MEDDOCS Open Access Publisher

Journal of Gynecology Case Reports

Open Access | Case Report

Vulvar Adenocarcinoma of Mammary Gland Type: Thinking Outside the Box. Report of Two New Cases and Comprehensive Review of The Literature

Claudia Mateoiu[1,14]; Cecile Colpaert[2]; Toshima Z Parris[3,4]; Katja Stenström Bohlin[5,6]; Isabelle Cadron[7]; Jenny Nyqvist-Streng[8,9]; Slavica Janeva[9,10]; Khalil Helou[3,4]; Per Karlsson[3,11]; Cleo De Backer[12]; Simona Stolnicu[13]; Anikó Kovács[1,14]*

[1]Region Västra Götaland, Department of Clinical Pathology, Sahlgrenska University Hospital, Gothenburg, Sweden.

[2]Laboratorium Pathologische Anatomie ZNK, Turnhout, Belgium.

[3]Department of Oncology, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.

[4]Sahlgrenska Center for Cancer Research, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.

[5]Department of Obstetrics and Gynecology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.

[6]Region Västra Götaland, Department of Gynecology and Reproductive Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden.

[7]Department of Gynaecology, AZ Turnhout Belgium.

[8]Region Västra Götaland, Department of Surgery, Skaraborg Hospital, Skövde, Sweden.

[9]Department of Surgery, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.

[10]Department of Surgery, Sahlgrenska University Hospital, Gothenburg, Region Västra Götaland, Sweden.

[11]Region Västra Götaland, Department of Oncology, Sahlgrenska University Hospital, Gothenburg, Sweden.

[12]Department of Medical Oncology, AZ Turnhout Belgium.

[13]Department of Pathology, University of Medicine, Pharmacy, Sciences and Technology "George E Palade" of Targu Mures, Targu Mures, Romania.

[14]Institute of Biomedicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.

***Corresponding Author(s): Anikó Kovács**

Department of Clinical Pathology, Sahlgrenska University Hospital, Gula stråket 8. 413 45 Gothenburg, Sweden.

Email: aniko.kovacs@vgregion.se

Received: Apr 02, 2026

Accepted: Apr 22, 2026

Published Online: Apr 29, 2026

Journal: Journal of Gynecology Case Reports

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Abstract

Adenocarcinoma of mammary gland type of the vulva is rare, with fewer than 100 cases reported since its first description by Greene in 1936. Here, we present two additional cases.

The first case is a 68-year-old patient successfully treated with local excision of the vulvar neoplasm, followed by re-excision. She received adjuvant endocrine therapy with the aromatase inhibitor exemestane for five years. Subsequently, she underwent radiotherapy both locally to the vulva and regionally to both inguinal areas. No recurrence has been detected 12 years after the initial vulvar surgery.

The second additional case is a 65-year-old woman. Biopsy of enlarged inguinal lymph nodes demonstrated ER- and PR-positive metastatic carcinoma with breast-like features. A paraclitoral nodule was surgically excised. Its histological examination demonstrated invasive tumor consistent with breast-like carcinoma of no special type, with adjacent ER-positive ano-

Cite this article: Kovács A, Mateoiu C, Colpaert C, Parris TZ, Bohlin KS, et al. Vulvar Adenocarcinoma of Mammary Gland Type: Thinking Outside the Box. Report of Two New Cases and Comprehensive Review of The Literature. J Gynecol Case Rep. 2026; 5(1): 1025.

Keywords: Mammary-like vulvar adenocarcinoma; Anogenital mammary-like glands; Ectopic vulvar breast-like adenocarcinoma; Vulvar adenocarcinoma of mammary gland type.

Abbreviations: AGMLG: Anogenital mammary-like glands; AR: Androgen receptor; DCIS: Ductal carcinoma in situ; ER: Estrogen receptor; H-E: Hematoxylin-eosin; HPV: Human Papilloma Virus; IHC: Immunohistochemistry; NGS: Next generation sequencing; NST: No special type; PR: Progesterone receptor; RTU: Ready to use; VAMGT: vulvar adenocarcinoma of mammary gland type.

genital mammary-like glands. Treatment with ribociclib and letrozole was started. Lung and lymph node metastases resolved, but bone marrow and liver metastases progressed. Treatment was changed to fulvestrant and weekly paclitaxel. The patient died more recently, 23 months after diagnosis.

In addition, we provide a comprehensive historical overview of vulvar adenocarcinomas of mammary gland type, including their immunohistochemical profiles, molecular analyses, and administered therapy. This overview not only sheds light on the development of histopathological diagnostic tools and the evolution of surgical and oncological treatment strategies over the past 90 years but may also assist pathologists in accurately diagnosing this rare malignancy and oncologists in choosing the appropriate treatment.

Introduction

Mammary-like carcinoma in extramammary sites is very rare, occurring most frequently in the axillary region. Vulvar Adenocarcinoma of Mammary Gland Type (VAMGT) is an unusual tumor arising from specialized anogenital mammary-like glands (AGMLGs), accounting for less than 10% of vulvar malignancies [1] and Table 1 [2-80]. The presence of ectopic breast tissue in the vulva was first described by Hartung in 1872, who postulated that ectopic mammary tissue can occur anywhere along the embryonic milk line between the axilla and the groin [81. Ectopic mammary tissue in the vulva is reported in 2–6% of women [30]. Greene diagnosed and subsequently reported on the first case of vulvar adenocarcinoma in 1936, noting its morphological resemblance to genuine breast adenocarcinomas [12].

However, more recent studies suggest that these glands derive from normal eccrine-type glands and are a normal constituent of anogenital tissue [82]. AGMLGs may display characteristics of eccrine, apocrine and mammary glands and can form lobules and acini similarly to breast tissue. They can be located in regions outside the caudal milk line, such as the interlabial sulcus (between the labia minora and majora), the perianal region and the paramedian zone of the perineum, resembling normal breast tissue [33,36,46,82,83]. Various lesions, both benign and malignant, may arise from AGMLGs, analogous to the spectrum of tumors seen in orthotopic breast tissue [1,84].

Another hypothesis suggests that adenocarcinomas arising from AGMLGs may originate through malignant transformation of pluripotent cells in the anogenital region [29].

VAMGT is predominantly diagnosed in postmenopausal women and is more frequent in parous patients [1]. The first diagnostic step is to exclude primary breast carcinoma and its metastasis in the vulva, metastasis of adenocarcinoma of other origins than breast and a primary malignant vulvar skin appendage tumor. The presence of Ductal Carcinoma in Situ (DCIS) supports the diagnosis of a primary vulvar neoplasm, as does the identification of AGMLGs in the vicinity of the tumor. However, the invasive component of this carcinoma may overgrow the preexisting AGMLGs or the carcinoma in situ component, complicating histopathological diagnosis. Immunohistochemical (IHC) markers that may aid in the diagnosis are the same as those used for primary breast carcinomas [74,85]. VAMGTs often metastasize to regional inguinal lymph nodes, whereas distant metastases are relatively uncommon [1]. Surgical management may range from local excision to radical vulvectomy, combined with the sentinel lymph node technique and/or (bilateral) inguinofemoral lymphadenectomy. However, for tumors confined to more superficial layers of the skin, less aggressive approaches—such as Mohs micrographic surgery—may be considered, particularly in elderly patients [26]. Although VAMGTs were historically thought to be rare, with just over 40 cases reported in the literature, we conducted a review indicating that the actual number is significantly higher. This tumor has been reported under a variety of nomenclatures, including: mammary-like adenocarcinoma, primary breast cancer of the vulva, mammary-like ductal carcinoma of the vulva, vulvar adenocarcinoma of mammary gland type, adenocarcinoma arising in vulvar breast tissue, adenocarcinoma arising in aberrant mammary gland in the vulvar area, “breast-like” adenocarcinoma of the vulva, infiltrating ductal carcinoma of the vulva, ectopic breast cancer of the vulva, carcinomas of anogenital mammary-like glands, apocrine adenocarcinoma of the vulva, primary ectopic breast carcinoma mimicking vulvar malignancy, and vulvar Paget’s disease with underlying adenocarcinoma simulating breast carcinoma. In addition, we report two new cases of VAMGT. The aim of this publication is to raise awareness of the existence of this rare vulvar adenocarcinoma and to provide guidance to pathologists on the criteria that should be considered when diagnosing this tumor.

