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Case Report

A vulvar mass as the first presentation in colorectal carcinoma: An unusual site of metastasis masquerading a primary cancer

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ABSTRACT

Objective: To demonstrate a case with a vulvar metastasis masquerading a primary vulvar malignancy. The clinical and histological features, mechanism, and impact to the prognosis are discussed.
Case report: A 58-year-old woman presented to gynecologist for abnormal vaginal discharge. A vulvar nodule was noticed during physical examination. Biopsy showed adenocarcinoma (ADC) and she was referred for further survey under the impression of Bartholin duct ADC. Later she was further found to also have a colorectal tumor with liver metastasis and subsequently received surgery under the suspicion of a double primary cancer involving the colon and vulva. The pathology revealed colorectal ADC with both hepatic and vulvar metastasis.
Conclusion: Secondary tumor in female genital tract is unusual and vulvar metastasis is the rarest kind. The clinical manifestation may be perplexing especially if a patient is presented with a nonspecific gynecological symptom such as abnormal vaginal discharge without any past history.

Introduction

Aside from the ovary, secondary tumor in the female genital system is unusual. Vulva is the rarest site of metastasis in the entire female genital tract [1]. Common malignancies, gynecological or non-gynecological, can be the source of metastasis in vulva [2]. Presence of vulvar metastasis may initially be mistaken as a primary vulvar malignancy when common gynecological complaints are presented [3]. Differentiating primary and secondary vulvar malignancy is crucial because vulvar metastasis is often a pre-terminal phenomenon [4].

As the incidence of colorectal carcinoma in Taiwan is rising, this common malignancy with metastasis at an unusual site may be encountered increasingly more. Here we describe a 58-year-old female with abnormal vaginal discharge and a vulvar mass as clinical presentations and was later diagnosed with colorectal adenocarcinoma (ADC) and metastases to both liver and vulva. This is a case with an unusual site of metastasis mimicking primary vulvar tumor.

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Case presentation

A 58-year-old para 2 postmenopausal woman with previous negative PAP smear results sought help at a district hospital for white and blood-tinged vaginal discharge lasting for a month. Rectal bleeding was also complained. She had neither abdominal discomfort nor any recent body weight loss. A fungating, immobile and ulcerative vulvar mass measuring 2.5 cm in greatest dimension was found near the left Bartholin duct. Initial biopsy revealed adenocarcinoma. She was therefore referred to our institution for further survey, under the impression of Bartholin duct ADC.

Series of blood tests showed that serum CA125 was 12.48 U/mL (normal <35 U/mL) and serum CEA was 3.54 ng/mL (normal <5 ng/mL). Both transvaginal sonography and pelvic examination revealed no abnormality except for the vulvar mass. Pelvic computed tomography (CT) revealed an ill-defined vulvar mass, compatible with the initial diagnosis of Bartholin duct ADC (Fig. 1A and B). A stricture lesion in the sigmoid colon was also noted (Fig. 1C). Colorectal tumor was therefore suspected. Multiple nodular lesions in the liver suggested liver metastasis (Fig. 1D). Flexible colonoscopy confirmed the presence of a sigmoid colon carcinoma.

Left radical vulvectomy with left inguinofemoral lymphadenectomy, sigmoid colectomy with radical lymph node dissection and partial hepatectomy were performed for the vulvar, intestinal

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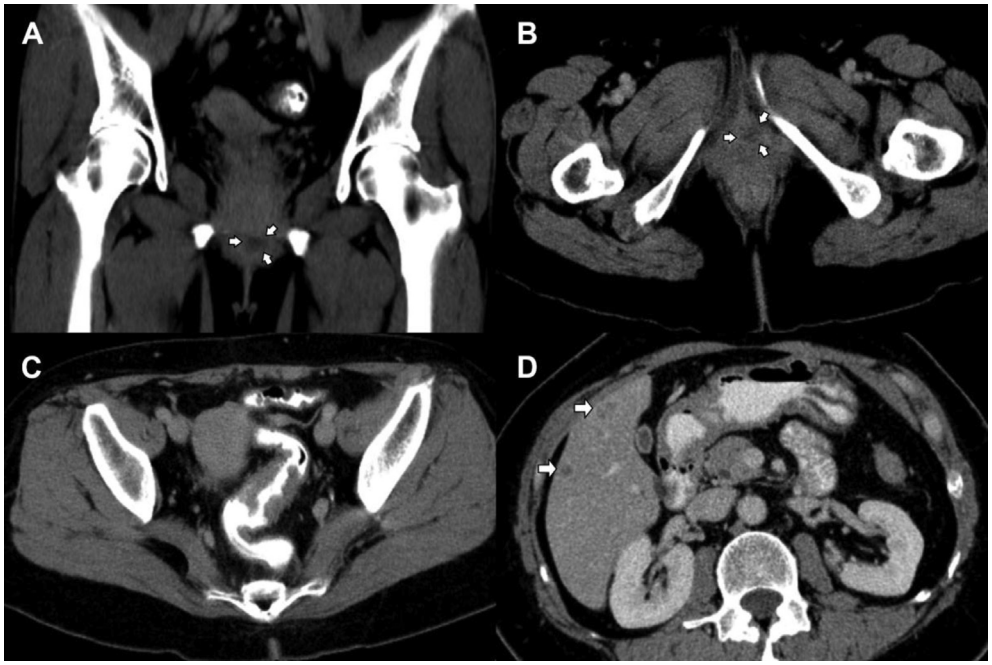

