PAGET'S DISEASE OF THE BREAST

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ABSTRACT

Paget's Disease of the Breast (PDB) is a type of adenocarcinoma that affects the areola-mammary complex. Its unusual presentation can be confused with inflammatory or dermatological conditions. PBD is associated with breast neoplasms and is characterized by the presence of Paget cells. There are theories about its origin, such as trophoepidermal and intraepidermal transformation. PDB is more common in women between 50 and 60 years old, usually associated with carcinoma in situ or invasive lesions. Diagnosis is difficult and can take years, requiring a biopsy for confirmation. Treatment involves surgery and radiotherapy, especially in advanced cases. Late diagnosis can impact the prognosis and quality of life of patients.

KEYWORDS: DIAGNOSIS; PAGET'S DISEASE MAMMARY; NEOPLASMS.

INTRODUCTION

Diseases with an unusual presentation are quite worrying in clinical practice and tend to cause concern in affected individuals, such as Paget's disease of the breast (PDB). This condition is characterized as a malignant entity with benign characteristics that affect the areola-mammary complex, being considered a type of adenocarcinoma, which may or may not be associated with cases of breast cancer (Figure 2)[1]. Its benign behavior can make early diagnosis difficult, as its presentation mimics inflammatory conditions or even dermatological disorders[2].

The name of the condition came from the discovery of James Paget, in 1874, who was a British surgeon and pathologist, who first described Paget's Disease with presentations in different places, which could be bone, mammary and extra mammary. Since the beginning of the discovery, there has been a correlation between the entity and neoplasms, such as the mammary gland[3]. Currently, PDB is known as a rare malignant skin condition of intraepithelial origin, characterized by the presence of Paget cells, which are large epidermal cells of adenocarcinoma, which lead to desquamation of the nipple epithelium[4].

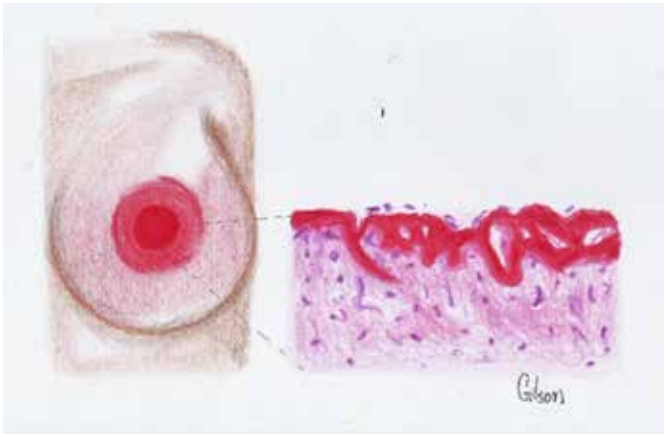

Figure 1 – Schematic representation of a breast with normal skin showing the layers of keratin, epidermis and dermis. Source: The author (2023)

Figura 2 - Desenho de mama esquerda apresentando Doença de Paget de aréola e mamilo. Fonte: O autor (2023)

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The presentation, usually confined to the nipple, is described as eczematous lesions in the periareolar region, which progress to bleeding or even growth of masses in the underlying tissues5. Thus, when faced with this pathological profile, many physicians mistakenly end up diagnosing the lesion as benign dermatitis, which can delay treatment and worsen the prognosis of young women[6]. The extra mammary or mammary description refers only to the site of appearance of the lesions, however, the histopathological examination reveals vacuolated squamous cells with bluish cytoplasm, which are highly infiltrated and diffuse[7].

Thus, the present study aimed to review some concepts related to Paget's disease, such as pathophysiology, epidemiological profile, tools for diagnosis and treatment.

PATHOPHYSIOLOGY

There are currently theories to explain the appearance of Paget's Disease, however, there are still factors that still do not make clear what the real explanation for the appearance of this condition is.

a) TROPHOEPIDERMAL THEORY

The trophoepidermal or epidermotropic theory concerns the transformation of Paget cells, which originate in the duct of apocrine glands, into underlying ductal carcinoma cells that migrate to the epithelial tissue of the nipple through the basement membrane[8]. This theory is supported by the high incidence of PDB in people with ductal carcinoma in situ and by the high level of expression of the HER2/neu oncogene in Paget[4] cells, suggesting that keratinocytes synthesize heregulin-alpha, a motility factor that attracts Paget for nipple[3].

b) INTRAEPIDERMAL ORIGIN OR TRANSFORMATION THEORY

It is suggested that the Paget cell is a pluripotent keratinocyte that has gone through the process of malignancy. This suspicion arises from the rare cases in which there is no malignancy adjacent to the nipple tissue[8]. This theory is based on the morphological similarity of Paget cells and Toker cells (benign epithelial cells of sebaceous glands present in the areolar skin in 10% of women)[4].

