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Renal Cell Carcinoma – The Vagabond

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ABSTRACT

Renal cell carcinoma (RCC) is an aggressive tumour, with potential for metastases, either synchronously or metachronously. Very unusual patterns of metastases from RCC have been reported in literature. We report three more unusual sites of metastases from RCC occurring in various body parts, which could be missed in the conventional post treatment follow up investigation protocols adopted for RCC. This probably highlights the importance ofregular self-physical examination of the entire body parts in a patient diagnosed to have RCC to identify unusual sites of metastases. Since RCC is generally chemo and radiation resistant, the results of treatment of metastases in unusual sites are generally poor.

KEYWORDS: *Renal Cell Carcinoma, Metastases, Synchronous, Metachronous, Targeted Therapy*

INTRODUCTION

Renal cell carcinoma (RCC) constitutes more than 90% of all malignant renal tumours, of which 80% belong to the clear cell carcinoma variety. Though RCC commonly metastasize to lungs, lymph nodes, liver, bones, brain, opposite kidney and adrenal glands in this preferred manner [1], it is also notorious to spread in an unpredictable manner to other body parts. The orbit, parotid gland, para nasal sinuses, tongue, tonsils, thyroid, heart, skin, various mucosal linings all have been reported to harbour RCC metastases [2]. Still rarer organs where RCC has been reported to have metastasized include scalp, forearm, breast, jaws, skeletal muscles and urinary bladder [3,4,5,6]. Disseminated metastases to rectum, lungs, ilium and lymph nodes simultaneously have also been reported by Zheng et al [7]. In this paper, we present reports of three cases of RCC which metastasized to very unusual sites, not reported so far in literature, treated in our centre.

CASE REPORT 1

A 52 year old lady, on investigations for total painless hematuria, was found to have a large necrotic mass in the left kidney (Fig1, Panel A& B) suggestive of RCC with no evidence of distant metastases. She underwent left radical nephrectomy and the histopathology report (HPR) was RCC-clear cell variety. There were no evidence of lymph node metastases. She was on regular follow up for 5 years and there was no local recurrence or metastases. After 5 years, she developed mild bleeding per vaginum with urinary obstruction lasting for 1 month. On examination, she had a friable mass of size 4 X 3 cm at the region of external urethral meatus, which was bleeding to touch (Fig 1, Panel C). Cystourethroscopy showed that the mass was arising from the external urethral meatus, with no involvement of rest of urethra or urinary bladder. The mass was excised and the HPR was suggestive of RCC-clear cell variety (Fig 1, Panel D). The patient was started on targeted therapy using Sunitinib. However she succumbed to disseminated pulmonary metastases in 6 months' time.

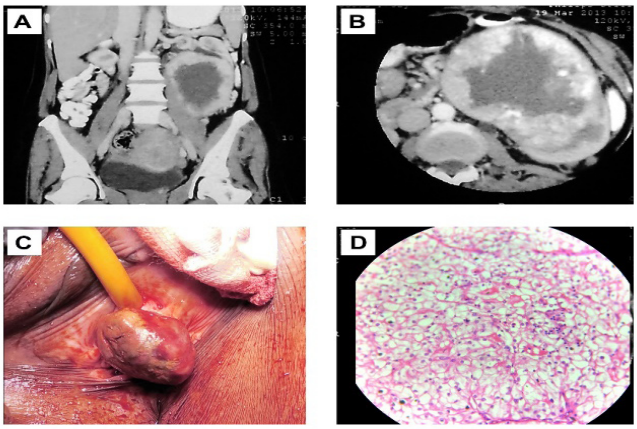

Fig 1, Panel A& B: CT images of large left RCC which was removed by radical nephrectomy

Fig 1, Panel C: Clinical picture of RCC metastasis at the external urethral meatus

Fig 1, Panel D: Histopathology picture of the RCC metastasis showing clear cell variety of RCC

CASE REPORT 2

A 49 year old lady underwent right radical nephrectomy through subcostal incision for suspected centrally located renal mass producing total painless hematuria (Fig 2, Panel

A). She had undergone total abdominal hysterectomy 8 years prior for fibroid uterus. The HPR of the renal mass was RCC-clear cell variety with no lymph node involvement. There was no evidence of metastases elsewhere. The patient was on regular follow up, with no evidence of local recurrence or metastases. At one year of follow up, she presented with a large subcutaneous mass in the region of right iliac fossa, separate from the deep muscles (Fig 2, Panel B). Since she was not willing for excision of the mass, a trucut biopsy from the mass was done for diagnostic purposes. The HPR was suggestive of RCC-clear cell variety (Fig 2, Panel C). The patient refused further treatment and died of disseminated disease in 3 months' time.

