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Pagets Disease of the Breast

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Abstract

Background: Paget's disease of the breast also called mammary Paget's disease [MPD] was first described by Sir James Paget an English surgeon and a medical pioneer in the 19th century in 1874. In his report, fifteen women with a chronic eczematous disease on the skin of the nipple and the areola also had an associated intra ductal carcinoma of the underlying mammary gland. It is a rare type of cancer that develops in the skin of the nipple, and sometimes the areola, for this reason patients tend to take it less seriously. **Conclusion:** The treatment for Paget's disease of the breast typically involves surgery, usually a mastectomy or breast conserving surgery with radiation, and effective chemotherapy or hormone therapy, depending on the underlying cancer's characteristics.

Keywords

Clinical Characteristics, Pathological Features, Treatment Modalities, Mammary Paget's Disease

1. Introduction

Paget's disease of the breast also called mammary Paget's disease [MPD] was first described by Sir James Paget an English surgeon and a medical pioneer in the 19th century in 1874. In his report, fifteen women with a chronic eczematous disease on the skin of the nipple and the areola also had an associated intraductal carcinoma of the underlying mammary gland. It is a rare type of breast cancer that develops in the skin of the nipple, and sometimes the areola, for this reason, patients tend to take it less seriously. The pathogenesis of mammary Paget's disease

continues to be deliberated. Two theories have been proposed: The epidermotropic theory which states that pagetoid cells are ductal carcinoma cells that migrated from the underlying breast parenchyma to the nipple epidermis. The in-situ transformation theory states that the pagetoid cells arise as malignant cells in the nipple epidermis, independent of another pathologic process within the breast parenchyma. This theory explains the Paget's disease without mass [1]. Diagnosis of MPD involves clinical evaluation, radiological investigations and histological confirmation of pagetoid cells. Treatment varies, initially requiring mastectomy, systemic therapy and radiotherapy. Treatment has evolved markedly to involve breast-conserving surgery, hormone and targeted therapies like HER2 where necessary [1]. This review will describe clinical characteristics, pathological features and treatment modalities of the MPD with highlight of some of our managed patients.

2. Methods

2.1. Epidemiology

It is reported in 1% - 3% of all primary breast cancers [2]. About 93% - 100% of MPD cases are associated with underlying breast cancer, usually centrally located close to the areola and often with multiple foci [3]. It is often associated with carcinoma *in situ* and/or invasive carcinoma of the breast [4]. MPD is often commoner in postmenopausal women in their sixth decades of life, though can be seen in adolescence and elderly patients [5]-[7].

2.2. Clinical Features

Mammary Paget's disease is insidious in onset and appears as a thickened, sometimes pigmented whipping lesion on the nipple, may extend into the areola in centrifugal growth pattern and in advanced cases may involve the surrounding skin (**Figure 1**). The changes and redness at onset may be mistaken for eczema [4] [8] [9]. Hyper pigmented lesions similar to superficial spreading melanoma have been reported. [3] MPD can also be seen in males but the prognosis is worse compared to females [3] [5] [9]. The lesion is unilateral but rarely bilateral, and may occur in ectopic and accessory nipples [6] [10] [11] [12]. A palpable underlying centrally located lump is seen in 93% - 100% and multifocality of the underlying carcinoma is between 42% to 63% in various studies [13] [14]. Chaudhary *et al.* reported that 455 of all palpable invasive cancers associated with MPD in their series were found at the upper outer quadrant [15]. Axillary lymph node enlargement may be seen in MPD with lumps [14]. MPD can be identified incidentally in the pathology of a resected mastectomy specimen [4].

2.3. Radiological Features

Bilateral mammography [MMG] will show suspicious lesions like masses, micro calcifications, multi-focal lesions and architectural distortions due to multicentricity. [16] [17] The sensitivity of MMG seems higher in the presence of a palpable

(a) (b)

Figure 1. Clinical appearance of MPD.

mass [16]. In a study MMG identified occult cancer in 8 (15%) out of 52 patients with Paget's disease [17]. In another study, 65% of MPD patients with negative MMG had an underlying unifocal cancer [18].

2.4. Pathological Features

This pathological features and immunohistochemical analysis help in the diagnosis of MPD. Commonly confirmed markers cytokeratin 7 (CK7) and Mucin 1 (MUC1) [1]. Histological sections show stratified squamous epithelium that is intensely infiltrated by malignant epithelial cells. The cells are large, hyper chromatic with marked nuclear pleomorphic, irregular nuclei with prominent nucleoli and abundant pale cytoplasm. The underlying dermis is infiltrated with mononuclear inflammatory (**Figure 2**). These cells may contain mucin and foamy cells with pale cytoplasm and hyper chromatic nuclei when stained with hematoxylin and eosin [19] [20].

