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CASE REPORT

Adenocarcinoma of mammary-like glands of the vulva: a case report and literature review

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A rare case of adenocarcinoma of mammary-like glands of the vulva is presented. The histological diagnosis as well as a review of literature are discussed.

Keywords: adenocarcinoma, mammary-like glands, breast cancer, vulval tumour

Case presentation

A 60-year-old woman was referred by a district hospital where she presented with a 3-month history of a painless vulval growth. She presented no other symptoms, had reached menopause at the age of 56 years and was not on hormonal therapy. The patient had a caesarean section in 1979 and had been on anti-hypertensives since she was diagnosed with hypertension in 2007. She is married, is employed as a domestic worker and does not smoke. On examination, she was generally well, with no palpable lymph nodes in either the axillae or groin. The breast examination revealed no masses or discharge, normal nipples and no skin changes.

The vulval examination showed a 2 × 3 cm hard mass on the left labia, and the patient underwent a wide local excision of this mass. Histology of the excision specimen showed a poorly differentiated carcinoma with areas resembling columnar cell hyperplasia and ductal carcinoma in situ of the breast. Immunohistochemical staining revealed a breast carcinoma-like immunophenotype with strong co-expression of estrogen receptors (ERs) and GATA binding protein 3 (GATA3), as well as negative staining for paired box 8 (PAX8) and Wilms Tumour 1 (WT1). GATA3 immunostaining is present in many tumours, particularly breast carcinomas, whereas PAX8 is expressed in normal female genital tract epithelium and carcinomas derived thereof (such as serous, endometrioid and clear cell carcinoma). WT1 is a marker of ovarian serous carcinoma and malignant mesotheliomas. The positive ER and GATA3 staining as well as the negative PAX8 and WT1 staining supports the morphologic diagnosis of an adenocarcinoma of mammary-like glands of the vulva and excludes other female genital tract adenocarcinomas. There was also no evidence of human papillomavirus involvement (non-block p16 staining).

The patient had a mammogram, and computerised tomography (CT) scans of the chest, abdomen and pelvis with no features suggestive of either a primary tumour in the breast, or any thoracic, abdominal or pelvic metastases. In view of the clinical findings of normal breasts, the negative imaging and the immunophenotype of the excision specimen, a diagnosis of adenocarcinoma of mammary-like glands of the vulva was made. The patient was referred to the combined oncology assessment clinic for further management, where she would have been offered a sentinel lymph node procedure, and adjuvant therapy dependent on the results of the lymph node histology and the immunohistochemical profile of the tumour. Unfortunately, she declined further surgery and defaulted her follow-up appointments.

Discussion

Vulval cancer accounts for 2–5% of gynaecological malignancies, with squamous cell carcinoma of the vulva contributing > 90%.[1] Vulval adenocarcinomas may be either primary or metastatic lesions, the latter accounting for 5–8% of all vulval malignancies.[2] Primary vulval adenocarcinomas include mucinous carcinoma, adenoid cystic carcinoma, Bartholin gland adenocarcinoma, carcinoma arising from Extramammary Paget disease (EMPD), and mammary-like adenocarcinoma.

Mammary-like tissue within the vulva was first described in 1872, and was believed to have been heterotopic tissue remnants from the embryonic milk line.[3] More recently, Van der Putte argued that anogenital mammary-like glands may rather derive from normal, local eccrine glands which elaborate into mammary-like tissues, explaining lesions that do not arise along the classically described caudal milk line, such as perianal lesions.[4] The histogenesis remains unclear; although previously suggesting the Van der Putte theory, the current World Health Organization (WHO) classification of female genital tumours lists the aetiology as 'unknown'.[5] Despite debate around the origin of these anogenital mammary-like glands, they are susceptible to the same pathologies as that seen in normal mammary tissue.[3,5,6]

Vulval mammary-like adenocarcinomas are rare lesions, with only approximately 37 cases previously documented in English literature.[7] The average age of patients is ~62 years,[7] and the tumours are locally aggressive, with lymph node metastases in ~60% of cases.[8] These lesions may resemble multiple subtypes of

breast carcinoma, including invasive ductal carcinoma, invasive lobular carcinoma, carcinomas with mixed ductal and lobular features, tubulolobular carcinoma, mucinous carcinoma and vulval adenoid cystic carcinoma.[3] These are typically positive for both oestrogen and progesterone receptors (luminal A/B type), with approximately 15% being HER2/neu positive, and with rare cases being triple-negative lesions.[7]

A diagnosis of primary ectopic breast cancer located in the vulva requires histopathologic evidence of mammary-like tissue, through morphology and immunohistochemical markers (such as hormone receptors, GATA3 and appropriate cytokeratin profiles), with clinical and radiological exclusion of primary breast carcinoma.[6,9]

In the case presented, both benign anogenital mammary-type glands and invasive disease were seen.