Case reports

Case 1

In 2014, a 68-year-old patient presented with an ulcerative lesion of the vulva that had persisted for eight months. Eight years prior, she had undergone a hysterectomy with bilateral salpingo-oophorectomy for a well differentiated invasive endometrioid adenocarcinoma confined to the inner half of the myometrium (FIGO stage IA). The patient reported no family history of breast carcinoma or other gynecological malignancies. Mammography excluded the presence of primary breast carcinoma. Surgical excision of the vulvar lesion was subsequently performed. Gross examination of the vulvar specimen, measuring 25×15×10 mm, revealed an ulcerated tumor measuring 10 mm in diameter. Microscopic evaluation showed normal squamous epithelium with a central area of ulceration. The adjacent dermal tissue contained skin appendages, including hair follicles and eccrine and apocrine sweat glands, without evidence of epidermal pagetoid involvement. Deeper in the dermis and subcutaneous tissue, a tumor mass exhibiting a mixed glandu-

lar and solid architecture was identified as a grade 2 invasive adenocarcinoma with moderate nuclear atypia. A grade 3 DCIS component with comedo-type necrosis was present, supporting the primary nature of the tumor. No ectopic breast tissue was observed in the vicinity of the tumor (Figure 2). Due to positive surgical margins, a re-excision was performed to achieve complete tumor removal. Inguinal sentinel lymph node surgery was not performed. IHC analysis revealed an invasive adenocarcinoma with strong positivity for GATA3, estrogen receptor (ER, 100%), progesterone receptor (PR, 10%), androgen receptor (AR, 80%), Cytokeratin 7, and MUC1. The tumor was negative for HER2 by HercepTest (score 1+), WT-1, PLAP, inhibin, TTF-1, GCDFP-15, MUC2, TAG-72, CD10, CD56, chromogranin, synaptophysin, p16, p63, CK5/6, calretinin, CDX2 and CK20. The Ki-67 proliferation index was 33%, determined as a global score using AI analysis (Table 2; Figure 3). Correlation of the histological features with the IHC profile strongly supported a diagnosis of primary VAMGT, accompanied by grade 3 DCIS. Next-Generation Sequencing (NGS) analysis using the GMS560 gene panel identified pathogenic mutations in *TP53* and *PIK3CA*, consistent with molecular alterations commonly observed in breast carcinomas. In addition, a variant of uncertain significance was detected in the *PCB1* gene. These findings provide important insights into the molecular profile of this rare tumor (Table 3). Adjuvant therapy included an aromatase inhibitor exemestane during a 5-year period. Radiotherapy was administered locally to the vulvar region (25 fractions of 2 Gy, total 50 Gy) and regionally to both inguinal regions (30 fractions, total 60 Gy). No recurrence has been detected 12 years after the initial vulvar surgery.

Case 2

In February 2024, a 65-year-old woman presented with enlarged left inguinal lymph nodes. Her medical history was unremarkable, except for episodic immunosuppressive therapy for polymyalgia rheumatica. Biopsy of the lymph nodes revealed metastasis from breast carcinoma of No Special Type (NST), ER positive, PR positive, and HER2 negative (score 0). However, no primary breast tumor was identified clinically or radiologically. PET-CT showed diffuse bone marrow metastases in the ribs and spine, ground-glass opacities in the lungs, and a small hypermetabolic lesion in the vulva. A peripheral lung biopsy confirmed lymphangitis carcinomatosa. On clinical examination, a paraclitoral nodule was detected in the right interlabial fold, which was surgically excised. The vulvar excision specimen measured 28×18×20 mm and contained a well-circumscribed 12 mm white solid nodule located in the dermis and subcutaneous fat, without epidermal involvement. Histology showed invasive carcinoma with features of grade 2 breast carcinoma (NST), including solid epithelial strands, moderate nuclear pleomorphism and rare mitoses. No in situ carcinoma was identified; however, ER-positive anogenital mammary-like glands were observed adjacent to the tumor (Figure 3.). Lymphovascular and perineural invasion were present. Resection margins were free of tumor. Immunohistochemistry demonstrated positivity for GATA3, ER (100% strong), PR (30% moderate) and HER2 (equivocal, score 2+). HER2 dual SISH showed no amplification. The Ki-67 proliferation index was very low (1%). Comprehensive genomic profiling using a 523-gene panel identified a subclonal pathogenic *BRCA2* mutation with a low variant allele frequency (4%). No other pathogenic mutations were detected. Homologous recombination deficiency testing was negative. Tumor mutational burden was low (4 mutations/Mb). Amplifications were detected in *FGFR1* and *CCND1*. Microsatellite Status was Stable (MSS).

Therapy was initiated with ribociclib (CDK4/6 inhibitor) and letrozole (aromatase inhibitor). Fifteen months after diagnosis, lung and lymph node metastases had been resolved, but bone marrow metastases progressed, and liver metastases developed. Treatment was switched to fulvestrant and weekly paclitaxel. Patient died 23 months after diagnosis.

Comprehensive literature review

A literature review was conducted using PubMed and ClinicalKeys®, starting with the keywords “mammary-like adenocarcinoma in the vulva,” “breast-like adenocarcinoma in the vulva,” and “vulvar adenocarcinoma.” References cited in articles discussing VAMGT were manually examined to ensure that no cases were missed. All published cases identified in our online search, including their histological subtypes, immunohistochemical phenotype and molecular characteristics if available are summarized in Table 1. Our two new cases included, there are now 94 cases reported in literature between 1936 and 2026. The median age at diagnosis was 54.6 years (range 39–89). In three cases, the exact age was not reported, with patients described only as being in their sixties, forties and seventies; for analysis, we estimated their ages as 65, 45 and 75 years, respectively.

Table 1: Review of the literature 1936-2025.

Name of the first author	Year	Type (invasive or in situ) of vulvar cancer	Pagetoid pattern	No. of patients	Age of patients in years	Tumor size in mm	Metastasis localisation	Therapy	ER PR AR Status; Molecular biological analysis	HER2 status	Number of reviewed vulva carcinomas cited by the authors
Greene HJ **(12)**	1936	Bilateral vulvar lesion: Two carcinoma types: adenocarcinoma and epidermoid carcinoma		1	49	The larger lesion was 8 x 6 inch	Inguinal lgl Widespread metastases	No therapy. The patient died 3 weeks after the diagnosis.			
Hendrix RC **(15)**	1956	Poorly differentiated invasive adenocarcinoma		1	58	20		Radical vulvectomy Patients refused inguinal and femoral lymph node dissection			1 case (Greene)

Guerry RL **(14)**	1976	Both in situ and infiltrating carcinoma from ectopic mammary tissue in the vulva and bilateral breast cancer		1	62	15	Axillary metastass (1/34) of the breast cancer. Carcinomatosis with cerebral metastases	Vulvar excision Bilateral mastectomy			2 cases (Greene and Hendrix)
Dietel M **(7)**	1981	Invasive apocrine adenocarcinoma	yes	1	70	80 multifocal and ulcerated	Bilateral inguinal lgll	Irradiation			
Guercio E **(13)**	1984	Invasive lobular carcinoma		1	49	60	Inguinal lgll (11/24)	Radical vulvectomy Bilateral inguino-femoral and pelvic lymphadenectomy			2 cases (Greene and Hendrix)
Cho D **(4)**	1985	Invasive adenocarcinoma with features of breast cancer		1	70	25	Inguinal lgll (2/9)	Radical hemivulvectomy Ipsilateral inguinal and deep femoral node dissection Tamoxifen	ER+ PR+		3 cases
Simon KE **(23)**	1988	Moderately differentiated invasive adenocarcinoma		1	60	20	Inguinal lgll (3 of 11) Liver Bones	Radical vulvectomy Bilateral inguinal and right deep pelvic node dissection Chemotherapy Irradiation Tamoxifen	ER+ PR+		5 cases
Rose PG **(22)**	1990	DCIS both invasive ductal and lobular adenocarcinoma		1	68	17	1 inguinal lgl	Radical vulvectomy Inguinal lymphadenectomy Radiation therapy Tamoxifen	ER+		4 cases
Pelosi G **(20)**	1991	In situ carcinoma within a papillary hydradenoma		1	40	15		Local excision	ER+ PR+		
Di Bonito **(6)**	1992	Invasive adenocarcinoma		1	42 in the abstract; 46 in the text	15	Inguinal lgll (11/13)	Radical vulvectomy Bilateral inguino-femoral lymphadenectomy			6 cases
Bailey CL **(2)**	1993	Infiltrating ductal carcinoma			65	30	Inguinal lgll (2/10)	Radical vulvectomy Bilateral inguinal-femoral lymphadenectomy Tamoxifen	ER+ PR+		4 cases + additional 2 cases
van der Putte SCJ **(24)**	1994	Invasive carcinoma	yes	1	51	10					6 cases
Levin M **(18)**	1995	Invasive carcinoma		1	62	25	Inguinal lgll (4/11) + bone	Excision Ipsilateral groin dissection Tamoxifen Irradiation	ER+ PR+	HER2 3+	11 cases 1936-1995
Kennedy DA **(17)**	1997	Poorly differentiated invasive and in situ ductal carcinoma; Prior primary breast carcinoma	yes	1	71	50	Inguinal lgll	Radical vulvectomy Bilateral inguinal lymph node dissection Chemotherapy Radiation therapy	ER- PR-		10 cases
Graf AH **(11)**	1998	Mucinous adenocarcinoma with neuroendocrine differentiaiton Obs! 16 months later bilateral breast carcinoma with other morphology		1	75	45		Radical vulvectomy Bilateral inguinal and femoral lymph node dissection Radiation therapy	ER- PR+	c-erbB2-	5 cases
Irvin WP **(16)**	1999	Poorly differentiated adenocarcinoma: invasive both ductal and lobular ?	Epidermis focally	1	64	30	Micrometastasis in 1 of 14 lgll	Excision Ipsilateral inguinofemoral lymphadenectomy Chemotherapy Pelvic irradiation Tamoxifen	ER+ PR+		8 cases

