

Synchronous of breast and vulvar Paget's disease: a case report

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Summary

Background: Synchronous Paget's disease of breast and vulva is extremely rare and has only been reported in the literature in one other case. **Case:** A 58-year-old postmenopausal woman was found to have crusting, bleeding, and discharge from left nipple, as well as vulvar pruritis at the same time. Biopsy of breast lesion demonstrated Paget's disease with an underlying foci of ductal carcinoma in-situ that required total mastectomy of left breast with sentinel node biopsy and breast reconstruction. For vulvar symptoms, the patient was initially diagnosed with dermatitis and topical ointment was prescribed. However, her symptoms persisted for the next several months, and she underwent vulvar biopsy that demonstrated Paget's disease. She underwent partial vulvectomy. Multiple episodes of recurrent vulvar Paget's disease were noted in the postoperative course that medical therapy with Imiquimod and a second partial vulvectomy was performed. **Conclusion:** Synchronous of breast and vulvar Paget's disease is presented. There was a delay in diagnosing vulvar Paget's disease in this experienced case. While coincidence of breast and vulvar Paget's disease is likely, ectopic mammary tissue in vulvar as well as secondary metastasis from a focal lesion of breast Paget's disease needs to be carefully evaluated whenever the patient complains of vulvar symptoms in the setting of breast Paget's disease.

Key words: Paget disease; Vulvar; Breast; Mammary; Synchronous.

Introduction

Mammary Paget's disease (MPD) is an adenocarcinoma localized within the epidermis of the nipple and/or areola and is typically associated with an in-situ or invasive carcinoma of the underlying breast tissue [1, 2]. Extra-mammary Paget's disease (EMPD) could be found in vulvar, perianal, or axillary regions, but is most commonly found in the vulvar region of postmenopausal Caucasians with ages around 65 to 70 years [1, 2]. EMPD shares histologic similarities with MPD, in that they both may be found within the epithelial sheaths of hair follicles, sweat gland excretory ducts, or secretory coils and they are characterized by large cells with clear cytoplasm, prominent nucleoli, and potential for invasion into the dermis [1, 3]. Although MPD has been found to be in association with underlying carcinoma in 67 to 100% of cases [4], EMPD is less often reported to be associated with underlying neoplasm [1, 3-11]. Co-incidence of MPD and EMPD are extremely rare clinical entity. To date, there have been only five reported cases of Paget's disease present in the breast and vulva of the same individual [3, 5]. Among these five cases, there is only one report demonstrating synchronous presence of breast and vulvar Paget's disease [5], highlighting possible lack of awareness of the two conditions that may possibly co-exist. Here, the authors report a case of synchronous MPD and EMPD where the diagnosis of vulvar Paget's disease was delayed and developed multiple recurrences.

Case Report

A postmenopausal 58-year-old Caucasian female, gravida 3 para 3, presented for gynecologic care with the chief complaint of occasional external vulvar pruritis for two to four months, as well as crusting, discharge, and bleeding from left nipple which did not resolve with treatment for presumptive eczema by primary care physician. She stated that these symptoms in vulvar and breast developed simultaneously. Past medical history was significant for prolonged QT syndrome, hypercholesterolemia, migraine headaches, and arthritis. Past surgical history included tubal sterilization, partial thyroidectomy, uterine curettage, and cold knife conization for cervical dysplasia. Family history was significant for breast cancer in her maternal grandmother. She did not smoke cigarettes, was on no special diet, and reported occasional alcohol use. Her last mammogram was one year prior to the visit and results were within normal limits. On initial physical examination, she had mild vulvo-vaginal atrophy and no external vaginal lesions were visualized. At time of initial presentation, she was being evaluated for possible MPD and underwent wedge biopsy of the left nipple.

Pathology evaluation of the breast biopsy revealed Paget's disease with an underlying foci of ductal carcinoma in-situ (DCIS) involving underlying ducts with grade 2 nuclear atypia and associated ulceration with granulation tissue. Immunohistochemistry was marked for negative staining for both estrogen and progesterone receptors. She was taken to operating room, and total mastectomy of left breast with sentinel node biopsy and breast reconstruction was performed without complication. Pathological evaluation of breast tissue confirmed Paget's disease of the nipple with no invasive tumor and negative lymph nodes. During her postoperative course, she kept complaining of continued right labial irritation that had not improved. The patient sought the second opinion for the evaluation of vulvar symptoms. On physical examination, right proximal labia majora was irritated, ulcerated, and erythematous with a white

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patchy lesion measuring approximately three cm. Biopsy of right labia showed EMPD with positive immunohistochemistry staining for mucicarmine, PAS-F, CEA, and CK7.

The patient was taken to the operative room and partial vulvectomy was performed and entire lesion was removed with a one cm margin. Pathology evaluation showed presence of Paget's disease in all surgical margins. No evidence of stromal invasion was seen at that time. She was placed on Imiquimod topical cream for five months for considering positive margin results. One year after vulvectomy, the patient was found to have a recurrence of EMPD proven by biopsy, with new erythematous lesions on the right periclitoral area and the left proximal labial near the labia minora. She underwent a second partial vulvectomy. Following two years after the second vulvectomy, she developed multiple recurrences in the vulvar and underwent two additional partial vulvectomy, as well as intermittent Imiquimod treatment. There was no sign of Paget's disease in contralateral breast.

