Adenocarcinoma of intestinal type of the vulva

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Abstract

Primary adenocarcinoma of the vulva is a rare disease, and usually arises in a Bartholin gland or occurs in association with Paget's disease. Furthermore, adenocarcinoma of intestinal type of the vulva is an extremely rare neoplasm, and few cases have been reported. The appropriate treatment for optimal prognosis is unclear. We report a case of adenocarcinoma of intestinal type of the vulva occurring in a 63-year-old female. The tumor was found near the urethra, and biopsy specimen showed a proliferation of signet ring cells embedded in an abundant myxoid stroma and irregular tubular structures of atypical columnar epithelium. An extensive workup showed no metastases. Local excision with a 2-cm lesion in the vulva side, bilateral superficial inguinal lymph node dissection and Cloquet lymph node biopsy were performed. Cancer cells contained mucinous materials in the cytoplasm, which exhibited diffuse positive staining for cytokeratin 20 and CDX2. The final pathologic diagnosis was adenocarcinoma of intestinal type of the vulva (pT1bN0M0). The patient received adjuvant external irradiation because of positive urethral surgical margin. She is well 1 year after therapy. Immunohistochemical staining for cytokeratin 20 and polyclonal CDX2 is helpful with investigation of adenocarcinoma of intestinal type, but long-term prognosis remains unclear.

Keywords Adenocarcinoma · Intestinal type · Immunohistochemistry · Vulva

Introduction

Primary adenocarcinoma of the vulva is rare, and most arise from Bartholin's gland or occur in association with Paget's disease [1, 2]. Adenocarcinoma of intestinal type is an extremely rare variant and few cases have been reported to date [3]. In this paper, we report a case of adenocarcinoma

of intestinal type of the vulva occurring in a 63-year-old Japanese female.

Case report

The patient, a 63-year-old Japanese woman, gravid 3, parity 2, was referred to our hospital because of postmenopausal bleeding. A papillary mass with easy contact bleeding, 18 mm in diameter was seen near the urethra (Fig. 1). Magnetic resonance imaging (MRI) of the pelvis revealed the 18 mm-sized enhanced mass, and uterus and both ovaries were normal shape and size. Scrape cytology and biopsy specimen showed atypical glandular cells in mucinous background. An extensive workup, including systemic positron emission computed-tomography (PET-CT), gastrointestinal tract fiberoptic, cystoscopy and mammography revealed no metastases. Serum CEA and CA125 levels were in the reference range. Local excision with a 2.0-cm tumor-free margin including subcutaneous tissue only on the vulva side, bilateral superficial inguinal lymph node dissection and Cloquet lymph node biopsy were performed. The surgical specimen showed a 2.0-cm lesion in the vulva side, which revealed

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Fig. 1 Gross examination. External genitalia. A papillary mass with easy contact bleeding mass was seen near the urethra

microscopic stromal invasion, reaching 1 mm in depth. The final pathologic diagnosis was adenocarcinoma of intestinal type of the vulva stage IB (pT1bN0M0). The patient received adjuvant external irradiation with 64 Gy because of positive surgical margin on the urethral side and remains well and free of disease 1 year after treatment.

Cytological findings

Scrape cytology specimens of the vulvar tumor revealed atypical epithelial cells in a mucinous background (Fig. 2a). Tumor cells formed palisading and loose clusters, and a cytoplasm with enriched mucinous material. The nuclei of the tumor cells were elongated and irregular, with a thin

nuclear membrane. Tumor cells had fine granular chromatin and small nucleoli, suggesting adenocarcinoma.

Pathological findings

Gross examination revealed a solitary mass arising in the surface epithelium of the vulva near the urethra. The cut section of the tumor showed a superficial polypoid mass measuring 2.0×1.8 cm. The pathological examination showed irregular tubular structures of atypical columnar epithelium with hyperchromatic nuclei, and a proliferation of signet ring cells embedded in an abundant myxoid stroma (Fig. 2b). The minimal stromal invasion to a depth of 1 mm was noted. No definite lymphatic invasion was seen. Immunohistochemically, the tumor cells showed diffuse positive staining for cytokeratin 20 and CDX2 (Fig. 3), whereas CK7 and GCDFP-15 (gross cystic disease fluid protein-15) were negative. These histochemical findings confirmed that the tumor was an intestinal type of neoplasm. The final pathologic diagnosis was adenocarcinoma of intestinal type of the vulva.

Discussion

Primary adenocarcinoma of the vulva is rare, and commonly originates from Bartholin's gland. Other possible origins are sweat glands and skene glands [1, 2]. Adenocarcinoma of intestinal type is diagnosed to distinguish it from tumors arising from Bartholin and other specialized

Fig. 2 Scrape cytology and pathology. **a** Atypical epithelial cells form loose clusters in a mucinous background. Tumor cells formed palisading and loose clusters, and a cytoplasm with enriched mucinous material. The nuclei of the tumor cells were elongated and irregular, with a thin nuclear membrane. **b** The minimal stromal invasion

to a depth of 1 mm was noted. The pathological examination showed irregular tubular structures of atypical columnar epithelium with hyperchromatic nuclei, and a proliferation of signet ring cells embedded in an abundant myxoid stroma

Fig. 3 Immunohistochemical examination. The tumor cells showed diffuse positive staining for cytokeratin 20 and CDX2

anogenital glands by WHO pathological classification 2014 [4]. This tumor is extremely rare, and its origin remains controversial. There are some reports about origins of vulvar intestinal-type adenocarcinoma. This tumor has been suggested to originate from the cloacal remnants [5–12]. It could be misplaced or aberrant tissue or might be a normal feature of that area. There are some cases originating from sweat glands or metastatic adenocarcinoma of the vulva, but true adenocarcinoma of intestinal type is an extremely rare variant (Table 1).

