European **Rev**iew for **Med**ical and **Pharmacol**ogical **Sci**ences 2021; 25: 4186-4187

Letter to the Editor

Paget's disease of the breast: strategy to improve oncological and aesthetic results

Dear Editor,

Paget's disease of the breast (PDB) is a rare clinical manifestation accounting for about 1-4 percent of overall presentations of breast cancer[1,2]; it is characterized by the persistence of some associated symptoms and signs, such as eczema, redness, ulceration, bleeding and often also itching of the nipple-areolar complex (NAC)[1,2]. PDB is usually unilateral even if some bilateral cases have been reported[3]. The essential requirement for a detailed diagnosis is the histopathological presence of malignant intraepithelial carcinoma cells (Paget cells) in the epidermis of the NAC[1,2].

The optimal management of this specific disease has been frequently debated over the years; we agree with Piras et al[4] that "actually, the standard treatment of PDB reflects oncological principles of breast carcinoma therapy, including the role of breast-preserving surgery". The Authors confirm in their systematic literature review that, in selected patients, breast conserving-surgery (BCS) followed by radiotherapy (RT) allows to achieve the same results as mastectomy[4].

However, we think that an adequate multidisciplinary knowledge of PDB and appropriate surgical expertise are essential tools in order to reduce the risk of local failure and improve aesthetic outcomes; technical skill but also repetitive performance of specific tasks are mandatory in order to optimize the results, such as:

- careful preoperative evaluation by physical examination, ultrasonography and mammography should always be performed focusing on possible associated glandular abnormalities; we underline that PDB is associated with an underlying breast cancer (in situ and/or invasive) in up to about 80% to 90% of cases although often without an evident breast mass or mammographic abnormality[3,5]; therefore, breast Magnetic Resonance Imaging (MRI) is recommended in patients with PDB in order to define the true extent of disease and identify possible underlying occult breast cancer[1,2,5]; histopathological diagnosis must be early established by full-thickness punch or wedge biopsy of the NAC; nipple scrape cytology can also accurately diagnose PDB; a confirmatory biopsy is also needed for any suspicious breast lesion associated to PDB and identified by imaging[1,2].
- a multidisciplinary discussion, in a dedicated "Surgery Board" is crucial to choose the more appropriate local treatment tailored to the patient; BCS and RT should be considered the gold standard of local treatment when a nipple-areolar resection and wide local excision of any underlying carcinoma are able to obtain both acceptable cosmetic results and negative surgical margins[4,6,7]; innovative oncoplastic techniques with the remodelling of breast tissue and placement of clips within the excision cavity as a "landmark" to define the tumor bed and guide adjuvant RT should be used in BCS to optimize oncological and aesthetic outcomes[8,9]. Skin-sparing mastectomy with immediate reconstruction is indicated for PDB associated with extensive or multicentric carcinoma, inadequate margins after BCS, contraindications to adjuvant radiotherapy and patient preference[4,6,7]. Staging and surgical treatment of the axilla in PDB depends on the underlying cancer; sentinel lymph node biopsy (SLB) is not necessary when BCS is used to treat pure PDB or PDB associated with DCIS; SLB should be performed in the presence of PDB with underlying invasive cancer treated with breast-conserving surgery. If a mastectomy is planned, SLB is always recommended in order to avoid complete axillary lymph node dissection in case an invasive component is revealed at final pathology of the gland (mastectomy precludes subsequent use of SLB)[6,7].

Corresponding Author: Gianluca Franceschini, MD; e-mail: gianlucafranceschini70@gmail.com

- a multidisciplinary dedicated "Tumor Board" is mandatory to select the possible adjuvant treatments after surgery; whole breast radiation should be always performed in patients treated with breast conservation and a radiation boost should be considered for the site of the resected NAC and any associated resected cancer site[1,2,4]. The use of adjuvant systemic therapies in patients with PDB should be based on the stage and biological characteristics of the underlying carcinoma. There are no data to support the use of endocrine therapy in patients with PDB without an associated invasive cancer or DCIS[1,2].

In conclusion, we strongly believe that adequate knowledge, dedicated training for proper technical skills and repetitive performance of standardized tasks in a multidisciplinary pathway are the most useful tools to choose the best local treatment for PDB.

Conflict of interest

The Authors declare that they have no conflict of interests.

ORCID ID

Gianluca Franceschini: 0000-0002-2950-3395.

References

1) Yasir M, Khan M, Lotfollahzadeh S. Mammary paget disease. 2021 May 7. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan.
2) Sandoval-Leon AC, Drews-Elger K, Gomez-Fernandez CR, Yepes MM, Lippman ME. Paget's disease of the nipple. Breast Cancer Res Treat 2013; 141: 1-12.
3) Franceschini G, Masetti R, D'Ugo D, Palumbo F, D'Alba P, Mulè A, Costantini M, Belli P, Picciocchi A. Synchronous bilateral Paget's disease of the nipple associated with bilateral breast carcinoma. Breast J 2005; 11: 355-356.
4) Piras A, Boldrini L, Venuti V, Sanfratello A, La Vecchia M, Gennari R, Sortino G, Angileri T, Daidone A. Mammary Paget's disease and radiotherapy: a systematic literature review. Eur Rev Med Pharmacol Sci 2021; 25: 1821-1827.
5) Samreen N, Madsen LB, Chacko C, Heller SL. Magnetic resonance imaging in the evaluation of pathologic nipple discharge: indications and imaging findings. Br J Radiol 2021; 94: 20201013.
6) Helme S, Harvey K, Agrawal A. Breast-conserving surgery in patients with Paget's disease. Br J Surg 2015; 102: 1167-1174.
7) Trebska-McGowan K, Terracina KP, Takabe K. Update on the surgical management of Paget's disease. Gland Surg 2013; 2: 137-142.
8) Franceschini G, Visconti G, Masetti R. Oncoplastic breast surgery with oxidized regenerated cellulose: appraisals based on five-year experience. Breast J 2014; 20: 447-448.
9) Franceschini G, Terribile D, Magno S, Fabbri C, Accetta C, Di Leone A, Moschella F, Barbarino R, Scaldaferri A, Darchi S, Carvelli ME, Bove S, Masetti R. Update on oncoplastic breast surgery. Eur Rev Med Pharmacol Sci 2012; 16: 1530-1540.

.

G. Franceschini, R. Masetti

Fondazione Policlinico Universitario Agostino Gemelli IRCCS; Multidisciplinary Breast Unit, Department of Woman and Child Health and Public Health; Università Cattolica del Sacro Cuore, Largo Agostino Gemelli, Rome, Italy