Discussion

In 1998, Popiolek *et al.* reported the first case of synchronous Paget's disease of the breast and vulva diagnosed within a period of seven months of each other [5]. In this experienced case, a 58-year-old female presented with vulvar pruritis, as well as crusting, bleeding, and discharge from the left nipple, which were both found to be Paget's disease. To the knowledge of the authors, this is the second case of synchronous Paget's disease of the mammary and extra-mammary tissues that is unique in that the diseases in the two areas developed simultaneously. The coexistence of Paget's disease in breast and vulva is extremely rare, and thus, entirely incidental existence of the two conditions may be a possibility. While the concurrent nature of these two lesions is most likely unrelated, the authors propose two additional hypotheses: the first hypothesis is that ectopic mammary tissue in vulva may exist; and the second is that secondary metastasis occurred from a focal lesion.

EMPD is a slow-growing tumor and therefore may result in a delayed initial diagnosis. In addition, it has relatively non-specific characteristics such as a scaling, crusty, and rash-like appearance that may lead to delayed treatment due to diagnosis as an inflammatory or infective skin condition [2]. In the experienced case, symptoms of EMPD were presented at the initial time of diagnosis of MPD and the authors estimated that they arose within the same chronologic time period due to the existence of external vulvar pruritis for several months prior to the initial diagnosis of MPD. This case of synchronous Paget's disease is very unusual because it is difficult to pinpoint which neoplasm arose first. The MPD was diagnosed prior to the vulvar EMPD, however, the patient complained of symptoms of vaginal pruritis several months prior to being diagnosed with MPD. Therefore, the authors believe that simultaneous formation of Paget's disease in the two distinct areas of the body has occurred as well as coexistence of these two entities during the same time period. It is extremely rare for synchronous Paget's disease to occur and the authors specu-

late that this experienced case may be the first to be reported in which Paget's disease arose in two separate areas of the body at the same time.

To explain the simultaneous presentation of these lesions, the authors explored the possibility that either of the two may have been due to secondary metastasis. In general, vulvar Paget's disease is considered to be a localized and non-invasive lesion. In a retrospective review of tumor registries for Paget's disease of the vulva, only 8% were associated with an underlying adenocarcinoma and 10% were associated with invasive disease [8]. The presented patient did not have underlying adenocarcinoma and did not exhibit inguinal lymphadenopathy at any time from initial presentation and throughout all follow up exams. In addition, initial biopsy of the vulvar lesion showed no invasion of underlying tissue. When MPD is confined to the nipple, the survival for patients is typically promising. Patients with MPD who only have nipple changes have been shown to have a five-year survival rate of 90 to 100%, while those with palpable breast tumors are at increased risk for invasive disease and have a five-year survival rate of 20 to 60% [9]. In the presented patient, the MPD pathology report showed evidence of associated DCIS, with no invasion of underlying tissues and negative lymph nodes on sentinel node biopsy. The pathology reports from either lesion do not support the invasive nature necessary for metastasis. Due to the non-invasive nature of these mammary and vulvar lesions, it is highly unlikely that either of these are secondary metastatic lesions and the authors believe they arose independently.

Several cases of primary breast cancer of the vulva have been reported in which the vulvar lesions simulate breast cancer histologically [6]. Ohira *et al.* reported a case of vulvar EMPD with underlying adenocarcinoma simulating breast cancer in which they proposed that ectopic breast tissue may exist in the vulva and be responsible for EMPD [6]. Primary breast cancer of the vulva is an infrequent occurrence and may be identified by three criteria: 1) a morphologic pattern consistent with breast carcinoma; 2) presence of estrogen and progesterone receptors; and 3) positivity of common biomarkers of breast cancer such as CEA, EMA, and glandular keratins [6]. Although the authors found histological similarities in the Pagetoid nature of the cells of both vulvar and breast tissues, they did not look for features of mammary tissue in the vulvar EMPD. The authors did find that the breast tissue was negative for both estrogen and progesterone receptors, however, they did not test the vulvar tissue for these receptors and cannot extrapolate that the vulvar tissue was negative for these two receptors as well. The authors did however find that the vulvar tissue was positive for biomarkers of breast cancer such as CEA and cytokeratin [7]. Due to the presence of two of the three criteria sufficient to describe primary breast cancer of the vulva, as well as the similarity in the Pagetoid nature of the two types of cells, it is possible that this case of EMPD may have derived from ectopic breast tissue present in the vulva, which appears to be uniquely susceptible to dysplastic and malignant change [7].



The existence of synchronous MPD and EMPD is still considered extremely rare, with only one other case reported by Popiolek *et al.* [5]. The authors believe that this is the first case reporting the coexistence of the two simultaneously. In addition, it is highly unlikely in this case that either breast or vulvar Paget's was due to metastasis from a primary lesion. Due to the synchronous occurrence of these two lesions, the authors cannot rule out the possibility that ectopic mammary tissue existed in the vulvar area in this patient. The incidental occurrence in this case points out that future investigation of EMPD should involve pathological specimen examination for signs of ectopic mammary tissue. Though the authors did not rule out that the vulvar Paget's disease arose from ectopic mammary tissue, it is an interesting theory that may prove to be true in future cases of synchronous Paget's disease.

In summary, synchronous of breast and vulvar Paget's disease is reported. In this experienced case, there was a delay in diagnosing vulvar Paget's disease most likely due to the lack of awareness of the possibility of coexistence. While coincidence of breast and vulvar Paget's disease is likely, ectopic mammary tissue in vulvar as well as secondary metastasis from a focal lesion of breast Paget's disease needs to be carefully evaluated whenever the patient complains of vulvar symptoms in the setting of breast Paget's disease.

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