

Intestinal-type adenocarcinoma of the Bartholin gland: A case report and literature review

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ARTICLE INFO

Keywords:

Bartholin gland
Adenocarcinoma
Intestinal type
Immunohistochemistry
KRAS mutation

ABSTRACT

Purpose: To report a case of intestinal-type adenocarcinoma of the Bartholin gland treated successfully with surgery and to review the current literature.

Methods: We report the case of a 45-year-old white woman with intestinal-type adenocarcinoma of the Bartholin gland treated with wide local excision followed by bilateral inguinal femoral lymph node dissection without adjuvant therapy. We also review the literature on the treatment and management of this rare tumor. We searched Pubmed / MEDLINE databases for previous case reports or series using the keywords “Bartholin gland”, “adenocarcinoma” and “intestinal type”.

Results: We found 19 cases of intestinal-type adenocarcinoma of the Bartholin gland published up to November 2020. The treatments described varied from case to case.

Conclusion: Intestinal-type adenocarcinoma of the Bartholin gland has been treated and managed in the same way as squamous carcinoma. Treatment of these cancers is understudied and involves local resection with curative intent. More case reports are needed to determine the best treatment strategies.

1. Introduction

Malignant tumors of the vulva account for less than 1% of all malignancies in women and 4–5% of all gynecological cancers; 90% have a squamous cell origin. Adenocarcinoma of the vulva is very rare and it can have a mucinous or papillary architecture. Intestinal-type adenocarcinoma of Bartholin gland is even rarer. It is defined as a primary invasive glandular epithelial tumor of intestinal type in the fourth edition of the WHO Classification of Tumors of Female Reproductive Organs, and is also known as cloacogenic carcinoma or cloacogenic adenocarcinoma (Kurman et al., 2014). Very few cases have been described in the literature. Clinical practice guidelines and unanimous agreement on treatment strategies are lacking.

2. The case

A 45-year-old white woman presented at the emergency room with a lump on her left labium majus that she had first noticed 6 months earlier. She described the lesion as being initially small and itchy and had not felt the need to treat the symptoms or consult with her general

practitioner. The lesion had grown in the past month, causing increasing pain and prompting her to seek emergency gynecological care. She denied urinary or digestive symptoms, abnormal uterine bleeding, chills or shivering, purulent discharge from the lesion, and foul-smelling leucorrhoea. Her past medical and surgical history was unremarkable. The patient had a long-term stable partner and denied being sexually active. The only obstetric/gynecological event of interest was a cesarean section 11 years earlier. She had experienced irregular periods in the past year and the results of a recent pap smear were normal. Physical examination revealed a lesion measuring 3–4 cm on the left labium majus. The lesion had a hard consistency and was painful to the touch. Bimanual vagina examination showed extension towards the rectum and midline. The inguinal and femoral lymph nodes were not enlarged on palpation. The rectal examination showed an intact mucous membrane. No vaginal or cervical lesions were detected during speculum examination. With a tentative diagnosis of an atypical Bartholin gland cyst, a pelvic magnetic resonance imaging (MRI) scan with contrast was performed. The MRI scan showed a perineal tumor invading the vagina and extending to the anterior border of the anal sphincter (Fig. 1). A subsequent staging study with computed tomography (CT) of the chest,

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<https://doi.org/10.1016/j.gore.2021.100836>

Received 25 March 2021; Received in revised form 6 July 2021; Accepted 13 July 2021

Available online 23 July 2021

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Fig. 1. MRI Scan. Perineal tumor invading the vagina and extending to the anal sphincter.

abdomen, and pelvis and colonoscopy was negative. The initial treatment was surgery with intraoperative biopsy, which revealed an adenocarcinoma component. Surgery consisted of wide local excision as far as, but not including, the rectovaginal septum, followed by, in accordance with oncological criteria, bilateral inguinal lymph node dissection (Fig. 2a) and left hemivulvectomy (Fig. 2b). The excised lesion measured 3 × 2.5 × 1 cm. The margins were negative for disease and the nearest margin was located at a distance of 5 mm. Histology showed a malignant tumor with a glandular and mucinous pattern in the proximity of the Bartholin gland (Fig. 3a). Immunohistochemistry was positive for intestinal markers (cytokeratin [CK] 20 and CDX-2) (Fig. 3b) and negative for CK7. CK20 positivity and CK7 negativity is the hallmark immunohistochemical profile of colorectal carcinoma. The

immunohistochemical study also showed conserved DNA mismatch repair proteins. Molecular analysis (Amgen) showed a mutation in exon 2 of the KRAS gene (p.G12D). Subsequent histology confirmed a diagnosis of Intestinal-type primary adenocarcinoma of the Bartholin gland (FIGO 2014 stage IB [pT2N0M0]).