Gull SE **(8)**	1999	In situ and invasive lobular carcinoma	yes	1	64	10	Inguinal lgll Skin (abdominal wall and back) Liver Local recurrence	Excision biopsy Tamoxifen Chemotherapy	ER+?		3 vulvar adenocarcinomas and 4 vulvar Paget's disease
Erb-Gremillet S **(9)**	1999	Infilrating adenocarcinoma		1	62	25		Total vulvectomy	ER+ PR+		11 cases
Neumann I **(19)**	2000	Invasive lobular carcinoma		1	60		Lgll in both groins (10/10 and 11/11)	Tamoxifen Chemotherapy Irradiation	ER+		12 cases
Gorisek B **(10)**	2000	Infiltrating ductal carcinoma		1	81	30		Wide local excision Adjuvant hormonal therapy	ER+ PR+		12 cases
Castro CY **(2)**	2001	Ductal carcinoma in situ		1	57	7		Wide local excision	ER+ PR+		12cases 1935-1997
Chung-Park M **(5)** Criteria till	2002	Invasive mucinous carcinoma		1	47	20		anterior radical vulvectomy Declined lymph node dissection	ER+ PR+ GCDFP-15-	HER2-	11 cases
Piura B **(21)**	2002	Invasive adenocarcinoma with apocrine (sweat) gland origin	yes	1	69	17	groin lgll bilaterally (6/7 and 1/8)	Radical vulvectomy Bilateral groin dissection Tamoxifen chemoptherapy irradiation	ER+ PR+		12 cases
Yin C **(25)**	2003	Invasive mucinous carcinoma		1	84	50	Lgl (1/11)	left partial vulvectomy	ER+ PR+ BRST-1+	HER2-	
Kiyohara T **(36)**	2003	Moderately differentiated apocrine adenocarcinma with signet ring cells	Yes with few pagetoid cells	1	72	40	Bilateral inguinal lgll Multiple bone metastases	Vulvar biopsy Chemotherapy Irradiation	ER- PR-		
Ohira S **(44)**	2004	invasive	yes	1	82	50	Left inguinal nodes	Local excision of the vulvar tumor Dissection of left inguinal lymph nodes	ER+		
Tanaka H **(45)**	2005	invasive		1	87	40	Multiple bone metastases Skin	Paclitaxel	ER- PR-		13cases
Gopinath D **(34)**	2006	Two foci of invasive lobular carcinoma; Infiltrating dermal lesion		1	81	40 and 10	CT showed bilateral inguinal lymph node and left obturator lymph node metastases	Anastrozole Chemotherapy Radiotherapy Bisphosphonate	ER+ PR+		13 cases
Lopes G **(38)**	2006	Primary ectopic breast cancer in the vulva Invasive mucinous carcinoma		1	44	20	Inguinal lgll (2/13)	Partial radical vulvectomy Bilateral groin dissection Chemotherapy Tamoxifen	ER+	HER2-	
North J **(43)**	2007	Purely differentiated adenocarcinoma T1 N1 M0		1	49	15	Inguinal lgl	Excision Neoadjuvant chemotherapy Tamoxifen Irradiation	ER+ PR+	HER2-	20 cases
Abbott JJ **(26)** Review Table side 130	2006	Primary infiltrative adenocarcinoma		1	51	10		Excision+ Mohs micrographic surgery	ER- PR-	HER2-	19 cases
Fracchioli S **(33)**	2006	Invasive micropapillary carcinoma	epidermis involvement	1	57	<10 mm	7/7 inguinal lgll, lungmetastases	Local excision + Vulvectomy chemotherapy	ER- PR- p53- CA19.9- c-ErbB2+ (?)		15 cases

Martinez-Palones JM **(39)**	2007	Invasive ductal carcinoma of mammary gland type Grade 2		1	49	35		Local excision of the tumor Ipsilateral inguinofemoral lymphadenectomy Tamoxifen	ER+ PR+	c-erbB-2 -	16 invasive cases 2 DCIS cases 1 case vulvar Paget's disease with underlying adenocarcinoma
Tseung J **(46)**	2008	Infiltrating ductal carcinoma	yes	1	49		Inguinal lymph node	Excision biopsy Fine needle biopsy of an inguinal lymph node	ER+ PR+		17 + 5 cases
Alsaad KO **(27)**	2009	Recurrent vulvar Paget disease Invasive apocrine	yes	1	89	47	2 inguinal lgll	Complete vulvectomy Left inguinal node dissection	ER- PR- AR+		
Fernandez-Figueras MT **(32)**	2010	Invasive tubulolobular carcinoma		1	45	20		Wide surgical excision Sentinel node biopsy + 2 other lgll			
Naseer MA **(42)**	2011	Invasive ductal carcinoma Grade 3		1	57	15	Inguinal lymph nodes (3/13	Bilateral inguinal lymph node dissection Chemotherapy Radiotherapy Aromatase inhibitor	ER+ PR+	HER2-	14 cases
Minhoto Diniz da Costa AT **(31)**	2012	Invasive adenocarcinoma with tubular pattern		1	82	20		Deep local excision Aromatase inhibitior (Letrozole) Radiotherapy	ER+ PR+		24 cases
Kajal B **(35)**	2013	Invasive apocrine adenocarcinoma		1	67	27		Local surgery	ER- PR-		
Bogani G **(29)**	2013	Mammary-like ductal carcinoma, moderately differentiated T2 N1 M0		1	71	10	Inguinal lgl (1/8)	Radical vulvectomy Bilateral inguinal superficial lymphadenectomy Neoadjuvant chemotherapy Tamoxifen Radiation therapy	ER+ PR+	Low + staining for c-erbB-2 (5%)	<30 cases
Lamb A **(37)**	2013	Infiltrating mammary adenocarcinoma with mucinous differentiation Hereditary breast and ovarian cancer		1	59	10		Radical vulvar local excision Tamoxifen	ER+ PR+ BRCA2 mutation	HER2-	just over 20 cases
McMaster J **(40)**	2013	Invasive adenocarcinoma grade 4		1	60	19		Wide local excision Inguinal lymph node survey Radiation therapy	ER+		Approx 25 cases
Benito V **(28)**	2013	Invasive adenocarcinoma grade 2		1	82	40	inguinal lgll (10/14); pelvic lgll (17/18)	Radical vulvectomy Bilateral inguinofemoral lymph node dissection Bilateral pelvic lymphadenectomy Anastrazole	ER+ PR+	HER2-	25 cases
Butler B **(30)**	2014	Invasive carcinoma in mammary-like glands		1	65	16		Local excision Ipsilateral groin sentinel lymph node dissection Letrozole	ER+ PR-	HER2-	25 cases
Meddeb S **(41)**	2014	Mammary-like adenocarcinoma	yes	1	41	15	Inguinal lgll (4/13)	Vulvectomy Bilateral inguinal lgl dissection	ER- PR-	HER2-	
Baykal C **(51)**	2015	Invasive mammary-like gland carcinoma grade 2		1	73	30	2 inguinal lymph nodes both sides Lung and bone metastasis L3 vertebra	Radical vulvectomy Bilateral inguinal lymphadenectomy Aromatase inhibitor, Zoledronic acid Radiotherapy Chemotherapy	ER+ PR+		26 cases

Villada G **(71)**	2015	Invasive lobular carcinoma	yes	1	60		Lgl	Wide local excision Wide re-excision Later partial radical vulvectomy Bilateral inguinal lymph node dissection	ER+	HER2+	6 cases of putative invasive mammary-like lobular carcinoma
Tran Tien AN **(70)**	2015	Collision of DCIS of AMLG and vulvar sarcomatoid squamous cell carcinoma		1	81	38	Inguinal metastasis of squamous cell carcinoma	Partial vulvectomy Inguinal dissection Local radiation therapy			34 cases
Cripe J **(54)**	2015	Invasive ductal carcinoma		1	62	13	Inguinal lymph nodes (2/17)	Wide local excision Re-excision because of local recurrence Inguinal-femoral lymphadenectomy Radiation therapy Chemotherapy Aromatase inhibitor	ER+ PR+	HER2-	22 cases
Aoyama K **(49)**	2016	Poorly differentiated invasive apocrine adenocarcinoma pT1b N2b M0, FIGO stage 3B (2008)	yes	1	57	35	Lgll in both inguinal regions	Radical vulvectomy Bilateral inguinal and pelvic lymphadenectomy Chemotherapy Radiotherapy Recurrence after radical surgery	AR+		
Tessier-Cloutier B **(69)**	2017	Mammary-like adenocarcinomas		7	Median age: 72 (53-86)	Between 18-70	Not sampled in 6 cases 1 case: lgll (2/8)	Surgery type known for 4 patients: Radical vulvectomy Wide local excision Hemivulvectomy Wide local excision	3 cases luminal B 2 cases HER2-enriched 1 case luminal A 1 case basal-like	2 cases HER2-enriched	30-40 cases
Konstatinova A **(60)**	2017	4 cases invasive carcinomas 3 cases DCIS	Yes in 6 cases	7	Median age: 67,7 (40-78)						
Ishigaki T **(59)**	2017	Invasive ductal carcinoma		1	72			Local excision Sentinel node Aromatase inhibitor	ER+ PR+ GCDFP15-+	HER2-	26 cases
Grewal JK **(58)**	2017	Poorly differentiated invasive adenocarcinoma Multiple masses Stage IV		1	60	25	Bilateral inguinal lymphadenopathy, retrocaval, external iliac, common iliac lymph nodes	Chemotherapy Trastuzumab and pertuzumab Radiotherapy	ER- GCDFP-15- Genomic characterization	HER2+	
Lopes A **(64)**	2017	Carcinoma analogous to invasive breast carcinoma not otherwise specified type, high grade		1	58	12		Wide vulvar excision Inguinal lymphadenectomy Chemotherapy Trastuzumab Aromatase inhibitor	ER+	HER2+	28 cases
Kredentser A **(61)**	2017	1.Invasive adenocarcinoma, high grade 2.Invasive adenocarcinoma with mucinous/colloid features 3.Invasive mucinous carcinoma		3	1.75 2.59 3.67	1. 10 mm 2. 9 mm 3. 30 mm	1. 2/5 superficial lgll 1/2 deep inguinal lgll 2. 1/2 SN	1.Radical hemivulvectomy Inguinal lgll dissection Radiation therapy Chemotherapy Trastuzumab 2.Hemivulvectomy Inguinal SN biopsy Chemotherapy Radiation therapy Tamoxifen 3.Hemivulvectomy Inguinal SN dissection Tamoxifen	1.ER+ PR- 2. ER+ PR+ 3. ER+ PR+	1. HER2 3+ 2. HER2-	29 cases

