients had wide excision with clear surgical margins and 1 completed the treatment with photodynamic therapy followed by topical use of imiquimod.[3] Interestingly, typical vascular patterns were found in the lesions of the scrotum but not in those of the axilla, possibly due to the axillary papillomatous epidermis and thicker dermis.[3] Navajas Hernández *et al*. reported a 85-year-old man with two decades of diagnosed ulcerative colitis (UC), who had been recently diagnosed with perianal primary Paget's disease and evolved to death before the radiotherapy management to control the invasive lesions.[4] The authors commented on the rarity of perianal PD (1.3% of all PD), the prevalence among 60–70 year-old women, the CK7 and 34ßE12 positive tumour markers and the lack of literature data establishing a relationship between UC and perianal PD.[4] Pérez *et al*.'s review focused on the diagnosis and treatment of localised or metastatic EMPD and called attention to the low incidence of this entity, the lack of randomised clinical trials and the role of publishing retrospective studies or case reports.[5] Furthermore, they also reported the case study of a 75-year-old woman with the diagnosis of vulvar PD and inguinal lymph node implants of a poorly differentiated adenocarcinoma.[5] CK7, EMA, androgen receptors and CEA positivity, CK20, estrogen and progesterone receptors and GCDFP 15 negative results confirmed metastases of the vulvar origin.[5] She started chemotherapy (carboplatin AUC-4 plus paclitaxel) with a lymph node partial response, followed by consolidation radiotherapy on the vulvar area plus pelvic and inguinal lymph node chains; as she had hepatic implants and the HER2 was positive 3+, the schedule was changed to trastuzumab and paclitaxel (suspended after neurotoxicity).[5] She was treated with only trastuzumab until she moved to another state when she was lost to follow-up. The authors commented on the few reported cases of anti-HER2 treatment and androgen and/or estrogen blockade with favourable outcomes, which may justify the routine evaluation of the HER2, androgen and estrogen receptors overexpression in vulvar PDs.[5] Sohn *et al*. performed a retrospective study to evaluate

the treatment outcomes among 37 patients with advanced and metastatic EMPD; 6 had locoregional and 31 had systemic chemotherapy as first-line treatments (22 platinum-based had an objective response rate [ORR] of 45.5%, and 8 taxane-based had 62.5%, while the systemic chemotherapy combined with anti-HER2 antibody had an ORR of 100%).[6] They stressed the lack of standard treatment for advanced or metastatic EMPD but trastuzumab plus taxane can propitiate longer survival than monotherapy or platinum- or taxane-based chemotherapy.[6]

Early diagnosis of EMPD often constitutes a challenging task for non-specialists, and due to rarity, advanced or metastatic stages have no established standard treatment. Classical dermoscopic patterns are useful to detect EMPD and improve the prognosis.

***Vitorino M. dos Santos[1] and Taciana A.M. Sugai[2]**

[1]Department of Internal Medicine, Armed Forces Hospital and Catholic University, Brasilia, Brazil; [2]Department of Neurophysiology, American Society of Neurophysiology, Brasilia, Brazil

**Corresponding Author's E-mail: vitorinomodesto@gmail.com*

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Response from the Authors

Dear Reader,

Thank you for your interesting comment on our research. EMPD is considered an infrequent entity, even more so outside the genital location. As you have emphasised, dermoscopy is an essential tool for the suspicion of this entity, but also for detection of recurrences, which are very common in this disease.[1] It is remarkable that Fang *et al*. mentioned the lack of vascular patterns in the axillary lesion, as was seen in our case. They try to explain this finding based on axilla's histology, with papillomatous epidermis and thicker dermis. The presence of papillomatous structures described in our report may be consistent with this fact. This characteristic could raise the suspicion of this tumour, in addition to the rest of the mentioned findings.[2]

Although the important role of non-specialists and dermatologists in recognising this entity through clinical and dermoscopics findings, it is histology that is the gold standard for EMPD's diagnosis. Biopsy should be performed in all these cases in order to establish a proper diagnosis, but also because it helps to distinguish between primary or secondary disease.[3]

We agree with the affirmation that strong evidence based on clinical trials and consensus to guide its management and treatment is mandatory, both in local EMPD disease but even more in advanced and metastatic EMPD.

Finally, EMPD is a rare cutaneous tumour where dermoscopy can be essential for early diagnosis, both of initial lesion or recurrences during the following, and robust scientific investigation is needed to improve the clinical attendance for these patients.

Maria Dolores Pegalajar-García,[1] Jose Mellado,[2] *Ricardo Ruiz-Villaverde,[1] Francisco J Navarro-Triviño[1]

[1]Dermatology Department, Hospital Universitario San Cecilio, Granada, Spain; [2]Pathological Anatomy, Analizalab-HLA Inmaculada, Granada. Spain

**Corresponding Author's e-mail: ismenios@hotmail.com*

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