Nipple Adenoma of the Breast: Case Report of Uncommon Benign Tumor and Brief Review of the Literature

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Abstract

Nipple adenoma is a very uncommon, benign proliferative process of lactiferous ducts of the nipple. It commonly presents unilaterally as a palpable nodule in the nipple or an erosive, scaly lesion of the nipple, with or without discharge. Resemblance to other conditions, such as Paget's disease of the breast, psoriasis, eczema or tumors of the breast can delay diagnosis. The gold standard for treatment is surgical excision; however, newer modalities such as Mohs microsurgery and cryotherapy have been used in limited cases. In this report, we present a case of nipple adenoma and a review of the current literature.

Keywords: Adenoma; Breast; Benign; Epithelial; Myoepithelial

Abbreviations

NA: Nipple Adenoma; IHC: Immunohistochemistry

Introduction

Nipple adenoma (NA) is an uncommon, benign lesion defined as 'a compact proliferation of small tubules lined by epithelial and myoepithelial cells, with or without proliferation of the epithelial component, around the collecting ducts of the nipple'[1].

NA presents most commonly in a middle-aged woman as a palpable nodule in the nipple with or without nipple skin erosion, crusting, inflammation, erythema, itching, and/or associated pain of the nipple region with or without discharge. The finding of serous and/or sanguineous discharge from the skin surface of the nipple profile is commonly reported as an initial presenting symptom and is generally secondary to the presence of a nipple skin erosive lesion [2]. Cases of nipple adenomas in men [3] and children [4-6] have been reported.

Resemblance to malignant conditions such as Paget's disease or adenocarcinoma, as well as dermatologic conditions such as psoriasis, eczema, allergic contact dermatitis, molluscum contagiosum, hidradenoma papilliferum, and syringocystadenoma papilliferum [7] can delay diagnosis.

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Treatment modalities include surgical excision, Mohs microsurgery, and cryotherapy [2]. Without treatment, nipple adenoma will continue to enlarge and cause local destruction of the nipple architecture [8]. Because this condition can be confused with malignancy, accurate diagnosis is important to prevent radical excision and unnecessary deformation of the breast [6].

Case Presntation

A 36-year-old woman presented with redness, and inflammation of the right nipple with itching and frequent non-bloody discharge. The patient reported no significant medical history of family history. Physical examination revealed a small indurated right nipple nodule. Mammography and breast ultrasound did not provide adequate information. Contrast-enhanced magnetic resonance imaging (MRI) suggested possible benign tumor with recommendation of tissue confirmation.

A multidisciplinary tumor board meeting recommended surgical excision of the nipple including the nodule with adequate safe surgical margins. The nipple was surgically removed followed by nipple reconstruction.

Microscopic examination of the excised nipple showed a dermal tumor infiltrating surrounding tissue measuring 0.8 cm (Figure 1A). The overlying skin showed hyperplasia with keratinization but no involvement by the adenoma. The proliferating tumor showed mixed pattern including papillomatosis and sclerosing papillomatosis giving pseudo-infiltrating architecture. Branched tubular structures with micropapillary epithelial hyperplasia were noted (Figure 1B). Tubules were lined by two cell layers. The cell lining did not show any evidence of atypia or malignant features (Figure 1C). Immunohistochemistry studies were utilized to assist with definitive diagnosis. The myoepithelial cells stained positive with P63 (Figure 1D) and M-actin (Figure 1E). The epithelial cells stained positive with cytokeratin CK 5/6 (Figure 1F). In addition, cytokeratin CK7 was positive highlighting the ductal