Eom H-J **(56)**	2017	Ectopic **male** breast cancer in the perineum: Multifocal invasive breast-like adenocarcinoma			70	17	Bilateral inguinal lgll	Local wide excision of the perineum Bilateral inguinal lymphadenectomy Hormonal therapy Adjuvant chemotherapy	ER+ PR+ PSA-	HER2-	
Al-Mansouri L **(47)**	2018	Primary adenocarcinoma of the ectopic breast tissue of the vulva		1	76		Large pelvic and vaginal mass Lgl metastasis, vulvar subcutaneous nodules	Radiotherapy Aromatase inhibitor Abraxane Femara chemotherapy	Vaginal mass: ER+ PR+	Vaginal mass: HER2-	28 cases
Li S **(62)**	2019	high grade invasive adenocarcinoma with apocrine feature and signet ring cells		1	69	46		Radical vulvar excision Aromatase inhibitor therapy Patient declined radiation and inguinal lymph node sampling Patient declined re-excision of the vulvar lesion;	ER+ PR+ AR+ Amsterdam 70-gene breast cancer gene signature: low risk of recurrence	HER2-	28 cases
Chow CY **(53)**	2019	Extramammary Paget disease with invasive vulvar adenocarcinoma Stage IIIB	yes	1	71	35	In 2 inguinal lgll	Radical vulvectomy Bilateral groin and pelvis dissection Post-adjuvant brachytherapy No chemotherapy	ER- PR-	HER2+	
Aramin H **(50)**	2019	Multifocal vulvar infiltrating ductal carcinoma grade 3 and DCIS Stage IIIB Obs! Metachronous breast carcinoma		1	43	multifocal	Bilateral inguinal SN	Radical hemivulvectomy Bilateral inguinofemoral sentinel node biopsy Systemic chemotherapy Taxol Herceptin	ER+ PR+	HER2+	30 cases
Matak L **(65)**	2020	Invasive lobular carcinoma Stage T1		1	60	5		Surgical removal Inguinal sentinel node	ER+ PR+		29 cases
Niakan S **(67)**	2020	Invasive lobular carcinoma of pleomorphic type		1	55	35	Brain metastasis	Neoadjuvant chemotherapy Partial radical vulvectomy Sentinel nodes Radiation Trastuzumab Lapatinib and capecitabine	ER- PR-	HER2+	36 cases
Deshmukh AA **(55)**	2020	Invasive differentiated adenocarcinoma grade 2 Obs! Prior DCIS in the breast		1	55		Inguinal lymph node (6/10)	Partial vulvectomy with re-excision Chemotherapy Radiation therapy Aromatase inhibitor	ER+ PR+	HER2-	<30 cases
Ananthula A **(48)**	2020	Mammary type adenocarcinoma Grade 3 Stage IV		1	47	27	Inguinal lgll (4/17) Distant lymph node and bone metastasis	Radical vulvectomy Bilateral inguinal lymphadenectomy Aromatase inhibitor CDK4/6 inhibitor	ER+ PR-	HER2-	36 cases
Farrag A **(57)**	2020	DCIS in ectopic breast tissue		1	53	20		Excision biopsy Tamoxifen Patient declined pelvic radiotherapy	ER+ PR-	HER2-	
Shah VI **(68)**	2021	Two cases of metaplastic mammary gland-like adenocarcinoma FIGO Stage IIIC	Yes in both cases	2	88 82	33 60	1.Metastasis in SN right inguinal region 2.MRI showed enlarged necrotic inguinal, aortocaval, para-aortic lgll	1.Anterior vulvectomy Bilateral SN sampling Adjuvant radiotherapy 2.Incisional biopsy, later palliative wide local excision Palliative radiotherapy	ER- in both PR- in both	HER2- HER2+	

Morais M **(66)**	2022	Invasive ductal carcinoma		2	1.In her 60s 2.In her 40s	1. 32 mm 2. 30 mm	1. no metastasis 2. lgl metastasis (inguinal and external iliac region/ganglia)	For both excisional biopsy 1.Aromatase inhibitor 2.Chemotherapy Radiotherapy	1.ER+/PR+ GCDFP15- 2.ER-/PR- GCDFP-15-	Both HER2-	36 cases until 2017
Castelow C **(52)**	2022	Invasive myoepithelial carcinoma (origin uncertain: from AGMLG? Skin adnex?)		1	40	38		Radical anterior vulvectomy Inguinal lymph node dissection Chemotherapy Radiation			7 vulvar myoepithelial carcinomas (1999-2022)
Lobrano R **(63)**	2023	Mammary-like infiltrating adenocarcinoma		1	88	20		Patient refused any further clinical investigation and treatment	AR+	HER2-	19 cases
Mansour M **(76)**	2023	Invasive ductal carcinoma grade 2 on mons pubis		1	74	150(!)		Local excision			31 cases
Si J **(78)**	2024	Encapsulated papillary carcinoma		1	73	25		Surgical enucleation No postoperative treatment	ER+ PR+		<40 cases
Tang H **(79)**	2024	Adenocarcinoma of AMGT arising from encapsulated papillary carcinoma with mucinous focus		1	69	21	1 groin sentinel node	Excisional biopsy Radical partial vulvectomy	ER+ PR+	HER2-	
Hu L **(75)**	2024	primary mammary-like vulvar adenocarcinoma (luminal B type / HER2+)		1	59	70 x 120(!)	Multiple inguinal, external iliac lgll	Excision	ER+ PR+	HER2+ Obs! The second triple positive case	41 cases
Wu F **(80)**	2024	Invasive ductal carcinoma grade 2		1	70+	20 mm DCIS and 8 mm invasive cancer		Wide excision Sentinel node from right inguinal region Adjuvant hormonal therapy	ER+ PR+	HER2-	30 cases
Barrios M **(72)** Obs! Primary tumor published by Lopes 2006	2024	2004: mucinous adecocarcinoma of ectopic mammary origin 2019: inguinal recurrence: invasive ductal carcinoma with mucinous differentiation		1	39 by the primary tumor; In her early 60s by recurrence	Recurrence in the lgll: 14	2004: 2/13 inguinal lgll	2004: partial vulvectomy Radiation therapy Hormonal treatment Chemotherapy Bilateral inguinal lymph node dissection 2019: Left inguinal mass: Letrozol and palbociclib Surgical excision Radiation therapy	Recurrence: ER+ PR-	HER2-	41 cases
Dai X **(73)**	2025	Non-special type invasive ductal carcinoma		1	70	30	Bilateral inguinal lymphadenopathy Metastasis in the urinary bladder and cervix	Vulvectomy Chemotherapy	ER- PR-	HER2-	
Markel L **(77)**	2025	Invasive mammary-like adenocarcinoma of the vulva T2 N0 M0		1	77	47 x 18 mm		Left radical vulvar excision Left inguinal sentinel lymph node Radiation Patient declined adjuvant treatment	ER+ Somatic BRCA1 mutation	HER2-	53 cases
Heller A **(74)**	2025	Mammary-type adenocarcinoma: 1 mucinous carcinoma, 1 with neuroendocrine features, 1 with lobular growth pattern		3	NA	NA	NA	NA	NA	NA	NA

Present Case 1	2026	Invasive vulvar adenocarcinoma arising from AGMLG		1	68	10 mm with ulceration	Inguinal lgll Bone marrow Lungs Liver	Vulvar excision Exemestane for 5 years Irradiation of vulvar region and both inguinal regions	ER+ PR+ Mutations in *TP53,* PIK3CA, and *PCB1* gene	HER2-	All publications cited above
Case 2	2026	Invasive vulvar adenocarcinoma arising from AGMLG		1	65	12 mm No ulceration.		Vulvar excision. Ribociclib and letrozole for 15 months. Fulvestrant and paclitaxel weekly.	ER+/PR+ Subclonal *BRCA2* mutation. *FGFR1* and *CCND1* amplifications.	HER2-	

Table 2: Antibodies, clones and dilutions used in this study.

