Clinicopathological features of an extramammary paget’s disease-associated sweat gland adenocarcinoma located in the right Groin

Yanfang Liang1*, Longbin Cao1, Bihua Lin2, Can Chen1, Jian Ruan1, Maofu Wei1, Keyuan Zhou2, Jincheng Zeng2

1Department of Pathology, Dongguan Hospital Affiliated to Medical College of Jinan University, the Fifth People’s Hospital of Dongguan, Dongguan 523905, China.
2Dongguan Key Laboratory of Medical Bioactive Molecular Developmental and Translational Research, Guangdong Provincial Key Laboratory of Medical Molecular Diagnostics, Guangdong Medical University, Dongguan 523808, China

Abstract: Extramammary paget’s disease (EMPD) is a rare malignant neoplasm. Especially, EMPD associated with cancer is extremely rare. Here, we report a rare case of EMPD associated with sweat gland adenocarcinoma (SGA) located in the right groin of a 73-year-old Chinese man. The histology of the excised lesion revealed a focus of sweat glands like-Paget’s cells and lower degree of differentiated carcinoma were observed on subcutaneous. The goblet cells of the skin stained strongly with alcian blue (AB) and periodic acid schiff (PAS). Laboratory tests revealed the man had an obviously rising CA125 level (46.58 U/ml), and tissues were immunostained positive for CK, CK5/6, CK7, CEA, CK19, GCDFP-15, Keratin, P53, P63, Ki-67, ER, and negative for HMB45, PR, CK20, Melan A. The report concludes that immunohistochemistry is required to confirm the diagnosis and differentiation of EMPD combined with SGA from pagetoid SGA and EMPD.

Keywords: Paget’s disease; Groin; Sweat gland adenocarcinoma; Histology, Immunohistochemistry

Received 23 January 2018, Revised 20 March 2018, Accepted 25 March 2018

*Corresponding Author: Yanfang Liang, lyfine84@126.com

1. Introduction

Paget’s disease, first described by Sir James Paget in 1874, is classified as mammary and extramammary. Extramammary paget’s disease (EMPD) is a rare malignant neoplasm that always affects apocrine-rich areas such as the penis, scrotum, vulva and perianal area[1]. EMPD is typically located in the hair-bearing skin of the axilla or genital area, and the pathogenesis is still unclear. The bulk of evidence points out that EMPD has an histogenetic origin from undifferentiated multipotent stem cells in the epidermal basal layer or infundibular stem cells of the hair follicle from epidermis or cutaneous adnexal structures, like apocrine glands[1-3]. Most patients with EMPD have a good prognosis because EMPD progresses slowly and is usually limited to the epidermis and cutaneous adnexal structures. EMPD associated with cancer is extremely rare, although there are publications linking it to tumors of the bladder[4,5], vulva[6,7], syringoma[8], vagina[9], and cervix[10]. Here, we report a rare case of EMPD associated with sweat gland adenocarcinoma (SGA) located in the right groin of a 73-year-old Chinese man.

2. Case presentation

A 73-year-old man, appeared no obvious incentive to local skin damage, measured 5 mm x5 mm in diameter, on right groin 2 month ago. An unclear ointment was used to treatment the skin damage but invalid. However, a granulation tissue with persistent burning pain and purulence was growing. Throughout the pathogenesis, the man was no chills, no fever, no nausea, no vomiting, no dizziness, no headache, no breathing difficulties, no blurred vision, no tinnitus, no tetany, no numbness, no obvious abnormalities in the urine, no significant changes in body weight, and without turning neck activity limitation.

3. Physical examination

Body temperature of 36.7 degrees, blood pressure 125/84 mmHg, pulse 72 beats/min, breathing 17 times/min, breath sounds clear lungs, abdomen flat, abdomen soft, no tenderness and without rebound tenderness, no shifting dullness, bowel sounds normal, 4 times/min, murphy’s sign (-), liver and spleen not touched, no percussion pain at both kidney region, no obvious abnormalities in the left groin and both testes. When the patient standing, a soft granulation tissue measured 16x16mm in diameter, higher than the skin was observed on right groin. And, when the granulation tissue are pressed, a small amount of purulent exudate draining from the tissue, but no tenderness.

4. Laboratory tests

Laboratory tests revealed an obviously rising CA125 level (46.58 U/ml), whereas the CEA level (1.92ng/ml), AFP level (2.18 U/ml), CA15-3 level (10.93 U/ml), CA 19-9 level (23.31 U/ml) and CA 72-4 level (0.826 U/ml)
were within normal limits.