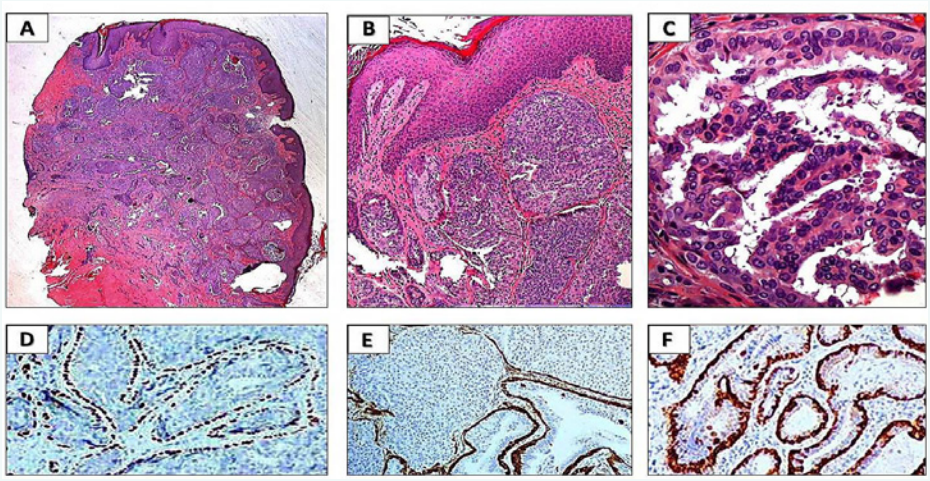

Figure 1 Microscopic examination of the excised nipple adenoma
1A: Dermal tumor infiltrating surrounding tissue measuring 0.8 cm (H&E stain x10)
1B: Mixed pattern including papillomatosis and sclerosing papillomatosis giving pseudo-infiltrating architecture (H&E stain x20)
1C: Tubules lined by two cell layers. The cell lining show no evidence of atypia or malignant features (H&E stain x40)
1D: Tumor cells positive for P63
1E: Tumor cells positive for M-actin
1F: Tumor cells positive for CK 5/6

epithelium. The histomorphologic features together with the IHC profile were diagnostic of a mixed type benign nipple adenoma, completely excised.

The patient was followed for 22 months with no complications or recurrence after which she was lost to follow up.

Discussion

Nipple adenoma (NA) is an uncommon, benign lesion defined as 'a compact proliferation of small tubules lined by epithelial and myoepithelial cells, with or without proliferation of the epithelial component, around the collecting ducts of the nipple [1]. 2012 WHO guidelines designates this condition nipple adenoma, however, in past literature it has been referred to as florid papillomatosis of the nipple ducts, erosive adenomatosis, as well as subareolar papillomatosis, and papillary adenoma of the nipple [9].

Clinically, it often presents as an indurated nipple nodule, a visible nipple skin erosive lesion, with or without serous or bloody discharge from the surface of the nipple skin. Nipple adenoma may mimic benign conditions such as allergic contact dermatitis, psoriasis, seborrheic keratosis, and infection. Nipple adenomas also bear histologic resemblance to sweat gland tumors, especially hidradenoma papilliferum and syringadenoma papilliferum [7]. More importantly, it may be confused with Paget's disease, keratoacanthoma, squamous cell carcinoma, or other unusual primary tumors of the nipple such as leiomyoma or mammary duct ectasia [5].

In the United States, breast cancer represents 29% of all new cancer diagnoses among women, second only to skin cancer [10]. Recognizing benign breast conditions, including those affecting the skin of the breast (like nipple adenoma), that can clinically and histologically mimic malignant conditions of the breast is therefore important to prevent radical excision and unnecessary deformation of the breast [6].

Due to the similarity in tissue density of the nipple to the surrounding skin and the underlying breast tissue, mammography and breast ultrasound cannot provide adequate information for confirming the presence of NA [2]. More advanced imaging modalities, such as breast magnetic resonance imaging (MRI), may be used to assess the extent of involvement of the tumor. The similarity in dynamic enhancement patterns between nipple adenoma and breast malignancy means the results of contrast-enhanced MRI should be interpreted with caution [8]. A biopsy is the gold standard for diagnosing NA.

