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An unusual case of post-menopausal bleeding

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Abstract

Background Metastasis from Renal cell carcinoma at presentation is seen in nearly one fifth of the patients and commonly occur to lung, bone and liver. Synchronous vaginal and cervical metastasis is extremely rare. Several pathways have been proposed of which blood reflux from left renal vein to ovarian vein is most plausible. The prognosis is usually very poor as they are often associated with disseminated metastasis.

Case presentation A 55-year-old women presented with post-menopausal vaginal bleeding, on examination a smooth mass occupying the vagina and obscuring the view of cervix with normal mucosa was found. Biopsy and Immunohistochemistry showed it to be renal cell carcinoma. Further investigations lead to identification of left renal mass with pulmonary, vaginal and cervical metastasis. Patient was started on Pazopanib 800 mg PO per day, and was lost to follow-up.

Conclusion Vaginal metastasis presenting as post-menopausal bleeding is one of the rarest presentation of renal cell carcinoma with only 3 cases reported in literature before this. Metastatic tumors to the vagina are more common than primary tumors and are mostly from cervix, endometrium and ovary. A high index of suspicion and through examination and investigation is the key to correct diagnosis and management.

Keywords Renal cell carcinoma, Vaginal metastasis, Venous reflux, Cervix, Kidney, Pazopanib

Introduction

Renal cell carcinoma (RCC) is the ninth most common neoplasm in United States, with an incidence of 2.2% among all cancer diagnosis with a life time risk of 1.3–1.8% It has more preponderance in males than females with a relative risk of 1.7 [1]. Only 10% of the RCC cases present with the classic triad of haematuria, flank pain and palpable masses, most of the RCC cases are diagnosed incidentally on imaging. Other common symptoms are fever, weight loss and leucocytosis. RCC is the deadliest urological cancer with a relative 5-year survival rate of 76%, and for metastatic disease it is only 12% [2].

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According to WHO 2016 classification, total 14 types of renal cell carcinomas are defined, among which clear cell carcinoma is the most common histologic subtype, accounting for 75% of cases and papillary renal cell carcinoma is the second most common subtype [3]. Most common site for metastasis is to lung, liver and bone, and 18–33% of RCC cases presents with metastasis at the time of diagnosis [4]. Most common risk factors associated with RCC are smoking, obesity, diet and alcohol, poorly controlled hypertension and occupational exposure [1].

Vaginal metastasis is very rare and around 100 cases have been reported in literature [4] while synchronous metastasis to vagina and cervix is seldom seen with only 6 cases reported in literature (Table 1) [5–10]. We report a case of RCC with cervical and vaginal metastasis, that presented with vaginal bleeding.

Table 1 Literature review of 6 previous cases of vaginal and cervical metastasis from renal cancer

Author name and year	age	Presenting complaints	Findings	Histopathology	Site	Treatment	Chemotherapy or immunotherapy	Follow up status
Young 2007 [5]	46y	Asymptomatic abdominal mass on left side, h/o irregular bleeding of 8 months which patient revealed 8 months after surgery	d/g with lung nodules and mass in upper pole of left kidney, vaginal mets was diagnosed 1 month after surgery	Clear cell ca.	vagina	Open radical nephrectomy and video assisted pulmonary wedge resection After 1 month hysterectomy and WLE of vagina	IL-2, INF alpha AND 5 FU	-
Godfrey 2010 [6]	61y	Postmenopausal bleeding	k/c/o polycystic kidney disease, d/g with cervical polyp and RCC of lt kidney	Clear cell carcinima	cervix	Lost to follow up	-	-
Pisvadia 2017 [7]	79y	Type 1 respiratory failure and chest pain and vaginal bleeding	k.c/o COPD, TY 2 DM, HTN, ANGINA, d/g with renal mass, liver and vaginal metastasis	Clear cell ca.	vagina	Palliative rx	Pazopznib 400 mg	alive
Chibuzo 2016 [8]	43y	Rt flank pain	Lost to follow up for three months, then diagnosed with rt renal mass and vaginal wall mass	Papillary renal cell ca.	vagina	Rt nephrectomy		Lost to follow up after surgery
Jimenez 2018 [9]	54y	Intermittent vaginal bleeding	h/o tah	Clear cell ca. with rhabdoid differentiaition	vagina	Left renal nephrectomy and adrenalectomy		Sunitinib 50 mg
Moradi A et al. 2020 [10]	40y	Intermittent vaginal bleeding	Cesarean Sect. 8 yrs back	Papillary renal cell ca.	vagina	Left radical nephrectomy	P T4N0M1	Sunitinib