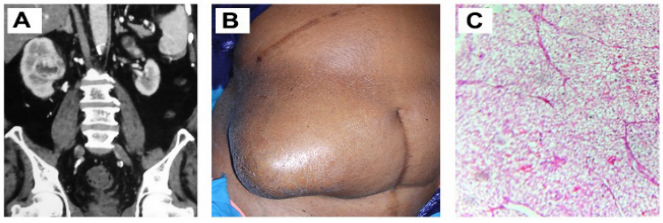

Fig 2, Panel A: CT image of right sided RCC which was removed by radical nephrectomy

Fig 2, Panel B: Clinical image of subcutaneous metastasis from RCC occurring in the right iliac fossa. The right subcostal scar of nephrectomy and midline lower abdominal scar of hysterectomy are also seen

Fig 3, Panel C: Histopathology picture of the RCC metastasis showing clear cell variety of RCC

CASE REPORT 3

A 58 year old lady who presented with total painless hematuria, on investigations was found to have a mildly enhancing mass in the region of left renal pelvis, extending to the inferior calyx (Fig 3, Panel A). Urine cytology was inconclusive of malignancy. With suspicion of transitional cell carcinoma of renal pelvis, radical nephro-ureterectomy with excision of cuff of bladder was done. The HPR was RCC-clear cell variety involving the renal pelvis with extension into the inferior calyx (Fig 3, Panel B). The renal parenchyma was uninvolved. There was no regional or distant metastases. The patient is on regular follow up for the last 8 years and there is no loco-regional or distant metastases so far.

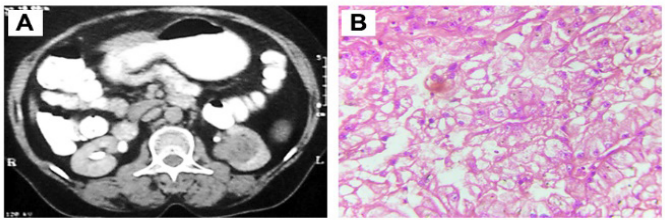

Fig 3, Panel A: CT image of RCC of the left renal pelvis

Fig 3, Panel B: Histopathology picture of RCC of left renal pelvis showing clear cell variety of RCC

DISCUSSION

It is now known that the metastasis from RCC occur synchronously with the primary tumour or metachronously, several years after the primary has been treated, in unusual fashion, completely bypassing the common sites of cancer metastases. The atypical presentations and rare metastases sites of RCC have been extensively reviewed by Sountoulides P et al [8]. Very unusual sites of metastases in scalp, chest and abdomen have also been reported in male patients with advanced malignancy [9,10].Generally the time interval to skin metastasis has been reported to vary from 10 to 60 months, depending on the tumour stage [11], though such time frames have not been identified in metachronous tumours occurring in other rare sites.

Vaginal metastasis from RCC presenting with vaginal bleeding, has been previously reported in literature [12,13]. Similarly solitary proximal urethral metastasis has also been identified in male patients with RCC [14,15]. However metastasis to external urethral meatus in female patients, as seen in our case has not been reported so far. The mode of metastasis to the lower genitourinary tract could be either by dissemination through urinary system or by hematogenous spread [16].

Although Kumar et al [17] reported isolated abdominal wall metastasis close to incision site, probably due to seeding of primary tumour cells during retrieval, in an elderly male patient who had undergone radical nephrectomy two years prior to presentation. However,subcutaneous deposit in the anterior abdominal wallaway from incision site, as seen in our patient has not yet been reported so far. Chan and Chua [18] also reported a rare case of advanced metastatic RCC which initially presented with back and forehead lumps. In our patient, the metastatic deposit was away from the incision site, free from both muscles and the overlying skin.

It is very unusual to see RCC occurring in the renal pelvi-calyceal system, completely by-passing the renal parenchyma, since there is no glandular tissue in the lining of this part of urinary system. Our third patient had RCC occupying the left renal pelvis with extension into the inferior calyces, probably as metastasis from a very small primary RCC, which was either burnt-out or clinically unidentifiable in the renal parenchyma, which misled us to a diagnosis of TCC of renal pelvis.

RCC is generally resistant to radiation, chemotherapy and hormonal therapy. Surgical excision and targeted therapy remain the mainstay of treatment of RCC with metastases [19]. Since the metastases to unusual body parts occur late in the course of oncogenesis of RCC, coupled with the advanced stage of disease, the results of treatment are also poor in such cases. Two of our patients succumbed to metastatic disease within a span of 6 months after diagnosis of metastases, though the patient with RCC in the renal pelvis has been surviving for the last eight years after surgery.

CONCLUSIONS

RCC is a potentially lethal aggressive cancer, with a vagabond nature metastasizing either synchronously or metachronouslyeven to unusual body sites. The disease is generally radiation and chemoresistant and surgery is the

only curable treatment option available. Targeted therapy could also be an adjuvant to surgery, useful in selected cases of metastases. Results of treatment of cutaneous, head and neck metastases in RCC are generally poor. Treatment of RCC with unusual sites of metastases, which are not surgically amenable still remains a challenge and the results of treatment are poor in such situations. Atypical presenting symptoms due to bizzare metastases pattern adds up to the delay in diagnosis. A thorough self-examination of body parts by the patients themselves should probably be included in the post-treatment follow up protocol of RCC, to identify the unusual metastatic sites so that the treating physician could be alerted regarding this.

PATIENT CONSENT

The patients have given necessary informed consent for analysis, reporting and medically publishing the images, as per the protocol of the treating institution. A copy of the written consent is available for review by the Editorial office/ Chief Editor/Editorial Board members of this journal.

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