Fig. 1. CT scan images for the lesions. (A) (B) Pelvic computed tomography (CT) revealing an ill-defined soft tissue mass (arrows), compatible with the initial diagnosis of Bartholin duct ADC. (C) A stricture lesion in the sigmoid colon. (D) Multiple nodular lesions (arrows) in random distribution in the liver suggesting metastasis.

and hepatic lesions, respectively. Final pathology confirmed an ADC arising from tubular adenoma in the sigmoid colon (Fig. 2A and B) with metastases to both vulva and liver (Fig. 2C and D). Microscopically, glands composed of pseudostratified columnar cells with abundant dirty necrosis observed in the vulvar tumor (Fig. 2D, left), resembling the primary sigmoid lesion. Immunohistochemical (IHC) stains demonstrated identical profile between the primary sigmoid tumor and its vulvar counterpart: CK7(−)/CK20(+)/CDX2(+)/focal p16(+) (Fig. 3). Pathologic staging was pT3N1bM1a, stage IVa. Molecular study showed negative HPV screening and a missense mutation (c.35 G > A, p.G12D) in exon 2 of K-ras gene. Expression of EGFR was proved by Dako EGFR pharmDx™ system (Agilent technologies, Santa Clara, CA, USA) using IHC stain.

After surgery, the patient received adjuvant chemotherapy using FOLFOX regimen for six courses and later shifted to oral Capecitabine (Xeloda®) for eight weeks due to poor tolerance. The

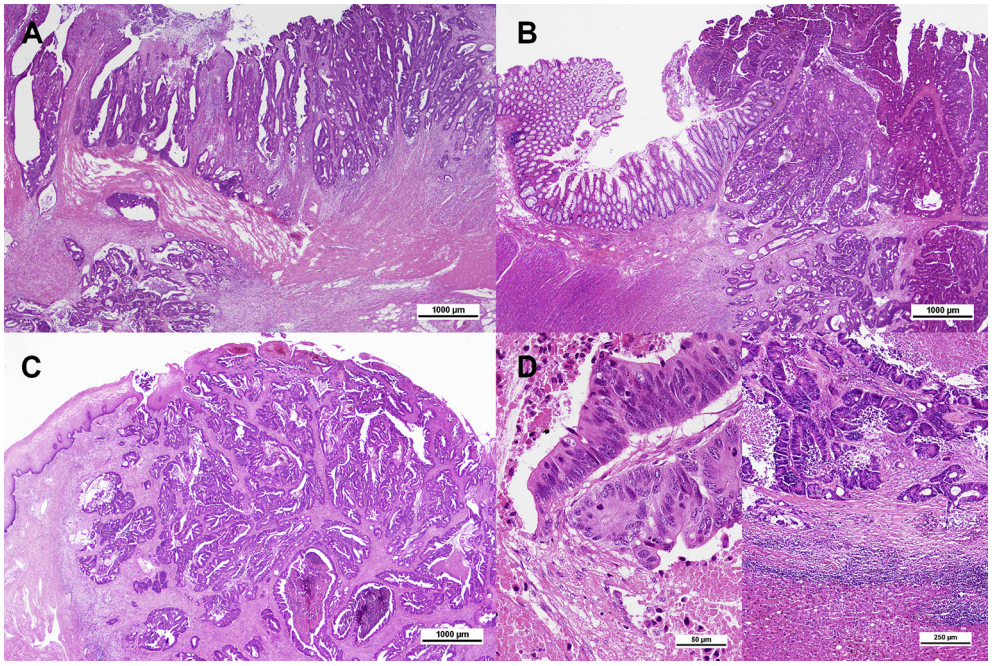

Fig. 2. Moderately-differentiated colorectal adenocarcinoma and its vulvar metastasis. (A) Main tumor in the sigmoid colon with deepest invasion to pericolic fat. (B) The sigmoid adenocarcinoma (right lower) is arisen from a tubular adenoma with high grade dysplasia (right upper). (C) Vulvar metastasis with surface ulceration. (C) Left: malignant glands composed of pseudostratified columnar cells with abundant dirty necrosis observed in the vulvar tumor resembling the primary sigmoid lesion. Right: Liver metastasis.