In our case, metastatic tumor was excluded by extensive workup, including systemic PET-CT, gastrointestinal tract fibroscope, cystoscope and mammography. Primary adenocarcinoma of the urinary bladder is another uncommon tumor, which has similar histopathological features. In the present case, the tumor was located near the urethra with slight invasion of the urethra.

Immunohistochemical study showed strong positive staining for cytokeratin 20 and polyclonal CDX2, supporting the diagnosis. The value of immunohistochemical staining was reported in previous cases [13, 14]. Intestinal-type mucinous carcinoma showed positive reaction for cytokeratin 20 and polyclonal CDX2, which is usually diffuse positive reaction in mullerian ducts of the female genital tract. We confirmed that CK7 and GCDFP-15 (gross cystic disease fluid protein-15) which indicate positive by sweat gland and ectopic mammary gland were negative. These histochemical findings confirmed that the final pathologic diagnosis was adenocarcinoma of intestinal type of the vulva.

The clinical management of this rare tumor is unknown. Our patient had an 18-mm nodule near the urethra in the midline vulva. Local excision with a 2.0-cm tumor-free margin including subcutaneous tissue only on the vulva side, bilateral superficial inguinal lymph node dissection and Cloquet lymph node biopsy were performed following Japanese gynecological cancer association guidelines because she had no severe medical complications [15]. Radical vulvectomy was also considered as the standard therapy. Recently, modified surgical management has been undertaken to avoid surgical complications [16, 17]. Radical local excision of the invasive lesion is the most appropriate for lesions on the lateral or posterior aspects of the vulva, where preservation of the clitoris is feasible. After surgery, radiation therapy seems to be clearly indicated in patients with involved surgical margins (<5 mm) [18]. The patient received adjuvant external irradiation because of positive surgical margin on the urethral side, but it is unclear whether adjuvant radiotherapy for adenocarcinoma of intestinal type of the vulva is effective. It is commonly recognized that adenocarcinoma is not highly susceptible to radiation therapy, but there is no additional effective chemotherapy for vulvar adenocarcinoma.

In conclusion, we have described adenocarcinoma of intestinal type of the vulva. Knowledge of this tumor is very limited due to the small number of cases. Almost patients including our case were observed without a recurrence in the short period prognosis only by surgical excision. We think surgical procedure is an appropriate treatment of this tumor.

Immunohistochemical staining for cytokeratin 20 and polyclonal CDX2 is helpful for investigating adenocarcinoma

Table 1 Clinical features and outcome of adenocarcinoma of intestinal type of the vulva

Author (year)	Age	Location	Lymph node metastasis	operation	Adjuvant therapy	Follow-up (mo)	Outcome
Tiltman and Knutzen (1978) [5]	50	Periurethral	Positive	MRV&LND	None	12	NED
Kennedy and Majmudar (1993) [6]	54	Left posterior	Negative	RV&LND	None	120	NED
Kennedy and Majmudar (1993) [6]	63	Posterior fourchette	Negative	WLE	None	48	NED
Ghamande et al. (1995) [9]	67	Vulva	Negative	RV&LND	None	Unknown	Unknown
Willen et al. (1999) [14]	57	Posterior part of vestibulum	Negative	WLE	None	26	NED
Zaidi and Conner (2001) [7]	43	Posterior fourchette	Negative	MRV&LND	None	18	NED
Rodriguez et al. (2001) [10]	69	Right labium majus	Negative	WLE	None	36	NED
Dube et al. (2004) [8]	58	Right labium majus	Negative	WLE	None	4.5	NED
Cormio et al. (2012) [11]	59	Vulva	Positive	RV&LND	Chemotherapy	54	DOD
Cormio et al. (2012) [11]	42	Vulva	Negative	RV&LND	None	39	NED
Sui et al. (2016) [3]	43	Hymen	Negative	WLE	Chemotherapy (PTX + CBDCA)	24	NED
Tepeoglu et al. (2016) [19]	40	Left labium minus close to urethra	Positive	WLE&LND	None	38	NED
Lee et al. (2017) [12]	64	Right posterior part of the major labium	Negative	WLE	None	12	NED
Present case	63	Periurethra	Negative	WLE&LND	Radiotherapy	12	NED

RV radical vulvectomy, MRV modified radical vulvectomy, WLE wide local excision, LND lymph node dissection, NED no evidence of disease, DOD died of disease, PTX paclitaxel, CBDCA carboplatin

of intestinal type, but long-term prognosis is still unclear. A successful treatment modality needs to be verified through several more cases.

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Compliance with ethical standards

Conflict of interest All authors have no conflict of interest to disclose.

Consent for publication The case report approval was obtained from the Hospital Research Ethics Board.

Informed consent Informed consent was obtained from individual participants included in the study.

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