Nasal metastasis as the first manifestation of a metachronous bilateral renal cell carcinoma

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Key words

Metastasis • Nasopharynx • Renal cell carcinoma

Summary

Renal cell carcinoma is one of the most common tumours to spread by extranodal metastases to the head and neck. Metastatic renal cell carcinoma to the head and neck area has been demonstrated mostly in the paranasal sinuses, parotid gland, the mandible, larynx and hypopharinx. Renal cell carcinoma should be excluded whenever a metastatic lesion is encountered in the head and neck area, even if the metastatic lesion is the first clinical presentation. The diagnosis of metastatic RCC should be suspected in any patient with even a remote history of renal cell carcinoma. We report a case of 79 year old woman with recurrent episodes of rhinorrhea, headache, hyposmia and monolateral right epistaxis, with a history of RCC. We describe RCC nasal metastases in a metachronous bilateral neoplasm, in which a second occult lesion debuted with a homolateral nasal metastases, ten years after left nephrectomy.

Introduction

Nasal malignant tumors, usually primary, are 0.3% of all neoplasms and 3% of all head and neck neoplasms [1]. Occasionally metastatic sinonasal tumors from infraclavicular sites, mainly the kidneys and, to a lesser degree, the lungs and breast, may manifest with nasal symptoms [2]. In particular, after lung and breast carcinomas, renal cell carcinoma (RCC) is the third most common neoplasm to metastasize to the head and neck region, but metastasis to the nasal cavity is an extremely rare occurrence. Several cases are reported in the literature to localization maxillary, ethmoid and in the nasal cavity [3]. The peculiarity of the case report described is metachronous bilateral renal neoplasm, in which a second occult lesion debuted with a homolateral nasal metastases.

Case report

A 79-year-old Caucasian woman presented to ENT Department of University of Catania with a eight months history of recurrent episodes of rhinorrhea, headache, hyposmia and monolateral right epistaxis. Her medical history was positive for hypertension, thyroid and RCC, reason why she underwent a left nephrectomy ten years previously. The histological diagnosis revealed clear cell renal carcinoma, staged as pT1bN0M0. The oncologic follow-up, run for the next five years has brought to light a complete remission of the neoplastic disease, it therefore did not need concomitant and/or additional treatments.

Laboratory tests showed normal haemoglobin levels (14 mg/dl), liver function, coagulation profile, serum calcium level, and other routine blood test results were all normal. On nasal endoscopy the examination showed a highly vascular reddish mass, readily bleeding in the right nasal cavity with complete obstruction of the nasal fossa (Fig. 1). Rather peculiar was the finding of like polypoid evidence in the contralateral nasal fossa. Presurgical computed tomography (CT) of the nose and paranasal sinuses revealed a soft-tissue mass including, maxillary sinus, ethmoid sinus and right nasal cavity, extending into the roof of nasophaynx. The mass was strongly enhanced on contrast enhanced viewing and lytic bone lesions of the right maxillary sinus were observed (Fig. 2). Magnetic resonance imaging (MRI) confirmed a nasal lesion, seen as a low signal area on

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Fig. 1. CT scan of the neck with contrast media axial, corona, sagittal mpr reconstructions in the right maxillary sinus, the right nasal cavity and ethmoid cells there is metastatic tissue with strong enhancement (arrows). The metastatic tissue borders on nasopharynx, coexists erosion of the medial wall of the right maxillary sinus.
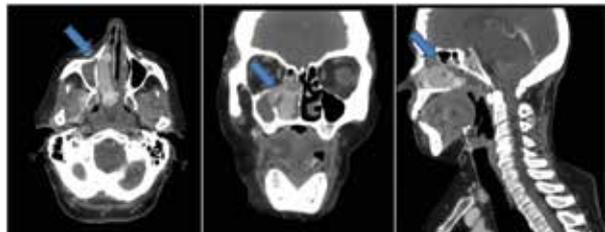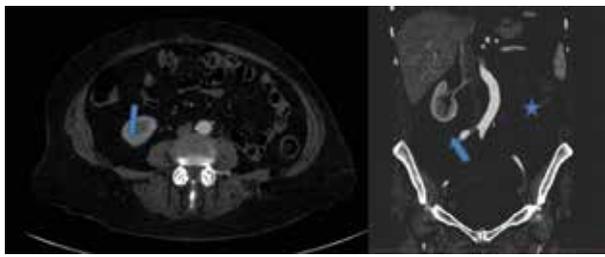

Fig. 2. Abdomen ct scan with contrast media: in the right kidney is appreciable metastatic centimeter area of enhancement (arrow), the left renal loggia is uninhabited for prior nephrectomy (star).