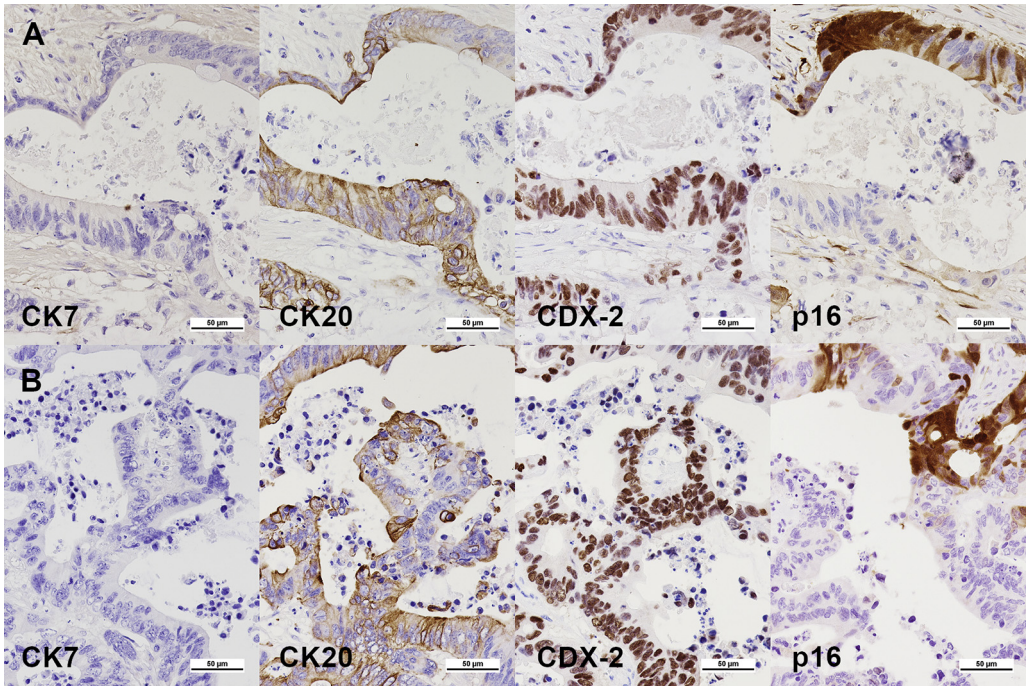

Fig. 3. The tumor cells in the primary sigmoid adenocarcinoma and its vulvar metastatic counterpart share the same immunoprofile. (A) The sigmoid adenocarcinoma is CK7(−)/CK20(+)/CDX-2(+)/p16 focal (+). (B) The vulvar metastatic counterpart is also CK7(−)/CK20(+)/CDX-2(+)/p16 focal (+).

patient has been stable with no recurrence after 48 months of follow-up by regular examinations of colonoscopy and serum CEA surveillance.

Discussion

Metastatic tumors involving the vulva are rare in the female genital tract [1]. These secondary tumors represent only 5–8% of all vulvar malignancies [2]. Due to its rarity, published literature has been predominantly case reports. Since the first reported series on vulvar metastases in 1973 by Dehner, only a total of three series have been published thus far [1,2,5].

The origin of the malignancy in vulvar metastases can be gynecological or non-gynecological. As described by Dehner and Neto, gynecological primaries were outnumbered non-gynecological ones with cervical squamous cell carcinoma (SqCC) as the majority [1,2]. Studies have shown that this phenomenon, in fact, also applies to other sites of metastases within the female genital tract [5]. In a series of 325 cases with metastases to the female genital tract, increasing ratio of gynecological to non-gynecological primaries was observed from ovary to vulva, consistent with the "drop metastasis" theory [5]. A case with tumor-to-tumor metastasis with endometrial carcinoma metastatic to SqCC of vulva has also been described [6].

