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ORIGINAL ARTICLE

Distant Metastases to Nasal Cavities and Paranasal Sinuses Case Series

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Abstract Metastatic tumors to the nasal cavity and paranasal sinuses are far less common than primary cancer in this location. Review of the 2004–2010 pathology records of patients with sinonasal malignancy, revealed three cases with distant metastases to this region from primary sites in kidney, prostate and breast. The clinical presentation, histopathological findings and clinical outcome is presented for each patient. Metastases to the nose and paranasal sinuses usually respond poorly to treatment and have a poor prognosis. This report highlights the importance of suspecting metastases in patients with a previous history of malignancy. Therefore, thorough history and clinical evaluation is mandatory in any known/treated case of cancer.

Keywords Paranasal sinus · Metastatic · Kidney · Breast · Prostate

Introduction

Primary malignant neoplasm is more common than metastatic cancer in the paranasal sinuses, and these occur most frequently in 40–60 age groups [1]. The clinical presentation is similar to that of primary tumors [1] and common symptoms include recurrent epistaxis, nasal obstruction and facial pain. The most common sites of metastatic involvement are the maxillary sinus, ethmoid sinus, frontal sinus, nasal cavity and sphenoid sinus [2].

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Case Reports

The 2004–2010 pathology records of nasal and paranasal sinuses in Khalili Hospital affiliated to Shiraz University of Medical Sciences, Shiraz, Iran were reviewed. The overall incidence of sinonasal malignancies was 2.5% (25 in 1,000 cases). There were 25 cases, 18 (72%) males and 7 (28%) females, whose ages ranged from 5 to 74 years. Epistaxis, rhinorrhea and nasal obstruction were the usual symptoms in patients. Lesions included primitive neuroendocrine tumor/Ewing's sarcoma (12%), malignant melanoma (12%), olfactory neuroblastoma (8%), rhabdomyosarcoma (8%), plasmacytoma (8%), small cell neuroendocrine carcinoma (8%), Non Hodgkin's lymphoma (8%), Sinonasal adenocarcinoma (4%), Adenoid cystic carcinoma (4%), Chondrosarcoma (4%), Chordoma (4%), nasopharyngeal carcinoma (4%), metastatic carcinoma (12%) (Table 1).

In this review, three cases with distant metastases were found. Whole-body bone scan with Tc-99m MDP revealed site of TC concentration compatible with metastasis. These cases illustrate atypical presentation of distant malignancies in the paranasal sinuses and nasal cavity.

Case 1

A 51-year-old Iranian man presented with repeated episodes of intractable epistaxis. He underwent radical left sided nephrectomy for renal cell carcinoma (RCC) 3 years ago. Last clinical and radiological work up in May 2008 revealed normal findings. Endoscopic examination of the right nasal

Table 1 The demographic and pathologic diagnosis of 25 tumors in nasal cavity and paranasal sinuses

	Tumor type	Patient age (year)	Patient sex
1	Rhabdomyosarcoma, alveolar type	5	Male
2	Rhabdomyosarcoma	4	Male
3	Olfactory Neuroblastoma	10	Female
4	Olfactory Neuroblastoma	12	Male
5	Primitive neuroendocrine tumor/Ewing's sarcoma	33	Male
6	Primitive neuroendocrine tumor/Ewing's sarcoma	25	Female
7	Primitive neuroendocrine tumor/Ewing's sarcoma	27	Male
8	Chondrosarcoma	67	Male
9	Chordoma	34	Female
10	Malignant melanoma	68	Male
11	Malignant melanoma	71	Male
12	Malignant melanoma	56	Male
13	Nasopharyngeal carcinoma	35	Male
14	Plasmacytoma	15	Male
15	Plasmacytoma	18	Male
16	Sinonasal adenocarcinoma, intestinal type	46	Female
17	Non Hodgkin's lymphoma, T cell type	37	Female
18	Non Hodgkin's lymphoma, Diffuse large B cell lymphoma	47	Female
19	Non Hodgkin's lymphoma, Diffuse large B cell lymphoma	40	Male
20	Small cell (Undifferentiated) neuroendocrine carcinoma	56	Male
21	Small cell (Undifferentiated) neuroendocrine carcinoma	60	Male
22	Adenoid cystic carcinoma	67	Male
23	Metastatic carcinoma (Renal cell carcinoma)	51	Male
24	Metastatic carcinoma (Ductal carcinoma Breast)	49	Female
25	Metastatic carcinoma (Prostatic adenocarcinoma)	74	Male

cavity revealed a dark hemorrhagic mass in the right middle meatus. A computed tomography (CT) scan revealed opacification of the ethmoid sinus with extension to the nasal cavity. Severe bleeding prompted removal of the tumoral tissue under general anesthesia. Histological findings revealed sheets of clear cells with hemorrhage and necrosis (Fig. 1). Immunohistochemical staining for cytokeratin and vimentin was positive, compatible with metastatic RCC. Treatment with palliative radiotherapy, external beam (40 Gy) was started, but the lesion was radioresistant. The patient developed lung metastasis and died.

