



COMPATIBILITY OF HISTOPATOLOGICAL WITH REGIONAL METASTASES IN SINONASAL CARCINOMA STAGE IV : TWO CASE REPORTS AND LITERATURE REVIEW

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ABSTRACT

Background: Sinonasal carcinoma is a malignant tumor found in the nasal cavity and paranasal sinuses. Symptoms and signs that are caused a rarely found in the early stages which make the diagnosis delay it reaches an advanced stage. Lymph nodes regional metastases in sinonasal carcinoma are rare, but the presence of positive nodules indicates a poorer prognosis. **Objective:** Reported differences in histopathological results and regional metastases in two cases of advanced sinonasal carcinoma (stage IV). **Cases:** We report two cases of male patients aged 52 years and 59 years with diagnosis sinonasal carcinoma stage IVB. In the first case T4bN2cM0 and the second case T4aN3bM0 with different histopathological results and clinical differences in lymph node metastases, and in these two patients underwent chemotherapy as the treatment. **Method:** Using book, guidelines, PubMed database, on google scholar, and manual research for the evidence and literatures. **Result:** Patients with squamous cell carcinoma have a greater risk of regional metastases than Adenocarcinoma. **Conclusion:** Regional metastases were determined by tumor histology type, tumor size, invasion of surrounding structures, transgression from bone to nasal cavity and early stage of treatment.

Keywords: Sinonasal carcinoma, regional metastases, lymph nodes, and histopathology

INTRODUCTION

Sinonasal carcinoma or malignancy of the nose and paranasal sinuses is a rare malignancy, and constitutes 1% of all malignant tumors in the body and 3% of malignancies in the head and neck area.

Based on the location, the maxillary sinus is the most common site (60–80%) followed by the nasal cavity (20–30%) and the ethmoid sinus \pm 15%, while the frontal sinus and sphenoid sinus are very rare (less than 1%). The ratio in men and women is 2:1 and

is often diagnosed at the age of 50-70 years.^{1,2}

Data from the ENT department of FKUI/RSCM for 10 years, this is the third ranks of malignancy after nasopharyngeal carcinoma and non-Hodgkins lymphoma of the head and neck malignancy.¹ A previous study by Novita (2013) at H. Adam Malik Hospital, Medan for the period January 2009-December 2011, there were 40 patients with sinonasal tumors, with squamous cell carcinoma as the most histopathological results (48.2%). The location of most benign and malignant tumors comes from the nasal cavity (72.7%) and the paranasal sinuses (79.3%).³

Although rare, lymph node examination should be performed. Cantù G et al in his study in Milan, Italy reported that from 305 cases of malignant tumor of the ethmoid sinus and 399 cases of malignant tumor of the maxillary sinus, presented with positive nodes was 1.6% and 8.3%, respectively.^{1,4} Lymph node metastases are a poor prognostic factor for patients with malignant tumors of the paranasal sinuses with a 5-year survival rate only 20% to 30%.⁵

Based on a study conducted by Wel- Ren et al (2008) by examining 2 fresh human cadavers to assess lymph flow in the nose and nasopharynx, it was found that there are 3 element lymphatic drainage: 1) the initial lymphatics (including capillary network and precollectors) in the wall of the nasal fossae and the nasopharynx; (2) the lymphatic collectors running in the parapharyngeal space; (3) the lateral

pharyngeal and retropharyngeal lymph nodes.⁶

Regional lymphatic drainage of the face and external nose is mainly by submandibular lymph nodes, whereas nasal cavity lymphatic drainage is by retropharyngeal and deep neck lymph nodes. Lymphatics from the upper part of the nasal cavity communicate with the subarachnoid space along the olfactory nerve.^{7,8}

Patients with positive lymph nodes have a 7-8 times risk of dying from nasoethmoidal carcinoma compared with negative lymph nodes. A recently published SEER (Surveillance, Epidemiology and End Results) analysis evaluated the risk of lymph node metastasis in 1283 patients with sinonasal SCCs. They found out that T4 carcinomas of the nasal cavity and tumor size larger than 2 cm were associated with significantly higher rates of positive lymph nodes, and that lymph nodes at neck levels I and II were most commonly affected.¹⁰

In the following, we reported two case reports of advanced stage sinonasal carcinoma (IVB) in two men with T4bN2cM0 and T4aN3bM0, respectively, who have different regional metastases.