In both series reported by Neto and Mazur, malignancies that originate from lower gastrointestinal tracts including colorectum and appendix are the most common non-gynecological source of vulvar metastasis. Our case was consistent with this statistical finding. Other primary malignancies in the stomach, breast, lung, appendix, and urinary system, as well as even lymphoma, have been reported [2,5].

Neto et al. reported the most common clinical presentation of a vulvar metastasis. It occurred predominantly in postmenopausal women (mean 54.8 years old) with a labium majus mass [2]. Our case was also a postmenopausal woman presented with a vulvar mass located near the Bartholin duct close to the left labium minus instead of labium majus.

Both Mazur and Brand pointed out that the initial impression of metastatic tumors including colorectal cancer could masquerade as gynecological primary tumors with abnormal vaginal discharge as the first sign of disease [3,5]. Ren et al. reported a case of colorectal adenocarcinoma metastasizing to vulva with similar vaginal bloody discharge as was observed in our case [8]. In fact, malignancies originating from gastrointestinal tract are the most common neoplasm to mimic gynecological primaries. Cases with kidney and breast cancer origins may also mimic vulvar primaries [5].

Vulvar metastases pose diagnostic difficulty, as they can mimic primary tumors. Therefore, past history is important, especially in the cases with long interval between excision of primary tumor and occurrence of metastasis [5,7,8]. In our case, the initial symptoms led to the impression of primary vulvar ADC. Pelvic examination and transvaginal sonography excluded possible malignancies from ovary to vagina. Despite a sigmoid lesion was also found subsequently, a double primary cancer was suspected first until pathology proof as a vulvar metastasis originating from the sigmoid tumor. Normal serum CA-125 and CEA levels were not contributory to the diagnosis at the time. Double primary cancer is not uncommon nowadays, abnormal vaginal discharge and rectal bleeding, as in our case, are possible to represent signs of two separate malignancies.

In the Neto series, rectal ADC represented the third common non-gynecological origin of vulvar metastasis [2]. The high possibility of a colorectal origin is an especially important issue in Taiwan, where the incidence of colorectal cancer is high (64.77 per 100,000) [9].

In the first case series comparing secondary tumors in each female genital organ, ovary and vagina were the most commonly involved organs whether the primaries were gynecological or non-gynecological [5]. Gastrointestinal malignancies especially those from colon and stomach were the most common non-gynecological sources of ovarian metastases. The "seed and soil" theory describes a tumor cell (seed) spawning easily in a fertile environment (soil) [6]. The rarity of cervical metastasis can also be explained by this theory, as it is small in size with reduced blood flow and distant

circulation. Also, its abundant fibrous composition further makes uterine cervix a barren place for metastasis [10]. In vaginal metastasis, the most gynecological origin is endometrial carcinoma; whereas SqCC of uterine cervix appears to be the most common origin (31.8%) of vulvar metastasis [2,5]. These statistics will decline in the future as PAP smear, HPV test, early treatment to the squamous intraepithelial lesion (SIL), and HPV vaccination can effectively prevent cervical SqCC occurrence. For vulvar metastasis, Valenzano et al. suggested altered lymphatic drainage after pelvic operation could be the reason [11]. However, since our patient never received any radical operation before, the exact mechanism of vulvar metastasis may be intricate to explain.

Dehner described two growth patterns for vulvar metastasis. The first pattern, observed in SqCC and urothelial carcinoma, was a Grenz zone between tumor and overlying epithelium. The second pattern was a direct invasion to the dermal papillae as seen in ADCs such as renal cell carcinoma, endometrial carcinoma, and ovarian carcinoma. Also, foci of lymphovascular invasion (LVI) were easier to be found deeper in the specimen. In our case, the overlying epithelium was ulcerated without Grenz zone. LVIs were mostly found superficially. Despite our observation was relatively different from Dehner's, the presence of LVI might still indicate the tumor spreading mechanism.

In the Neto series, 93.9% of cases had multiple organ metastases, consistent with the common concept that the presence of vulvar metastases is a pre-terminal event and is often associated with systemic metastasis [4]. Most patients expired within 12 months upon diagnosis of a vulvar metastasis [1]. While the concurrent multiple liver metastases found in our patient also indicated systemic metastasis, she has remained stable for 48 months after treatments. Since the latest and largest series published decades ago, advancement of cancer treatments such as new chemotherapy regimen and target therapy has lengthened life expectancy in such patients.

Vulvar metastasis is not commonly seen. Despite its low incidence, accurate diagnosis of metastasis is essential as the treatment and prognosis are different. Metastasis should also be suspected for patients with common gynecological complaints.

Conflicts of interest

The authors have no conflict of interest relevant to this article.

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