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MISCELLANEOUS

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Metastatic renal cell carcinoma presenting as epistaxis

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Abstract Metastatic tumors in the nasal and paranasal sinuses are very rare. The origin of metastatic tumors in the nasal or paranasal sinuses is often renal cancer. Renal cell carcinomas are known for their tendency to early metastasis, and symptoms due to the metastatic lesion may be the only initial manifestation. In this paper we deal with the case of a 73-year-old patient who presented with recurrent epistaxis. The presence of a primary renal cell carcinoma was recognized only after surgical removal of the metastatic tumor. The presentation, difficulties in diagnosis and treatment of this tumor are discussed, with a review of the literature.

Keywords Renal cell carcinoma · Metastasis · Ethmoid sinus · Nasal endoscope

Introduction

Primary carcinoma of the paranasal sinuses constitutes approximately 0.3% of all human cancers [1]. Most malignant tumors occurring in the nasal and paranasal sinuses are primary tumors, and metastatic tumors in these areas are extremely rare [2]. Metastatic renal cell carcinoma to the paranasal sinus is seen as an intranasal mass causing recurrent epistaxis, nasal obstruction, facial pain or orbital mass. These symptoms may precede those of the primary tumor.

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Case report

A 73-year-old male presented with repeated episodes of massive epistaxis. His occupation was not related to woodwork. He had been treated previously at a private otolaryngologic clinic for intermittent episodes of spontaneous epistaxis for 6 months. He had no other complaints. Due to profuse bleeding and the anemic condition of the patient, detailed intranasal examination was not possible, and nasal packing was inserted in the nasal cavity initially to control the bleeding. When the patient's condition stabilized several days later, endoscopic examination of the right nasal cavity revealed a dark red, irregular, hemorrhagic tumorous lesion in the right middle meatus (Fig. 1). There was no associated cervical lymphadenopathy or evidence of regional or distant metastasis. Biopsy of the intranasal mass was attempted, but hemorrhage from the mass soon caused the attempt to be aborted.

Paranasal sinus CT scans showed a soft-tissue mass extending from the right posterior ethmoid sinus into the right middle meatus. This mass was strongly enhanced on contrast-enhanced viewing. There was displacement of adjacent bone, but no lytic bone lesions could be observed (Fig. 2). Soft tissue density was also seen in the right maxillary sinus, but no bone destruction could be detected. MRI showed a 3×2-cm-sized mass in the right posterior ethmoid sinus. The mass was seen as a low signal area on T2-weighted imaging and was moderately enhanced by gadolinium.

The patient underwent tumor removal with nasal endoscopy under general anesthesia. An elongated, slightly necrotic, pinkish

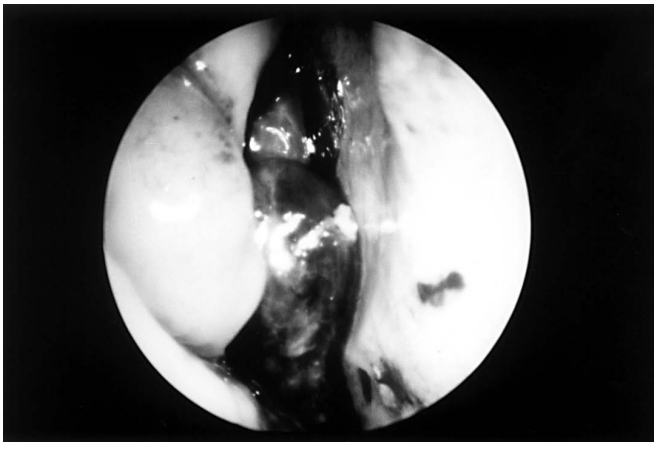

Fig. 1 Endoscopic view showing a necrotic, magenta-colored mass filling the right nasal cavity