Antibody	Clone	Catalog number	Dilution	Source
AR	441	sc7305	1/50	Santa Cruz
CALR	DAK-Calret 1	IR627	RTU	Agilent
CD10	DAK-CD10	IR786	RTU	Agilent
CD56	123C3	IR628	RTU	Agilent
CDX2	DAK-CDX2	IR080	RTU	Agilent
CHROA	LK2H10	MAB5268	1/6000	Sigma Aldrich
CK20	KS20.8	IR777	RTU	Agilent
CK5/6	D5/16B4	IR780	RTU	Agilent
CK7	OV-TL 12/30	GA619	RTU	Agilent
ER	EP1	GA084	RTU	Agilent
GATA3	L50-823	390M-16	1/100	CellMarque
GCDFP-15	23A3	GA077	RTU	Agilent
HercepTest		SK001	RTU	DAKO
HER2 SISH	Probe cocktail	00-6043		VENTANA Dual ISH DNA Probe Coktail
INHIBIN	R1	IR058	RTU	Agilent
Ki-67	MIB-1	GA626	RTU	Agilent
MUC1	014E	FDV-0012B	1/2000	Funakoshi
MUC2	Ccp58	PA0155	RTU Bond	Leica
p16	BC42	SKU:3231	RTU	BioCare Med.
p53	DO-7	IR616	RTU	Agilent
PLAP	8A9	IR779	RTU	Agilent
PR	PgR 1294	GA090	RTU	Agilent
SYNAP	DAK-SYNAP	IR660	RTU	Agilent
TAG72	B72.3	MS-138-P1	1/200	ThermoScientific
TTF1	SPT24	NCL-L-TTF1	1/100	Triolab
WT1	6F-H2	IR055	RTU	Agilent

Table 3: Molecular characteristics for the present cases.

Genes	Codon	Amino acid change	Coding	Classification	Allele frequency %	Assessment
Case 1.						
PIK3CA	H1047R	p.H1047R	c.3140A>G	Tier 2C	55%	Pathogenic
TP53	Y220C	p.Y220C	c.659A>G	Tier 2C	51%	Pathogenic
PCBP1	G216dup	p.G2016dup	c.645_647dupGGG	Tier 3	33%	Uncertain significance
Case 2. Comprehensive genomic profiling using a 523-gene panel identified a subclonal pathogenic *BRCA2* mutation with a low variant allele frequency (4%). Amplifications were detected in *FGFR1* and *CCND1*.						

Table 4: Summary of published cases of vulvar adenocarcinoma arising in AGMLGs with reported molecular analyses.

No	Authors Year of publication	Patient age	Molecular analysis performed with results
1	Lamb (37) 2013	59	BRCA2 mutation (8765delAG) Hereditary breast and ovarian cancer
2	Grewal (58) 2017	60	Genomic analyses: Single-nucleotide variants, copy number variants, structural variants, transcriptomic analysis, mutational signatures
3	Li S (62) 2019	69	Amsterdam 70-gene breast cancer gene signature: low risk of recurrence
4	Deshmukh (48) 2020	55	Genomic testing for tumor origin by Rosetta Genomics: primary mammary-like carcinoma
5	Lobrano (76) 2023	88	Next generation sequencing: Pathogenic mutation of AKT1 gene, pathogenic frameshift insertion of JAK1 gene, two likely pathogenic frameshift deletions of the KMT2C gene, two variants of unknown significance involving ARID1A and OR2T4 genes, two CNVs of the BRCA1 gene were identified
6	Hu L (80) 2024	59	5 genomic variants detected: ERBB2_NAGLU fusion at ERBB2 exon 15 and intron 1 of NAGLU, ESR1-CCDC170 fusion, MYC gain, PIK3CA p104_G106delinsR and TP53 c1180_*del TGAC
7	Markel (74) 2025	77	Somatic BRCA1 mutation (variant p.S770, c.2309C>G)

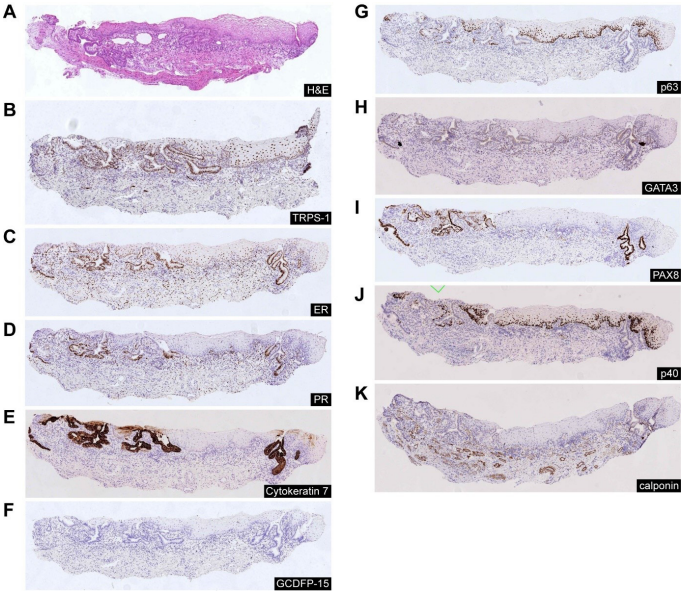

Figure 1: Normal AGMLGs of the vulva. Vulvar skin biopsy 2.8×0.6 mm. A 23-year-old female patient, clinically diagnosed as endometriosis. **(A)** H-E staining. B-K: IHC staining; **(B)** TRPS-1+ **(C)** ER+ D: PR+ **(E)** Cytokeratin 7+ **(F)** GCDFP-15 mucoapocrine marker **(G)** p63 +/- **(H)** GATA3 **(I)** PAX8 J: p40 +/- **(K)** calponin.

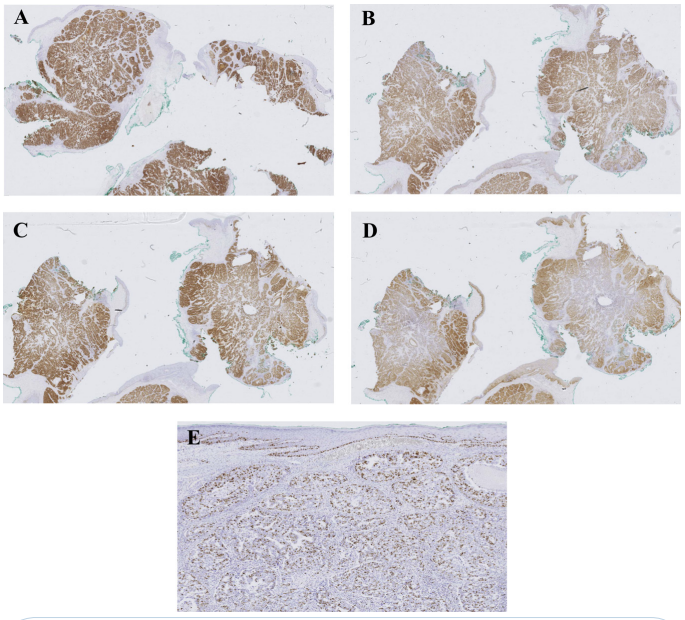

Figure 3: Case 1. Digital images of the positive immunohistochemical findings of the VAMGT. **(A)** Cytokeratin 7 **(B)** GATA 3 (C) ER (D) AR E. Ki67 proliferation index: 33% as global score.

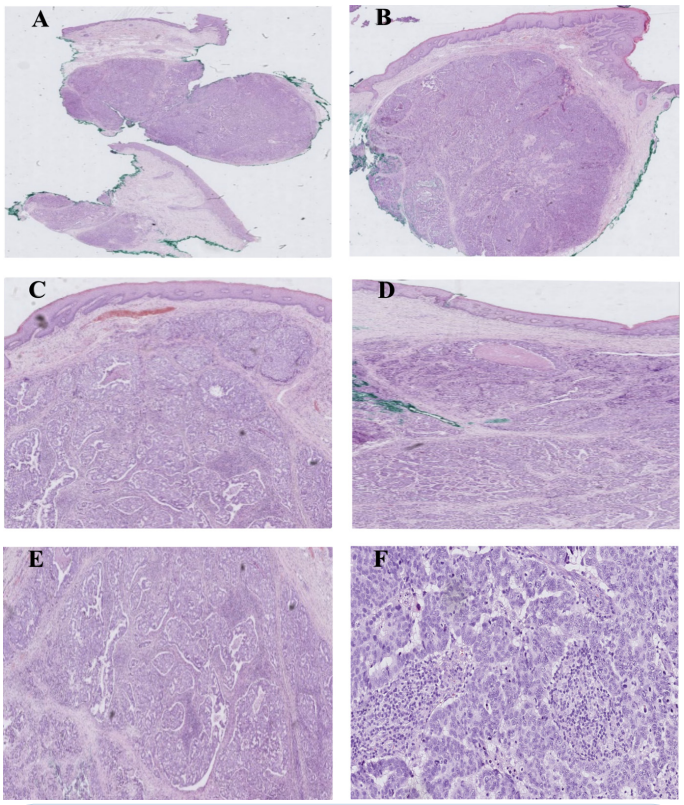

Figure 2: Case 1. Morphological features of VAMGT in H&E staining. **(A-B)** Normal histological squamous epithelium with tumoral mass deeper in the dermis. **(C)** Tumoral mass exhibiting a mixed glandular and solid architectural pattern. **(D-E)** The solid areas are arranged mainly in cribriform patterns. **(F)** The tumor cells displayed moderate nuclear atypia.

