A case of extra mammary Paget disease with an unusual immunophenotype

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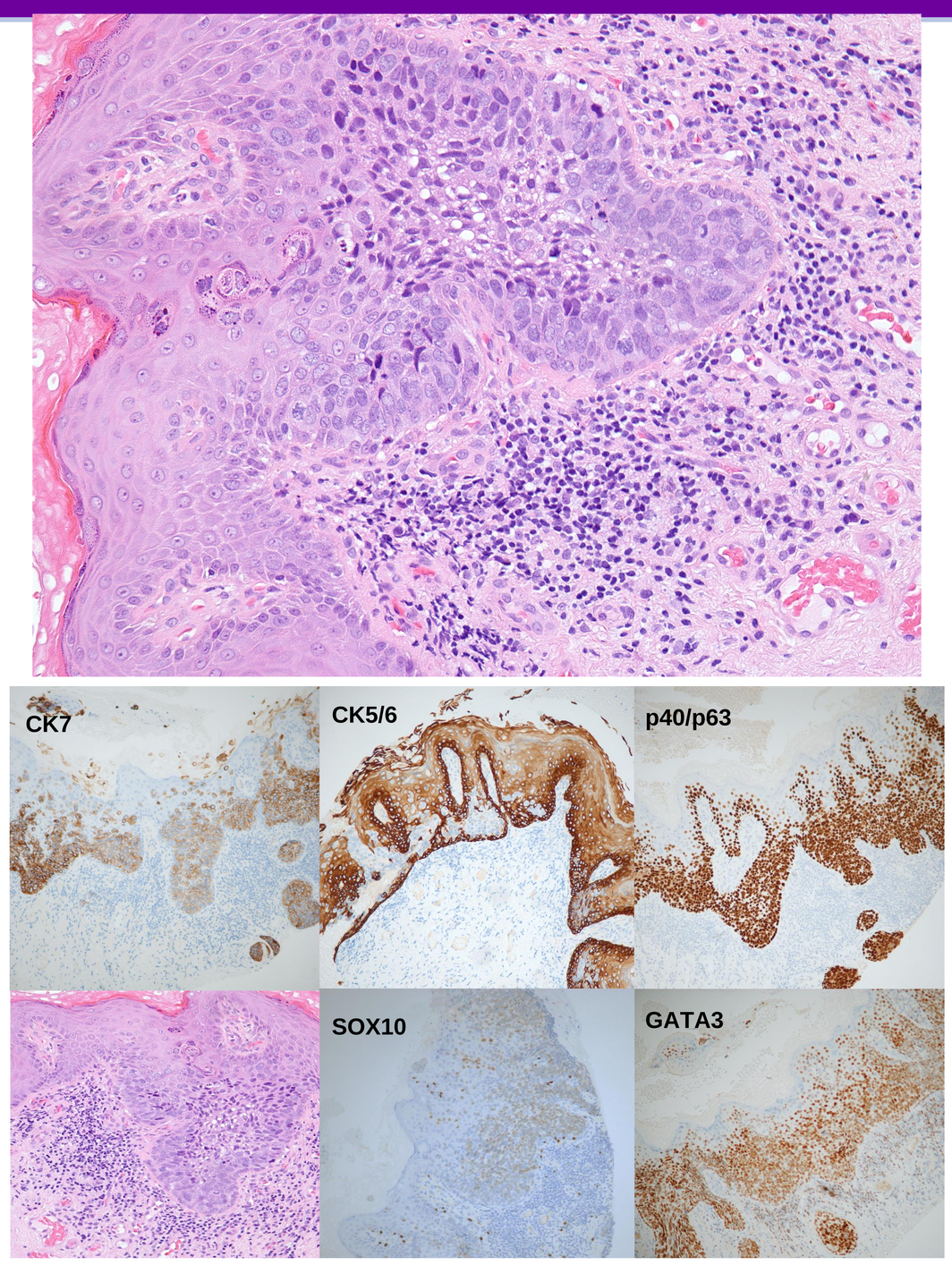
INTRODUCTION