: h/o- history of; d/g- diagnosed; ca.- carcinoma; WLE- wide local excision; IL- interleukin; IFN- interferon; 5FU - 5 uro uracil ; K/C/o Known case of; RCC-renal cell carcinoma; COPD- chronic obstructive pulmonary disease, TY2- type 2; DM- diabetes mellitus; HTN - hypertension; rx-treatment; Rt- right; h/o- history of; TAH-transabdominal.hysterectomy;

Case report

A 55-year-old female presented to surgical oncology OPD (outpatient department) with complaints of white discharge for 4 months and postmenopausal bleeding for 1 month duration. She has attained menopause 10 years before, and there was no significant history of medical or surgical illness, family history or habits.

On examination, her ECOG (eastern cooperative oncology group) status was 1, vitals were stable, and there was no palpable generalized lymphadenopathy. Abdomen was soft, non-tender and no organomegaly or free fluid was present. Vaginal examination revealed a normal cervix with a soft friable growth felt just below the cervix in posterior fornix and appeared separate from cervix. Digital rectal examination showed that the bilateral parametria and rectal mucosa were free of infiltration. Speculum examination of the vagina showed a globular fragile growth of around 4 × 4 cm, that was arising from posterior vaginal wall, cervix could not be seen separately (Fig. 1). She had undergone a trans abdominal ultrasound of pelvis before coming to outpatient that showed endometrial thickness of 1 mm, with bilateral atrophied ovaries, a relatively well-defined heterogeneous mass in upper part of vagina with internal cystic spaces and raised internal vascularity of 5.1 × 4.0 cm, suggestive of vaginal carcinoma. Based on the clinical findings and ultrasound a clinical diagnosis of carcinoma of the vagina, FIGO stage 1(T1N0MX) was made. A vaginal biopsy was taken and contrast enhanced computerized tomography (CECT) thorax, abdomen and pelvis was advised. CECT abdomen showed soft tissue density mass of 7.1 × 4.4 × 7.2 cm with non enhancing necrotic area involving mid and lower pole of left kidney with extension of tumour thrombus into left renal vein (Fig. 2). Pelvic CT showed necrotizing enhancing lesion in the vagina, cervix and lower segment of the uterine cavity (Fig. 3) and CECT thorax showed multiple enhancing soft tissue density nodules in bilateral lung fields suggestive of diagnosis of metastatic renal cell carcinoma. Histopathological examination of the vaginal biopsy showed stratified squamous epithelium with acanthosis and regenerative atypia, and proliferating blood vessels, lined by plump endothelial cells (Fig. 4), immunohistochemistry (IHC) showed strong positivity of PAX 8 and CD10, and focal positivity for EMA, the ki67 was 8–10% (Fig. 5), suggesting the diagnosis of metastatic renal cell carcinoma. Due to advanced nature of disease, she was

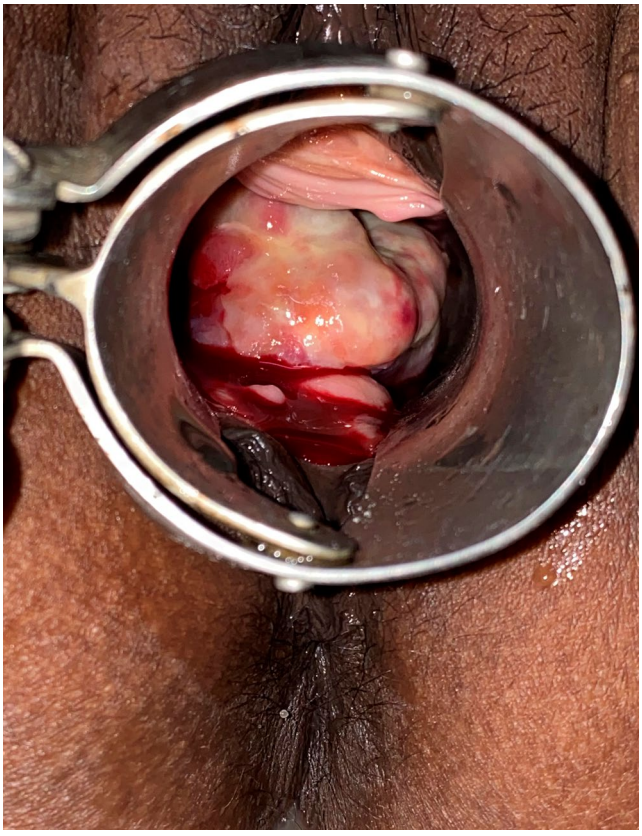

Fig. 1 Per speculum examination showing mass occupying the vagina with normal looking stretched mucosa, the cervix is not visualized and presence of blood in the vagina