T2-weighted, the lesion appeared hyperintense on T2 weighted imaging (T2WI) and isointense on T1WI, with strong enhancement (Fig. 3). Trans nasal endoscopic surgery under general anesthesia was performed, using monopolar electrocautery, to biopsy. Histological examination of the specimen revealed clear cell carcinoma of renal origin, clear-cell type RCC. The tumor was composed of cells interspersed with abundant thin walled vessels that result in a sinusoidal vascular pattern, characterized by a clear cytoplasm surrounded by a distinct cell membrane. Nuclei were round and uniform, with finely granular chromatin, with inconspicuous nucleoli at 10x objective (Furhman nuclear grade 2) (Fig. 4). Immunohistochemically, the tumour cells were strongly positive for vimentin (Fig. 5A), CD10 (Fig. 5B), and pancytokeratin (Fig. 5C), but negative for CK20, CK7 and S100. Abdomen CT, performed later, found a solid mass at the lower pole of the right kidney and urinalysis revealed microscopic haematuria. In relation to old age and in order to low extension of the lesion that did not reach cribra lamina, if only with a perilesional oedema, the tumors was resected by an entirely extra cranial approach through a paralateral rhinotomy incision, with partial right maxillectomy. The margin of resection were free of the tumor. The surgical approach has been characterized by a profuse bleeding intraoperative, which required a blood transfusion of three bags of packed red blood cells and an anterior and posterior nasal packing. Patient maintained full bed rest in a 30-degree upright position until the third postoperative day. Nasal packing was gradually removed within 48 hours. Intravenous third-generation cephalosporin therapy was started the day before surgery and continued for at least 5 days. The patient was therefore staged as T1aN0M1 and she has been started to biological treatment for RCC.

Fig. 3. MRI sequences: (arrows) presence of tissue at the intermendia signal intensity on T2 axial (a), sagittal (b), coronal (c) and isointense in T1-weighted sequences (d); intense enhancement on T1-weighted sequences with contrast media (e).
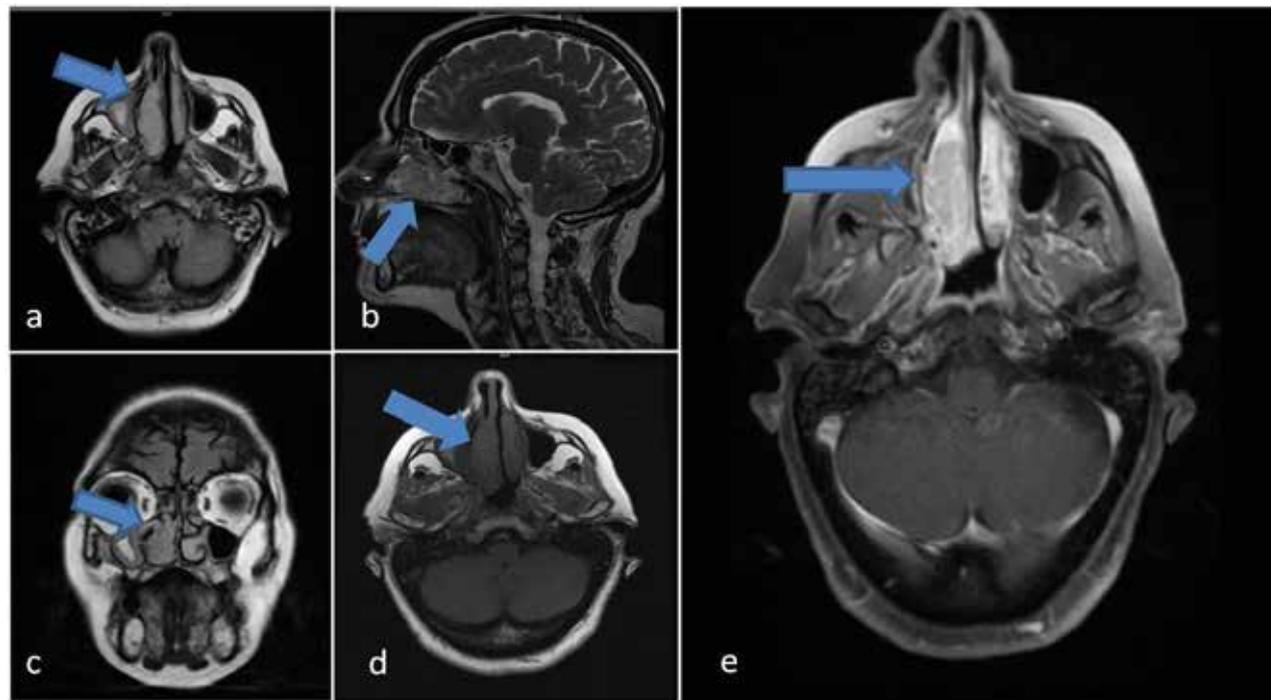
Fig. 4. Histological examination revealed a proliferation of cells interspersed with abundant thin walled vessels that result in a sinusoidal vascular pattern, characterized by a clear cytoplasm surrounded by a distinct cell membrane. Nuclei were round and uniform, with finely granular chromatin, with inconspicuous nucleoli (arrow).
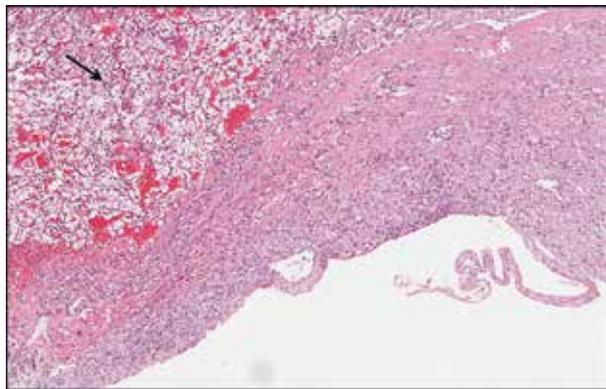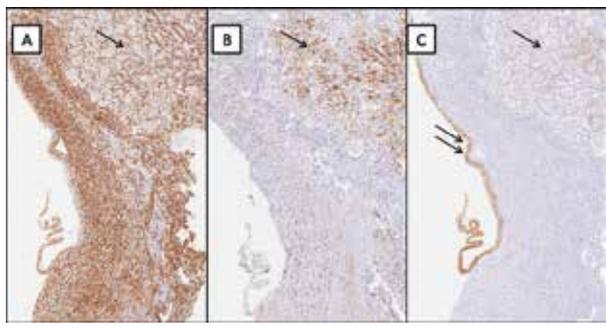
Fig. 5. (a) Neoplastic cells show strong staining for vimentin (arrow) (b) Neoplastic cells show strong staining for CD10 (arrow). (c) Neoplastic cells show weak staining for pancytokeratin (arrow); nasopharyngeal epithelium show strong staining for pancytokeratin (arrows).