3. Discussion

Intestinal-type primary adenocarcinoma of the Bartholin gland is rare. It can arise from ectopic tissues or embryonic remnants (Ghamande et al., 1995). The main entity that should be considered in the differential diagnosis is metastasis from colorectal mucinous carcinoma, as it has identical histological, immunohistochemical, and molecular characteristics. It usually presents as a solitary pruritic vulvar mass. We reviewed the few cases reported in the literature to synthesize the limited evidence available. The clinical characteristics and treatments used are summarized in Table 1, alongside the details of the current case.

The urethra, the lower two-thirds of the vagina, and the rectum are embryologically derived from the cloacal membrane. It has been hypothesized that intestinal-type primary adenocarcinoma of the Bartholin gland may originate from remnants of gastrointestinal tissue that persist following the division of these structures during embryological development (Tiltman and Knutzen, 1978). The labia majora and minora develop from labioscrotal and urethral folds, respectively. These anatomic structures are also involved in cloacal development, and, as occurs with primary colorectal adenocarcinoma, may undergo malignant transformation (Lee et al., 2017). Other proposed mechanisms are ectopic intestinal epithelium or intestinal metaplasia in tissues originating from Müllerian ducts (Kennedy and Majmudar, 1993). The exact mechanism by which primary intestinal-type adenocarcinoma of the vulva develops remains to be elucidated.

KRAS mutations are observed in approximately 40% of colorectal cancers. They are associated with resistance to anti-epidermal growth factor receptor therapy and have been implicated in tumor invasion and metastasis. Their prognostic significance in intestinal-type primary adenocarcinoma of the Bartholin gland is not known. Close clinical follow-up is therefore necessary.

CT of the chest, abdomen, and pelvis, pelvic MRI and colonoscopy were negative, ruling out colorectal carcinoma. Microscopic examination of the tumor specimen confirmed a diagnosis of primary intestinal-

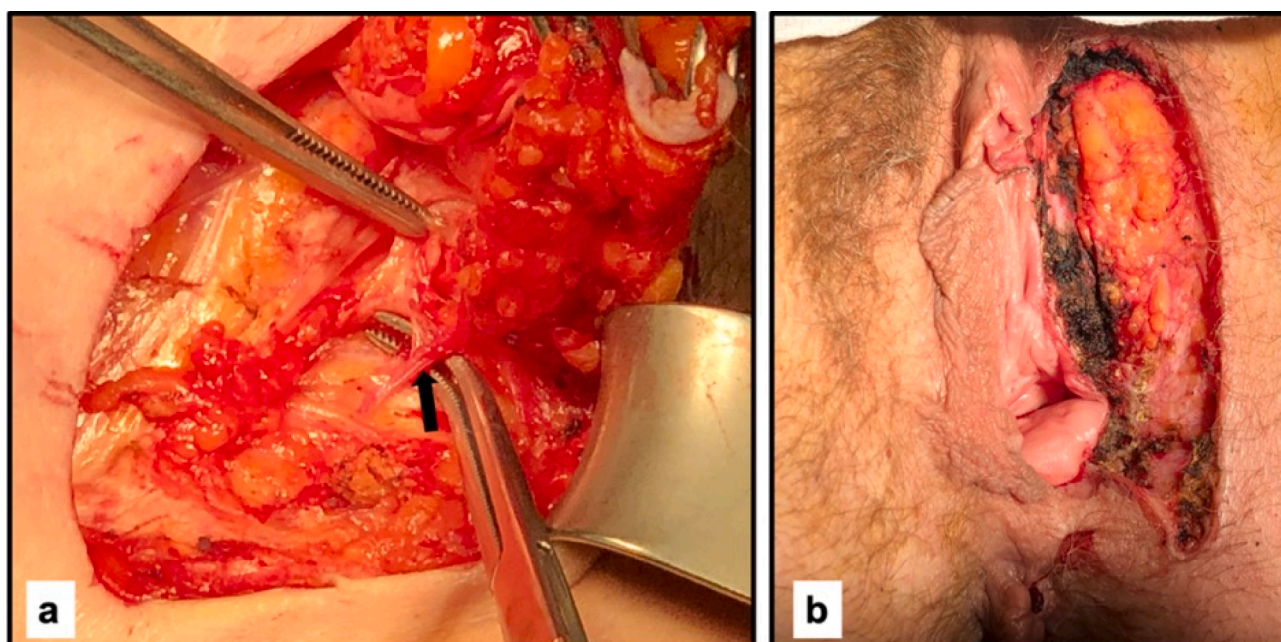


Fig. 2. Surgical treatment. (a) Inguinal lymph node dissection with saphenous vein preserved and (b) Wide local excision. Left hemivulvectomy.

