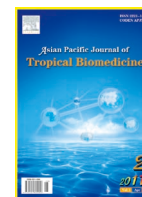




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## Intraductal papilloma of the breast in association with preoncogenic gene of breast cancer

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### ABSTRACT

We reported a case of an African American woman who went to the hospital with palpable right breast lump with bloody nipple discharge at University of Texas Medical Branch at Galveston. The modalities of breast imaging included mammography and ultrasonography. The method used for viral identification was Linear Array HPV genotyping test. Intraductal papilloma revealed as high density tubular or rounded lobular masses with partially circumscribed, obscured margins and clustered punctate microcalcifications on mammograms. Ultrasound showed as intraductal masses with dilated ducts. The core biopsy demonstrated duct filled with papillary lesion and post excision revealed intraductal papilloma. HPV DNA types 16, 33, 58 and 71 were detected after use of Linear Array HPV genotyping test.

## 1. Introduction

Breast cancer is the most prevalent cancer among women in the United States and the second most common cause of cancer death in women (after lung cancer). In 2007, breast cancer is expected to cause 40 910 deaths (7% of cancer deaths; almost 2% of all deaths) in the US[1,2]. Many risk factors have been associated with the pathogenesis of this disease, including family history, viral infection, environmental pollutants, hormones and alcohol consumption[3–8]. There is a strong inherited familial risk in only 5% of breast cancer case[9] with two autosomal dominant genes, BCRC1 and BCRC2. The association between the Human Papillomavirus (HPV) and cervical cancer is well-known and well-documented[10]. More recently, HPV has been shown to be present in 11%–86% of breast carcinoma, the number varying depending on racial, epidemiological factors and experimental factors[11]. In this report, we presented a case of benign intraductal papilloma which had HPV type 16 that can be possible opportunity of breast cancer.

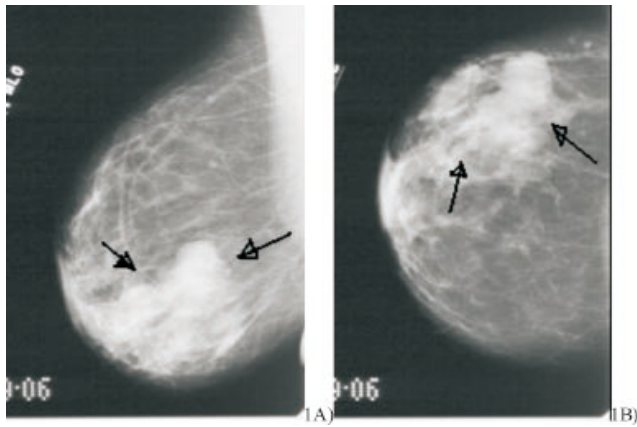
## 2. Case report

A 49– year old African American woman went to the hospital with palpable right breast lump with bloody nipple discharge. No family history of breast cancer was found. Physical examination showed retroareolar mass at 7 o'clock, measuring about 50 mm. She has been palpated her right breast mass since 1997, data record revealed subareolar mass with hard consistency and slightly mobile, size about larged bean. She was loss follow-up on that time.

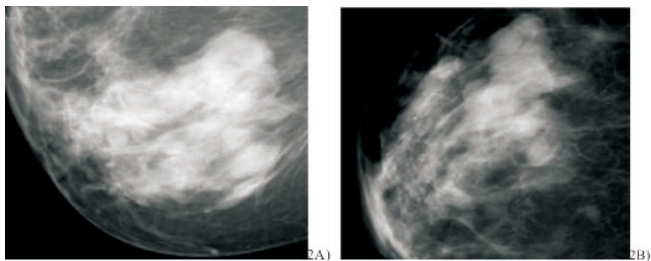
Mammograms demonstrated slightly high density tubular and rounded lobular masses with partially circumscribed, obscured margins measuring 50 mm involving in right lower outer quadrant (Figure 1A, 1B). On magnification views (craniocaudal and mediolateral projections) presented greater than ten clustered punctate microcalcifications scatter at lower outer quadrant (Figure 2). Ultrasound showed numerous intraductal masses and dilated ducts with dimension subcentimeter at the site of masses on mammograms (Figure 3A, B). The core biopsy revealed duct filled with papillary lesions. She underwent excisional biopsy with bracket wire-localization of the affected area. The pathological report demonstrated benign intraductal papilloma with associated post obstructive changes, cystic secretory hyperplasia associated with calcification (Figure 4). HPV DNA types 16, 33, 58 and 71 were also detected (Figure 5). There was no malignancy indentified.