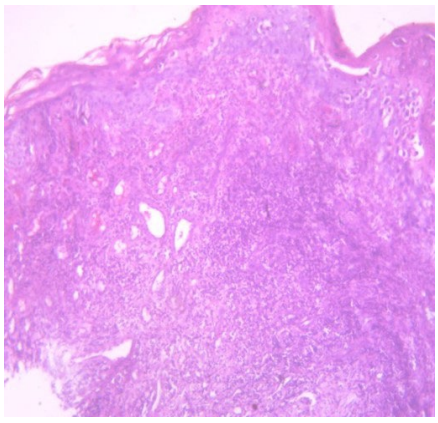

Figure 2. Microscopy of MPD.

2.5. Some Treated Case Scenario

Patient 1 A 62 years old woman with itchy, discharge and superficial ulceration of left breast. Clinical evaluation confirmed nipple erosion with no palpable lump. Wedged biopsy with histology was consistent with Paget's disease, mammography didn't reveal any lesion. Immunohistochemistry shows hormone receptor positive

Treated by neoadjuvant chemotherapy, excision biopsy, radiotherapy, and hormone therapy. Currently on follow-up clinic visits.

Patient 2 A 60 years old woman itchy, superficial ulceration and hyper pigmented right breast. Clinical evaluation revealed an underlying palpable breast mass of 3 cm by 4 cm in diameter. Wedge biopsy with histology was consistent with Paget's disease, mammography showed underlying breast mass and discreet ipsilateral axillary lymph nodes. Immunohistochemistry is hormone receptor positive.

Treated with neoadjuvant chemotherapy, modified radical mastectomy, adjuvant chemotherapy, radiotherapy, and hormone therapy.

On follow-up clinic visits.

Patient 3 A 70 years old woman with itchy, dry scaly, superficial ulcerated hypo and hyper pigmented left breast nipple and areola region. Clinical evaluation confirmed nipple erosion with no palpable lump. Wedged biopsy with histology was consistent with Paget's disease, mammography didn't reveal any lesion. Immunohistochemistry shows hormone receptor positive

Treated by neoadjuvant chemotherapy, excision biopsy, radiotherapy and hormone therapy. Currently on follow-up clinic visits.

3. Discussion

Paget's disease of the breast represents 3% of breast cancer types, diagnosis and treatment vary [2] [20]. Presentation varies too as this pathology can come with or without an underlying mass. Some of the clinical features are more constant like, itchy, ulceration and pigmentation whether hyper- or hypo- depending on skin colour of the patient as seen in our patients and other studies [5] [20]. Confirmation of diagnosis is by histology of the biopsied tissue. Wedge biopsy is preferred over fine needle aspiration, brush and punch biopsies as it is likely to represent all levels of the tissue layers as done in our patients [20] [21]. The use of immunohistochemistry is also necessary to enhance diagnosis, receptor status, and further treatment plans as obtainable in our patients [22]. Treatment is multi modal and multidisciplinary, though varies, with surgical treatment the most inconsistent. In the past mastectomy with/without axillary dissection was given even in the absence of clinical evidence of malignancy [20] [21]. Currently patients are treated with other forms of surgical oncological options as long as the patient merits it, like wide local excision, breast conserving surgery and mastectomy are all standard options of surgical treatment as offered to patients in our centre [20]. These patients also benefit from radiotherapy, chemotherapy and hormonal treatment if their tumor is hormone receptor positive. MPD with underlying breast

lumps are staged and managed based on the stage of the invasive cancer. MPD are followed up on clinic visits.

Prospectively, studies have shown that those patients with MPD without DCIS or invasive cancer stand a chance to benefit from reconstructive surgeries of nipple reconstruction like nipple tattoos, nipple creation using tissue from other parts of the body or prosthesis without affecting local recurrence or survival rates [23].

4. Conclusions

The treatment for Paget's disease of the breast typically involves surgery, usually a mastectomy or breast conserving surgery with radiation, and effective chemotherapy or hormone therapy, depending on the underlying cancer's characteristics

Ethics Statement

Authors declare that a written informed consent was obtained from the patients for the publication of these cases.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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