CASE REPORT

Case 1: A male patient, 52 years old, with chief complaints of nasal blocked especially on the right side since 2 years ago, and within 6 months also felt on the left side,

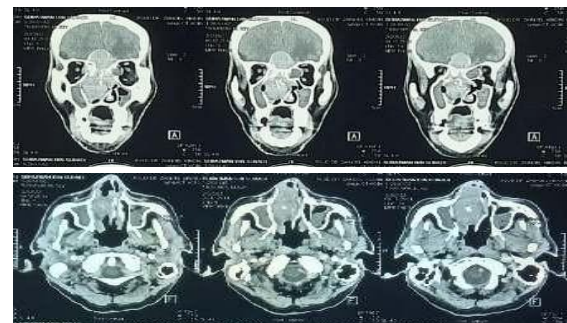
accompanied by a protuberant nose. There is with discharge of mucus and sometimes accompanied by blood. The blood that comes out is fresh red with a volume of \pm $\frac{1}{4}$ - $\frac{1}{2}$ of glass or 1 small towel. The patient also complained of swelling in the right eyelid for the last 6 months and blurred vision. Headache for 3 years. The patient as a wood worker and is a home builder with cutting ceramics, which he has been working on for 30 years.

From the physical examination, we were found that on the nasal side there was protuberant on the dorsum of the right nose with a size of 2x1x1 cm, hard palpable, tenderness (-), no crepitus. A narrow nasal cavity on both sides, a reddish-white mass appears to fill the right nasal cavity, with a ridged appearance, look likes fragile and bleeds easily, and the impression that the septum is deviated to the left due to mass pressure. Air passage is absent on the right side and decreases on the left side. Examination of the neck revealed no enlarged lymph nodes.

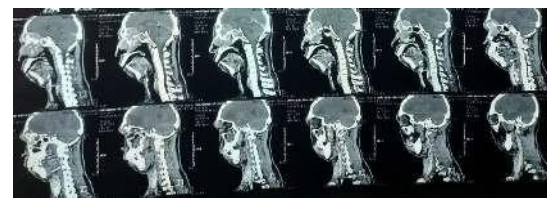


Figure 1. Clinical photo of case 1

Histopathological examination revealed adenocarcinoma with acute inflammation. Laboratory results and chest X-ray were within normal limits.



(a)



(b)

Figure 2. CT scan with contrast of paranasal sinuses from Case 1. (a) Coronal and axial sections, (b) Sagittal sections.

The CT scan with contrast of paranasal sinuses showed a solid sinonasal mass that had infiltrated intracranially and destroyed the left ethmoid bone. Multiple lymphadenopathy is seen in both right and left region, at level I, II, III and V (largest size \pm 1.7 cm x 1.1 cm).

The patient was diagnosed with T4bN2M0 sinonasal carcinoma (stage IV B) and underwent chemotherapy with Cisplatin and Docetaxel regimens.

Case 2. A male patient, 59 years old, with chief complaints of swelling on the right side of the nose since the last 6 months, which was getting bigger and caused both nasal blocked. The snot out mixed with blood (+), with volume of 1-2 tablespoons. The patient also complained of a lump on the left neck and under the chin that had been seen for the last 6 months.

Patient had history of surgery at nose in 2019 and continued with chemoradiation but not complete. The patient has been working as an interior worker since more 30 years, and smokes 2- 3 packs/day for more than 20 years.



Figure 3. Clinical photo of case 2

Based on physical examination, at nasal area, it appeared that the mass was pushed to the right dorsum of the nose with size of 6.5 x 5.3 x 2.5 cm, the surface was bumpy, palpable hard, hyperemic and vascularized, there was no tenderness. Both nasal cavities are narrow, making it difficult to assess into the nasal cavity. On the hard palate, the surface is uneven, palpable the soft part in hard palate the impression of destruction. On the colli visible enlargement of the lymph nodes.

In Dextra, level I: size 5.5 x 3.8 x 3 cm, level IIa, size 2.7 x 2.5 x 2 and at level V, 4.9 x 3.9 x 1.5 cm, with a flat surface, hard palpable, well demarcated, fixed, not

hyperemic and not tenderness. In sinistra, at levels II, III and V simultaneously, size 7.2 x 7 x 3.8 cm with a bumpy surface, hard palpable, well demarcated, fixed, not hyperemic and not tenderness.



Figure 4. Enlargement of the lymph nodes in case 2

From the laboratory results, it was leukocytosis at 19.410/mm³, chest x-ray within normal limits and from soft tissue colli photo, its right-left soft tissue swelling in the colli region accompanied by calcification with good airways space.