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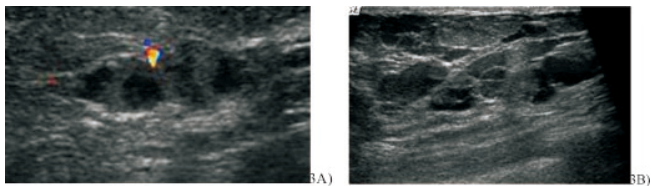
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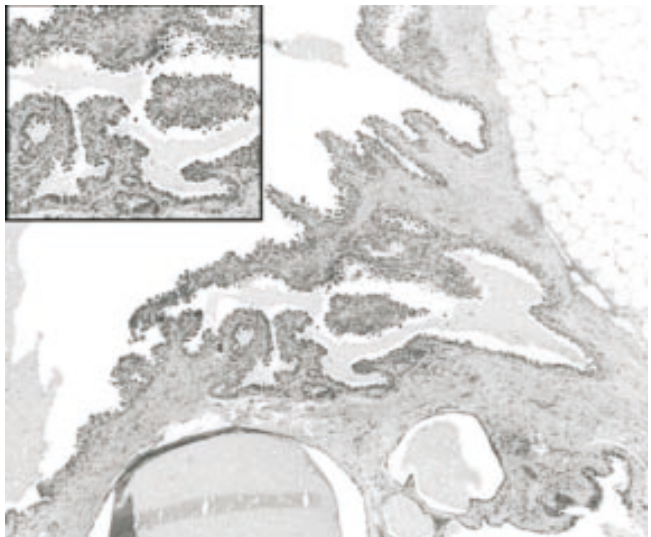
**Figure 1.** Mammograms of mediolateral (A) and craniocaudal (B). It showed a slightly high density tubular and rounded lobular masse with partially circumscribed, obscured margins, measuring 50 mm almost involving the entire lower outer quadrant of right breast.



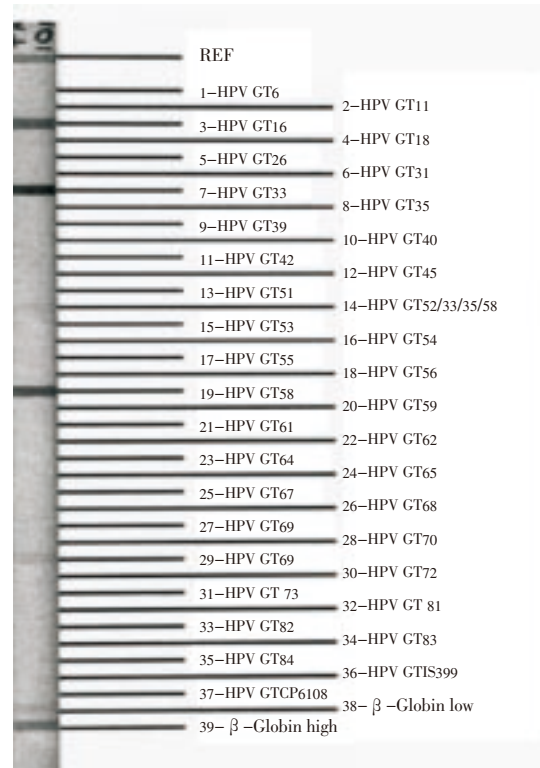
**Figure 2.** Right magnification views. Mediolateral (A) and craniocaudal (B) demonstrated multiple clusters of punctate microcalcifications at lower outer quadrant anterior and middle depth.