- Extra mammary Paget disease (EMPD) is an intraepithelial carcinoma which most commonly involves the vulva.
- It is rare, accounting for less than 1% of all vulvar malignancies and predominantly affects patients in the sixth and seventh decades[1].
- There are two types, primary and secondary.
- Primary EMPD is thought to be an intraepidermal carcinoma arising from cutaneous apocrine glands in apocrine rich areas (including the vulva, groin, inguinal area, penis and scrotum). It is usually intraepidermal in origin but may represent colonisation from an underlying apocrine or adnexal adenocarcinoma[2,3].
- Secondary EMPD arises due to intraepidermal spread from a distant tumour, which is usually of urothelial or colorectal origin. As such it occurs in the perineal areas near these organs[4].

HISTORY

- Here we present the case of a woman in her mid-fifties who presented with a 6 year history of soreness and vulval itch affecting the right labium.
- She has a prior history of malignant melanoma excised from the shoulder with no evidence of local or regional recurrence.
- She had no significant comorbidities or other known medical history.
- Examination revealed a slightly macerated appearance of the right inner labium.
- The clinical impression was of possible EMPD or vulval intraepithelial neoplasia (VIN).
- A punch biopsy of the area was taken.

MICROSCOPIC IMAGES



MICROSCOPIC INTERPRETATION

- The epidermis was mildly acanthotic and hyperkeratotic.
- A population of moderately atypical cells with basaloid features was present in the epidermis which showed upward “Pagetoid” extension.
- The basal layer was preserved but attenuated (the so-called “Eyeliner” sign); however the atypical cells colonised the adnexal epithelium.
- These cells displayed an unusual immunophenotype staining positively for basal markers including CK5/6 (weak, focal), p40 and p63 and negatively for ER, PR, GCDFP15, EMA, CK20, S100, Uroplakin 2, BerEP4 and mucin (DABPAS).
- This immunophenotype is highly unusual for primary EMPD which would not normally stain for basal markers; it is also classically positive for GCDFP15 and mucin (not present in all cases).
- CK7, GATA3, p16, AE1/3, Cam 5.2 and SOX10 were also positive. The KI67 proliferation index was very high.
- Overall this was thought to represent EMPD with a basal immunophenotype akin to a basal-like breast carcinoma.
- The referring physician was advised to exclude the less likely possibility of spread from an underlying sweat gland tumour or a basal-like breast carcinoma.

DISCUSSION

- **The differential diagnosis for the case included malignant melanoma in situ and pagetoid Bowen disease (squamous cell carcinoma in situ)[3].**
- **SOX10 positivity precluded a diagnosis of Bowen disease in this case. The lack of typical morphological features and S100 negativity as well positivity of cytokeratins (CK7 and CK5/6) do not favour malignant melanoma in situ.**
- **The negativity for CK20; lack of staining for mucin and positivity for CK5/6 render secondary EMPD from a colorectal primary unlikely. Likewise the negativity for CK20 and Uroplakin 2 preclude secondary EMPD from a urothelial primary.**
- **The patient has been referred for further investigations and review by the gynaecology team for consideration of surgical treatment.**

REFERENCES

1: Parker LP, Parker JR, Bodurka-Bevers D, Deavers M, Bevers MW, Shen-Gunther J, Gershenson DM. Paget's disease of the vulva: pathology, pattern of involvement, and prognosis. Gynecol Oncol. 2000 Apr;77(1):183-9.
2: Guerra, R.; Misra, S. (2013). "Management of Extramammary Paget's Disease: A Case Report and Review of the Literature.". Case Rep Dermatol Med 2013 **3**: 4.
3: Raju, RR.; Goldblum, JR.; Hart, WR. (Apr 2003). "Pagetoid squamous cell carcinoma in situ (pagetoid Bowen's disease) of the external genitalia.". Int J Gynecol Pathol 22 (2): 127-35.
4: Feuer GA, Shevchuk M, Calanog A. Vulvar Paget's disease: the need to exclude an invasive lesion. Gynecol Oncol. 1990 Jul;38(1):81-9.

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