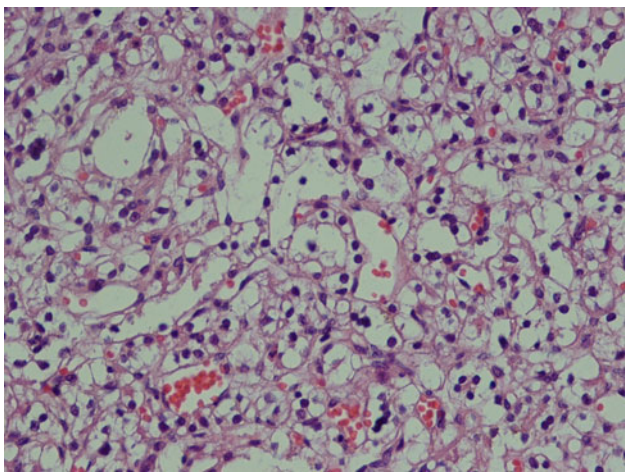

Fig. 1 Histologic findings of metastatic renal cell carcinoma with clear cytoplasm and rich vascular stroma (H&E ×400)

Case 2

A 74-year-old Iranian man presented with nasal congestion and rhinitis He was treated with antibiotics for 3 weeks with

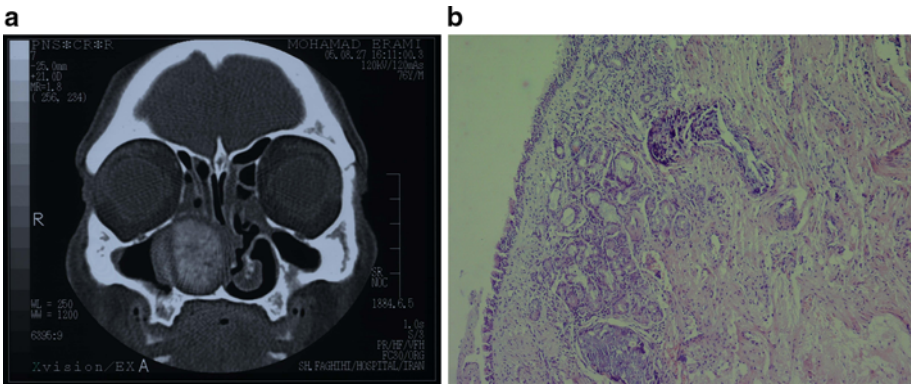

Fig. 2 **a** CT scan revealing opacification of the right maxillary sinus with tumoral lesion. **b** Presence of atypical malignant cells with overlying normal nasal mucosa (H&E ×400)

no improvement. The patient was known to have had prostatic adenocarcinoma, Gleason grade 8 since 2003. Last clinical follow up in September 2007 revealed normal prostatic specific antigen (PSA). CT scan showed a soft tissue mass in the maxillary sinus with extension to nasal cavity (Fig. 2a). Biopsy of the left nasal mass was reported as poorly differentiated carcinoma (Fig. 2b) with focal positive immunohistochemical staining for prostatic specific antigen. Serum prostate specific antigen (PSA) was also markedly elevated. PSA is an antigen present in prostatic acini, ducts or secretions and can be used as a specific marker of tumors of prostatic origin [3]. Chemotherapy with 4000 rads of radiation therapy to sinus area was started. He developed disseminated disease and died 11 months later.

Case 3

A 49-year old Iranian woman, with a known history of infiltrative ductal carcinoma of the left breast, was referred to Otolaryngology due to symptoms of nasal obstruction with onset 1 month previously. The primary tumor had been diagnosed 2 years previously and the patient had undergone radical mastectomy with concurrent chemo-radiation. One year after the initial diagnosis, the laboratory results of tumor markers CA 15-3 and CEA were negative and after that the patient lost her follow up. For new admission, computed tomography (CT) of the paranasal sinuses showed unilateral sphenoid and ethmoid opacification. The patient underwent tumor resection with nasal endoscopy under general anesthesia, and histology of the biopsy specimen revealed a nest of malignant epithelial cells beneath the respiratory epithelium (Fig. 3). Tumor cells tested positive for oestrogen receptors (ER). Combined chemotherapy regimen with mitomycin, folinate, and 5-fluorouracil (Mi/Fo/FU) was initiated but the patient died 6 months after surgery.