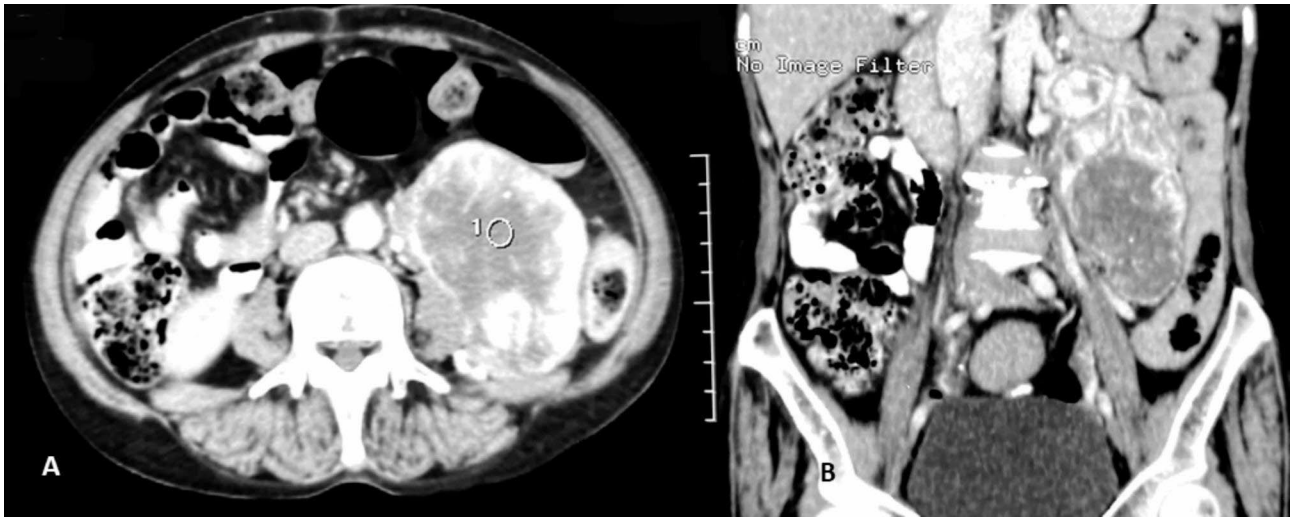

Fig. 2 Computerized tomographic scan of the abdomen showing (**A**) Axial view of the Mass in the left kidney (**B**) Sagittal section showing mass in the left kidney with tumour thrombus in inferior vena cava