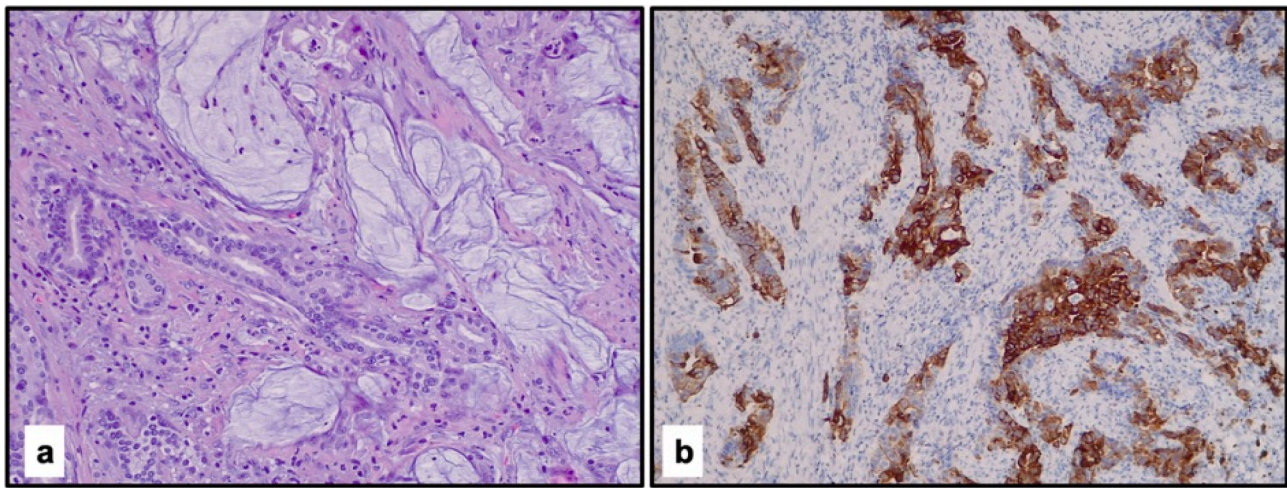


Fig. 3. Histopathology. (a) Hematoxylin eosin staining, glandular structures with intracytoplasmic mucin and (b) Immunohistochemistry, positive for cytokeratin [CK] 20.

Table 1

Overview of cases of intestinal-type mucinous adenocarcinoma of the vulva in the literature until November 2020.

Author (year)	Age (years)	Tumor location	Lymph node metastasis	Operation ^{a,b,c,d}	Adjuvant Therapy	Follow-up (months)	Outcome ^{e,f}
Tiltman and Knutzen (1978)	50	Periurethral	Positive	MRV & LND	None	12	NED
Kennedy and Majmudar (1993)	54	Left posterior	Negative	RV & LND	None	120	NED
Ghamande et al. (1995)	63	Posterior fourchette	Negative	WLE	None	48	NED
Willén et al. (1999)	67	Vulva	Negative	RV & LND	None	17	NED
	57	Posterior part of vestibulum	Negative	WLE	None	26	NED
Ohno et al. (2001)	92	Vulva	Positive	None	Radiotherapy	10	DOD
Zaidi and Conner (2001)	43	Posterior fourchette	Negative	MRV & LND	None	18	NED
Rodriguez et al. (2001)	69	Right labium majus	Negative	WLE	None	36	NED
Liu et al. (2003)	49	Left labium majus	Negative	WLE & LND	None	24	NED
Dubé et al. (2004)	64	Right labium majus	Negative	WLE	None	4,5	NED
Cormio et al. (2012)	59	Vulva	Positive	RV & LND	None	54	DOD
	42	Vulva	Negative	RV & LND	None	39	NED
Tepeoğlu et al. (2016)	60	Vulva	Positive	WLE & LND	None	38	NED
Sui et al. (2016)	43	Hymen	Negative	WLE	Chemotherapy	24	NED
Tulek et al. (2016)	62	Vulva	Positive	WLE	Chemotherapy	36	DOD
Matsuzaki et al. (2017)	68	Periurethral	Negative	WLE	None	60	NED
He et al. (2017)	63	Vulva	Negative	WLE	None	26	NED
Lee et al. (2017)	64	Right labium majus	Negative	WLE	None	12	NED
Kaltenecker et al. (2019)	53	Left labium majus	Positive	None	Chemotherapy + Radiotherapy	12	DOD
Current study (2020)	45	Left labium majus	Negative	WLE & LND	None	8	NED

^a WLE, wide local excision.
^b MRV, modified radical vulvectomy.
^c RV, radical vulvectomy.
^d LND, lymph node dissection.
^e NED, no evidence of disease.
^f DOD, died of disease.

type adenocarcinoma of the Bartholin gland. Wide local excision with curative intent is considered to be sufficient and safe in squamous cell vulvar carcinoma (Hacker et al., 1984), but little has been reported on the treatment of intestinal-type primary adenocarcinoma of the Bartholin gland. Prognosis is largely linked to lymph node status. In our case, wide local excision and left hemivulvectomy achieved clear margins. Bilateral inguinal-femoral lymph node dissection was also performed, with no evidence of tumor involvement in the 16 lymph nodes analyzed. Follow-up with pelvic MRI 6 months after surgery showed postoperative changes with no signs of residual tumor or local-regional lymph node enlargement.

Standardized guidelines are lacking for the diagnosis, treatment, and

follow-up of Bartholin gland cancer (Di Donato et al., 2017). Case reports such as this can aid decision-making regarding the diagnosis and treatment of this tumor.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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