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Case Report

A tale of two rare entities: extramammary Paget's disease and hepatocellular carcinoma - a singular case report

Sumedha Gupta[1]*, Dheer Singh Kalwaniya[2], Sufiyan Zaheer[3], Pallavi Mourya[1]

[1]Department of Obstetrics and Gynaecology, VMMC and Safdarjung Hospital, New Delhi, India
[2]Department of Surgery, VMMC and Safdarjung Hospital, New Delhi, India
[3]Department of Pathology, VMMC and Safdarjung Hospital, New Delhi, India

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***Correspondence:**
Dr. Sumedha Gupta,
E-mail: sumedhagupta91@gmail.com

ABSTRACT

This case report underscores the intricate challenges in managing extramammary Paget's disease (EMPD) of the vulva, a rare neoplasm with diverse clinical manifestations. The presented case, involving a postmenopausal woman, highlights the complexity of EMPD diagnosis and its association with underlying malignancies, particularly hepatocellular carcinoma (HCC). Despite initial management with 5% Imiquimod cream, the patient's clinical course revealed the aggressive nature of the disease, as evidenced by the development of invasive HCC. The rapid deterioration and subsequent demise of the patient emphasize the need for comprehensive monitoring and early intervention in cases of EMPD, considering its potential association with internal malignancies. The discussion delves into the typical presentation of Paget's disease, its association with adnexal carcinomas, and the challenging link between EMPD and internal malignancy. The retrospective analysis of cases in the literature further underscores the variability in underlying adnexal carcinoma rates, emphasizing the complexity of this association. In this particular case, immunohistochemical markers failed to establish a direct correlation between vulval EMPD and hepatocellular carcinoma, highlighting the need for continued research and understanding of the intricate pathogenesis of EMPD and its relationship with internal malignancies.

Keywords: Extramammary Paget’s disease, Hepatocellular carcinoma, Vulva

INTRODUCTION

Extramammary Paget Disease (EMPD) of the vulva is a rare neoplasm, presenting a formidable challenge in its therapeutic management. The pathological manifestation originates within the epidermis or adnexal structures, including hair follicles and sebaceous glands. It is distinguished by the presence of loosely cohesive Paget cells, which tend to form clusters in epithelial nests and are dispersed throughout the epithelium.[1] Invasion into the dermal layer is a rare occurrence, with invasive EMPD accounting for less than 2% of all vulvar malignancies. Extramammary Paget Disease is additionally linked to vulvar adenocarcinoma and, in a notable percentage of cases ranging from 11% to 54%, is associated with malignancies beyond the vulva. These encompass various malignancies such as those affecting the breast, intestines, and urologic system.[2] There have been numerous instances of EMPD linked to bladder carcinoma, prostate cancer, kidney tumors, and colon malignancies.[3,4] The connection between extramammary Paget's disease (EMPD) and hepatocellular carcinoma (HCC) seems to be exceptionally uncommon based on our current knowledge. Here in, we present a case of extramammary Paget’s disease with Hepatocellular carcinoma.

CASE REPORT

A 68-year-old postmenopausal woman presented with perineal itching and burning sensations persisting for 2 years. Initially treated conventionally, her condition progressed to an erythematous, oozing vulvar lesion (Figure 1).

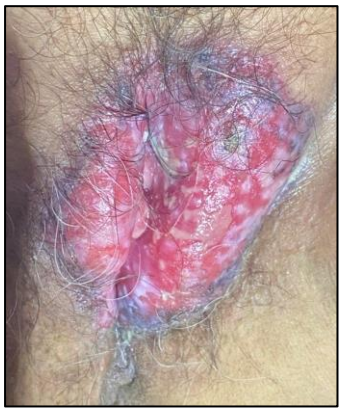

Figure 1: Erythematous area with scaly and crusty surface involving whole of the labia majora, labia minora, clitoris along with part of mons pubis with surrounding area of hyperpigmentation.

A vulvar biopsy confirmed Extramammary Paget's disease without underlying invasive malignancy (Figure 2).

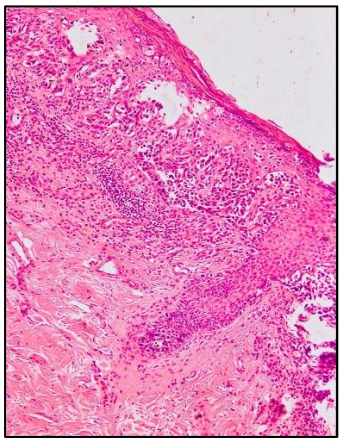

Figure 2: Basal epidermis showing pagetoid cells forming nests and present individually, underlying dermis showing only chronic inflammation in superficial areas.