Figure 3 – Paget's disease in the left breast, showing erythematous squamous plaque affecting the entire areola and nipple, exceeding the areolar limits.

EPIDEMIOLOGY

The epidemiological profile of PDB seems to be related to female patients, aged between 50 and 60 years, with a worse prognosis when the condition occurs in males9. PDB can appear in isolation, without association with other conditions, however, in most cases, in about 32 to 41% of cases, there is a correlation with carcinoma in situ or more invasive lesions10. It is present in 1 to 3% of cases of primary breast cancer, with 93 to 100% of these associated with underlying breast cancer, commonly in central and multifocal tumors, predominantly located near the areola[4].

Figure 4 – Right breast eczema showing desquamative lichenified plaque partially affecting the nipple-areolar complex. Treated with topical corticosteroid therapy. Source: The author (2023).

DIAGNOSIS

Because it is a rare and poorly studied condition, PDB is difficult to diagnose, and it can take years for a professional to identify and treat the disease correctly. In the literature, there are reports of cases that had a delay between 10 and 15 years in diagnosis[7]. Initially, PDB appears as an irritation, rash or crack in the nipple, which may take months or years to reach the areola and periareolar region, evolving as an erythematous and scaly disease11. In more advanced cases, there may be skin ulceration and nipple retraction, the latter being a pathognomonic sign of PDB[11]. There may also be cases of hyperpigmented lesions that can be confused with melanomas[8].

Therefore, PDB is commonly identified with eczema, dermatitis or psoriasis, leading to an ineffective topical treatment, which delays the diagnosis of the disease. Therefore, to avoid misdiagnosis, when faced with eczematous, pigmented, crusted lesions or with signs of chronic inflammation in the nipple, the most appropriate conduct is to perform a biopsy[4].

The nonspecific presentation, associated with the epidemiology of the disease, makes diagnosis difficult in most cases. For this reason, the protocol for diagnosis should begin with a good physical examination, performing inspection maneuvers and palpation of the breast tissue

and, in this case, the areolas and nipples. Inspection begins with the assessment of lesions that may or may not be clearly present. For this, the use of a dermoscope is indicated for enlargement of the area and careful investigation. However, the final diagnosis must be made by collecting material for histopathological analysis. As previously described, in the case of PDB, vacuolated squamous cells with diffuse tissue invasion and bluish cytoplasm will be seen, thus characterizing the presence of Paget cells[4,7].

TREATMENT

The surgeries are mainly indicated when there is an association of PDB with in situ carcinomas, and breast segmentation may be performed in case of early diagnosis. However, due to epidemiological characteristics and late diagnosis, in many cases radical treatments are required, such as mastectomy, followed by radiotherapy for better prognosis of patients[11].

Segundo a revisão sistemática de Lin et al (2022), mastectomia ou cirurgia conservadoras da mama associado ao tratamento radioterápico obtiveram os melhores prognósticos em relação à reincidência, metástase e taxa de mortalidade[12]. Porém, a abordagem conservadora sem radioterapia obteve uma taxa significativa de recidiva para DMP, sendo recomendado principalmente a associação dos tratamentos quando há presença de lesões de carcinomas in situ ou de perfil invasivo[12].

According to the systematic review by Lin et al (2022), mastectomy or breast-conserving surgery associated with radiotherapy treatment obtained the best prognosis in terms of recurrence, metastasis and mortality rate12. However, the conservative approach without radiotherapy obtained a significant rate of relapse for PDB, and the combination of treatments is mainly recommended when there are carcinoma lesions in situ or with an invasive profile[12].

CONCLUSION

It can be concluded, therefore, that the difficulties in diagnosing PDB are mainly related to its clinical presentation, as well as to the epidemiological profile of the condition. These factors may hinder treatment with more conservative approaches and directly impact the quality of life of patients. Thus, when diagnosed late, the therapeutic association between surgical and radiotherapeutic methods is strongly recommended.

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