Extramammary Paget's Disease of the Vulva: A 10 year review of cases in a tertiary cancer centre and a proposed immunopanel

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INTRODUCTION and AIMS

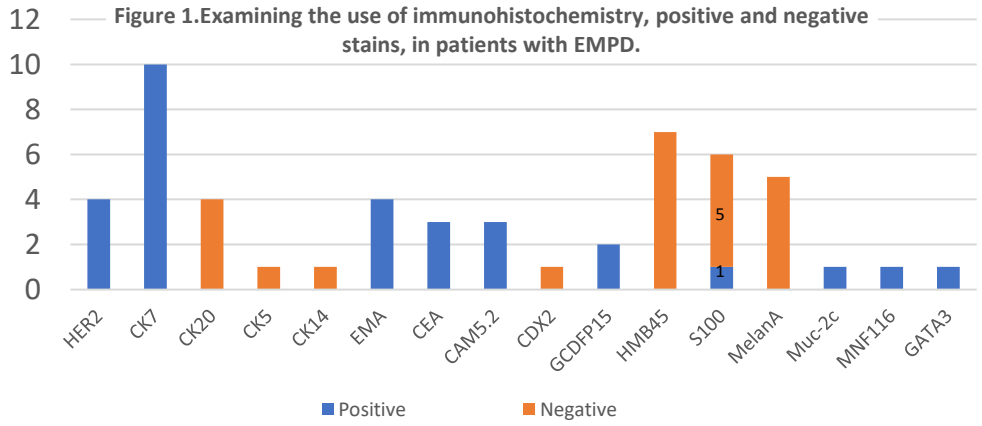
Extramammary Paget's disease (EMPD) of the vulva is a rare neoplasm typically affecting women over the age of 60. Primary EMPD arises as an intraepithelial neoplasm of the epidermis. It is thought to originate from pluripotent stem cells in the epidermis. Secondary EMPD develops from direct extension from an underlying internal neoplasm. Most EMPD is diagnosed as carcinoma in situ. When invasive disease occurs it is aggressive. The treatment and prognosis for primary and secondary EMPD differs, therefore accurate diagnosis is critical (1). The differential diagnosis of EMPD includes malignant melanoma and pagetoid VIN. Secondary EMPD can arise from colorectal, urothelial or cervix. The aim of the study was to determine how many cases of EMPD had been diagnosed at our centre in the past decade and to find out which IHC markers were used. Our second aim was to develop a small panel of IHC that would aid diagnosis.

METHODS

Our database (Co-path) was searched for Paget's Disease and Vulva from 01/01/2012 to 01/01/2022. The diagnosis and type of IHC used was documented. The follow up plans and notes on an electronic record were examined

RESULTS

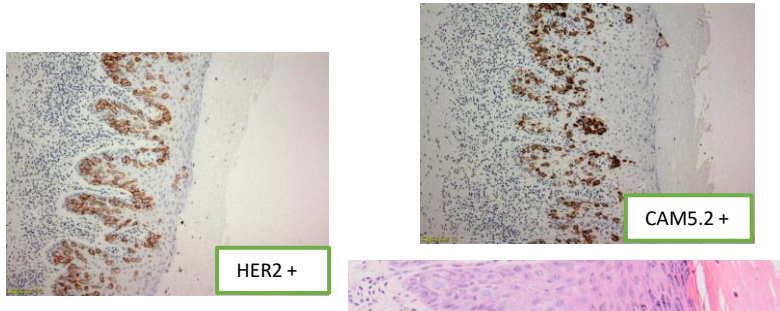
18 cases were identified (mean age 75.5 years) and all were diagnosed as primary EMPD. There were no secondary EMPD cases. 11/18 cases had IHC performed (61%). CK7 was tested in 10 cases. CK20 was tested in 4 cases. No cases used uroplakin or p16. Melanoma markers were performed in 7 cases. Other markers included HER2, CK20, CEA, EMA and GCDFP-15 (Figure 1.). 5 patients are still having active follow up. 1 patient finished follow up 2 years ago, and 1 patient had follow up 1 year ago. 1 patient is deceased. No clinical data could be found for 10 patients.