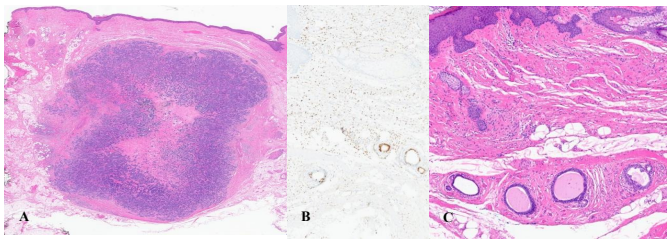

Figure 4: Case 2. **(A)** VAMGT. H&E staining. **(B)** ER IHC staining. **(C)** Normal AGMLGs in the vicinity of the tumor.

Discussion

The presence of mammary tissue in the vulvar region is a well-recognized phenomenon in certain Cetacea, such as whales, porpoises, and dolphins, whose nipples are located on either side of the genital slit [86]. Early studies described vulvar adenocarcinomas as arising from supernumerary or aberrant mammary glands, vulvar breast tissue or ectopic mammary tissue [12-15,23]. Denise Cho and Rose later referred to this tumor type as primary breast cancer of the vulva [4,22]. Even mammary-type DCIS has been reported [3,20,60,70]. Those invasive VAMGT that were not morphologically specified in these early studies can be interpreted as ductal-type (NST), [2,4,6,9,14,15,17,18,23,26,28-30,39-48,50,51,53-56,60,63,66, 69,73,75,76,80,82]. Later on, more specific subtyping of the VAMGT was introduced, such as the lobular type [8,13,19,34,65,67,71], the tubular type [31], the tubulo-lobular type [32], the mucinous type [5,25,37,61,64,72], the micropapillary type [33], the apocrine type [7,21,27,35,49], the metaplastic type [68], the myoepithelial type [52] and the encapsulated / intracapsular type [78,79] of VAMGTs. A combination of different carcinoma-types was reported by Greene [12] Rose and Irvin [16,22], Graf [11], Kiyohara and Li S [36,62], and Tien AN Tran [70]. There have been cases described in which VAMGT was associated with extramammary Paget's disease of the vulvar skin (sometimes referred to as epidermal involvement or a pagetoid pattern) [7,8,16,21,24,27,33,36,41,44,46,49,53,60,68, 71]. VAMGT and extramammary Paget's disease may represent a shared pathological continuum, as they exhibit a spectrum of changes analogous to those seen in the breast [60,69].

VAMGTs are listed in both the WHO Female Genital Tumours classification and the AJCC Cancer Staging System. These classifications specify the specific glandular origin of vulvar adenocarcinomas, such as Bartholin gland, Skene gland, mammary-gland type or sweat gland origin [1,87-89]. From a pathological perspective, VAMGTs should be differentiated from adenocarcinomas arising in the Bartholin gland. The latter typically involves the anatomical region of the Bartholin gland and often demonstrates a transition zone between benign Bartholin gland tissue and the tumor. Microscopically, they show variable differentiation, sometimes with a papillary exophytic architecture involving the surface epithelium, but more commonly with predominantly glandular structures in deeply infiltrative areas. They may be of mucinous type; when present, the mucinous subtype can exhibit intestinal differentiation with goblet cells and large extracellular mucin pools. In contrast to VAMGTs (which can be positive for ER, PR, HER2, mammaglobin, GCDFP-15, and GATA3), adenocarcinomas of Bartholin gland origin are usually negative for ER, PR, and HER2, and typically show a CK7+, CK20+, CDX2+, and GATA3– immunophenotype (88). Notably, both tumor types are generally p16- and HPV-negative. Only rare HPV-associated cases have been reported in the literature; these cases display distinct morphology, typically resembling HPV-associated adenocarcinomas, characterized by mucin-poor tumor cells, hyperchromatic nuclei, numerous mitotic figures, and frequent apoptotic bodies. VAMGTs should also be distinguished from benign mammary-type tumors of the vulva, such as papillary hidradenoma, which may present with an ulcerated surface and clinically mimic malignancy. Histologically, papillary hidradenoma shows complex branching and interconnecting epithelial tubules and papillae lined by a subepithelial myoepithelial cell layer positive for calponin and p63, in contrast to VAMGTs, in which myoepithelial cells are absent. Similarly to the breast, purely in situ carcinoma may also arise from Anogenital Mmammary-Like Glands (AGMLGs) [3,20]. Furthermore, tumor-like lesions of the vulva may mimic VAMGT, such as Bartholin gland hyperplasia, which typically exhibits preserved acinar–ductal architecture. Finally, metastatic adenocarcinoma to the vulva—particularly of colorectal origin—should be included in the differential diagnosis; clinical history and immunohistochemical profile are essential for accurate distinction. To ensure that an adenocarcinoma is related to AGMLGs, several factors may assist in the differential diagnosis, such as (a) tumor localization in the interlabial sulcus and (b) positive IHC expression of ER and PR [4]. However, the site of origin may no longer be identifiable in larger tumors that have grown far beyond the interlabial sulcus. Moreover, there was a wide variety of primary mammary-like carcinomas that do not express ER or PR. Among the reported cases, several tumors were ER negative, [11,17,26,27,33,35,36,41,45,53,67,68,73], however not all cases were tested by IHC. Levin [18] first described a HER2-positive VAMGT, followed by subsequent reports [50,53,58,6,64,67,68,71,75]. However, not all cases reported in the literature were tested for HER2 status. Breast cancer molecular subtyping, using surrogate categories such as luminal/non-luminal type, triple negative, HER2 positive subtypes etc., can also be applied to VAMGT [69]. Due to the lack of consistently available IHC biomarker data for the previously reported cases, we did not perform retrospective subtyping or related statistical analyses [55]. An ectopic male breast cancer in the perineum had been described as a multifocal invasive breast-like carcinoma [56].

Given the rarity of these VAMGTs, optimal treatment strategies are not yet established. However, oncological treatment and follow-up protocols generally mirror those used for orthotopic primary breast carcinomas, including wide local excision, sentinel lymph node biopsy and/or inguinofemoral lymphadenectomy, adjuvant systemic therapy and locoregional radiotherapy. Similar to breast carcinomas, prognosis varies depending on stage and histological subtype. Two reported cases of VAMGT have been treated with neoadjuvant therapy [43,67]. North et al. reported a poorly differentiated tumor (ER+/PR+/HER2-, T1N1M0) treated with four cycles of 5-FU/epirubicin/cyclophosphamide followed by 13 weeks of docetaxel, resulting in a partial response in the left inguinal lymph nodes and complete clearance at the primary site [31]. Niakan described a non-luminal, HER2-positive invasive lobular carcinoma of pleomorphic type treated with neoadjuvant trastuzumab, pertuzumab, carboplatin, and docetaxel, achieving a complete pathological response upon surgical excision [67]. Despite the absence of standardized diagnostic and treatment guidelines, an accurate histopathological diagnosis remains crucial, ideally made in consultation with pathologists subspecialized in breast pathology. Differential diagnosis includes adenocarcinomas arising from skin appendages and metastatic breast carcinomas [90]. Diagnosis is further complicated given that some malignancies with identical morphological features can originate primarily in both the breast and skin appendages (e.g., adenoid cystic carcinoma, apocrine adenocarcinoma). Tumor involvement of the epidermis, presenting as extramammary Paget's disease, may also be observed in vulvar adenocarcinomas. Moreover, a wide variety of rarer breast carcinoma subtypes can develop in the vulvar region, including primary apocrine carcinoma, mucinous adenocarcinoma, neuroendocrine carcinoma and adenoid cystic carcinoma. These tumors may originate not only from AGMLGs but also from sweat glands, giving rise to malignant breast-like lesions. Despite compiling all cases reported in the medical literature over the past nine decades, it is not possible

to microscopically re-evaluate these historical cases to determine whether they truly meet the current criteria for VAMGT. It is possible that some tumors originated from skin appendages when their features overlapped completely with those of breast carcinoma subtypes, such as invasive apocrine carcinomas [49]. Pelosi [20] reported a case in which apocrine DCIS of mammary type arose within a papillary hidradenoma of the vulva. In cases where differential diagnosis requires IHC—such as triple-negative adenocarcinomas—antibodies commonly used to identify primary breast carcinomas (cytokeratin 7, GATA3, mammaglobin, TRPS1) can also be applied to vulvar adenocarcinomas [74]. However, these markers are not entirely specific for breast lesions and may also stain adenocarcinomas originating from skin appendages [85]. Relatively few cases have undergone genomic characterization, although integrative genomic analyses could aid in selecting more targeted therapies [58]. Some patients with VAMGT have been found to carry *BRCA1* or *BRCA2* mutations (Table 4) [37,55,58,62,63,75,77]. In conclusion, VAMGTs are rare tumors that intersect two areas of cancer management. Consequently, their histopathological evaluation and treatment require a multidisciplinary approach, involving both pathologists and oncologists with subspecialty expertise in breast carcinoma, to ensure that patients receive appropriate, targeted therapy.

