Sinonasal Metastasis: A Clinico-pathological Series of Seven Cases.

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Abstract: Introduction: Metastases to the sinonasal region is rare and presents with features overlapping with various regional neoplastic/non-neoplastic lesions. This series aims to highlight the clinical presentations and diagnostic difficulties of sinonasal metastases. Material and Method: A review of pertinent demographic and laboratory data for patients diagnosed with metastases to the sinonasal region, over a period of 6 years (2012-2017) was done. Results and Discussion: Seven cases (males-6, females-1) of sinonasal metastases were identified. The age ranged from 41-72 years. The common clinical presentation was nasal obstruction, epistaxis, and pain. Grossly tumors were irregular masses (mean size – 4.1cm) with maxillary sinus as the most common site. The histologic types included Squamous cell carcinoma (3 cases), clear cell renal cell carcinoma (2 cases), and one case each of infiltrating ductal carcinoma, and eccrine spiradenocarcinoma. The site of the primary tumor was larynx (2/7), kidney (2/7), breast (1/7), lung (1/7), and neck (1/7). The mean time interval between the primary tumor and metastasis was 4.5 months. All cases were managed with resection of the metastatic tumor. Metastatic breast and renal tumors comprise of the primary tumors of the region. Metastatic tumours to the region are uncommon and results from widespread primary, Their signs and symptoms are similar as those of the primary tumours and commonly includes features of obstruction, epistaxis and pain. Renal cell carcinoma is the most widely reported metastatic tumour to the sinonasal region, other includes metastasis from breast, colon, lung, thyroid, prostate, and female genital tract.

Materials and Methods
This was a six-year (January 2012-December 2017) retrospective study. Seven cases diagnosed as metastasis to nasal cavity, paranasal sinuses and nasopharynx were identified after reviewing the departmental archives and were included in the study. Following permission from the institutional ethics committee approval, pertinent demographic data were obtained from the medical record department. Laboratory investigations, histopathology and immunohistochemistry slides (if available) were retrieved and reviewed. The following patient data were collected and analysed: age, gender, clinical symptoms, site of sinonasal metastasis at time of presentation, histologic reports, radiographic findings and treatment modalities.

Results
Seven cases were identified from the archives. The age ranged from 41-72 years. Six cases were males and one female (M: F-6:1). The most common clinical presentation was nasal.
obstruction seen in all cases (7/7), followed by epistaxis (4/7), and pain (4/7). Two patients showed bilateral cervical lymphadenopathy. The most common site of involvement was the maxillary sinus (3/7), followed by the nasal cavity (2/7) and nasopharynx (2/7). All cases were irregular grey-white grossly and showed surface ulceration. The size ranged from 2-7 cm (mean ~4.1cm) in the greatest dimension. The site of primary tumour were larynx (2/7), kidney (2/7), breast (1/7), lung (1/7) and neck (1/7). The mean time interval between the primary tumour and metastasis for six cases was 4.5 months. One case presented with synchronous metastasis with the primary renal cell carcinoma. All cases were managed with resection of the metastatic tumour.

The histopathological types of metastasis were Clear cell renal cell carcinoma (RCC) (2 cases), squamous cell carcinoma (SCC) supraglottis (2 cases), squamous cell carcinoma- lung (1 case), infiltrating ductal carcinoma (1 case), and eccrine spiradenocarcinoma (1 case). The metastasis of RCC presented with nasal obstruction and epistaxis with localisation in the lateral wall and other in the floor of nasal cavity. Histopathology showed sheets of clear cells positive for CD10 (Figure 1).

One case was synchronous with the primary in left kidney. Both were disease free on an average follow up period of 11 months. Three cases of SCC (well differentiated) were identified; two in maxillary sinus while one in the roof of nasopharynx. Apart from nasal obstruction, one case showed erosion of wall of maxillary sinus, and cervical lymphadenopathy. The primary tumour was supraglottic in two cases, and one lung carcinoma. One case showed liver metastasis, while two were disease free for an average follow up of 24 months. One case of metastatic infiltrating ductal carcinoma (IDC) (Figure 2) presented with lesion in right fossa of Rosenmuller showing increase uptake on bone scan. Following resection, the patient was disease free for the available follow up period of 10 months. One case of eccrine spiradenocarcinoma in the left maxillary sinus presented with nasal obstruction and epistaxis, three months following the diagnosis of primary on the nape of neck. The metastasis showed undifferentiated hyperchromatic cells forming the bulk of tumour and the infiltrating edge, a differentiation to polygonal cells and squamous cells was seen in the islands located close to the mucosa (Figure 3). The patient was disease free for an available follow up of 18 months. The demographic details, clinical presentation, diagnosis and follow up is summarised in Table 1.

Figure 1: (A) Heterogeneously enhancing mass in the left nasal cavity with erosion of wall and spread to sinuses. (B) Tumor composed of clear cells with rich interstitial capillary network (H&E, 100x). (C) The tumours cells show membranous positivity for CD10 (200x).

