Cervical Metastasis from Renal Cell Carcinoma

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To the Editor: A 43-year-old woman, having a renal cell carcinoma (RCC) treated with radical nephrectomy 15 months ago in West China Hospital, was consulted to our gynecology outpatient clinic for a 3-month history of vaginal bleeding in March 2008. Before the clinic, blood transfusion was given to the patient at a local hospital due to heavy vaginal bleeding.

Colposcopy revealed a cervical mass of 5 cm × 6 cm as well as a hard nodular bleeding mass. A computed tomography scan showed a 4.3 cm × 3.7 cm × 3.7 cm mass in the cervix, consistent with recurrence of RCC, and negative pelvic lymph nodes. A biopsy and pathology revealed clear cell adenocarcinoma with hemorrhage and necrosis. Immunohistochemical staining showed positive staining for vimentin, cytokeratin (CK), epithelial membrane antigen (EMA), cluster of differentiation-10 (CD-10), human chorionic gonadotropin, and carcinoembryonic antigen, confirming cervical metastasis of RCC. The patient underwent the radical hysterectomy and was lost to follow-up in the Wenchuan earthquake 2 months postoperation. The pathological examination showed that cervical metastatic RCC infiltrated in half of the cervical wall, and the immunohistochemical staining showed that RCC features [Figure 1], secretory endometrium, vaginal margins of resection, and vessel were free of tumor.

The first case of cervical metastasis of RCC was reported in 1985,[1] and the primary location of RCC was left kidney. Usually, the metastasis occurred on the same side as the primary renal tumor. Retrograde flow of contrast medium from the left renal vein to the left ovarian vein, and uterovaginal venous plexuses and subsequently to the right ovarian vein has been demonstrated angiographically. Therefore, the most convenient path of spread seems to be retrograde venous extension. To our knowledge, the patient was the first case of cervical metastasis of RCC from the right kidney, same side as primary cancer. This could be explained by venous plexus or retrograde flow via inferior vena cava and right ovarian vein although there is no direct communication between the right ovarian vein and the right renal vein.

The major clinical presentation of all the three cases was vaginal bleeding,[1-3] one case showed cervical polyp,[4] and one case showed renal mass.[5] History of RCC and histopathology are very useful for diagnosis of metastasis of RCC. Immunohistochemical staining has been widely used to distinguish metastatic RCC from the primary carcinoma of genital tract cell. Traditionally, the positive staining of CK and vimentin is used to determine RCC. Metastatic clear cell carcinoma (CCC) of the gynecologic tract usually shows constant positivity of CD-10, which is in sharp contrast to the constant negativity of all primary gynecologic CCC, regardless of the original site. Therefore, CD-10 may be used to distinguish the primary and metastatic CCC of gynecologic tract. CK and EMA are markers of epithelial origin, and vimentin and CD-10 are markers of RCC. Therefore, both vimentin and CD-10 positive indicate that the tumor is derived from the kidney. Currently, CD-10 is used for the diagnosis of RCC and differential diagnosis. Taken together, the combination of histologic and immunohistochemical features with clinical findings will be helpful in differential diagnosis as in this case.

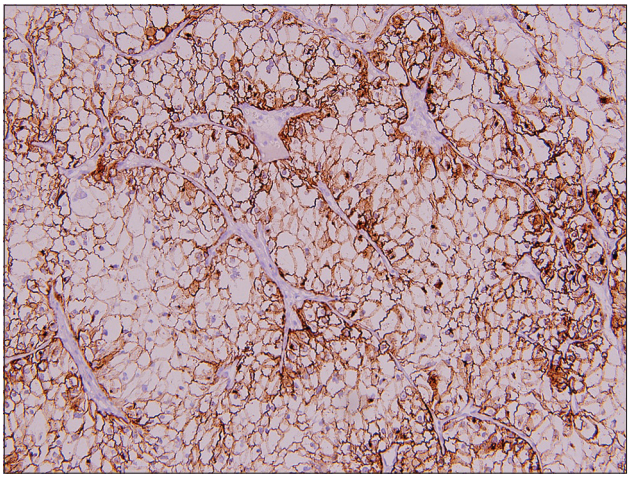

Figure 1: The tumors cells with immunohistochemical staining of cluster of differentiation-10 were shown in small frame (original magnification, ×200).

Treatments to cervical metastasis of renal cancer are various due to limited cases and lack of experiences. In this case, the patient underwent radical hysterectomy without pelvic lymph node

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Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.179790

Received: 28-11-2015 **Edited by:** Li-Min Chen
How to cite this article: Wang WX, Zhang WJ, Yang KX, Tang X, Peng ZL. Cervical Metastasis from Renal Cell Carcinoma. Chin Med J 2016;129:1005-6.

dissection because of negative finding of CT scan. Bozaci *et al*. reported a case of cervical and vaginal metastasis from RCC with radiotherapy. Radiotherapy may be alternative treatment, especially for patient with vaginal metastasis or with deep infiltration of cancer, positive resecting edge, and lymph node metastasis.[3]

With the development of molecular targeted therapy for cancer, molecular targeted therapy for metastatic RCC has also made a major progress. Bevacizumab combined with interferon-α has been used to treat metastatic RCC. It has been reported that a patient with cervical metastasis of RCC was given biological targeted therapy (sunitinib) and survived for 4 years.[3]

In summary, the best way of treatment to cervical metastasis of RCC is surgery. Adjuvant radiotherapy or molecular targeted therapy may also be useful according to the metastasis site and histological and pathological features of RCCs in the different patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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