Author declarations

Ethics approval

Case 1

This study was approved by the Ethical Committee of the Department of Medicine, Linköping, Sweden (Ethics code: Diary Number 2020-00955). According to our university policy, informed consent was not required, as the study does not include any identifiable patient information.

Case 2

Written informed consent was obtained from the patient prior to her death, which occurred shortly before submission of the manuscript for publication. Publication of the case report was approved by the Ethical Committee of AZ Turnhout, Belgium, on January 29, 2026.

Acknowledgments

The authors thank biologists Niklas Dahr and Josefin Andersson for their technical support.

Author contributions

AK: Conceptualization; Literature review; Data curation; Writing – original draft; Visualization; Table preparation; Histological image acquisition to Case 1. SS: Writing – review & editing (Discussion section, differential diagnosis of vulvar lesions). CC: Writing – original draft (Case 2). Histological image acquisition to Case 2. All other co-authors: Writing – review & editing; Critical revision of the manuscript for important intellectual content.

Funding

This study was funded by the Stiftelsen Assar Gabrielssons Fond, Sweden, Grant ID: F24-126.

Data availability

Not applicable. This manuscript does not report data generation or analysis.

Disclosure

The authors state they have no competing interests.

References

1. World Health Organization Classification of Tumours Editorial Board. Female genital tumours. Lyon (France): International Agency for Research on Cancer; 2020.
2. Bailey CL, Sankey HZ, Donovan JT, Beith KA, Otis CN, Powell JL. Primary breast cancer of the vulva. Gynecol Oncol. 1993; 50: 379-83.
3. Castro CY, Deavers M. Ductal carcinoma in-situ arising in mammary-like glands of the vulva. Int J Gynecol Pathol. 2001; 20: 277-83.
4. Cho D, Buscema J, Rosenshein NB, Woodruff JD. Primary breast cancer of the vulva. Obstet Gynecol. 1985; 66: 82S.
5. Chung-Park M, Liu CZ, Giampoli EJ, Emery JD, Shalodi A. Mucinous adenocarcinoma of ectopic breast tissue of the vulva. Arch Pathol Lab Med. 2002; 126: 1216-8.
6. Di Bonito L, Patriarca S, Falconieri G. Aggressive "breast-like" adenocarcinoma of vulva. Pathol Res Pract. 1992; 188: 211-4.
7. Dietel M, Bahnsen J, Stegner HE, Hölzel F. Paget's disease of the vulva with underlying apocrine adenocarcinoma. Pathol Res Pract. 1981; 171: 353-61.
8. Gull E, Al-R, Sarah. Paget's disease of the vulva with underlying lobular breast carcinoma. J Obstet Gynaecol. 1999; 19: 320-1.
9. Erb-Gremillet S, Gunther M, Amiaux F, Parache R, editors. Carcinome vulvaire de type mammaire. Ann Pathol. 1999.
10. Gorisek B, Zegura B, Kavalar R, But I, Krajnc I. Primary breast cancer of the vulva. Wien Klin Wochenschr. 2000; 112: 855-8.
11. Graf A, Su H, Tubbs R, Hacker G, Dietz O, Staudach A. Primary neuroendocrine mucinous adenocarcinoma of the vulva. Anticancer Res. 1998; 18: 2041-5.
12. Greene HJ. Adenocarcinoma of supernumerary breasts of the labia majora. Am J Obstet Gynecol. 1936; 31: 660-3.
13. Guercio E, Cesone P, Saracino A, Gatti M, Arisio R, Oberto F. Adenocarcinoma in aberrant mammary gland of vulva. Minerva Ginecol. 1984; 36: 315-9.
14. Guerry RL, Pratt-Thomas HR. Carcinoma of supernumerary breast of vulva. Cancer. 1976; 38: 2570-4.
15. Hendrix RC, Behrman S. Adenocarcinoma in supernumerary mammary gland in vulva. Obstet Gynecol. 1956; 8: 238-41.
16. Irvin WP, Cathro HP, Grosh WW, Rice LW, Andersen WA. Primary breast carcinoma of the vulva. Gynecol Oncol. 1999; 73: 155-9.
17. Kennedy DA, Hermina MS, Xanos ET, Schink JC, Hafez G. Infiltrating ductal carcinoma of the vulva. Pathol Res Pract. 1997; 193: 723-6.
18. Levin M, Pakarakas R, Chang H, Maiman M, Goldberg S. Primary breast carcinoma of the vulva. Gynecol Oncol. 1995; 56: 448-51.
19. Neumann I, Strauss H, Buchmann J, Koelbl H. Ectopic lobular breast cancer of the vulva. Anticancer Res. 2000; 20: 4805-8.
20. Pelosi G, Martignoni G, Bonetti F. Intraductal carcinoma in vulvar mammary-type epithelium. Arch Pathol Lab Med. 1991; 115: 1249-54.
21. Piura B, Gemer O, Rabinovich A, Yanai-Inbar I. Primary breast carcinoma of the vulva. Eur J Gynaecol Oncol. 2002; 23: 21-4.

22. Rose PG, Roman LD, Reale FR, Tak WK, Hunter RE. Primary adenocarcinoma of the breast in vulva. Obstet Gynecol. 1990; 76: 537-9.

23. Simon KE, Dutcher JP, Runowicz CD, Wiernik PH. Adenocarcinoma in vulvar breast tissue. Cancer. 1988; 62: 2234-8.

24. Van der Putte S, Van Gorp L. Adenocarcinoma of mammary-like glands of the vulva. J Cutan Pathol. 1994; 21: 157-63.

25. Yin C, Chapman J, Tawfik O. Invasive mucinous adenocarcinoma of ectopic breast tissue. Breast J. 2003; 9: 113-5.

26. Abbott JJ, Ahmed I. Adenocarcinoma of mammary-like glands of the vulva. Am J Dermatopathol. 2006; 28: 127-33.

27. Alsaad KO, Obaidat N, Dube V, Chapman W, Ghazarian D. Vulvar apocrine adenocarcinoma. Pathol Res Pract. 2009; 205: 131-5.

28. Benito V, Arribas S, Martínez D, Medina N, Lubrano A, Arencibia O. Metastatic adenocarcinoma of mammary-like glands of vulva. J Obstet Gynaecol Res. 2013; 39: 450-4.

29. Bogani G, Uccella S, Cromi A, Casarin J, Donadello N, Ghezzi F. Primary mammary-like ductal carcinoma of the vulva. Am J Dermatopathol. 2013; 35: 685-7.

30. Butler B, Leath CA, Barnett JC. Primary invasive breast carcinoma in vulva. Gynecol Oncol Case Rep. 2014; 7: 7-9.

31. da Costa ATMD, Coelho AM, Lourenço AV, Bernardino M, Ribeirinho AL, Jorge CC. Primary breast cancer of the vulva: a case report. J Low Genit Tract Dis. 2012; 16: 155-7.

32. Fernandez-Figueras MT, Michal M, Kazakov DV. Mammary-type tubulolobular carcinoma of anogenital mammary-like glands. Am J Surg Pathol. 2010; 34: 1224-6.

33. Fracchioli S, Puopolo M, De La Longrais IR, Scozzafava M, Bogliatto F, Arisio R, et al. Primary "breast-like" cancer of the vulva. Int J Gynecol Cancer. 2006; 16: 423-8.

34. Gopinath D, Sasson S, Nuttall I. Primary lobular carcinoma of the vulva: a case report. Gynecol Surg. 2006; 3: 220-2.

35. Kajal B, Talati H, Daya D, Alowami S. Apocrine adenocarcinoma of the vulva. Rare Tumors. 2013; 5: 140-1.

36. Kiyohara T, Kumakiri M, Kawami K, Kouraba S, Takeuchi A, Sawai T, et al. Apocrine carcinoma of the vulva. Int J Dermatol. 2003; 42: 71-4.

37. Lamb A, Darus CJ, Skripenova S, Weisberg T, Miesfeldt S. Association of primary breast cancer of the vulva with hereditary cancer. J Clin Oncol. 2013; 31: e231-e2.

38. Lopes G, DeCesare T, Ghurani G, Vincek V, Jorda M, Glück S, et al. Primary ectopic breast cancer presenting as a vulvar mass. Clin Breast Cancer. 2006; 7: 278-9.

39. Martinez-Palones J, Perez-Benavente A, Diaz-Feijoo B, Gil-Moreno A, Roca I, Garcia-Jimenez A, et al. Sentinel lymph node identification in vulvar ductal carcinoma. Int J Gynecol Cancer. 2007; 17: 471-7.

40. McMaster J, Dua A, Dowdy SC. Primary breast adenocarcinoma in ectopic vulvar tissue. Case Rep Obstet Gynecol. 2013; 2013: 721696.

41. Meddeb S, Rhim MS, Mestiri S, Kouira M, Bibi M, Khairi H, et al. Mammary-like adenocarcinoma of the vulva with Paget's disease. Pan Afr Med J. 2014; 19.

