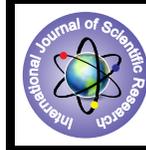


## Vulval Cancer in A Breast Cancer Survivor: Can Human Papilloma Virus (HPV) Be A Connecting Link?



### Medical Science

KEYWORDS : Vulval Cancer, Breast cancer, HPV

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### ABSTRACT

**Introduction:** The majority of molecular mechanisms in the genesis of breast cancer are not known. There is growing evidence to support the possible role of HPV in the development of breast cancer. On the other hand, the causal relationship of HPV to vulval cancer is well established. We hereby report a case of vulval cancer in a breast cancer survivor and propose that HPV might be the connecting link.

**Case report:** A 73 years old postmenopausal woman, a known case of breast cancer was referred to our Gynecological Oncology Department in August 2013 after excisional biopsy of her 1x1cm sized vulval lesion by her primary gynaecologist. Histopathology revealed high grade squamous cell carcinoma. She reported history of breast cancer two years back for which she underwent modified radical mastectomy with axillary lymph node dissection in Oct 2011. Histopathology showed intraductal carcinoma. She was staged as T2 N1 M0 and received adjuvant chemotherapy till March 2012. Mammo-sonography of her opposite breast done at that time showed two punctuate calcification in retroalveolar region which on Fine Needle Aspiration Cytology, revealed intraductal papilloma. She also reported history of total abdominal hysterectomy with bilateral salpingo-oophorectomy in September 2012 for an adenexal mass which was of benign histology. After work up, radical vulvectomy and bilateral groin dissection was done. Histopathology revealed squamous cell carcinoma in situ in 1.5 cm lesion around excisional biopsy (squamous cell carcinoma) site. She was staged as T1N0M0 cancer vulva and kept on observation. On two years of follow up, patient was alive and disease free.

**Conclusion:** HPV might be linked to vulval cancer development in the breast cancer survivor. Breast cancer survivors should undergo screening for premalignant cervical and vulval lesions during their follow up.

**Introduction:** The majority of molecular mechanisms in the genesis of breast cancer are not known. There is growing evidence to support the possible role of HPV in the development of breast cancer [1-4]. On the other hand, the causal relationship of HPV to vulval cancer is well established [5-7]. We hereby report a case of vulval cancer in a breast cancer survivor and propose that HPV might be the connecting link.

**Case report:** A 73 years old postmenopausal woman, a known case of breast cancer was referred to our Gynecological Oncology Department in August 2013 after excisional biopsy of her 1x1cm sized vulval lesion by her primary gynaecologist. Histopathology revealed high grade squamous cell carcinoma (Fig. 1)

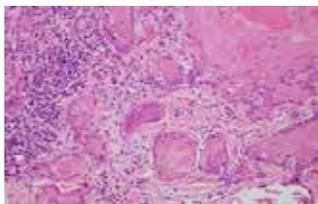


Fig 1. Squamous cell carcinoma vulva (H&E,10X)

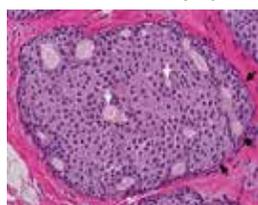


Fig 2. Intraductal carcinoma breast(H&E,40X)

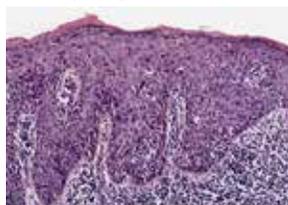


Fig 3. Vulval intraepithelial neoplasia III (H&E,10X)

She reported history of breast cancer two years back for which she underwent modified radical mastectomy with axillary lymph node dissection in Oct 2011. Histopathology showed intraductal carcinoma. (Fig. 2) She was staged as T2 N1 M0 and received adjuvant chemotherapy till March 2012. Mammo-sonography of her opposite breast done at that time showed two punctuate calcification in retroalveolar region which on Fine Needle Aspiration Cytology, revealed intraductal papilloma. She also reported history of total abdominal hysterectomy with bilateral salpingo-oophorectomy in September 2012 for an adenexal mass which was of benign histology. After work up, radical vulvectomy and bilateral groin dissection was done. Histopathology revealed vulval intra-epithelial III (Fig.3) in 1.5 cm lesion around excisional biopsy (squamous cell carcinoma) site. She was staged as T1N0M0 cancer vulva and kept on observation. On two years of follow up, patient was alive and disease free.

**Discussion:** Vulval cancer exists as two separate entities. The first type is associated with human papilloma virus infection which leads to vulval intra-epithelial neoplasia and finally, vulval cancer. Ngan HY detected HPV in 48% of vulval cancer specimens of which HPV type 16 and 18 were present in 96% of cases. The second type involves vulvar non-neoplastic epithelial disorders (VNED) and advanced age, leading to cellular atypia and cancer[5,8]. In this case report, histopathology showed vulval intra-epithelial neoplasia as well as vulval cancer. It is interesting to note that vulval intra-epithelial neoplasia associated vulval cancer is uncommon for the age group to which our patient belonged. However, this is the type of vulval cancer which is associated with HPV infection and lead us to suspect that vulval cancer in our case might be HPV associated.

Breast cancer is the second most common cancer in women in India and is showing a fast rising trend in major metropolitan cities in India [9]. Majority of molecular mechanisms involved in breast cancer are not known. A causal relationship between HPV and breast cancer has been suggested [1,10,11], and a review of 20 studies shows that nearly a quarter of breast carcinomas tested for HPV were HPV-positive [12]. Recent studies suggest the association of HPV infection with breast cancer pathogenesis. Type 16, 18 and 33 have been isolated in various studies [1,10,11]. Heng et al. reported the association of HPV 16 in 46% of breast carcinomas in patients with a history of CIN III lesions [10].

Mechanism of transmission of virus to breast is not clear. One possibility is transmission of virus from ano-genital organs to the breast due to altered sexual practices. Earlier studies have indicated that it could be due to hematogenous route [13-17]. It could be related with changes in the level of expression of integrins, particularly with that of the  $\alpha$ -6 integrin [18], and also of Heparan sulfate proteoglycans (HSPG) [19], which are putative candidates for HPV cell receptors [20].

In the light of recent evidence and from the studies of pre-cancerous cervical lesions, we extrapolate that HPV might be the connecting link in the development of vulval neoplasia in our breast cancer survivor patient. In an era of increased awareness and better diagnostic and therapeutic facilities, more of breast cancer survivors are seen. We suggest screening for cervical and vulval cancer during their follow up. We also suggest breast cancer screening in patients with cervical and vulval premalignant and malignant lesions.

**Conclusion:** HPV might be linked to vulval cancer development in the breast cancer survivor. Breast cancer survivors should undergo screening for premalignant cervical and vulval lesions during their follow up.

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