There are no guidelines for the management of primary vulval mammary-like gland carcinoma, and treatment of this rare tumour type is usually extrapolated from the treatment guidelines of primary breast carcinoma.[7] Most cases in the literature have been treated surgically, with radical wide local excision and either sentinel lymph node procedure or inguinofemoral lymphadenectomy.[9] Adjuvant therapy may include various combinations of chemotherapy, radiation and hormonal treatment with tamoxifen or aromatase inhibitors, depending on the final histology results and stage of the cancer, as with primary breast carcinomas.[7] Neoadjuvant chemotherapy prior to surgical excision has also been described.[7]

Of the 37 cases reported in the English literature, 22 received adjuvant therapy in the form of hormonal therapy (tamoxifen in the majority of cases, and seven patients received aromatase inhibitors). Eleven patients had radiotherapy and at least four of these had positive lymph nodes (Table I).

Conclusion

Adenocarcinoma of mammary-like glands of the vulva is an extremely rare cancer, presenting with a specific histological type which needs to meet appropriate diagnostic criteria, and current data suggest managing this rare tumour in a similar manner to primary breast cancer in terms of chemotherapy and adjuvant

Table I: Summary of reported cases of mammary-like adenocarcinoma of the vulva[7,9]

Year	Age	Operation	Adjuvant therapy	Histology	ER	PR	Her2	LN	Outcome	Follow-up (months)
1935	59	None	None	Adenocarcinoma	*	*	*	*	Dead	1
1956	58	Vulvectomy	None	Adenocarcinoma	*	*	*	*	Dead	4
1976	62	Partial	None	Ductal carcinoma	*	*	*	*	Dead	24
1984	49	Radical vulvectomy + LND	RT	ILC	*	*	*	*	*	*
1985	70	Hemi vulvectomy + LND	Tamoxifen	Adenocarcinoma	+	+	*	2/9	DF	24
1988	60	Vulvectomy + LND1	CT + Tamoxifen	Adenocarcinoma	+	+	*	3/11	Dead	27
1990	68	Vulvectomy	RT + Tamoxifen	Ductal carcinoma	+	-	*	1/15	*	*
1991	40	Partial	None	IDC	+	+	*	*	*	*
1992	46	Vulvectomy + LND	None	Adenocarcinoma	*	*	*	11/13	DF	4
1993	65	Vulvectomy + LND	Tamoxifen	Ductal carcinoma	+	+	*	2/20	DF	12
1994	62	Partial + LND	Tamoxifen	Adenocarcinoma	+	-	+	4/11	DF	24
1997	71	Vulvectomy + LND	CT + RT	Adenocarcinoma	-	-	*	9/9	DF	15
1998	64	Partial + LND	CT + RT + Tamoxifen	Adenocarcinoma	+	+	*	1/14	DF	4
2000	81	Partial	Tamoxifen	Adenocarcinoma	+	+	*		DF	19
2000	60	Hemi-vulvectomy + LND	CT + RT + Tamoxifen	ILC	+	+	*	21/21	DF	20
2001	57	Partial	None	DCIS	+	+	*	*	*	*
2002	69	Vulvectomy + LND	CT + Tamoxifen	Adenocarcinoma	+	+	*	7/15	DF	14
2002	47	Vulvectomy	None	Mucinous	+	+	-	*	DF	36
2003	84	Partial + LND	None	Mucinous	+	+	-	1/11	DF	9
2006	44	Partial + LND	CT + Tamoxifen	Mucinous	+	*	-	2/13	*	*
2006	57	Vulvectomy + LND	CT + Tamoxifen	Adenocarcinoma	-	*	*	7/7	Rec	36
2006	49	Partial + LND	CT + Tamoxifen	Ductal carcinoma	+	+	-	5/7	*	*
2006	51	Partial	None	Ductal carcinoma	-	-	-	*	*	*
2007	49	Partial + SNLB + LND	Tamoxifen	Ductal carcinoma	+	+	-	0/14	*	*
2008	49	Partial	*	Adenocarcinoma	+	+	*	*	*	*
2011	57	Partial + LND	CT + Aromatase	Ductal carcinoma	+	+	-	3/13	*	*
2012	82	Partial	RT + Letrozole	IDC	+	+	*	*	DF	48
2012	82	Radical vulvectomy + LND Partial	Anastrozole	Adenocarcinoma	+	+	-	*	*	*
2013	60	Vulvectomy + SLNB + LND	RT	IDC	+	*	*	*	*	*
2013	71	Partial + LND	CT + Tamoxifen	IDC	+	+	*	1/8	DF	24
2013	59	Radical vulvectomy + LND	Tamoxifen	Adenocarcinoma	+	+	-	*	*	*
2013	65		Letrozole	DCIS	+	-	-	*	*	*
2014	73	Partial	RT + Aromatase inhibitor	Adenocarcinoma	+	+	*	*	*	*
2015	62	Partial + SLNB	CT + RT	IDC	+	+	-	*	Rec	13
2016	72	None	Aromatase inhibitor	IDC	+	+	-	0/1	DF	6
2018	76	Partial vulvectomy + SLNB	RT + Letrozole	Adenocarcinoma	+	+	-	*	*	*
2020	58		RT + Trastuzumab	ILC	-	-	*	*	DF	48