42. Naseer M, Mohammed S, George S, Majumdar SD. Primary ectopic breast cancer mimicking vulval malignancy. J Obstet Gynaecol. 2011; 31: 553-4.

43. North J, Perez D, Fentiman G, Sykes P, Dempster A, Pearse M. Primary breast cancer of the vulva. Aust N Z J Obstet Gynaecol. 2007; 47: 1.

44. Ohira S, Itoh K, Osada K, Oka K, Suzuki A, Osada R, et al. Vulvar Paget's disease with adenocarcinoma. Int J Gynecol Cancer. 2004; 14: 1012-7.

45. Tanaka H, Umekawa T, Nagao K, Ishihara A, Toyoda N. Adenocarcinoma of mammary-like glands in the vulva. Int J Gynecol Cancer. 2005; 15: 568-71.

46. Tseung J, Russell P. 'Breast-like' lesions in the vulva. Pathology. 2008; 40: 321-6.

47. Al-Mansouri L, Poursoltan P, Simons M, Muljono A, Boyages J. Primary breast cancer of the vulva. J Obstet Gynaecol Res. 2018; 44: 2190-4.

48. Ananthula A, Lockwood B, Savage J, Malak S, Chen C, Makhoul I, et al. Primary breast carcinoma of the vulva metastatic to lymph nodes. Perm J. 2020; 24: 19.084.

49. Aoyama K, Matsushima H, Sawada M, Mori T, Yasukawa S, Kitawaki J. Apocrine adenocarcinoma of the vulva. Case Rep Obstet Gynecol. 2016; 2016: 1712404.

50. Aramin H, Koirala P, Shah A, Adams K, Buza N, Desai S, et al. Metachronous vulvar ectopic breast cancer. Gynecol Oncol Rep. 2019; 30: 100515.

51. Baykal C, Dünder I, Turkmen I, Ozyar E. Mammary gland-like carcinoma of vulva: case report and review. Eur J Gynaecol Oncol. 2015; 36: 333-4.

52. Castelow C, Carter E, DePasquale S. Primary myoepithelial carcinoma of the vulva. Gynecol Oncol Rep. 2022; 44: 101116.

53. Chow CY, Namuduri RP, Yeo YC, Mihir G. Diagnostic challenge of primary adenocarcinoma of the vulva. Proc Singap Healthc. 2020; 29: 50-4.

54. Cripe J, Eskander R, Tewari K. Sentinel lymph node mapping of vulvar breast cancer. World J Clin Oncol. 2015; 6: 16.

55. Deshmukh AA, Greenwalt J, Whitworth JM, Fox MD, Crozier JA. Mammary-like carcinoma of the vulva. Breast J. 2020; 26: 1242-4.

56. Eom HJ, Ko BS, Song IH, Gong G, Kim HH. Ectopic male breast cancer in the perineum. J Breast Cancer. 2017; 20: 404-7.

57. Farrag A, Jafar W, Ahmed O, Buhlaigaqh T, Ansari J. Ductal carcinoma in situ in ectopic breast tissue of the vulva. Glob J Med Ther. 2020.

58. Grewal JK, Eirew P, Jones M, Chiu K, Tessier-Cloutier B, Karnezis AN, et al. Genomic characterization of mammary-like adenocarcinoma. Mol Case Stud. 2017; 3: a002170.

59. Ishigaki T, Toriumi Y, Nosaka R, Kudou R, Imawari Y, Kamio M, et al. Primary ectopic breast cancer of the vulva treated with excision and sentinel node biopsy. Surg Case Rep. 2017; 3: 69.

60. Konstantinova AM, Spagnolo DV, Stewart CJ, Kacerovska D, Shelekhova KV, Plaza JA, et al. Spectrum of changes in anogenital mammary-like glands. Am J Surg Pathol. 2017; 41: 1053-8.

61. Kredentser AM, Kredentser DC. Adenocarcinoma of the vulva arising in ectopic breast tissue. J Gynecol Surg. 2017; 33: 22-6.

62. Li S, Schwartz M, Everest S, Blank SV. Primary breast cancer of the vulva with concurrent malignancies. Gynecol Oncol Rep. 2019; 27: 35-7.

63. Lobrano R, Manca A, Sini MC, Palmieri G, Petrillo M, Cossu A, et al. Mammary-like adenocarcinoma of the vulva with sequencing analysis. Pathologica. 2023; 115: 101.

64. Lopes A, Louis JS, Balancin ML, Nogueira-Rodrigues A, Silva LC, Paulino E, et al. Primary breast carcinoma in the vulva. Clin Breast Cancer. 2018; 18: e291-e4.

65. Matak L, Dukić B, Tupek T, Lisica-Šikić N, Mikuš M. Primary ectopic lobular breast cancer of the vulva. J Obstet Gynaecol. 2020; 40: 727-30.

66. Morais M, Silva JV, Tavares MV. Primary vulvar adenocarcinoma of mammary gland type. BMJ Case Rep. 2022; 15: e245580.

67. Niakan S, Love H, Cao Q, Kawar N. Primary invasive lobular carcinoma of vulvar mammary-like glands. Clin Case Rep. 2021; 9: 118-22.

68. Shah VI, Bergin L, Rowlands GL, McCluggage WG. Unusual manifestations of vulval Paget disease. Int J Gynecol Pathol. 2022; 41: 476-83.

69. Tessier-Cloutier B, Asleh-Aburaya K, Shah V, McCluggage WG, Tinker A, Gilks CB. Molecular subtyping of mammary-like adenocarcinoma of the vulva. Histopathology. 2017; 71: 446-52.

70. Tran TA, Deavers MT, Carlson JA, Malpica A. Collision of ductal carcinoma and vulvar carcinoma. Int J Gynecol Pathol. 2015; 34: 487-94.

71. Villada G, Farooq U, Yu W, Diaz JP, Milikowski C. Extramammary Paget disease with underlying carcinoma. Am J Dermatopathol. 2015; 37: 295-8.

72. Barrios M, Perez NE, Briski LM, Pluguez-Turull C. Recurrent ectopic breast adenocarcinoma of the vulva. BMJ Case Rep. 2024; 17: e257791.

73. Dai X, Lei H, Jie R. Primary vulvar adenocarcinoma of mammary gland type. Int J Womens Health. 2025; 17: 399-405.

74. Heller A, Harigopal M, Ahmed AJ, StClair S, Collins V. TRPS1 staining in vulvar mammary-like glands. Int J Gynecol Pathol. 2026; 45: 39-43.

75. Hu L, Tiesinga J. Primary vulvar adenocarcinoma: genetic characteristics. Pathol Oncol Res. 2024; 30: 1611376.

76. Mansour M, Zahra O, Nabulsi D, Alhamwi A, Chahin M, Yousef D, et al. Ectopic ductal breast carcinoma of the vulva. Ann Med Surg. 2023; 85: 5138-44.

77. Markel L, Rivera L, Ordobazari A, Hakam A, Hoffman MS, Wenham RM, et al. Mammary-like adenocarcinoma of the vulva with BRCA1 mutation. Gynecol Oncol Rep. 2025; 101957.

78. Si J, Yi J, Shen Y. Encapsulated papillary carcinoma of vulvar mammary-like glands. AME Case Rep. 2024; 8: 91.

79. Tang H, Laskin WB, Luan Y, McNiff JM, Zhan H. Adenocarcinoma of anogenital mammary gland type. J Cutan Pathol. 2024; 51: 604-8.

80. Wu F, Andaleeb U, Ahmed I. Extramammary breast cancer of the vulva. BMJ Case Rep. 2024; 17: e259567.

81. Hartung E. Ueber einen Fall von Mamma accessoria. 1875.

82. Van der Putte S. Mammary-like glands of the vulva and their disorders. Int J Gynecol Pathol. 1994; 13: 150-60.

83. Kazakov DV, Spagnolo DV, Kacerovska D, Michal M. Lesions of anogenital mammary-like glands: an update. Adv Anat Pathol. 2011; 18: 1-28.

84. Arora K, El-Zaatari ZM, Schwartz MR, Ro JY. Lesions of anogenital mammary-like glands. Ann Diagn Pathol. 2020; 47: 151551.

85. Zengin HB, Bui CM, Rybski K, Pukhalskaya T, Yildiz B, Smoller BR. TRPS1 expression in sweat gland neoplasms. Dermatopathology. 2023; 10: 75-85.

86. Simpson EJ. Functional morphology of the reproductive system in cetacea. In: Norris KS, editor. Whales, dolphins and porpoises. Berkeley: University of California Press; 1966. p. 310-1.

87. Desouki MM, Fadare O, editors. Primary adenocarcinomas of the vulva. Semin Diagn Pathol. 2021.

88. Kozakiewicz B, Dmoch-Gajzlerska E, Roszkowska-Purska K. Carcinomas and sarcomas of Bartholin gland. Eur J Gynaecol Oncol. 2014; 35: 2014.

89. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, et al. AJCC cancer staging manual. CA Cancer J Clin. 2017; 67: 93-9.

90. Buitrago-Flechas SM, Barrera-Latorre SJ, Morante-Caicedo C. Ectopic mammary tissue in vulva. Rev Colomb Obstet Ginecol. 2021; 72: 271-90.