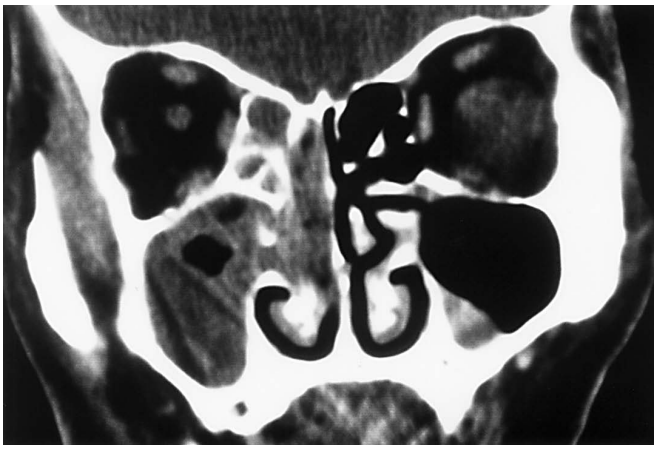

Fig. 2 PNS CT scan showing a soft tissue mass occupying the right ethmoid sinus

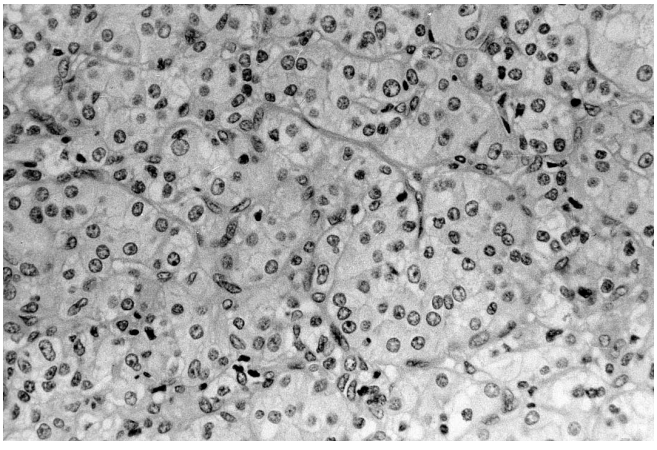

Fig. 3 Histologic findings showing metastatic renal cell carcinoma, with characteristically clear cytoplasm (HE ×400)

polypoid mass was seen to extend into the right nasal cavity from the right posterior ethmoid sinus. The left maxillary sinus was full of tissue with hyperplastic mucosa. The tumor was removed en bloc. The excised tumor showed extensive hemorrhagic appearance and was yellowish-gray in color. The margins of resection were free of the tumor. The pathologic findings were consistent with metastatic renal cell carcinoma (Fig. 3). Immunohistochemical staining for cytokeratin, epithelial membrane antigen and vimentin was positively compatible with metastatic renal cell carcinoma. Immunohistochemical examination showed a negative staining for S100 and melanoma-specific marker HMB-45. The metastatic foci contained focal, diastase-sensitive and periodic acid Schiff (PAS)-positive material, which was indicative of glycogen in the cytoplasm of the clear cells.

In order to confirm the presence of a renal malignancy, further studies were performed. Urinalysis revealed microscopic hematuria. Abdominal CT scan showed an 8×8×7-cm-sized lobulated mass in the upper pole of the left kidney, with extension to the left adrenal gland.

The patient underwent radical nephrectomy of the left kidney. The pathology result was consistent with renal cell carcinoma. The patient is alive and free of nasal symptoms 3 year after surgery. No signs of recurrence or metastasis have been noted. Since the lesion was invading the bone, external beam radiotherapy (40 Gy) was administered in 15 fractions, although these lesions are not noted for their radiosensitivity.

Discussion

When a tumorous condition is detected in the nasal or paranasal sinuses, a primary nasal or paranasal tumor is first suspected, but metastatic tumors from other primary sites should also be considered. Of all primary tumors that arise below the level of the clavicle, renal cell carcinoma is overall the third most common neoplasm to metastasize to the head and neck region, after lung and breast carcinomas, and most of these metastases occur in the thyroid gland [1]. However, renal cell carcinoma is the most frequent infraclavicular tumor to metastasize to the nasal cavity and paranasal sinuses. Therefore, even though it is rare for renal cancer to metastasize to the nasal or paranasal sinuses, renal cancer must be first suspected when investigating metastatic tumors in this region.