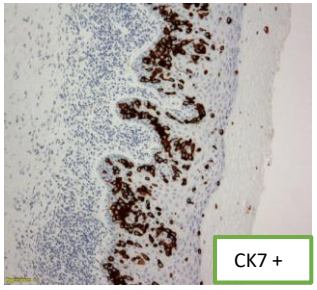


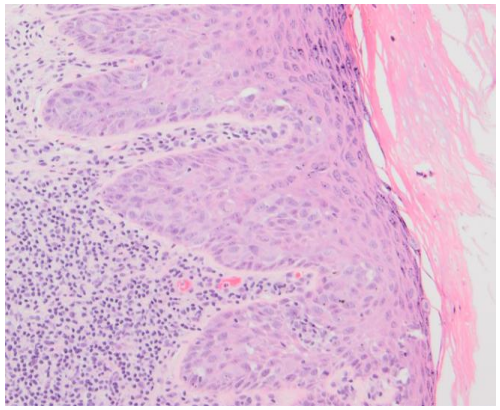
DISCUSSION

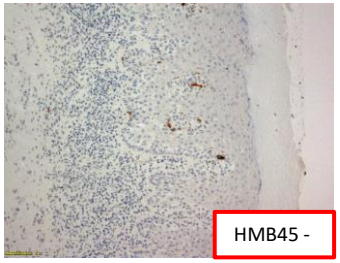
IHC should be used in all cases of EMPD to differentiate between primary disease, secondary disease and malignant mimics. Cases at our centre over the last decade were not sufficiently worked up to definitively rule out secondary EMPD or malignant mimics. We propose a panel of IHC that is performed on all suspected EMPD of the vulva (Table 1.) Emerging data supports testing for HER2 expression as overexpression is strongly associated with invasion and lymph node metastasis. Importantly, HER2 could also be used as a therapeutic target in EMPD (2).

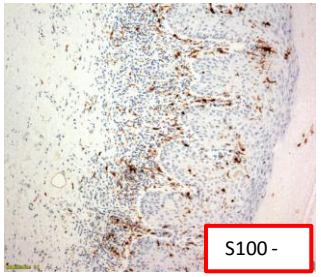
References
1) Ishizuki S, Nakamura Y. Extramammary Paget's Disease: Diagnosis, Pathogenesis, and Treatment with Focus on Recent Developments. *Curr Oncol*. 2021;28(4):2969-2986. Published 2021 Aug 5. doi:10.3390/curroncol28040260
2) Masuguchi S, Jinnin M, Fukushima S, Makino T, Sakai K, Inoue Y, Igata T, Ihn H. The expression of HER-2 in extramammary Paget's disease. Biosci Trends. 2011 Aug;5(4):151-5. doi: 10.5582/bst.2011.v5.4.151. PMID: 21914949.

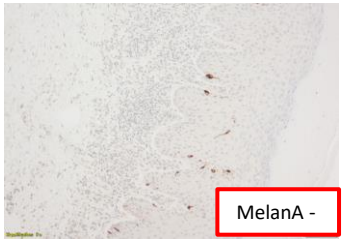












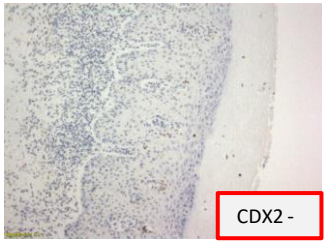


Table 1. Proposed immunohistochemical panel for suspected EMPD of the vulva

IHC	Reason
CK7	+ primary EMPD
HER2	+/- primary EMPD. Immunotherapy potential
CAM5.2	+ primary EMPD
CEA	+ primary EMPD
P16	+ VIN, + adenocarcinoma cervix, +/- primary EMPD Block positive: consider HPV PCR
HMB45, MelanA, S100	+ malignant melanoma
CDX2, CK20, uroplakin3	+ secondary EMPD (colorectal, urothelial)