Case Report

Extramammary Paget’s disease of the axilla: a case report and a review of literature

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Abstract: Extramammary Paget’s disease (EMPD) is a rare type of intraepithelial adenocarcinoma not including the breast tissue. It is an uncommon malignancy accounting for 6.5% of all Paget’s disease. Because of its non-specific clinical appearance, patients often were diagnosed as benign dermatology diseases and so the correct diagnosis can be delayed. Therefore, the thorough examination, early diagnosis, appropriate treatment, and long-term follow-up are important factors. Herein we describe a rare case of primary Extramammary Paget’s disease of the unilateral axilla with a review of the relevant literature.

Keywords: Paget’s disease, axilla, extramammary, immunohistochemical staining

Introduction

Extramammary Paget’s disease (EMPD) is a rare type of intraepithelial adenocarcinoma not including the breast tissue and often involves the apocrine gland-bearing areas such as vulva, scrotum, penis, axilla and even eyelids [1]. It is an uncommon malignancy accounting for 6.5% of all Paget’s diseases [2, 3]. There are only a few hundred cases reported in the world literature [4]. Because of its non-specific clinical appearance, patients often were diagnosed as benign dermatology diseases and so the correct diagnosis can be delayed. The average interval from the beginning of the symptoms to correct diagnosis is about two years [5]. Herein we describe a rare case of primary Extramammary Paget’s disease of the unilateral axilla with a review of the relevant literature.

Case report

A 53-year-old man presented with an erythematous and painless patch in his right axilla with gradual growth for 2 years. At the beginning, the lesion appeared as a small round and well-defined mass. He went to the local hospital and has received the treatment of topical corticosteroids and antibiotics from the dermatologist for about 1 year without improvement. Then he received no treatment in the next year. And the lesion increased gradually up to 4 cm in diameter with localized desquamated erosions and leuko-keratotic foci on the surface (Figure 1). In his left axilla, there is also a small reddish well-demarcated plaque. He denied any pruritic symptoms and any other systemic symptoms such as a headache, bone pain or weight changes. His medical history was normal and he had no family history of cancer especially breast cancer.

On physical examination, there was an erythematous patch measuring 2.5×4 cm in the right axilla with irregular margins and exudative surface. While in his left axilla, a smaller reddish well-demarcated lesion measured about 1×1 cm was marked. There was no evidence of lymphadenectomy in his bilateral axilla and breast. The ultrasound of breast and axilla showed no abnormal changes or lymphadenopathy except the focal lesion in the right axilla. He was also examined by chest X-ray, computed tomography scan, as well as blood tests including tests for tumor markers and carcino-embryonic antigen. These examinations showed no internal abnormality.
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Then the patient received treatment of wide local excision. The histology of the excised lesion showed abundant Paget’s cells diffused in small clusters or singly within the epidermis. Compared with the normal cells, these Paget’s cells were large and round with prominent central nuclei and abundant pale, clear cytoplasm. Intraductal carcinoma of apocrine was seen infiltrating in the dermis (Figures 2, 3). Immunohistochemistry showed that the tumor cells were positive for CK7, CEA, and GATA3 while negative for PR, CK5/6, and P63. (Figure 4) However, he refused skin biopsy in the left axilla for some reason.

The patient is now healthy without recurrence for 6 months and still under the follow-up.

Discussion

James Paget reported the first malignant areola skin change associated with breast carcinoma in 1874. Extramammary Paget’s disease was first recognized and reported in 1889 by Radcliffe Crocker [2, 6]. Perianal EMPD was first reported in 1893 and the first case of vulva EMPD in 1901 [7].

EMPD is an infrequent type of intraepithelial adenocarcinoma in areas rich in apocrine glands, which often are the reproductive organs such as the vulva in women, scrotum and penis in men. The most common site is the vulva. However, axilla, buttocks, thighs, even the eyelid, external auditory canal and other sites have also been reported [1, 4, 6-8].

EMPD often affects patients between the ages of 50 and 80 years and the average age is approximately 75 years, most frequently in Caucasians. Women are more susceptible than men with a ratio about 4:1 of women to men [4, 6].

Clinically, the EMPD lesions and the symptoms are nonspecific. The potential lesions are usually unilateral, scaly, erosive, or oozing erythema and the advanced lesions are well-demarcated, round, ovoid, or polycyclic pink or red or white eczema-like plaque with slow growth [6, 9, 10]. Patients often suffer from itching, burning, pain and other asymptomatic presentations [4]. Chiu and Yang reviewed seven patients with EMPD of the axillary region and found that the typical symptoms were nonspecific and one-third of their patients suffered from pruritus [11]. Zollo and Zeitouni in their study reported...
that pruritus was the most common symptom, occurring in around 60% of patients, while other presenting symptoms included irritation, burning, tenderness, pain, bleeding, and edema. The disease was asymptomatic in 10% of the patients [6]. Therefore, the presentations of EMPD can mimic other dermatological diseases so that diagnosis is always delayed [3]. Most patients are first misdiagnosed as benign dermatological conditions and inflammatory skin conditions like Bowen disease, various tinea infections, psoriasis, eczema, tinea corporis, mycosis fungoides, Langerhans cells histiocytosis, and irritant dermatitis and are initially treated with topical steroids and antifungal ointments [4, 7, 11, 12].

