The Journal of Medical Research

Case Report

JMR 2023; 9(2):16-19
March- April
ISSN:2395-7565

www.medicinearticle.com
Received:14-02-2023
Accepted:08-04-2023
DOI: 10.31254/jmr.2023.9202

Extramammary Paget's disease and papillary thyroid carcinoma: two related or unrelated diseases?

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Abstract

Extramammary Paget's disease (EPD) is a rare tumor occurs mainly in areas with numerous apocrine and or eccrine sweat glands. We report a 49-year-old woman who had referred to another hospital with the complaint of an erythematous and pruritic plaque on the vulva for 6 months. An incisional biopsy had been taken and pathological result was reported as invasive SCC. In her past medical history, there was a history of total thyroidectomy due to follicular variant of papillary thyroid carcinoma two years ago. The patient had been received radioactive iodine for 3 times, however her Iodine isotope scans were still positive. Then she was visited at our hospital for definite treatment. According to the pathologic report she underwent vulvectomy with inguinal lymph node dissection. Histological examination revealed primary invasive Paget disease of the vulva and there was one inguinal lymph node involvement. Second vision of the initial incisional biopsy was also compatible with primary invasive Paget disease of the vulva. We ruled out the possibility of metastatic deposits of thyroid carcinoma in the vulvar lesion and inguinal lymh node by IHC stains. Accurate classification of Paget's disease is essential for appropriate treatment. IHC stains are necessary to differentiate it from other tumors. The possibility of associated malignancy should be considered. To the best of our knowledge this case is the first case of primary Paget disease of the vulva in association with thyroid carcinoma.

Keywords: Paget's disease, Papillary thyroid carcinoma.

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INTRODUCTION

Paget disease (PD) was introduced by Sir James Paget in 1874 for first time but in 1888 Crocker described EPD [1]. The hallmark of Paget disease whether mammary or extra mammary is the presence of large mucin producing tumor cells in the epithelium. The most common anatomical site of EPD is vulva [2]. On the other hand, EPD accounts for lower than 2% of all the vulvar malignant tumors [3]. This disease more frequently involves middle aged to elderly Caucasian ladies. EPD of vulva is classified to primary (cutaneous or type 1) or secondary (metastatic) one [4]. This classification is of clinical importance. Secondary EPD of vulva is further subclassified into type2 that originate from a GI malignancies and type3 from a urogenital tract tumors [4]. Type 1 or cutaneous form is subdivided into three subtype: type 1a (in the absence of dermal invasion), type1b (with dermal invasion) and type 1c (with underlying cutaneous adenocarcinoma) [5]. It is estimated that in about one quarter of the cases, there is dermal invasion and in these cases the outcome is somewhat ominous. Invasive EPD of the vulva accounts for 1 to 2 percent of all of vulvar malignancies [6]. EPD could be associated with other malignant tumors. The most accompanying malignancies are breast, other female genital tract neoplasms, liver, biliary tract and basal cell carcinoma [5]. Here we report a case of invasive vulvar Paget disease in a woman with a history of follicular variant of papillary thyroid carcinoma which initially misdiagnosed as vulvar SCC.

CASE REPORT

A 49-year-old Iranian woman referred to gynecologic outpatient clinic with chief complaint of an erythematous and pruritic plaque on the vulva for 6 months. She denied other symptom related to her vulvar lesion. Topical creams were ineffective. Two months ago she was visited at another medical center. At that center an incisional biopsy was taken and the histopathologic result was invasive SCC. Then she

had come to our center for definitive treatment. In her past medical history there was a history of total thyroidectomy due to follicular variant of papillary thyroid carcinoma two years ago. The patient had been received radioactive iodine for 3 times, however her Iodine isotope scans were still positive. On general appearance she was an alert conscious middle aged lady. There was no evidence of icterus, cyanosis or edema. Surgical scar related to previous thyroidectomy was seen in the front of her neck. On physical examination cardiovascular, respiratory system and abdomen were unremarkable. Breasts were normal in shape and no mass was found on palpation. External genitalia examination showed an erythematous large plaque nearby 4.5 cm in the greatest diameter on the right labium majus that extend to the perineum. Its surface was excoriated in some foci. On vaginal examination no specific abnormalities were found in the cerviv. Inguinal lymph nodes were impalpable. Lab data composed of hematology and biochemistery including tumor markers were unremarkable. According to the pathologic report, she underwent vulvectomy with inguinal lymph node dissection. Histopathology showed skin tissue that epidermis was infiltrated by large neoplastic cells. These cells had pleomorphic nuclei sometimes with a prominent nucleolus and abundant pale cytoplasm (Fig-1). In the cuts of the series prepared from the sample, a small focus of dermal invasion was found (Fig-2). There was also one inguinal lymph node involvement (Fig-3). Based on the alluded microscopic description EPD of the vulva, malignant melanoma and Bowen disease were at the forefront of differential diagnoses. So we designed the IHC panel accordingly. IHC revealed that the cells were positive for CK7, EMA and CEA and negative for CK20, p16, CDX2 and CK5/6 (Fig-4). Due to the history of thyroid cancer in the patient, we ruled out the possibility of metastatic deposits of thyroid carcinoma in the vulvar lesion and inguinal lymh node by IHC stains. Thyroglobin and TTF1 were negative in both of them. So the final diagnosis was primary invasive Paget disease of the vulva. Second vision of the initial incisional biopsy was also compatible with primary invasive Paget disease of the vulva. In order to exclude associated malignant tumors breast sonography, mamography, upper and lower GI endoscopy, cystoscopy, Pap smear and abdominal CT scan were performed which all were within normal limits.

