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Adenoma of the nipple: a mimic of breast malignancy

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Abstract

Adenoma of the nipple is a very uncommon benign neoplasm of lactiferous ducts. Its clinical presentation is variable and it can be easily misdiagnosed as a malignancy such as mammary Paget disease or breast intraductal carcinoma. Although dermoscopy and imaging tests such as ultrasonography or mammography can be of help, histological examination is mandatory to confirm the diagnosis. We describe the clinical, dermoscopic, and histopathological findings in a patient with nipple adenoma and discuss the clinical and histological differential diagnosis as well as the different treatment options.

Keywords: adenoma, breast, erosive adenomatosis, nipple, tumor

Introduction

Adenoma of the nipple (AN), previously known as erosive adenomatosis of the nipple or florid papillomatosis of the nipple, is a rare benign breast tumor which originates in the lactiferous ducts of the nipple. It commonly appears in women in their fourth or fifth decade of life and is exceptional in men and children [1,2].

Case Synopsis

A healthy 49-year-old woman presented to our outpatient department with a reddish nodule with a crust on the surface on the nipple of her right breast

(**Figure 1**). The lesion was painful with friction and had been present for several months. Physical examination revealed a firm and poorly delimited nodule with a rough surface. Dermoscopy showed white and yellow hyperkeratotic scales, pink-white clods and red structureless areas (**Figure 2**).

There was no evidence of nipple discharge or axillary lymphadenopathy. No palpable masses were detected in the breast and the patient denied family history of breast cancer. A wide incisional biopsy of the lesion revealed superficial papillomatosis and a proliferation of small ducts coated by a double layer of epithelial and myoepithelial cells and immersed in a desmoplastic stroma (**Figure 3A**). Focal squamous metaplasia was present. Cytological atypia was not



Figure 1. Clinical image showing a reddish firm nodule with a crust on the surface on the right nipple.



Figure 2. Dermoscopy shows white and yellow hyperkeratotic scales, pink-white clods and red structureless areas.

observed. Immunohistochemical staining with p63 confirmed the presence of myoepithelial cells in the ductal proliferation (**Figure 3B**). Mammography and breast ultrasound were performed to evaluate the extension of the lesion, showing normal breast tissue.

Case Discussion

Adenoma of the nipple clinically presents as a unilateral erosive nodule. It is often asymptomatic, but patients sometimes present with swelling and complain of itching, pain, and/or erythema. Serosanguinous discharge, although rare, results in the formation of a superficial crust [1-3]. In advanced stages or larger lesions the nipple may become nodular, firm, or even deformed [2].

From a clinical point of view, the differential diagnosis of AN is broad and includes multiple conditions; mammary Paget disease is the most important. Similar to AN, Paget disease can also present with serosanguineous discharge, erosion, and pain. However, the peak incidence is later in life (between the sixth and seventh decades of life) and approximately 50% of patients also present with an associated palpable mass in the breast. In this setting, although ultrasonography has proved useful in determining the diagnosis, histological

examination if still fundamental [4]. Other nipple diseases that should be included in the clinical differential diagnosis are atopic and contact dermatitis of the nipple, psoriasis, extragenital primary syphilis, lactiferous duct ectasia, herpes simplex virus infection, impetigo, nipple wart, and other rare benign tumors such as leiomyoma, neurofibroma, or fibroma of the nipple [1-3,5].

Dermoscopic findings of AN have only been described in four cases so far and differ among each other, which makes it difficult to establish a specific dermoscopic pattern. In general, the dominance of red and white color and regularity of vascular structures (red dots in linear, radial, or semicircular patterns) are the signs that can lead to the diagnosis of AN [2,6]. Therefore, dermoscopy can be a useful diagnostic tool and can help in the differentiation of AN from other nipple lesions such as Paget disease,