Figure 5. Chest x-ray and Soft tissue colli of the case 2

From the CT scan with contrast of paranasal sinuses showed an inhomogeneous mass filled the right maxillary sinus and expanded to the orbital, subcutaneous layer of the maxillary region, infiltrating the pterygopalatine fossa, right pterygomaxillary fissure and has destroyed os maxillary and hard palate. As well as multiple malignant lymphadenopathy at levels I, II, III and V on both right and left side.

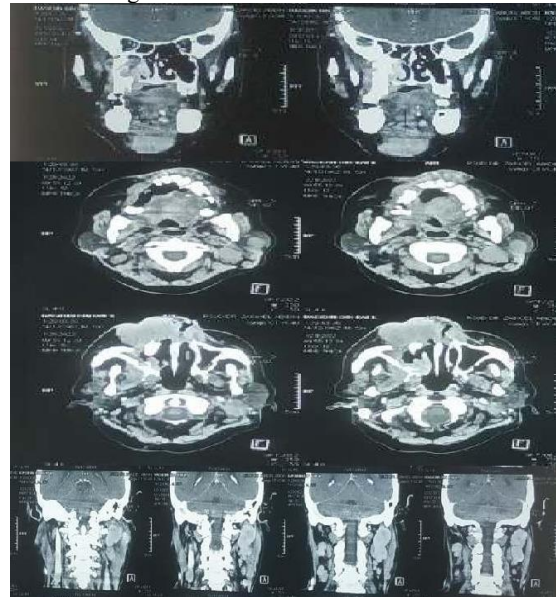


Figure 6. CT scan with contrast of paranasal sinuses of case 2

The FNAB was performed on the right and left colli, the results obtained were Malignant smear metastatic carcinoma, and from biopsy through the right buccogingiva, we got the result of histopathological as Non-Keratinizing Squamous Cell Carcinoma.

The patient was diagnosed with recurrent sinonasal carcinoma T4N3bM0 (Stage IV B), and underwent chemotherapy with regimens of ifosfamide, cisplatin and paclitaxel.

METHOD

Literature sources come from books, research journals and guidelines by searching in the PubMed database, Web of Science, Google Scholar using the keywords: “sinonasal carcinoma”, “enlargement of lymphnode”, “regional metastases”, “histopathology”.

The literature search was performed using the following inclusion criteria: 1) Sinonasal carcinoma, 2) lymph node, 3) regional metastases, 4) histopathology type of sinonasal carcinoma. The literature about other distant metastases, surgical treatment are excluded from the analysis.

RESULTS

From this case report, both cases occurred in men with an age range of 50-60 years, worked as a carpenter and was diagnosed with sinonasal carcinoma stage IVB, both of which had different histopathological results, the first case with adenocarcinoma, and the second case with Non-Keratinizing Squamous Cell Carcinoma. In the first case, did not show enlarged of lymph nodes clinically, although radiologically, lymphadenopathy was found in the colli (with largest size \pm 1.7 cm x 1.1 cm). In the second case, there was enlargement of the lymph nodes in the right and left colli clinically at levels I, II, III and V, this is in accordance with the radiological findings on the CT scan with contrast of paranasal sinuses.

Sinonasal carcinoma metastases to the lymph nodes very rare because the nasal cavity and paranasal sinuses are very poor with the lymphatic system, except when the tumor has infiltrated to the soft tissues of the nose and cheeks which are rich in lymphatic system. Regional metastases have been estimated to occur in about 3 - 33%. There are several factors that significantly increase the incidence of regional metastases, there are histological type of tumor, tumor size (advanced T), invasion of surrounding structures, transgression from bone to nasal cavity and early stage of treatment. Regional metastases were largely determined by histopathological type, with the highest rates being esthesioneuroblastoma (37%), neuroendocrine carcinoma (27%), squamous cell carcinoma (20%), melanoma (16.2%), adenocarcinoma (7.4%) and no regional metastases were found in the adenoid cystic.¹¹ This is also in line with the results of the FNAB colli in the second case which showed a Malignant smear metastatic carcinoma.

Both of these patients underwent chemotherapy as treatment, and this correspond with NCCN guideline 2022.