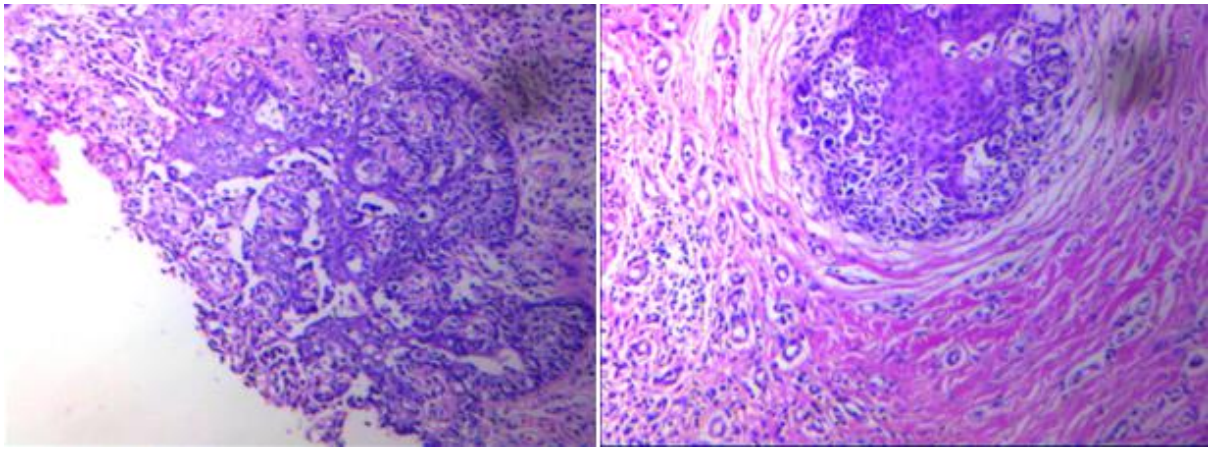

Fig-1: Sections show that epidermis is infiltrated by large neoplastic cells. These cells had pleomorphic nuclei sometimes with a prominent nucleolus and abundant pale cytoplasm (X10).

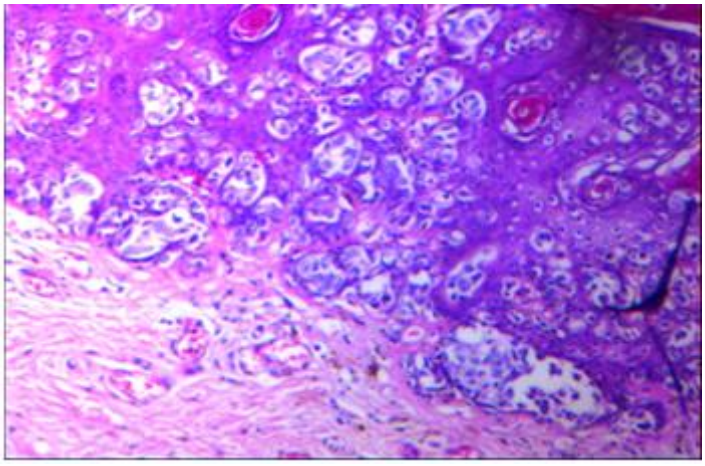

Fig-2: A small focus of dermal invasion was found (X40)

