

## SINONASAL MALIGNANT TRANSFORMATION OF SQUAMOUS METAPLASIA

Boia ER<sup>1,2</sup>, Balica NC<sup>1,2</sup>, Flavia Baderca<sup>3,4</sup>, Simina Boia<sup>5,6</sup>

### Abstract

Introduction. The aim of this study was to correlate the mother's biological status and related extrinsic factors during pregnancy and growth retardation and anemia in neonates. Material and method. We have done a prospective study on 75 mothers who delivered in 2013 in Obstetrics and Gynecology Clinics of Emergency County Hospital Timisoara and their newborns. Maternal extrinsec factors pre- or during pregnancy were related with the percentage distribution of neonates with IUGR and anemia. Results. Smoking habits (53%), lack of education (44%) and precarious socioeconomic conditions (42.7%) were the first three extrinsec factors well represented. The percentage distribution of newborns was 43% AG Sinonasal squamous cell carcinomas are relatively uncommon, representing only 3% of all head and neck malignancies. The treatment modality (surgery, radiotherapy, chemotherapy) poses several challenges. First of all, the patients are often diagnosed with advanced stage disease. Secondly, close proximity of critical structures and complex anatomy of the region, compromise surgical removal and radiation deliverance. Thirdly, important uncertainty issues surround fundamental aspects of treatment hence the optimal therapy protocol remains to be determined. We present an 18-year-old male patient with right sinonasal non-keratinizing squamous cell carcinoma and hard palate, middle infraorbital area, middle cranial fossa space involvement. Admission clinical signs and symptoms were: recurrent sinusitis, right sinonasal tumor and bilateral cervical lymph node involvement. A biopsy was performed and sent to the Pathology Service. The specimen was prepared with the routine histological technique. On hematoxylin eosin slides, the lesion was polypoid showing a connective tissue core with seromucous acini and moderate quantity of inflammatory cells (neutrophils, eosinophils, lymphocytes, histiocytes). The overlying epithelium was pseudostratified, being composed of ciliated columnar cells and presenting areas of squamous metaplasia. From these zones, originated a malignant tumor formed by epithelioid cells, with eosinophilic cytoplasm and vesicular nucleus containing prominent nucleolus. The cells were disposed in sheets, surrounded by fibrous connective stroma. Moreover, as precursor lesion, at transition site between normal

epithelium and malignant tumor, was noted severe dysplasia. The histopathological aspects were consistent with a non-keratinizing squamous carcinoma arising in a fibro-glandular polyp with concomitant severe epithelial dysplasia, as a precursor lesion.

The patient underwent radiochemotherapy for primary tumor and cervical lymph nodes metastases; at 12 months after treatment no recurrence was noted.

**Keywords:** Sinonasal squamous cell carcinoma, cervical lymph nodes, malignant transformation, squamous metaplasia, severe epithelial dysplasia

### Introduction

Sinonasal squamous cell carcinomas are relatively uncommon, representing only 3% of all head and neck malignancies. Together with adenocarcinomas, squamous cell carcinomas are associated with a number of environmental factors such as smoking and alcohol use, exposure to heavy metals such as chromium and nickel and with workers in the leather, textile, furniture and wood industries (1, 2, 3, 4, 5)

The patient with sinonasal squamous cell carcinoma always describes a long standing disease with unspecific symptoms such as nasal obstruction, nasal discharge, minor epistaxis, headache and/or facial pain, other patients are asymptomatic. In more advanced stages patients may present facial swelling, vision changes or neurologic deficits (3, 4, 5)

Clinical investigation usually shows an exophytic tumor that tends to be friable, ulcerated and necrotic with increasing tumor size. On the other hand, sinus tumors are well-circumscribed, expansive and erosive to adjacent bony walls (1, 3, 4, 5)

Sinonasal squamous cell carcinomas can originate from epithelium of nasal cavity and paranasal sinuses. Early diagnosis is sometime difficult due to non-specific signs and symptoms and similar to those of allergic reaction, nasal polyposis and chronic sinusitis. In differential diagnosis, the most frequent suspicioned is a schneiderian papilloma and, at younger patients, angiofibroma (6)

Usually, the patients with sinonasal carcinoma present to the physicians earlier than those with maxillary sinus mucosa tumor.