According to the *WHO Classification of Tumors of the Breast* [9], the 4 most common recognized histological subtypes of NA are: (1) adenosis type, (2) epithelial hyperplasia or papillomatosis type, (3) sclerosing papillomatosis or pseudo-infiltrating type, and (4) mixed type. The adenosis type is localized to the dermis and shows proliferating glands extending from collecting ducts. This type lacks hyperkeratosis, inflammation, erosion, and/or ulceration. The papillomatosis type has hyperplasia of the collecting duct epithelia, forming solid tufts, and hyperplastic glandular ducts. The sclerosing papillomatosis type is characterized by a pseudo-infiltrating pattern with proliferating epithelium extending into the stroma. The papillomatosis type is most commonly misdiagnosed as Paget's disease, but the presence of two prominent cell layers, the absence of cytologic atypia, and the presence of intraductal papillomatosis means that adenocarcinoma and therefore Paget's disease can be excluded in most cases [7]. The presence of superficial keratocysts, intraluminal giant cells, intraductal papillomatosis, and the

absence of true papillae support a diagnosis of NA over sweat gland tumors [7].

Immunohistochemistry (IHC) studies can be used to demonstrate the presence of two cell layers (i.e., epithelial and myoepithelial cells). p63, calponin 1, h-caldesmon, CK5/6, CD10, or alpha smooth muscle actin and smooth muscle myosin are specific for identifying myoepithelial cells. Cytokeratin CK7 highlights the ductal epithelium and further supports a diagnosis of nipple adenoma [11].

Nipple adenomas are biologically benign and complete surgical excision is standard therapy. Successful management with minimally invasive procedures, including Mohs micrographic surgery or cryosurgery, has also been reported but was restricted only to cases that were detected early on [8]. Without surgical excision, nipple adenoma will continue to enlarge and cause local destruction of the nipple architecture [8].

Although nipple adenomas are most commonly diagnosed in middle-aged women, cases of men and children have been reported. Albers et al reported a case of an 8 year old girl who presented with multiple white and flesh-colored lesions, measuring 1-2mm, scattered across her trunk and limbs. The child's right nipple had a 4 mm, crusted, translucent papule. The initial diagnosis was molluscum contagiosum and the patient was treated with cantharidin. At follow-up, all lesions except the one on her nipple had resolved. A biopsy demonstrated that the remaining lesion was a nipple adenoma [5]. Clune et al reported the case of a 5-month old female infant presenting with a slowly enlarging nipple lesion. At the age of 23 months, a shave excision of the mass showed nipple adenoma [6]. Fujisawa et al reported a case of a 2 year old boy who presented with a firm, erythematous mass of the right nipple expressing serous discharge. Biopsy and subsequent excision confirmed a diagnosis of nipple adenoma [4]. Although almost all reported cases of nipple adenoma arose from central mammary tissue, Shioi et al described a case of nipple adenoma in axillary accessory breast tissue. In their case, an 82 year old woman presented with a well-defined, painful, eczematous 8 mm mass in her right axilla. Upon excision, histological examination showed branched tubular structures with micropapillary epithelial hyperplasia, consistent with a "mixed type" nipple adenoma [12].

Occasional cases of malignancy co-occurring with nipple adenoma have been reported. Burdick et al described a case of a 53 year old man who presented with a bleeding left nipple. Over 8 years, the patient was followed and the mass continued to enlarge, with occasional bloody discharge. Biopsy of the mass demonstrated a nipple adenoma with an adjacent, well-defined area of Paget cells [3]. Sasi et al reported the case of a 63 year old woman presenting to the clinic with an eczematous, crusted right nipple that was inverted and expressing yellow discharge. The patient had a history of left-sided ductal carcinoma in situ and nipple adenoma. Upon surgical excision, histopathological examination showed that the right breast had evidence of nipple adenoma making this a case of bilateral nipple adenoma with metachronous breast cancer in the left breast [13]. Although cases of nipple adenoma co-occurring with malignancy have been reported, the association between the two entities remains unclear. Regular follow-up with patients with a history of nipple adenoma is recommended to exclude breast cancer [8].

We hope that reporting this case will raise the awareness of pathologists and clinicians to include the nipple adenoma in the differential diagnosis of nipple lesions. Early proper diagnosis of this benign tumor is essential to prevent radical excision and unnecessary deformation of the breast.

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