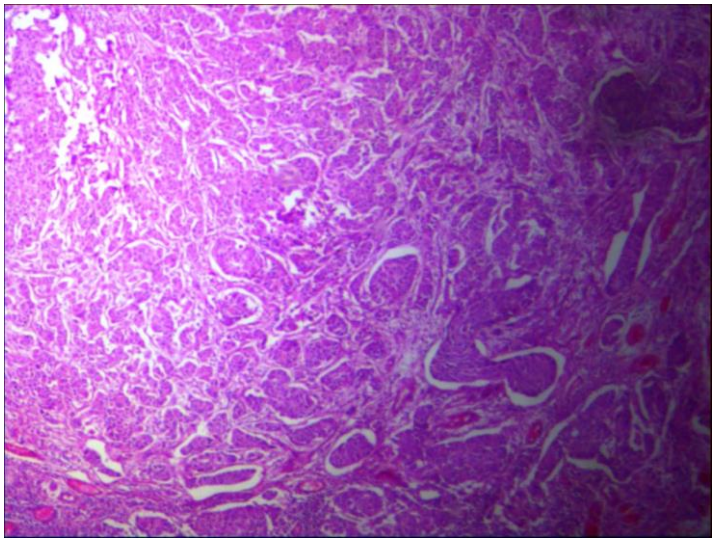

Fig-3: There was also one inguinal lymph node involvement (X10)

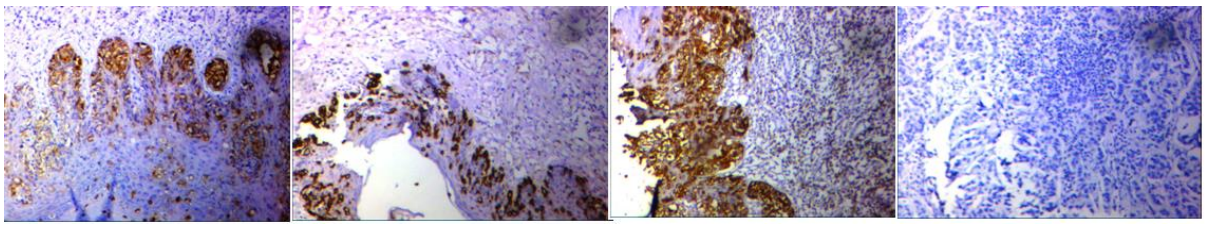

Fig-4: Tumor cells were positive for CEA, CK7, EMA and negative for TTF1 (IHC stain X10)

DISCUSSION

Vulvar cancer is the fourth most common malignancy of the female reproductive system. It accounts for 5% of female genital malignancies. EPD of the vulva was introduced by Radcliffe Crocker in 1889 at first. EPD of the vulva is more common in middle aged to elderly women. The appearance of the lesion is as an erythematous plaque with different size. There are usually crusted areas. If the patient complains of pain and bleeding, the possibility of dermal invasion is higher. In about 10% of cases there are foci of invasion, and in these cases the tumor can metastasize [7]. The etiology of the disease is obscure. Since the gross appearances of the disease are nonspecific, the diagnosis is hard. As a result the role of histology and IHC stains are crucial. The most important clinical differential diagnoses are melanoma, hidradenitis suppurativa, psoriasis, and contact dermatitis. On the other hand, the most important microscopic differential diagnoses include malignant melanoma, sebaceous carcinoma, eccrine porocarcinoma, mycosis fungoides and Bowen disease [8].To established the diagnosis, ancillary techniques are necessary. Paget cells are positive for CK7, EMA, CEA and mucin while in malignant melanoma these markers are negative and neoplastic cells are positive for HMB45 and S100 [9]. Metastatic carcinoma could be ruled out by squamous-cell differentiation markers such as p63 [10, 11]. A precise clinical history and physical examination are essential to exclude the possibility of secondary PD. A relatively significant percent of EPD patients are susceptible to secondary malignancy. This malignant tumor could be synchronous or metachronous [12]. This suggests that the cancer monitoring system is defective in these patients. Therefore, early detection of secondary cancer in these patients can save their lives. A thorough examination of the skin, the gastrointestinal tract, bladder and breasts is recommended. Radical surgery should be performed when EPD of vulva has an invasive component [13]. In the case of inoperable disease radiation therapy is an alternative option [14]. Although surgery is the treatment of choice [15], local relapse is seen frequently because getting a negative surgical margin is difficult [16]. If regional lymph nodes are involved, radiotherapy can be useful. The result of one study showed [17] that the most important predictors of distant metastasis and survival were dermal invasion and regional lymph node involvement. Thus close follow up of these patients is highly recommended.

CONCLUSION

In conclusion accurate classification of Paget's disease is essential for appropriate treatment. IHC stains are necessary to differentiate it from other tumors. The possibility of associated malignancy should be considered. To the best of our knowledge this case is the first case of primary Paget disease of the vulva in association with thyroid carcinoma.

Acknowledgements

None.

Contributions: All the authors contributed in the preparation of this research and article.

Conflict of Interest: None.

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