DOI: 10.1515/sjdv-2017-0015

# DERMOSCOPY CASE OF THE MONTH Mammary Paget's Disease - a Case Report

Tatjana ROŠ<sup>1,2</sup>, Marijana BADRKIĆ<sup>2</sup>, Marijana MACANOVIĆ<sup>2</sup>, Nenad ŠOLAJIĆ<sup>2,3</sup>,

Branislava GAJIĆ<sup>1,2</sup>

<sup>1</sup>Clinic of Dermatovenereology Diseases, Clinical Center of Vojvodina, Novi Sad, Serbia
<sup>2</sup>Faculty of Medicine, University of Novi Sad, Serbia
<sup>3</sup>Department of Pathology, Oncology Institute of Vojvodina, Sremska Kamenica, Serbia

\*Correspondence: Tatjana Roš, E-mail: tatjana.ros@mf.uns.ac.rs

UDC 616.5:618.9]-006.6-07

# Abstract

Mammary Paget's disease is a rare intraepithelial carcinoma of the nipple/areola complex often associated with ductal breast carcinoma. We report a case of a 55-year-old female patient with a classical form of mammary Paget's disease associated ductal ipsilateral breast carcinoma. Dermoscopy of Paget's disease revealed a whitish-pink area with polymorphous vessels organized in irregular nests separated by pale streak-like structures, with peripheral light brown diffuse pigmentation. Dermoscopic features described in this case are in agreement with rare previous reports and may contribute to better differentiation of mammary Paget's disease from clinically similar lesions.

**Key words:** Paget's Disease, Mammary; Skin Neoplasms; Diagnosis; Nipples; Breast Neoplasms; Dermoscopy; Case Reports

#### Introduction

Mammary Paget's disease (MPD) is a rare intraepithelial carcinoma of the nipple/areola complex frequently associated with ductal carcinoma in situ (DCIS) or invasive ductal breast carcinoma. MPD accounts for 1-5% of all breast carcinomas. It is most commonly diagnosed in postmenopausal women, in the sixth decade of life. Less frequently, MPD affects men, having a worse prognosis, although there is no evidence that the disease in men has a different course (1). Clinical presentation of MPD is often tricky and dermoscopic patterns are currently not defined. The diagnostic hallmarks of MPD are epidermal Paget's cells, but whether they originate from underlying ductal breast carcinoma or mutated keratinocytes is still debatable. Sometimes, even histological features are not distinct enough and ancillary diagnostic techniques are required.

# **Case Report**

A 55-year-old female was referred for a dermatological assessment of an erythema-

tous, slightly scaling asymptomatic plaque spreading irregularly from the left nipple to



**Figure 1.** Erythematous, scaling plaque affecting the nipple/areola complex and the surrounding skin of the left breast



**Figure 2 A, B.** Dermoscopic examination (carried out with DermLite Pro HR; 3 Gen) shows a whitishpink area with polymorphous delicate dotted and irregular linear vessels partially organized in irregular nests separated by pale streak-like structures, fine scales at the surface and light brown diffuse pigmentation at the periphery of the lesion

the areola and the surrounding skin for more than a year (Figure 1).

Dermoscopy revealed a whitish-pink area with polymorphous delicate dotted and irregular linear vessels organized in irregular nests and separated by pale streak-like structures, with light brown diffuse pigmentation at the periphery of the lesion (Figure 2. A, B).

The nipple/areola complex with the underlying breast tissue was excised, fixed in buffered formalin and sent to the Pathology Department for examination. Histopathological findings on standard hematoxylin-eosin (HE) sections revealed large atypical neoplastic polygonal epithelial cells infiltrating the epidermis and infundibular region of hair follicles. The neoplastic cells were arranged in small solid groups and rare adenoid formations haphazardly distributed throughout the epidermis. The dermis displayed reactive changes including telangiectasia and chronic inflammation (Figure 3. A, B). Along with Paget's disease, multifocal in situ and invasive ductal breast carcinomas were found. Since the sentinel lymph node biopsy was positive, subsequent left axillary dissection was performed. Histopathological examination revealed metastatic carcinoma in additional 5 lymph nodes. Hormonal receptor status of the primary ductal carcinoma was as follows: estrogen receptors positive, progesterone receptors negative and human epidermal growth factor receptor type 2 (HER2/neu) strongly positive (3+).