DISCUSSION

In epidemiology, sinonasal carcinoma more common in men with ratio 2:1 and was diagnosed more often in the 50- 70 years age group.^{1,2} Men whose jobs are exposed to wood with exposure to other chemicals are 20 times more likely malignancy, with a relative risk of 70%. Wood dust/dust with a size of $5\mu\text{m}$ which is continuously exposed to with a latency period of about 35 years is at risk of developing to sinonasal carcinoma, with hardwood dominantly having adeno- carcinoma histologically and softwood dust being predominantly squamous cell carcinoma.¹²

Tobacco smoking can increase the risk of sinonasal carcinoma two to three times higher than that of non smokers, and exposure to passive smoker can also be a risk factor for sinonasal carcinoma.^{3,10}

The symptoms of sinonasal carcinoma can vary, according to the location experienced. Symptoms usually develop as a result of obstruction of the nasal cavity or involved sinus or when the tumor penetrates the wall of the involved sinus and produces symptoms of local invasion of adjacent tissue or bleeding. Symptoms can be in nasal, orbital, alveolar and intracranial symptoms.^{1,9,12}

Based on the anatomical location and the symptoms that arise, the first case with the possibility of a mass originating from the nasal cavity and ethmoid sinus, while the second case with the possibility of originating from the maxillary sinus which has expanded anteriorly

and infiltrated the dorsum of the nose and the skin of the cheek.¹²

Ohngren described an imaginary plane defined by a line connecting the medial canthus of the eye to the angle of the mandible. This plane divides the nasal cavity and antrum of maxillary into two parts. The anatomical area located anteroinferior to this plane is called the "infrastructure," and the area located posterosuperior to the plane is called the "superstructure." In superstructural lesions, symptoms appear at an advanced stage and resection is more difficult because the tumor has extended to the infratemporal fossa, pterygomaxillary fossa, orbital and to the middle cranial fossa and/or anterior cranial fossa. Tumors of the maxillary antrum as infrastructure can extend through the floor of the antrum into the oral cavity, through its medial wall into the nasal cavity, as well as through parts of the anterior wall to skin of the cheek, or through the lateral wall into the masticator space. The cure rate is lower when compared to infrastructure.^{7,9} Almost all intestinal-type adenocarcinomas (ITAC) are located in the olfactory groove of the ethmoid sinus, whereas SNSCC occurs mainly in the nasal cavity and maxillary sinus.¹³

Sinonasal SCCs are characterized by aggressive bony destruction of the adjacent sinus walls. Hypoxia is a common feature in most cases of SCC, and prolonged oxygen deprivation often leads to chronic hypoxic stress and consequent tumor necrosis. Thus, intratumoral necrosis is also one of the characteristic findings in SCCs. On CT, sinonasal adenocarcinomas appear as a soft-tissue mass and occasionally exhibit areas of calcification, which reflect the mucin content. In unilateral olfactory cleft adenocarcinomas, the bulging of the nasal septum across the midline and widening of the olfactory cleft are observed. High-grade adenocarcinomas often show bone destruction. Adenocarcinomas arising from the ethmoid sinus may potentially extend to the skull base and intracranially to the frontal lobes.¹⁴

In sinonasal carcinoma, in general level II is the most commonly affected lymphatic basin, occurring in 69% of patients with regional metastases. Followed by level I (45%), level III (29%), level IV (21%), V (17%), retropharynx (17%), and parotid gland (14%). Lymph nodes are more common ipsilateral to the location of the tumor; however 22% of lymph node metastases occurred on the contralateral side of the tumor. Bilateral regional metastases can occur in approximately 39% of either the first appearance or recurrence after procedure. Histological type with a high-risk group for malignancy was significantly associated with the incidence of contralateral regional metastases.¹¹

Based on the 2018 AJCC, these two cases were at stage IVB which is an advanced stage. Based on the NCCN 2022, the management of patients with sinonasal carcinoma depends on the staging, and based on the type of tumor, the general condition of the patient and comorbidities. Patients with T4b, N0-3 or unresectable lymph nodes, or T4a, N+ sinonasal carcinoma and a history of recurrence with locoregional recurrence or previous history of radiotherapy, may receive reirradiation and chemotherapy and best supportive care.¹⁵

The use of high doses of intra- arterial cisplatin administered selectively through a vein that feeds the tumor together with intravenous infusion of a neutralizing agent (sodium thiosulfate) and concomitant radiotherapy has been reported by several authors to be effective in the treatment of advanced sinonasal carcinoma.⁹

Reported two cases of advanced sinonasal

carcinoma with different regional metastases. In both cases, there were differences in regional metastases due to the histological type of tumor, tumor size (advanced T), invasion of surrounding structures, transgression from bone to nasal cavity and early stage of treatment. And according to the literature states that patients with squamous cell carcinoma have a greater risk for regional metastases compared to adenocarcinoma.

This case report can be the first step to conduct research/study on type of histopathology with regional metastases in sinonasal carcinoma.

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