Case Report

Nephrogenic epistaxis

Rajeev Kumar1, MS, DNB, Kapil Sikka1, MS, DNB, Rakesh Kumar1, MS, Priti Chatterjee2, MD

ABSTRACT Metastatic renal cell carcinoma (RCC) in the nose and paranasal sinuses is very rare. We report an unusual case of metastatic RCC that presented as recurrent epistaxis ten years after curative nephrectomy. The purpose of this report is to draw the attention of clinicians to the possibility of metastatic RCC in patients with recurrent epistaxis and nasal mass. We also discuss treatment options and review the relevant literature.

Keywords: epistaxis, metastatic renal cell carcinoma, paranasal sinus tumours, radiotherapy, targeted molecular therapy

INTRODUCTION
Metastatic deposits in the nose and paranasal sinuses are very rare. Even so, renal cell carcinoma (RCC) is reported to be the commonest tumour metastasising to the nose and paranasal sinuses.1,2 Metastatic RCC can present as recurrent epistaxis, nasal obstruction, pain, swelling or solitary periorbital mass. We herein report the case of a patient with recurrent epistaxis who was diagnosed with metastatic deposits of clear cell RCC (ccRCC) in the paranasal sinuses after a long latency period of ten years.

CASE REPORT
A 42-year-old Indo-Aryan man presented to the Department of ENT, All India Institute of Medical Sciences, New Delhi, India, with recurrent epistaxis during the preceding nine months. He had three episodes of spontaneous nasal bleeding, with the epistaxis being moderate in volume (20–25 drops per episode). There was associated melaena, suggestive of ingestion of blood. The patient also had left-sided progressive nasal obstruction, which was associated with purulent nasal discharge for three months. There was no history of headache, facial pain, postnasal drip or visual disturbances. The patient, who had undergone curative nephrectomy for ccRCC (stage T1N0M0) 10 years previously, had been disease free since and was on regular follow-up for RCC.

Anterior rhinoscopy revealed pale polypi filling the left nasal cavity, and the presence of purulent discharge. The rest of the examination, including vision and extraocular movements, was normal. There were no palpable neck nodes. Contrast-enhanced computed tomography of the paranasal sinuses showed a markedly enhancing, lobulated, soft tissue lesion (measuring 3 cm × 2.5 cm) involving the left frontal and ethmoid regions, with expansion of the surrounding structures (Fig. 1).

There was no bony erosion or destruction, and no intraorbital or intracranial extensions were seen. Endoscopic biopsy under general anaesthesia for tissue diagnosis was planned for the patient. Endoscopy of the left nasal cavity showed multiple pale polypi, which were removed. Behind the polypi was a reddish, friable mass involving the ethmoids and frontal recess area, which was biopsied and sent for histopathological analysis. The mass was noted to be intensely vascular. Postoperative histopathology surprisingly showed features suggestive of ccRCC. Haematoxylin and eosin staining showed a tumour composed of cells with clear cytoplasm and a centrally located nucleus with distinct nucleoli. There were thin-walled capillaries in between the tumour cells. These cells were positive for pancytokeratin, CD10 and vimentin. The above morphological and immunohistochemical features suggested a diagnosis of metastatic RCC (Figs. 2a & b).

Following histopathology, a urology consultation was sought for the patient. Positron-emission tomography with computed tomography (PET-CT) was performed, which showed metastatic nodules in the bilateral lungs and the left frontoethmoid sinuses. Following discussions with radiation and medical oncologists at the hospital, the patient was started on sunitinib, an epidermal growth factor receptor (EGFR) inhibitor, for pulmonary metastasis. High-dose radiotherapy was also initiated for metastatic frontoethmoid disease. Currently, the patient has completed radiotherapy and is on molecular targeted therapy.

DISCUSSION
Metastatic RCC to the nose and paranasal sinuses is very rare. To
Case Report

The best of our knowledge, only 26 such cases have been reported so far. Our patient is unusual given the very late metastasis seen, which was diagnosed ten years after initial curative nephrectomy. Only one study has previously presented a patient with such late distant metastatic deposits in the paranasal sinuses, in whom metastasis was seen 17 years after initial treatment. The lungs, liver and bones are the usual sites of metastatic deposits. There are dual modes via which RCC can metastasise to the nose and paranasal sinuses and paranasal sinuses. The caval route describes the dissemination of tumour cells through the inferior vena cava to the right side of the heart, lungs, left side of the heart and maxillary artery, finally seeding in the nose and paranasal sinuses. Another route that has been described is the retrograde flow of tumour cells from the inferior vena cava to the sacral plexus and then to the paraspinal venous plexus. The tumour emboli reach the cranium by retrograde flow, and then reach the internal jugular vein through the intracranial vascular sinuses by a combination of anterograde and retrograde flows, which further allows the tumour to seed in the paranasal sinuses by unusual flow patterns. In our patient, the presence of seedings in the lungs suggested dissemination via the caval route.

Recurrent epistaxis is the most common mode of presentation for this metastatic disease, although it can also present as nasal obstruction, swelling, pain or solitary periorbital mass. Therefore, a high index of suspicion is needed when patients present with recurrent epistaxis, and metastatic RCC should be included in the possible differential diagnosis. Metastatic deposits from RCC are present in approximately 15% of patients at the time of presentation, although long latency periods of up to 20 years has been reported in the literature. In our patient, the latency period was ten years.

Contrast imaging of the paranasal sinuses followed by endoscopic biopsy are the initial investigations recommended for the management of such patients. Once confirmed by histopathological analysis, the work-up should include disease recurrence at the primary site as well as other distant sites. PET-CT has been the preferred imaging modality in the modern era, as it provides details of both the anatomical and physiological presence of disease. PET-CT, when performed in our patient, revealed metastatic deposits in both the lungs and the left paranasal sinus. In cases where PET-CT is not available, the diagnostic work-up should include routine urine examination for malignant cells, ultrasonography KUB (kidney, ureter and bladder), and CT of the abdomen and chest.

Treatment options are limited for metastatic RCC and prognosis is usually poor. If the metastatic deposit is solitary in the paranasal sinus, aggressive surgery has been recommended. Surgery is also advised to prevent recurrent epistaxis and subsequent anaemia. Nonsurgical treatment modalities such as radiotherapy, immunotherapy, and combined radiotherapy and chemotherapy have shown no long-term survival benefits. Ziari et al reported complete response after treating a patient with high-dose intensity-modulated radiation therapy (4,500 Gy in 15 fractions) along with interleukin and thalidomide for solitary paranasal metastasis. In our case, the patient was started on targeted therapy (EGFR inhibitor) for pulmonary metastasis and high-dose radiotherapy for the metastatic deposits in the paranasal sinuses.

The five-year survival rate for patients with multiple organ metastasis of RCC has been reported to range from 0% to 7%. However, patients with a solitary metastasis treated with surgery have been reported to have a two-year survival rate of 41% and a five-year survival rate of 13%.

In summary, metastatic deposits of RCC are very rare in the nose and paranasal sinuses. We herein presented the case of a patient with recurrent epistaxis who was diagnosed with metastatic deposits of ccRCC in the paranasal sinuses ten years after curative nephrectomy. Recurrent epistaxis, which is the most common presentation of metastatic RCC, might be the only clue to the disease, either occult or recurrent. A high index of suspicion should therefore be exercised by clinicians for the diagnosis of metastatic RCC in patients presenting with recurrent epistaxis when the setting is either occult primary or very late recurrences.

REFERENCES