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Clinical abnormalities of the nipple-areola complex: The role of imaging



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KEYWORDS

Breast; Nipple; Abnormality; Tumor Abstract Clinical examination of the nipple is part of normal breast screening procedures. Abnormal processes of benign or malignant nature may be reflected by erythema, erosion, swelling or acquired inversion. In patients presenting with a persistent unilateral nipple lesion, it is advisable to collect a sample to exclude Paget's disease of the nipple, a rare form of ductal carcinoma *in situ* (DCIS). Imaging should be performed to detect breast cancer, which is found in more than 80% of cases, and determine its possible multifocal nature. Breast MRI is indicated if breast-conserving surgery is planned. The main differential diagnoses are erosive adenomatosis and eczema of the nipple. Acquired inverted nipple is generally of inflammatory origin. It is usually diagnosed by conventional breast examination but breast MRI can be helpful when in doubt about possible underlying neoplasia.

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Introduction

Clinical assessment of the nipple-areola complex (NAC) is a normal part of breast screening procedures. Clinical changes such as erythema, erosion, swelling or retraction of the breast may be signs of a process of benign or malignant nature. Radiologists should therefore be familiar with the main diagnoses that can be made as well as the imaging findings for each condition.

We shall successively review the conditions that cause superficial changes to the NAC and acquired nipple inversions.

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Abbreviations: EAN, erosive adenoma of the nipple; NST-WHO 2012, Invasive carcinoma of no special type according to the 2012 WHO Classification; MRI, magnetic resonance imaging; NAC, nipple-areola complex; DCIS, ductal carcinoma *in situ*.

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Superficial changes of the nipple-areola complex

Paget's disease of the nipple

Paget's disease of the nipple is often diagnosed at a late stage; 6 to 12 months after the first symptoms appear. Lesions are practically always unilateral. At an early stage, the nipple is pruritic, then becomes bright red and shiny. At an intermediate stage, the nipple becomes thicker, rougher and scaly. Late stage Paget's disease manifests as nipple erosion, with oozing ulceration and indurated crusting with clearly defined borders. Concurrently, the nipple gradually flattens. The nipple extends centrifugally and very gradually towards the areola (Fig. 1a-d). Bloody and/or serous nipple discharge or the presence of a palpable lump is associated with the condition in one to two thirds of cases [1-5].

Diagnosis can be made by scrape cytology of the nipple but nowadays nipple-areolar punch biopsies are performed more and more frequently because they provide more representative samples [6] (Fig. 2a–d).

Temporary improvements have been reported, as have pigmented forms that mimic malignant melanoma [7]. In such cases, surgical biopsy should be favored over punch biopsy.

Paget's disease of the nipple is characterized by infiltration of the nipple epidermis by DCIS cells. It accounts for less than 3% of all breast tumors [1,2]. Depending on patient populations, the average age at diagnosis ranges from 51 to 70 years (extreme values of 24 and 90 years) [3–5].

Histopathological assessment reveals the presence of Paget cells within the epidermis of the nipple (large cells with clear cytoplasm and large irregularly-shaped hyperchromatic nuclei that are frequently undergoing mitotic division). Two theories have been developed to explain the origin of Paget cells: first, according to the migratory theory, Paget cells migrate from an underlying breast carcinoma. On the other hand, the transformation theory holds that epidermal keratinocytes become malignant independent of any other malignancy of the breast [8].

Paget's disease of the nipple is associated with underlying breast cancer in more than 80% of cases, both near to and at a distance from the NAC [2,4,5,8-10] (Figs. 3 and 4a-b). Carcinoma *in situ* accounts for less than half of the cases, and invasive carcinoma accounts for one to two thirds of cases [4,8,10]. Ductal carcinoma predominates [1,10], although all histological types can be observed.

Carcinomas associated with Paget's diseases are generally found to be more aggressive: their histological grade is often higher, and they are more often hormone-receptor negative and C-erb 2 positive (80% of cases) than cancers that are not associated with Paget's disease [5,9,11,12].

Three factors of poor prognosis have been described for Paget's disease: the presence of a palpable lump, lymph node involvement and the invasiveness of the associated breast cancer [2,3,11]. Nonetheless, a recent study demonstrated that, even when the pathological grade and prognostic factors are equivalent, the survival of patients with invasive carcinoma and Paget's disease of the nipple is lower than that of patients with invasive cancer but

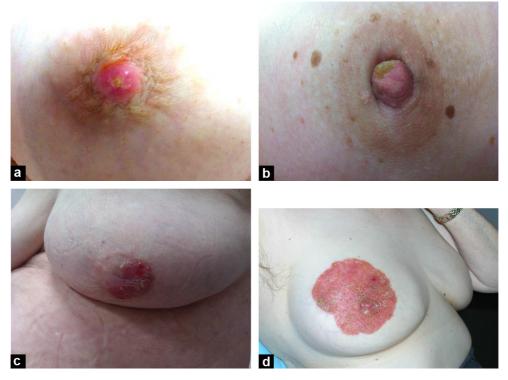


Figure 1. Different clinical stages of Paget's disease of the nipple: a: early stage: red, shiny nipple; b: intermediate stage: thickened, rough nipple; c: late stage: scaly, erythematous lesion with ulcerations and nipple flattening; d: very late stage: centrifugal extension of the nipple towards the areola, perfectly defined edges and entirely flattened nipple. Source: Imagerie de la femme, sénologie, Anne Tardivon, Éditions Lavoisier.

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