# Discussion

MPD skin lesions are usually scaly, erosive or exudative eczema-like plaques of the nipple/areola complex, tending to spread to the surrounding skin and to cause destruction of the involved structures (1). Cases of pigmented MPD lesions have also been described. Patients may complain of itch or pain. Clinical presentation, therefore, poses a diagnostic problem since MPD may mimic a variety of inflammatory, microbial and neoplastic diseases, such as eczema, psoriasis, tinea, impetigo, lichenoid keratosis, erosive adenomatosis, Bowen's disease, basal cell carcinoma or even melanoma.

Besides the usual diagnostic procedures (a comprehensive history of the lesion, complete skin examination, microbial smear and culture from the skin lesion), it is advisable to use dermoscopy in further diagnostic work-up.

On dermoscopy examination, eczema and psoriasis present with yellowish to whitish scales and patchy or uniformly distributed dotted vessels, whereas Bowen's disease presents with scales and glomerular vessels (2, 3). In pigmented Bowen's disease, small brown globules regularly packed in a patchy distribution and structureless grey to brown pigmentation can also be seen (3). Errichetti et al. have reported dermoscopy findings in a case of erosive adenomatosis of the nipple: whitish/yellowish hyperkeratosis and sparse dotted vessels on a reddish-whitish background (4). The dermoscopic features of lichenoid keratosis vary, depending on the age of the lesion, so pinkish background, annular granular structures, gray pseudonetwork and diffuse blue-gray dots can be seen (5).

Typical dermoscopic features of basal cell carcinoma and melanoma are numerous and well described, pointing to the histologic type, tumor thickness and other prognostic factors (6, 7).

Pigmented MPD is a rare subtype, but extremely challenging, since it is dermoscopically indistinguishable from melanoma. Reports of pigmented MPD describe diffuse brown pigmentation, reticular pigmentation, irregular black dots, blue-gray dots, scar like depigmentation and streaks (8 - 10).

Dermoscopic patterns of classical nonpigmented MPD are often described as nonspecific. However, we have compared our observations to several other published cases (11 - 13) and noticed similarities among them, with correspondence to what we may expect in histopathology. Common features include a variable degree of pinkish background with polymorphous vessels that may represent dermal inflammation with irregular elongation of rete ridges and irregularly dilated capillaries typical for malignant neoplasms. Other common features are streak-like structures (described elsewhere as whitish reticulation, shiny-white streaks or chrysalis-like structures), separating aforementioned pinkishvascular areas and giving a partially lobular look to the lesion. It is our assumption that clusters of Paget's cells are more translucent than keratinocytes, depicting nests in the dermoscopy images. Streak-like structures could be reflections of uninvolved epidermis or fibrosis in advanced stages of the disease.

Following a diagnostic algorithm, if a suspicion of neoplastic lesion remains, biopsy with histopathological examination is required. The diagnosis of MPD is based on the presence of large epidermal Paget's cells with clear and abundant cytoplasm, pleomorphic and hyperchromatic nuclei and prominent nucleoli. These cells are usually clustered into solid nests and occasionally into glandular structures, mainly but not exclusively confined to the basal half of the epidermis. Intracellular mucin and acinar formation are helpful histopathological features favoring MPD over melanoma and Bowen's disease, the two most frequent diagnostic pitfalls (1).



**Figure 3 A.** Histopathologic findings on standard hematoxylin-eosin sections (HE,  $\times$  100): neoplastic large atypical polygonal Paget's cells with clear cytoplasm infiltrating the epidermis, arranged in solid groups; telangiectasia and chronic inflammatory infiltrate in the dermis

**Figure 3 B.** Histopathologic findings on standard hematoxylin-eosin sections (HE,  $\times$  200): neoplastic large atypical polygonal Paget's cells with clear cytoplasm infiltrating the epidermis and infundibular region of hair follicles, arranged in small adenoid formations; telangiectasia and chronic inflammatory infiltrate in the dermis

Inability of standard histopathological examination to distinguish the aforementioned entities demands immunohistochemical staining. Paget's cells show overexpression of low molecular weight cytokeratins, especially cytokeratin 7, but it had been observed that MPD has a similar immunohistochemical staining pattern and hormone receptor reactivity as that of the underlying breast carcinoma. The Paget's cells of the nipple are often HER2 positive (1, 14). Based on such findings, along with the presence of acinar arrangement of neoplastic cells, immunohistochemistry and receptor status of MPD were not performed in our case, since it would be irrelevant for the future therapeutic approach.

#### Conclusion

Timely recognition of MPD is of great importance, not only because it is a cancer, but because of a high probability of an associated, prognostically more serious ductal breast carcinoma. Dermatologists are usually first in line to face MPD, so they should use all the available tools in order to make a proper diagnosis. Dermoscopic features described in this case are in agreement with rare previous reports and may contribute to better differentiation of MPD from other clinically similar lesions. The spectrum of disorders entering the differential diagnosis can be narrowed by comparison of dermoscopic findings with other dermoscopically described entities and by clinico-dermoscopic correlation.