There are two routes for renal cancer to metastasize to the nasal and paranasal sinuses. One is the caval route in which tumor cells travel through the inferior vena cava, the right heart, the lungs, the left heart and the maxillary artery to reach the nasal and paranasal sinuses [3]. The other is the vertebral plexus route, in which tumor cells do not flow into the inferior vena cava, but travel through the venous plexus, the intracranial venous plexus and the cavernous venous plexus to reach the nasal and paranasal sinuses. Emboli can enter the cranial vault through a combination of anterograde and retrograde flow in the intracranial vascular sinuses, arriving at the internal jugular vein, where further unusual flow patterns would allow the emboli to seed structures and develop metastasis in the paranasal sinuses [4]. In the present patient, since lung or liver metastasis was not seen, the vertebral venous plexus was believed to have been involved.

The renal clear-cell carcinoma may metastasize when the diameter of the primary tumor exceeds 3 cm. Because of the slow growth at the initial stage in about 60% of the cases, the primary lesion receives little attention until symptoms occur because of metastasis [5].

Symptoms of metastatic tumors to the paranasal sinuses include epistaxis, nasal mass or swelling, nasal obstruction and pain, in decreasing order of frequency. The vascular stroma of these metastatic deposits accounts for the fact that the most common symptom of these sinonasal lesions is epistaxis [6]. The high vasculature of renal cell cancer leading to bleeding is probably caused by the fact that most of them have a von Hippel-Lindau gene mutation causing upregulation of hypoxia-induced factor (HIF) 1α, which in turn leads to angiogenesis through VEGF upregulation [7, 8]. When there is uncontrollable bleeding, immediate surgical removal is very important.

When cancer is diagnosed in a paranasal sinus, a thorough search for a distant primary tumor must be made to rule out metastatic disease. Renal cell carcinomas are known to metastasize early, and symptoms due to the metastatic lesion may be the initial and only manifestation. Twenty-five percent of the patients with renal cell carcinoma have distant metastatic lesions at the time of initial assessment.

The original classic triad of flank pain, hematuria and palpable mass occurs in only about 10% of the patients, and palpable mass occurs in only about 10% of the patients. However, intermittent microscopic hematuria occurs in 90% of the patients [9]. Since symptoms of metastatic tumors often precede those of a primary tumor in renal cancer, hemorrhagic tumorous conditions must be diagnosed with this point in mind, even in the absence of a past history of renal cancer.

Preoperative diagnosis of a metastatic tumor is often difficult, because severe and recurrent bleeding and often significant necrosis hinder getting a credible histopathologic specimen. Biopsy should be done very carefully for fear of violent sudden bleeding. In our patient, the diagnosis remained equivocal for some time because repeated episodes of massive epistaxis precluded a thorough intranasal examination. The hemorrhagic nasal and paranasal tumors such as hemangioma, angioendothelioma, angiofibroma, melanoma and primary nasal adenocarcinoma have to be differentiated from metastatic clear-cell carcinoma.

Even though many metastatic tumors originating from renal cancer develop in multiples, most metastatic tumors in the nasal or paranasal sinuses are single and treated surgically [6, 10]. Patients with a single resectable metastatic lesion should be treated aggressively, since they have an excellent chance for extended survival before further progression of this disease. However, even if multiple tumors are found in the nasal and paranasal regions and other organs, surgery will be effective in preventing epistaxis and subsequent anemia [11]. Non-surgical treatment modalities such as chemotherapy, immunotherapy, radiotherapy and chemotherapy with drugs such as vinblastine, hydroxyurea or methyl-GAG have failed to improve survival significantly, and where possible, surgery is the mainstay of treatment and offers the best hope for survival [12].

In conclusion, the case described here is unusual because the primary tumor had not declared its presence and also because of its unusual site. Early diagnosis and surgical removal of both primary and metastatic tumors are important to prolong the patient's life. When a patient presents with persistent epistaxis with an intranasal necrotic mass, the possibility of metastatic renal cell carcinoma should be considered.

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