Figure 2: Tumor composed of sheets of cells with vesicular pleomorphic nuclei and moderate amount of eosinophilic cytoplasm (H&E, 200x), showing nuclear positivity for estrogen receptors (inset, ER, 100x).

Figure 3: (A) Enhancing soft tissue mass lesion in the left maxillary sinus with bony erosion and extension to nasal cavity. (B) The tumor is lined by respiratory epithelium and shows focal squamous differentiation, the invading part consists of hyperchromatic small cells (H&E, 200x)

Discussion
Metastasis to the sinonasal region are tumours that originate from but are not in continuity with primary malignant neoplasms of other sites. This definition however excludes leukaemia and lymphomas. The majority of patients presenting with sinonasal metastasis are over 50 years and shows a male preponderance.(1,3,5,6) The common presenting features includes epistaxis, nasal obstruction and facial pain, patients with locally aggressive disease can present with orbital symptoms like proptosis, diplopia and ptosis. These may remain confined to one region or show bony erosion and local spread to surrounding area.(1,5,6)

Metastatic pathway to the sinonasal region is via haematogenous or lymphatic route. The low pressure Bateson’s plexus and valve less network of veins provide communication with the azygous system. An increase in the intra-abdominal pressure may push the tumour emboli to the head and neck. Lymphatic spread occurs via tumour emboli entering the thoracic duct from the regional lymph nodes, they can reach the head and neck circulation via retrograde flow from intercostal, supraclavicular or mediastinal vessels.(2) The maxillary sinuses owing to its rich vascular supply forms a fertile soil for metastasis to grow and hence is most frequently involved.(1–4)
RCC accounts for more than half of the reported cases of sinonasal metastasis and shows a predilection for maxillary sinuses (54%); only about 11% are localised to the nasal cavity. RCC metastasis is usually present with recurrent epistaxis and nasal obstruction. It metastasises early and can present as the first sign of an occult malignancy. Clear cell RCC is the most common histologic type documented in the metastasis, however, biopsies can be difficult to interpret where haemorrhage and necrosis predominate the lesion. Such cases require the use of ancillary techniques like immunohistochemistry for confirmation. Markers like RCC, CD10 can be used not only to confirm a metastatic RCC but also to exclude the diagnosis of recently described clear cell carcinoma in the sinonasal tract.(2,5) The present study reports two cases of metastatic clear cell RCC. Metastatic SCC is usually a diagnostic dilemma as SCC is the most common primary malignancy occurring in the head and neck region. Lung SCC metastasising to the paranasal sinuses have been documented in the literature. Metastasis of a laryngeal SCC is usually synchronous and is stage IV primary.(1,3) The present series describes two case of a supraglottic SCC and one lung SCC metastasis to the maxillary sinus and roof of nasopharynx. The laryngeal SCC metastasis also has bilateral cervical lymphadenopathy emphasising a widespread metastasis. Metastasis of an IDC of breast involves the paranasal sinuses and nasal cavity. Ductal carcinoma are the most common type and in absence of morphological clues immunohistochemical markers like oestrogen receptor (ER), progesterone receptor, mammaglobin, or GATA3 can aid the diagnosis.(1–4,10,11) The present series describes a case of metastatic IDC to the fossa of Rosenmuller. Eccrine spiradenocarcinoma is a malignancy of the sweat glands. The most common site is trunk followed by face and neck accounts for around 0.08% of these malignancies. Nasal bridge and lateral wall has been reported as an unusual site for the primary malignancy. Wide spread metastasis has been documented to other solid organs, skin and bones, however no reports were found of metastatic eccrine spiradenocarcinoma in the maxillary cavity and paranasal sinus.(12–14) The present case of eccrine spiradenocarcinoma in the maxillary sinuses occurring three months after the diagnosis of a primary in the nape of neck in the present series is believed to be the first report of this rare presentation. The patient presented with nasal obstruction, epistaxis and pain. The metastasis was seen seeded in the left maxillary sinus and extending to the nasal cavity. Histopathology showed a tumour composed of undifferentiated cells in the advancing edge causing bone destruction along with brisk mitotic activity and foci of squamous differentiation. The metastasis was managed by a wide local excision. The overall prognosis of sinonasal metastasis is grim as it signifies an advanced stage of the malignancy. Palliative therapy like embolisation of feeder vessel is used in specific cases like those of a RCC to prevent bleeding during surgery. In cases of breast metastasis, systemic therapy with bevacizumab, trastuzumab and docetaxel are being evaluated in therapeutic protocols. Minimally invasive surgical techniques are increasingly being employed in management of these metastasis as it minimizes patient morbidity, ensure decreased local or systemic toxicity, and provide rapid symptom improvement and months of improved quality of life as compared to the traditional modalities.(1–4,15)

**Conclusion**

A sinonasal metastatic lesion can be associated with significant local symptoms, a markedly diminished quality of life, and a grim prognosis. Owing to the overlapping features, a high index of suspicion is needed in patients with history of other malignancies for an early diagnosis. Wide local resection carries risk of significant deformity, and systemic therapies are marred by toxicities. Palliative therapy with endoscopic resection and radiotherapy have gained importance in management of these lesions.

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