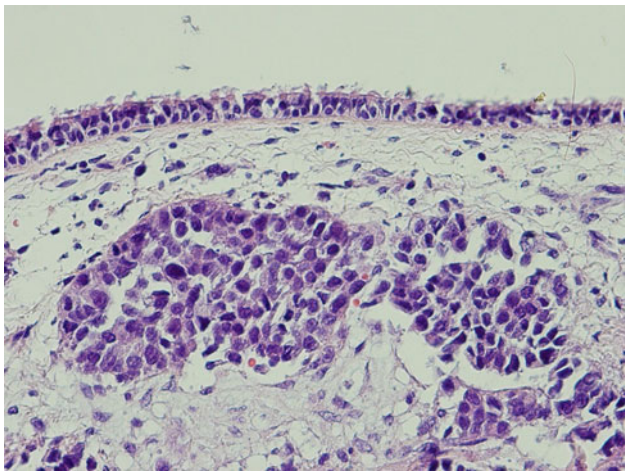

Fig. 3 Nests of malignant epithelial cells beneath respiratory mucosa. (H&E ×400)

Discussion

Metastasis to the paranasal sinuses is extremely rare and diagnosis is often delayed. The signs and symptoms are usually vague and nonspecific [1]. It may be present with nasal or orbital symptoms. Nasal symptoms include epistaxis, nasal swelling, nasal obstruction and facial pain [4, 5]. Orbital symptoms include proptosis, diplopia, decreased vision and ptosis [4, 5]. All the patients in this study presented with nasal symptoms. In literature review, RCC accounts for most cases [6, 7], while metastatic tumors from the breast [8, 9], colon [10], stomach [11] and prostate [3, 12] have also been reported.

RCC has a rich vascular stroma. Therefore, the most common symptom of these sinonasal lesions is epistaxis and surgery must be undertaken with caution [7, 13]. RCC can metastasize early, and symptoms of metastatic tumor may be the first clinical presentation [13]. Metastatic RCC is usually resistant to radiotherapy and chemotherapy. According to the National Comprehensive Cancer Network practice guidelines for kidney cancer [14], post-nephrectomy patients who develop a metachronous metastasis may benefit from metastasectomy. If multiple metastases coexist, systematic therapy with Interferon α, interleukin 2, temsirolimus, surutinib and bevacizumab are currently evaluated in therapeutic protocols.

Prostatic carcinoma is one of the most prevalent malignancies in the adult male population. Seventy percent of patients with prostate carcinoma will present with distant metastasis [3, 12]. Bone involvement is common, especially in the pelvis, ribs and spine. Metastatic carcinoma to the sinonasal tract from prostate carcinoma is rare [12].

Although the majority of patients with metastatic prostate cancer initially respond to androgen deprivation therapy, almost all patients will eventually develop castration-resistant prostate cancer. Recently cabazitaxel, docetaxel-and Sipuleucel-T were improve overall survival in patients with symptomatic metastatic prostatic cancer [15].

Breast carcinoma is a common primary malignant tumor in females. The most common sites for secondary breast cancer metastases are the lungs, liver, ovaries and adrenal glands [8]. Metastases of the skull base with paranasal sinus involvement are also reported. The neoplastic cells spread to the central nervous system and paranasal region by the hematogenous route [8, 9]. If metastases exist, systematic therapy with bevacizumab, trastuzumab and docetaxel are currently evaluated in therapeutic protocols [16].

In respect of evaluation of carcinoma of unknown primary site, paranasal sinus CT scan may provide some views about the benign or malignant nature of the lesion, such as bone erosion and remodeling (signs of malignant and metastatic lesions), hypervascularity or expansion of the sphenopalatine foramen. Magnetic resonance imaging (MRI) shows the true extent of the lesion and provide more information such as infiltration of the skull base and leptomeningeal metastases. Combined positron emission tomography/computed tomography (PET/CT), using the radiotracer (18) F-fluoro-2-deoxyglucose (FDG), is useful for the detection of primary tumors [17, 18] .

The vertebral venous plexus has been postulated as a possible route for the hematogenous dissemination of cancer cells to the head and neck. This low-pressure plexus communicates with the pelvic veins, intercostal veins, vena cavae and the azygos system. The malignant cells travel upwards to the pterygoid plexus, cavernous sinus and finally the nasal and paranasal sinuses. Thus, neoplastic cells from prostatic carcinoma or RCC may spread to the paranasal sinuses by the vertebral plexus route [2, 13–15].

If clinical picture like rhinosinusitis in old age patient not respond to routine treatments, the possibility of a neoplastic process should be considered. Overall, in these situations, the diagnosis is usually delayed and the prognosis is poor.

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