Figure 1. Gross and HE staring findings. A: Gross findings; B: HE staring.

Figure 2. Tissues were strained by alcian blue (AB) and periodic acid schiff (PAS).

5. Gross findings

Macroscopically the skin biopsy with skin ulcer defect measured 30×20×15mm and incorporated a slightly raised dark red nodule measuring 15×15mm in maximum diameter (Figure 1A).

6. Histopathological findings

The histology of the excised lesion revealed a focus of sweat glands like-Paget's cells and lower degree of differentiated carcinoma were observed on subcutaneous. Paget's cells, characterized by the presence of large round or oval cells with abundant granular/dusty or pale cytoplasm, pleomorphic vesicular or irregular nuclei and prominent nucleoli (Figure 1B). These cells were arranged in small clusters or dispersed singly, formed adenoid structure, solid nests, infiltrated full-thickness rind but more intensive at the basal layer of the epidermis and very different with the surrounding epithelial cells. Large roundness or oval tumor cells, visible nucleoli and mitotic, were arranged in solid small nests, trabecular-like, partly formed adenoid structure and keratin pearls. The surrounding skin was atrophy, dyskeratosis and depigmentation. Superficial dermis could be seen a significant inflammatory response, lymphocytes, plasma cells, neutrophil infiltration (Figure 1B). The goblet cells of the skin stained strongly with alcian blue (AB), and periodic acid schiff (PAS), seen in Figure 2.

Figure 3. Tissues indicated proteins were detected by IHC.
7. Immunohistochemical findings

Tumor tissues were immune-positive for p53(+++), p63(+), Ki-67(+), CK(+++), CK5/6(+), Melan A(+), CK7(+++), CEA(+), CK19(+++), GCDFP-15(+), Keratin (+), ER(60%+), and negative for HMB45(-), PR(-), CK20(-) (Figure 3).

8. Discussion

In here, we reported a rare case of EMPD associated with SGA located in the right groin of a 73-year-old Chinese man, mainly according histopathological and immune-histochemical findings. EMPD is a rare malignant neoplasm usually found in apocrine-rich areas with a high rate of local recurrence. The initial manifestation of cutaneous EMPD includes edness, roughness, itchiness of the skin lesion and less metastasis[2,11]. Notably, sweat gland adenocarcinomas, derived from sweat ducts, eccrine and apocrine glands, or sebaceous portion, is often observed with lymph node metastases, hematogenous spread or bone metastasis[12]. Therefore, the relationship between them has drawn much attention. Histopathological examination is an important tool in the diagnosis of EMPD. Consistent with previous reports, in this study, immune-histochemical stains for CK, CK7, CK19 were strongly expressed in both characteristic Paget cells, while stains for CK20 were completely negative[6,8,11]. CK7 has been used as a marker of EMPD. The tumor cells in Paget's disease expressed p53, Ki-67, CK, Melan A, CK7, CEA, CK19, GCDFP-15, Keratin and ER, but were negative for HMB45, PR and CK20. Absence of mucin and diffuse positive staining for p63 and CK5/6 support the diagnosis of SGA. It could differentiate from other dermal based primary apocrine adenocarcinomas. In the dermis, primary apocrine adenocarcinomas were present in adnexal epithelium. The tumor had papillary and micropapillary architecture covered by tumor cells, along with infiltrative smaller tumor cell clusters surrounded by stromal retraction. There was striking nuclear pleomorphism with frequent mitotic figures. The tumor cells showed strong positive immunostaining with CK20, EMA, CEA, and low molecular weight cytokeratin, with patchy positiveness for CK7[13,14]. There was no tumor cell immune-staining with ER, GCDFP, or PSA[13,14]. This report concludes that immune-histochemistry is required to confirm the diagnosis and differentiation of EMPD combined with SGA from pagetoid SGA and EMPD.

Acknowledgements

This study was supported by grants from the National Natural Science Foundation of China (81500007); the Science and Technology Project of Guangdong Province (2014A020212298), the Medical Science Foundation of Guangdong Province (A2015206).

Disclosure of conflict of interest

The authors have no conflicts of interest to declare.

Ethics approval and consent to participate

Informed consent was obtained from all study subjects, and the studies were approved by the Internal Review Board of Human Assurance Committee at Fifth People's Hospital of Dongguan and the Guangdong Medical University.

References

[10] Milne JA, Mair J, Phillips DL. Carcinoma of the cervix uteri presenting as Paget's disease of the vulva, with a note on the pathogenesis of the