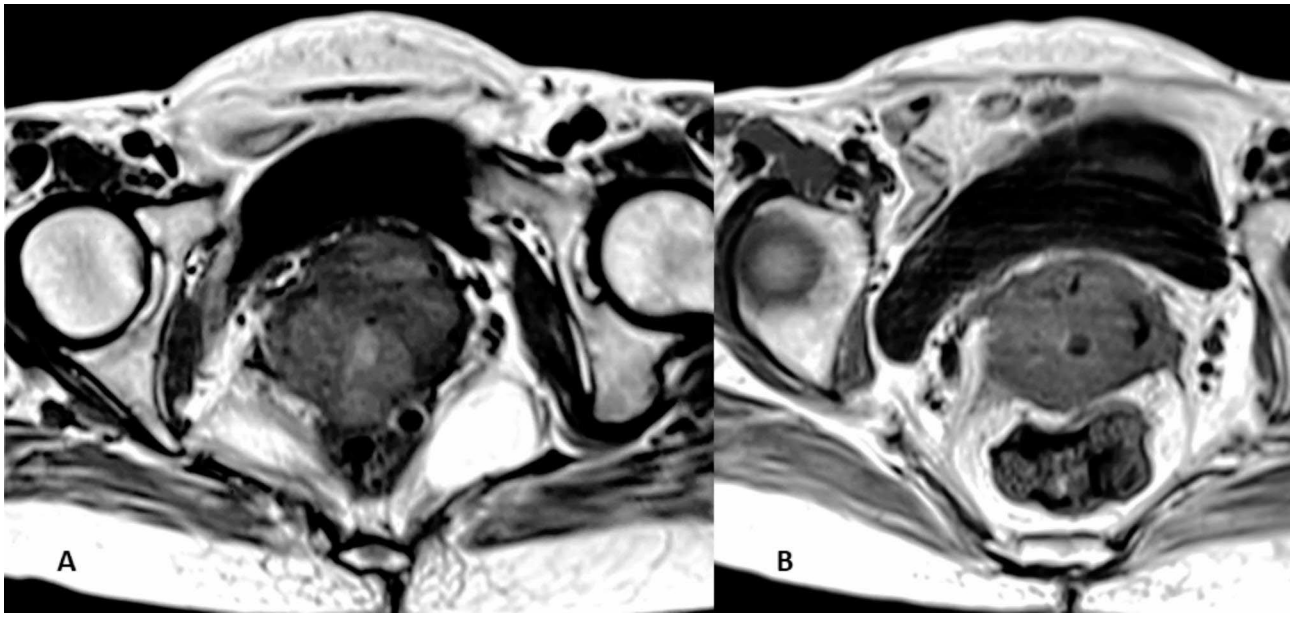

Fig. 3 Magnetic resonance imaging of the pelvis showing (**A**) Mass occupying the vagina (**B**) Mass involving the cervix

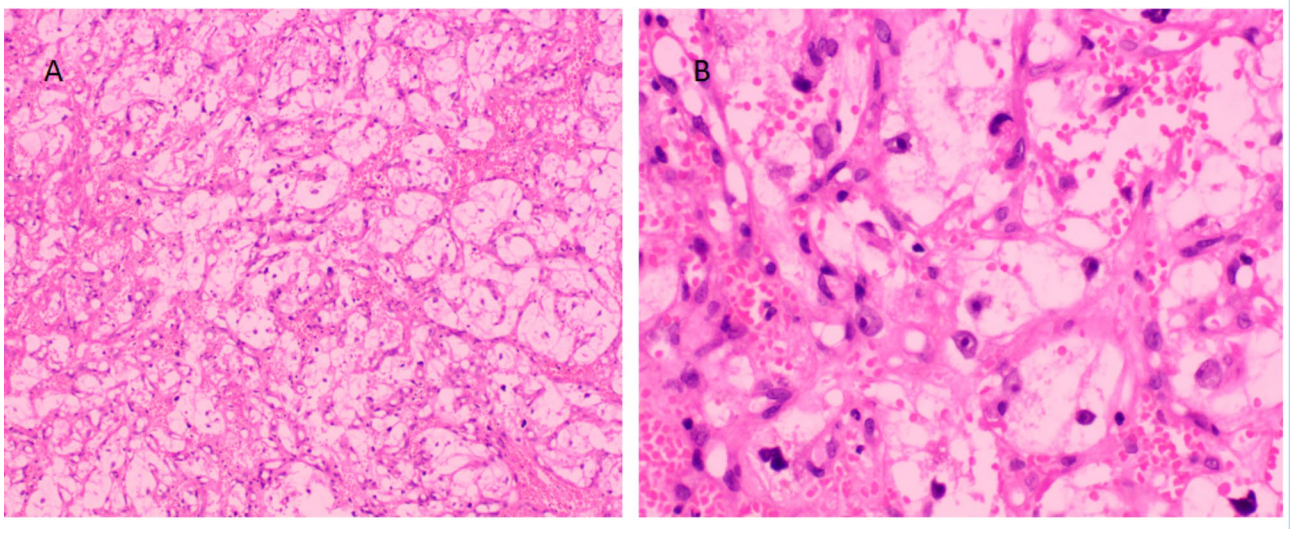

Fig. 4 Photomicrograph showing showed stratified squamous epithelium with acanthosis and regenerative atypia, and proliferating blood vessels, lined by plump endothelial cells (**A**) H &E 10 x (**B**) H&E 40x

started on oral Pazopanib 800 mg OD, and was later lost to follow-up.