CT – chemotherapy, DCIS – ductal carcinoma in situ, Dead – death from disease, DF – disease free, ILC – invasive lobular carcinoma, IDC – invasive ductal carcinoma, LND – (inguinal) lymph node dissection, LND1 – (inguinal + pelvic) LND, Rec – recurrence, RT – radiotherapy, SLNB – sentinel lymph node biopsy, * – unknown

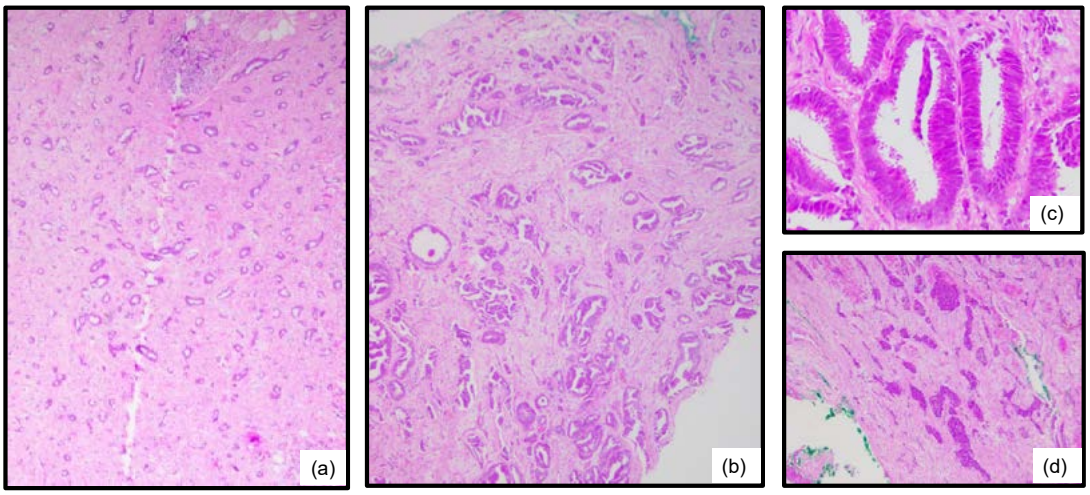

Figure 1: Vulval mammary-like carcinoma, demonstrating various morphologies, including well-formed tubules (a, H&E, 4X); complex glands (b, H&E, 4X); areas of columnar cell change (c, H&E, 20X); and solid areas (d, H&E, 4X)

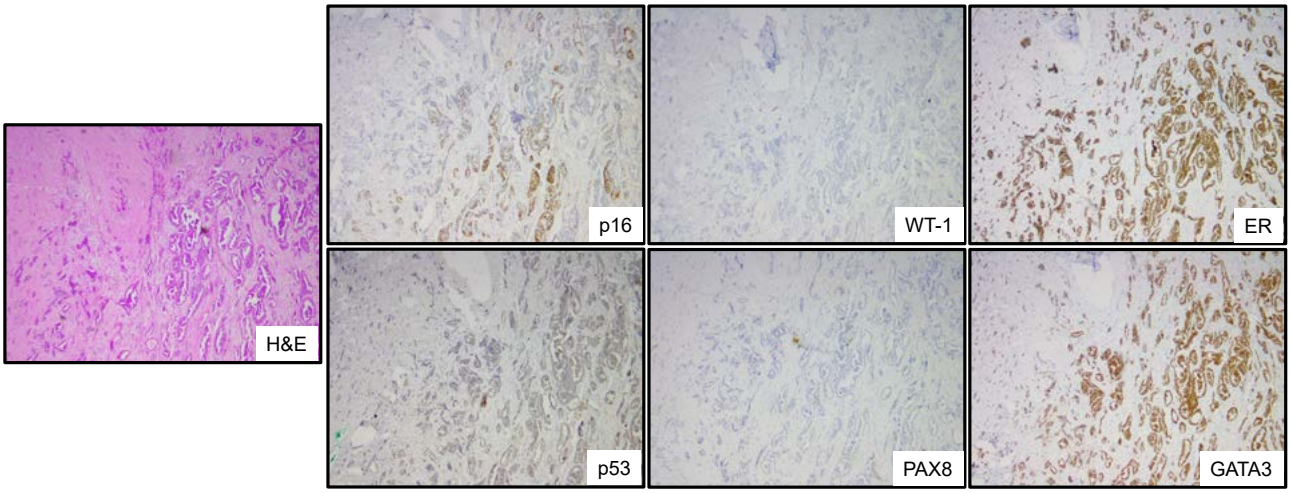

Figure 2: Immunohistochemical profiling
Note: All images at 4x magnification

therapy, though the principles of surgical management of cancer of the vulva are followed. A separate guideline for this type of tumour should be developed based on the available evidence.

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