Treatment commenced with 5% Imiquimod cream applied locally for 12 weeks. Subsequent pelvic magnetic resonance imaging revealed an ill-defined enhancing soft tissue mass involving the urethra anteriorly and anal canal posteriorly. Upper gastrointestinal tract endoscopy, colonoscopy, and cystoscopy were conducted to rule out underlying malignancy, all yielding normal results. However, the patient developed anorexia and nausea, leading to admission for further evaluation, which revealed deranged blood sugar and a subsequent diagnosis of Diabetes mellitus. Routine laboratory tests indicated liver function abnormalities, with elevated serum AST and ALT levels. Upper abdominal ultrasonography revealed multiple hypodense lesions in both liver lobes, suggestive of metastasis. Positron emission computerized tomography (PET-CT) and tumor marker assessments were then performed. While serum carcinoembryonic antigen levels were normal, alpha-fetoprotein levels were elevated. PET-CT scans confirmed multiple enhancing lesions in both liver lobes (Figure 3) and bony lytic lesions with hypermetabolic uptake in the vulva.

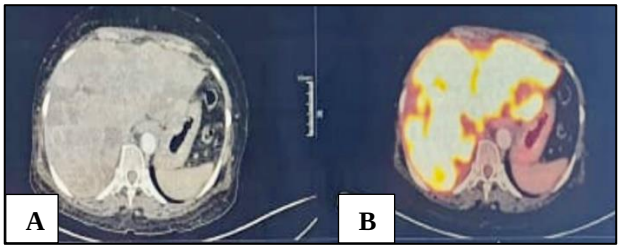

Figure 3 (A and B): Liver is enlarged with multiple enhancing lesions in both lobes of the liver (SUV max - 11.4).

A sono-needle biopsy revealed hepatocellular carcinoma (HCC), with tumor cells positive for CK 7, HMWCK, ER, and CD34, and negative for CK20. The case was discussed in a multidisciplinary tumor board meeting, and chemotherapy was advised. Unfortunately, the patient's condition deteriorated rapidly, leading to her demise within one month.

DISCUSSION

Paget's disease usually appears in apocrine gland-containing areas; it presents as an intraepidermal adenocarcinoma affecting the breast's nipple and/or areola (called mammary Paget's disease, or MPD) or extramammary areas such as the axilla, anogenital, and perineal skin (called extramammary Paget's disease, or EMPD). Ninety percent of instances of EMPD involve individuals over the age of fifty. It mostly affects the vulva, then the perianal area, and is more common in females than males.[5] The condition primarily affects elderly people between the ages of 65 and 70.[6] Pruritus is the most typical extramammary Paget's disease presenting symptom. Our patient also presented with an itchy lesion over the vulva. The clinical presentation resembles that of Paget's disease in breasts. Sometimes lesions exhibit hypo- or hyperpigmentation.[7] Morphological features show intracellular mucin presence in many cases, and positive immunohistochemical staining for glandular cytokeratins, EMA, and CEA are indicators of Paget's disease. EMPD is characterized by erythematous and eczematoid plaques that can be solitary or multifocal. Itching is the most typical symptom. It is frequently misdiagnosed as an inflammatory or infectious disease, and the diagnosis is often made 2-4 years after the disease first manifests.[3]

Since its original description by James Paget in 1874,8 MPD has typically been linked to underlying breast cancer. Although EMPD and MPD have many clinicopathological characteristics, the link between EMPD and underlying malignancies is significantly less common. Crocker originally identified EMPD in 1889.[9] Chanda conducted a retrospective review of 197 cases of EMPD that were published in the English literature between 1962 and 1982.[5] Of these, 46 cases (or 24%) had an underlying adnexal carcinoma (Bladder cancer, renal cell carcinoma and prostate cancer). Depending on the affected anatomic areas, there have been reports of varying incidences of underlying adnexal cancer. For vulvar EMPD patients, reported rates range from 14% to 20%, while for perianal EMPD patients, they range from 50% to 86%.[10] According to Lai et al, out of 33 patients, 7 (21.2%) had underlying adnexal cancer (Rectosigmoid and prostate).[3] In Wada and Urabe's study, no patient had underlying adnexal cancer; however, in Yang et al report, some did.[4] The link between internal malignancy and EMPD is a challenging one to answer. The literature appears to provide the notion that EMPD develops concurrently with or before internal malignancy and is linked to underlying malignancy.

In our presented case, the localization of the underlying malignancy was found to be unrelated to vulval Extramammary Paget's Disease (EMPD), as verified through immunohistochemical markers. Vulval EMPD, without evidence of invasive malignancy, exhibited positive immunostaining for CK7, CEA, GATA-3, GCDFP-15, and p16, with negative staining for CK20. Conversely, hepatocellular carcinoma displayed positive immunoreactivity for CK7 and HMWCK, while being negative for CK20. Consequently, immunohistochemistry failed to reveal any discernible correlation between vulval EMPD and hepatocellular carcinoma. The standard approach for EMPD management involves surgical intervention. However, significant resections are often complicated by a heightened risk of local recurrence attributable to the multicentric nature and indistinct margins of the disease, as documented in relevant literature references.[12]

CONCLUSION

Extramammary Paget's disease (EMPD) frequently goes undiagnosed because it appears as an uncommon tumour that affects the skin that has apocrine glands. Notably, it has a significant correlation with internal or adnexal cancers. It is advisable to consider EMPD and do a comprehensive skin biopsy when patients come with vague, nonresponsive skin lesions. Continued research efforts are warranted to enhance our understanding of EMPD's underlying mechanisms and optimize therapeutic strategies for improved patient outcomes.

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