# Abbreviations

MPD - mammary Paget's disease DCIS - ductal carcinoma in situ

HE - hematoxylin-eosin

HER2/neu - human epidermal growth factor receptor type 2

# References

- Karakas C. Paget's disease of the breast. J Carcinog. 2011;10:31.
- Errichetti E, Stinco G. <u>Dermoscopy in general derma-</u> tology: a practical overview. Dermatol Ther (Heidelb). 2016;6(4):471–507.

- Zalaudek I, Argenziano G, Leinweber B, Citarella L, Hofmann-Wellenhof R, Malvehy J, et al. Dermoscopy of Bowen's disease. Br J Dermatol. 2004;150(6):1112-6.
- Errichetti E, Avellini C, Pegolo E, De Francesco V. Dermoscopy as a supportive instrument in the early recognition of erosive adenomatosis of the nipple and mammary Paget's disease. Ann Dermatol. 2017;29(3):365-7.
- Watanabe S, Sawada M, Dekio I, Ishizaki S, Fujibayashi M, Tanaka M. Chronology of lichen planus-like keratosis features by dermoscopy: a summary of 17 cases. Dermatol Pract Concept. 2016;6(2):29–35.
- Lallas A, Apalla Z, Argenziano G, Longo C, Moscarella E, Specchio F, et al. The dermatoscopic universe of basal cell carcinoma. Dermatol Pract Concept. 2014;4(3):121-4.
- Deinlein T, Arzberger E, Zalaudek I, Massone C, Garcias-Ladaria J, Oliveira A, et al. Dermoscopic characteristics of melanoma according to the criteria "ulceration" and "mitotic rate" of the AJCC 2009 staging system for melanoma. PLoS One. 2017;12(4):e0174871.
- Longo C, Fantini F, Cesinaro AM, Bassoli S, Seidenari S, Pellacani G. Pigmented mammary Paget disease dermoscopic, in vivo reflectance-mode confocal microscopic, and immunohistochemical study of a case. Arch Dermatol. 2007;143(6):752-4.
- Hida T, Yoneta A, Nishizaka T, Ohmura T, Suzuki Y, Kameshima H, et al. Pigmented mammary Paget's disease mimicking melanoma: report of three cases. Eur J Dermatol. 2012;22(1):121-4.
- Lee JH, Kim TH, Kim SC, Kim YC, Roh MR. Pigmented mammary Paget disease misdiagnosed as malignant melanoma. Ann Dermatol. 2014;26(6):747-50.
- 11. Crignis GS, Abreu Ld, Bucard AM, Barcaui CB. Polarized dermoscopy of mammary Paget disease. An Bras Dermatol. 2013;88(2):290–2.
- Oliveira A, Zalaudek I, Arzberger E, Massone C, Hofmann-Wellenhof R. Reflectance confocal microscopy for diagnosis of mammary Paget's disease. Acta Derm Venereol. 2016;96(7):980–2.
- Ozdemir F, Turk BG, Yaman B, Pellecani G, Ozdemir N, Karaarslan I, et al. Reflectance confocal microscopy of mammary Paget disease. Dermatol Pract Concept. 2017;7(4):75-80.
- Sek P, Zawrocki A, Biernat W, Piekarski JH. HER2 molecular subtype is a dominant subtype of mammary Paget's cells. An immunohistochemical study. Histopathology. 2010;57(4):564-71.

# Padžetova bolest dojke – prikaz slučaja

# Sažetak

Padžetova bolest dojke je redak intraepitelijalni karcinom koji zahvata strukture mamile i areole, često udružen sa duktalnim karcinomom dojke. Prikazujemo pacijentkinju staru 55 godina, sa klasičnim oblikom Padžetove bolesti i pridruženim duktalnim karcinomom iste dojke. Dermoskopskim pregledom uočeni su polimorfni krvni sudovi na beličastoružičastoj podlozi, organizovani u nepravilna gnezda koja su razdvojena bledim trakastim strukturama, a na periferiji lezije bledosmeđa difuzna pigmentacija. Dermoskopske karakteristike opisane u ovom slučaju u skladu su sa malobrojnim objavljenim prikazima i mogu doprineti boljoj diferencijaciji Padžetove bolesti dojke od klinički sličnih lezija.

**Ključne reči:** Padžetova bolest dojke; Kožne neoplazme; Dijagnoza; Bradavice; Neoplazme dojke; Dermoskopija; Prikazi slučajeva