Discussion

RCC represents 3% of all adult malignancies and occurs more frequently in the fifth and sixth decades of life. It's the most frequent infraclavicular tumor to metastasize to the nasal cavity and paranasal sinuses and it may metastasize when the diameter of the primary tumor exceeds 3 cm [3]. Choong et al., analyzed 301 cases of metastatic RCC treated over a period of 20 years, and found only 4 cases of nasal metastases (1.3%). In two of these four cases, nasal lesion was the first presenting feature of RCC [4]. In another large series of 1785 patients of surgically treated RCC, incidence of atypical metastases was 1.88% (37 cases). Among these 37, only 3 patients had metastases to the nasopharynx region [5]. A review of 98 paranasal sinus metastases revealed that RCC comprised 54% of the primary tumors with a predilection for the maxillary antrum (36%), ethmoidal sinuses (25%), frontal sinus (17%), and nasal cavity (11%) [6]. 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 [7]. The other is the vertebral plexus route, less commonly followed, in which tumor cells do not flow into the inferior vena cava, but via Batson paravertebral plexus of avalvular veins, which surrounds the vertebrae and communicates with pelvic veins caudally, intercostal veins cranially, and IVC in the abdomen (through azygous veins). Through this route, the tumor cells may bypass the lungs [8]. 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 [9]. Thirty percent of patients present a distant metastasis and only 10% exhibit the classical presentation of the tumor with flank pain, palpable mass and gross haematuria. Intermittent haematuria, however, may be present in 90% of patients [10]. 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 13]. RCC comprises a histologically diverse group of solid tumors but the most common histological variant being the clear cell RCC (85%) [11]. This variant is associated with loss of function of the von Hippel Lindau gene, which leads to up-regulation of the hypoxia inducible factor (HIF) and, finally, increased function of the vascular endothelial growth factor (VEGF) [12]. Therefore, sinonasal metastases of RCC origin are characterized by a propensity for severe bleeding, like in the case described by us. A differential diagnosis of nasal bleeding lesions should include angiofibromas, hemangiopericytomas, hemangiomas, and other less vascular benign lesions and/or malignant such as adenocarcinomas, melanomas and metastatic tumors from the breast and lungs have to be differentiated [13-15]. A paranasal sinus CT scan may provide some hints about the benign or malignant nature of the lesion, such as bone erosion and remodeling (signs of malignant and metastatic lesions), hypervascularity, expansion of the sphenopalatine foramen and pterygopalatine fossa (angiofibromas). Magnetic resonance imaging (MRI) shows the true extent of the lesion, infiltration of the skull base and leptomeningeal metastases. Biopsy of a suspicious nasal lesion is imperative to guide further workup, but severe hemorrhage may occur [16]. Some authors advocate selective embolization prior to tumor biopsy particularly if there is a known history of nephrectomy [8 17]. Biopsy of RCC nasal metastasis may prove non-diagnostic due to diffuse necrosis of the lesion so several attempts are sometimes necessary. Its histopathologic characteristics include the presence of encapsulating connective tissue, clear cell borders, round or oval nuclei, and abundant clear cytoplasm that contains cholesterol, phospho-lipids, and glycogen. Approximately 50% of specimens express vimentin, with most also staining positive for CD10, EMA, and