**Figure 3.** Ultrasonography revealed numerous intraductal lesions with dimation subcentimeter at the site of mammographic findings.



**Figure 4.** Photomicrograph of the intraductal papillary lesion showing multiple fibrovascular core and epithelial proliferation.



**Figure 5.** HPV genotyping was positive for genotypes 16, 33, 58, and 71.

### 3. Discussion

Human papilloma virus infections vary in United States of America, with one reviewed finding reported values anywhere from 14% to 90%[12]. It has been shown that HPV types 16 and 18 can immortalize normal breast epithelium[13]. This raised the possibility that HPV may be etiologically related to some cases of breast cancer. There is some evidence that breast carcinogenesis may in some cases be initiated or promoted by a viral agent. The relationship between virus and mammary tumors is known from induction of mammary cancer in mice with the mouse mammary tumor virus (MMTV)[14,15]. The intermediate DNA of MMTV can integrate into the genomes and perturb the activity of a proto-oncogene, inducing accelerated cell growth[14]. Particles similar to this mouse virus were also observed in human breast cancer tissue, indicating a possible viral etiology in human breast cancer[16]. More recently, a number of researchers have detected HPV DNA in breast carcinoma. A majority of these studies used paraffin embedded tissue samples of invasive carcinoma, benign lesions and normal tissue, and detected and typed the HPV DNA by PCR-based methods. These studies cover geographically and racially diverse populations[11,17-27]. The breast carcinoma cases that were found to be associated with HPV varied from 11% in the Japanese study[19] to 86% in the German study[20]. This correlation was relatively high up to 64% (seven out of 11) when the breast cancer patient had a known history of cervical carcinoma[28]. Six patients had the same HPV type (HPV-16) in cervical cancer, and in the corresponding breast cancer and/or axillary lymph node tissue[28]. HPV DNA might be transported from the original site of infection to breast tissue by the bloodstream, and may possibly be involved in the carcinogenesis of breast neoplasia in some patients[28]. The author believed of the direct contact of HPV to the nipple since there were many studies also detected the other

types of HPV DNA which not commonly seen from cervix. De Villiers *et al* and Yu *et al* also reported positive for HPV DNA in benign breast tumor<sup>[19–20]</sup>, but other reports did not. These maybe due to most published studies therefore used methods restricted to the detection of specific, single, or combinations or groups of HPV types. Only in the study of de Villiers *et al* was primer combinations used, which allowed the detection of a wide range of HPV types<sup>[20]</sup>.

We report a case of benign intraductal papilloma of the breast. HPV types 16, 33, 58 and 71 were identified by Linear Array HPV genotyping test, which can detect up to 37 different HPV genotypes. The HPV type 16 was the same as other reported of breast carcinoma<sup>[19,21,22,24–25]</sup>, indicating possible etiology or preoncogenic gene of breast cancer by this virus<sup>[14,16]</sup>. The HPV 33 was detected in this case found in benign breast tumor in Yu *et al*<sup>[19]</sup>. The HPV 58 and 71 had never reported in other studies also detected in our case. This case report also emphasized detection of papilloma virus infections in tissues largely depends on the method used<sup>[20]</sup>.

The HPV types 6, 11, 16, 18, 31, 33, 35, 39, 52 and 58 are frequently associated with genital lesions and are therefore most often targeted for HPV detection. The use of type-specific primers may increase the number of positive samples but is biased with regard to the HPV types involved, because other HPV types present cannot be detected<sup>[20]</sup>.

In conclusion, human papilloma viruses related to breast cancer are controversial. Although many studies supported the possibility of HPV associated with breast carcinoma. The presence of preoncogenic gene in our case probably illustrates the potential to have subsequent breast cancer and the patient should have been follow-up regularly after excision. Further larger epidemiologic studies are still indicated with the used of detected methods which have greater sensitivity and specificity.

### Conflict of interest statement

We declare that we have no conflict of interest.

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