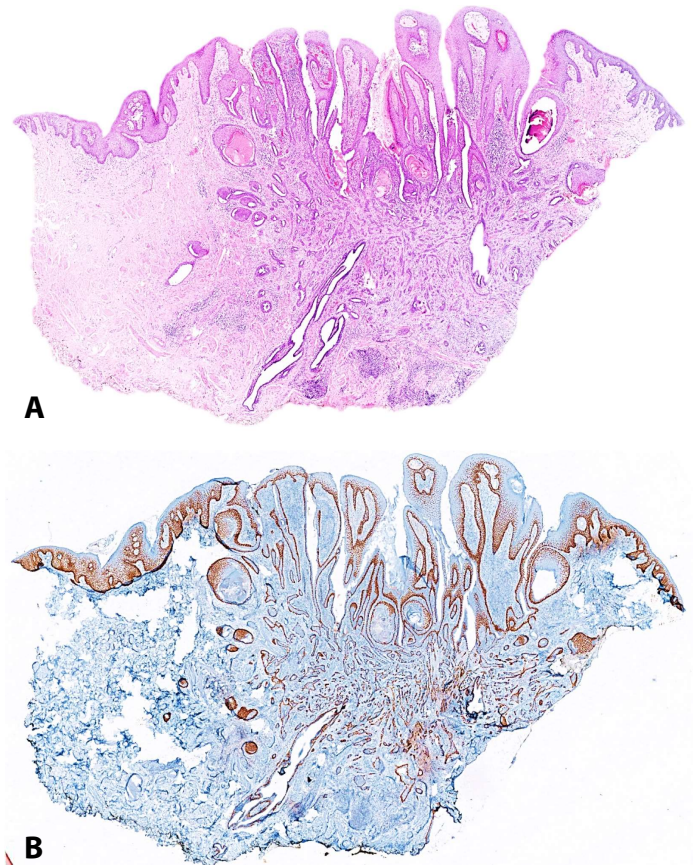


Figure 3. Histological images consistent with adenoma of the nipple. **A)** Superficial papillomatosis and a proliferation of small ducts, coated by a double layer of epithelial and myoepithelial cells, immersed in a desmoplastic stroma. H&E, 10 \times . **B)** Immunohistochemical staining with p63 highlights the presence of myoepithelial cells in the ducts, 10 \times .

in which light brown diffuse pigmentation, irregularly distributed blue-gray dots, irregular black dots, and irregular vessels can be found [6].

Histological examination is the gold standard for the diagnosis of AN. Histopathology reveals a glandular, relatively well-circumscribed, non-encapsulated proliferation in the dermal stroma of small and medium caliber ducts, coated by a characteristic double layer of cells, which are composed of an external layer of cubic or flattened myoepithelial cells and an internal layer of cuboidal or cylindrical epithelial cells, which can present apocrine secretory projections on its luminal border. Immunohistochemistry with myoepithelial markers such as p63, p40, h-caldesmon, calponin 1, α -smooth muscle actin, CK 5/6, or CD10 is helpful in highlighting the myoepithelial cell layer in the ducts [2,7]. Cytological atypia is rare. The overlying epidermis can show hyperkeratosis and acanthosis. Sclerosis/fibrosis may distort glands, mimicking an invasive growth pattern. Various growth patterns have been described: 1) the papillomatous pattern in which the ductal epithelium has a florid papillary hyperplasia with occasional mitosis; 2) the sclerosing papillomatous pattern, which has florid papillary hyperplasia and distorted architecture related to stromal fibrosis creating tubular, solid and glandular structures and giving the tumor a pseudo-infiltrating appearance; 3) the adenosis pattern, which consists of proliferating round glands with evident myoepithelial hyperplasia; and 4) the mixed proliferative pattern which is a combination of the three patterns [2,3,7,8]. Our case presented with histologic features consistent with the sclerosing papillomatous growth pattern.

Distinguishing AN histologically from in situ and invasive breast ductal carcinoma is paramount and must always be performed. The following histopathological findings support the diagnosis of AN: lack of cytological atypia, presence of two types of tubular epithelial cells, intraductal papillomatosis, symmetry, distinct circumscription, and superficial localization in the subareolar tissue. In this context, the use of p63 may be extremely useful as its expression is lost or may appear discontinuous in ductal carcinoma. Other possible entities that should be considered include syringomatous adenoma of

the nipple, intraductal papilloma, adenomyoepithelioma, and benign apocrine tumors such as syringocystadenoma papilliferum and hidradenoma papilliferum, though they differ from AN in their histological and anatomical localization [2,3].

The treatment of choice is surgical excision, with partial or complete resection of the nipple. Mohs micrographic surgery [9] and nipple splitting enucleation technique [10] can remove the tumor completely and preserve this important area cosmetically, functionally, and psychologically. Alternative treatment interventions include cryotherapy, cryosurgery, or radiofrequency, especially in those cases in which preservation of intact nipple tissue is preferred [1-3]. Local recurrence is not infrequent, especially in incompletely excised lesions or when conservative treatment methods are used.

Although the coexistence of AN and ipsilateral or contralateral breast cancer has been reported in the literature, this association is difficult to establish. Currently, it remains unclear as to whether AN represents a risk factor for the development of breast carcinoma or acts as a premalignant lesion [1-3]. The majority of authors believe that the probability of developing breast cancer in patients with AN is similar to that of the general population. Nevertheless, since this possibility cannot be fully excluded, regular follow-up after treatment is recommended in these patients [1,2].

Conclusion

Clinicians should consider AN as one of the conditions in the differential diagnosis in patients with an erosive nodule on the nipple. Histological examination is essential to rule out breast malignancies such as ductal carcinoma or Paget disease and avoid unnecessary and aggressive treatments. Although AN is not a malignant lesion, its association with breast cancer remains unclear. Therefore, it is important to follow these patients over time.

Potential conflicts of interest

The authors declare no conflicts of interest

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