pancytokeratin. However, the histologic subtype is not a recognized prognostic factor in RCC [18]. If the histological specimen shows clear cells, the abdomen should be investigated with ultrasonography and CT. Other sites prone to RCC metastasis, such as the lungs, brain and bone, should be screened with CT and bone scintigraphy, respectively. The 5-year survival rates are 81%, 74%, 53%, and 8% in stages I to IV, respectively, according to the National Cancer Database. Also the presence of vascular invasion and capsular infiltration, microvessel density and tumor necrosis are important clinic-histological prognostic factors. However, low performance status (70 or less in Karnofski's scale), thrombocytosis, and neutrophilia, one and a half times higher than normal levels of serum LDH, low hemoglobin, corrected serum calcium levels higher than 10 mg/dL are poor prognostic indicators [19]. Treatment options of RCC are variable and prognosis depends on clinical, radiological, serological and histological factors. According to the The National Comprehensive Cancer Network practice guidelines for kidney cancer, patients with a resectable primary tumor and a single metastasis or post-nephrectomy patients who develop a metachronous metastasis may benefit from nephrectomy and metastasectomy or metastasectomy respectively [20] [21]. 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. Excision of solitary metastatic lesions after nephrectomy results in a 41% survival at 2 years and 13% at 5 years, regardless of the interval between nephrectomy and diagnosis of metastases, and so it provides some survival advantage in select patients [22]. At the sinonasal level, this option must take into account the choice of surgical approach. The lateral rhinotomic approaches offer excellent exposure of the maxillary ethmoidal region with a degree of 5-year survival ranging from 25% to 65% [23]. Also more control than the upper limits of the disease was achieved with the association to craniofacial approaches that saw the prognosis of malignant lesions involving the skull base significantly improve front. However, it is known that transfacial approaches may be followed by sequelae such as facial aesthetic deformities, strictures of the nasal vestibule, anesthesia or pain in the infraorbital and lacrimal dysfunction. The transcranial approaches may be associated with persistent symptoms such as headache, diplopia and anosmia. Moreover, the intraoperative blood loss is often considerable and the postoperative course is characterized by a long period of hospitalization. Some surgical schools, in an attempt to reduce postoperative morbidity, have applied to this disease micro-invasive techniques such as micro-endoscopic intranasal. More recently, endoscopic resection seems to be the best treatment for small localized paranasal and nasal metastases. The choice of a laser surgery does not appear applicable [27]. Nasal surgery will be also effective in preventing epistaxis and subsequent anemia. It is important to note the fact that owing to the vascularity of the tumor, surgery must be undertaken with caution. If the primary tumor is potentially resectable but multiple metastases coexist, nephrectomy and systematic cytoreductive therapy is likely to benefit. If the primary tumor is unresectable and the nasal metastasis causes epistaxis and visual disturbances, the patient may receive systemic therapy or resection or radiotherapy of the metastasis [21]. Sabo et al., have even reported complete regression of nasopharyngeal metastasis of RCC with radiotherapy and brachytherapy [28]. A reasonable options to employ radiotherapy followed by surgical resection of any residual metastatic lesion. This strategy can also be helpful even if the primary tumor is unresectable [22].

Conclusions

The case treated by us is interesting, especially in relation to the development of a small tumor metachronous controlateral, to the previous appeared ten years before, which made its debut with ipsilateral nasal metastases. It is important to recognize metastases from renal cell carcinoma, especially if they were in unusual sites, such as the nasopharynx, nasal cavity, and paranasal sinuses, because they can be misdiagnosed as primary malignant or benign diseases, particularly for those patients without a clinical history and in relation to nonspecific symptoms of the lesion. Nasal metastases are associated with poor prognosis. The surgical management is recommended for isolated metastasis, but patient can be selected for targeted therapy or radiotherapy.

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