The precise pathogenesis of EMPD has not been entirely explained and the pathogenetic mechanism now is controversial. Ogawa et al. reported that during embryonic life, histogenetically similar cells migrated together and transformed to multicentric malignant [13]. Current evidence suggests EMPD is heterogeneous and the multicentric theory that oncogenic stimulus can generate intraepidermal and adnexal adenocarcinoma has been accepted, [9] so multicentricity of Paget’s disease should be considered when encountering APD [14, 15]. Moreover, clinically palpable lymph nodes can be an important prognostic factor for this disease [16]. Besides, it has been reported that there were only 12 cases of axillary Paget’s disease in the literature and only one case of APD was bilateral [17]. In our case, bilateral axillary Paget’s disease was considered but the sufficient evidence was lack.

Much of the research has stated that EMPD is classified into primary and second EMPD. Although the hypothesis of histogenesis of EMPD is still controversial, some studies have stated that the primary EMPD may involve intraepidermal neoplasm of the epidermal while the second EMPD may spread from an underlying internal malignancy [7, 18].

![Image](image.png)
fore, the diagnosis of EMPD should be made by a thorough investigation of the underlying internal carcinoma of other sites, frozen section analysis, skin biopsy and immunohistochemical staining. FDGPET is said to be a useful method to detect the precancerous lesions and metastases [19].

Although the frozen section analysis of EMPD in the operation can be misleading to some degree, it is still an important method for primary diagnosis. Histological examinations show that Paget cells are atypical with large centrally situated nuclei with nuclear atypia and abundant cytoplasm, distributed singly or in groups within the epidermis and epithelium of adnexal structures [7, 12, 13].

Previous studies of immunohistochemical reviews have emphasized that Paget’s cells typically stain for markers of apocrine and eccrine derivation. Low molecular weight cytokeratin (CK), gross cystic disease fluid protein (GCDFP-15), periodic acid-Schiff (PAS) and carcinoembryonic antigen (CEA) are positive while S100 and higher CKs are negative [7, 20]. Whorton et al. stated in their study that CK7 was one of the important markers to help confirm the diagnosis [1]. And the primary EMPD is positive for CK7 and GCDFP-15 while negative for CK20 whereas the second EMPD is on the contrary [7].

In our case, the patient was positive for CK7, CEA, and GATA3 while negative for PR, CK5/6, and P63. The immunohistochemistry confirmed the lesion as a kind of adenocarcinoma rather than the epithelium-originated cancers. Besides, it could also state that the intraepidermal neoplasm was primary EMPD instead of second EMPD with underlying internal carcinoma of the mamma accessoria.

The managements of EMPD include wide local excision, Mohs’ micrographic surgery (MMS), topical and systemic chemotherapy, laser therapy and radiotherapy, and surgery remains the major treatment especially MMS [7, 21]. Because EMPD is a kind of intraepithelial neoplasm, its irregular margins and multifocal non-contiguous features can often lead to recurrence after treatments. The rate of recurrence is different in methods. A study showed the recurrence ranging from 15% to 60% depending on the size of margins after local resection [4]. Compared to wide local resection, MMS shows a reducing local recurrence rate [6, 7, 11]. Besides, chemotherapy and radiotherapy can be adjuvant therapy to surgery and have shown some benefit for reducing the recurrence [6, 7, 21]. Therefore, long-term follow-up including both local recurrence and associated internal malignancy for every patient is essential [7].

Conclusion

EMPD is a kind of rare acquired skin disorder which mimics the benign cutaneous lesions. The middle-aged patient in our report is not a postmenopausal woman and younger than the typical age group. The unusual location of the lesion and atypical presentation made the diagnosis more difficult. Considering its non-specific clinical features, the early diagnosis should be confirmed. Furthermore, the examination of internal malignancies of other sites should be performed. Until now, although there are a multitude of methods to treat EMPD, a high rate of recurrence cannot be ignored. Therefore, early diagnosis, appropriate treatment as well as long-term follow-up should be paid attention to. While considering the multicenter propensity and irregular histology, more accurate tumor markers and therapies are needed.

Disclosure of conflict of interest

None.

Abbreviations

EMPD, Extramammary Paget’s disease.

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