Discussion

Vaginal bleeding as the first presenting symptom of renal cell carcinoma has not been reported before. Vaginal metastasis from RCC is very rare phenomenon. In most of the cases, vaginal metastasis is diagnosed in long term after surgery as metachronous metastasis. Peham in 1906 [11], reported the first case of vaginal metastasis, after this around 100 cases have been reported in literature. To the best of our knowledge, in literature, only 5 cases of synchronous vaginal metastasis and 2 cases of synchronous cervical metastasis has been reported in English literature, among which 3 patients have initial presentation as vaginal bleeding (Table 1) [5–10], none of these presented with vaginal lesion first. In most of the patients with vaginal metastasis, primary location reported was left kidney and metastasis was discovered in lower third of vagina on same side. In our case too, primary tumour was located in left kidney. The most frequent primary carcinomas metastasizing to uterus and cervix are the breast, stomach, ovarian and colorectal cancers [12].

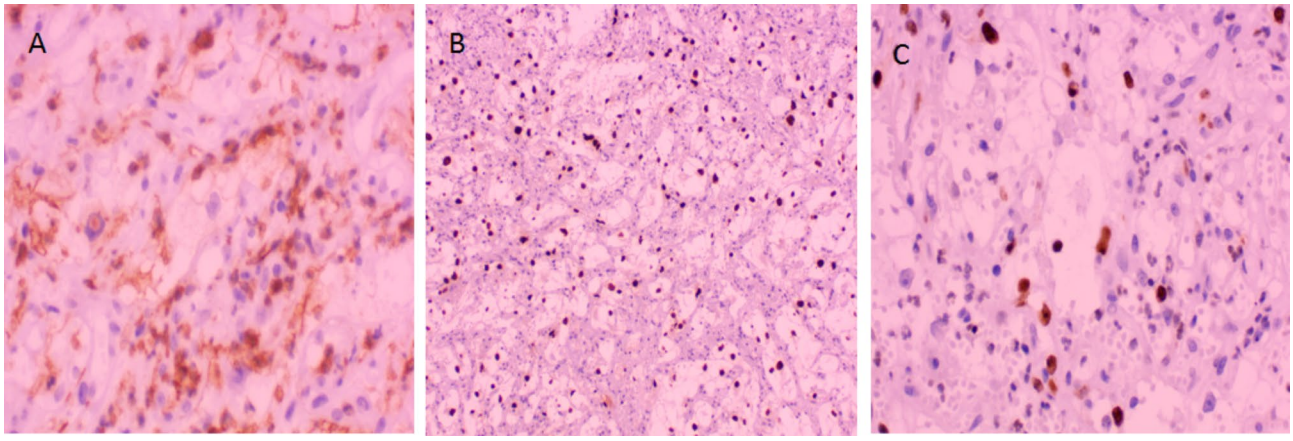

Fig. 5 Photomicrograph showing immunohistochemistry (**A**) CD10 magnification 40X (**B**) PAX 8 magnification 40X (**C**) Ki67 magnification 40x

Several routes of spread are demonstrated for the origin of vaginal metastasis like urinary, lymphatic and systemic. Mulcahy and Furlow [13] radiologically demonstrated the venous pathway, from blood reflux to left ovarian vein from left renal vein, from there to the ovarian plexus and the ureterovaginal plexus. On reviewing the literature, almost 80% cases metastasizing to vagina originated from left kidney. Lymphatic route is unlikely because no direct communication between lymphatics of kidney and vagina has been demonstrated. Urinary tract is also improbable because none of the patient with vaginal metastasis reported had metastatic lesion in ureter or bladder. Systemic circulation via the renal vein to inferior vena cava possibly has a role in diffuse pulmonary metastasis, but this route was also disregarded because it will also have nidus to different other organs other than lungs and vagina [13].

Most common site for genital tract metastasis in RCC is ovary [14]. In our case diagnosis is supported by IHC in which it can differentiate primary clear cell carcinoma of genital tract and metastatic clear cell carcinoma. Strong nuclear staining of CD 10 suggests metastatic clear cell carcinoma, which is also a marker of RCC [15]. PAX 8 also shows positivity in 88–100% cases of RCC, and in 100% cases of renal collecting duct carcinoma [16].

Conclusions

A case of RCC with synchronous cervical and vaginal metastasis, presenting as postmenopausal vaginal bleeding is being reported. Although it is very rare, per vaginal bleeding and vaginal metastasis, should be kept as differential diagnosis for post menopausal or post coital bleeding.

Author contributions

RP: Worked up the case, collected material and prepared the draft manuscript. JK: Helped with literature search and draft manuscript preparation. MS: Histopathological diagnosis and pathological part of manuscript and discussion. MP: Concept and design, editing of the manuscript for final content. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics and consent

Written informed consent was obtained from the patient for publication of case and accompanying images.

Competing interests

The authors declare no competing interests.

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