<sup>1</sup> ENT Department, "Victor Babeș" University of Medicine and Pharmacy, Timisoara, Romania

<sup>2</sup> ENT Department, Emergency City Hospital, Timisoara, Romania

<sup>3</sup> Department of Microscopic Morphology, "Victor Babeș" University of Medicine and Pharmacy, Timisoara, Romania

<sup>4</sup> Service of Pathology, Emergency City Hospital, Timisoara, Romania

<sup>5</sup> Periodontology Department, "Victor Babeș" University of Medicine and Pharmacy, Timisoara, Romania

<sup>6</sup> Periodontology Department, Emergency City Hospital, Timisoara, Romania

E-mail: eugen\_boia@yahoo.com, balica@umft.ro, falviabaderca@yahoo.com, siminalugojan@gmail.com

From histopathologic point of view sinonasal tumors are include squamous cell carcinoma, adenocarcinoma, adenoid cystic carcinoma, melanoma, and esthesioneuroblastoma. Some of these histopathological subtypes correlate with specific clinical aspects and aggressiveness as sinonasal undifferentiated carcinoma (7, 8)

Because of earlier presentation to the physician, the prognostic is better for sinonasal carcinoma than those from nasal sinuses.

The mainstay of the treatment remains surgery with excision of the tumor in free margins.

### Case presentation

The male patient GV, 18-year-old, was admitted on October 2012 in ENT Department, "Victor Babes" University of Medicine and Pharmacy from Timisoara with the following diagnosis: right sinonasal tumor with bilateral cervical lymph node involvement.

The patient is a student; he was a heavy daily cigarette smoker for the last 2 years (16 per day). No other comorbidities were associated.

Hospital admission symptoms and signs consisted in: permanent right nasal obstruction, mucopurulent nasal discharge, cheek paraesthesia, cephalgia. Clinical examination revealed: obstruction of the right nasal fossa by a polypoid mass, right sinonasal tumor with hard palate involvement and bilateral cervical lymph node masses.

$0^{\circ}$  nasal and rhinopharynx endoscopic exam showed an exophytic tumor mass extending from the right middle meatus, to the hard palate, right maxillary sinus, nasal septum and left nasal fossa.

Cranial contrast enhanced CT scan highlighted a non-homogenous tumor mass in the right maxillary sinus and right nasal fossa (invading the medial, inferior and anterior maxillary sinus walls and extension into the left nasal fossa) (Figure 1). Fluid accumulation in the ethmoid, frontal and sphenoid sinuses were also visible. Bilateral cervical lymph node masses of approximately 20 mm were present.



Fig. 1. A non-homogenous tumor mass in the right maxillary sinus and right nasal fossa, invading the medial, inferior and anterior maxillary sinus walls and extension into the left nasal fossa.

Blood tests revealed: low white blood cell count (6200/mm<sup>3</sup>) with neutrophilia (78.4%), lymphopenia (17.2%) and monocytopenia (4.4%), high erythrocytes sedimentation rate (88 mm/h), low red blood cell count (3.62 million per mm<sup>3</sup>), and low hemoglobin (10.6 g/dl) and hematocrit (33.6%) levels.

Biopsy was performed for diagnosis. The tissue specimens were processed according with the routine histological technique. The specimens were fixed in 4% v/v buffered formalin and paraffin embedded. Three micrometers thick serial sections were stained with hematoxylin–eosin (HE). Histopathologic evaluation was performed with Leica DM750 microscope and images were acquired using Leica DMshare system.

On hematoxylin eosin slides, the lesion was polypoid showing a connective tissue core with seromucous acini and moderate quantity of inflammatory cells (neutrophils, eosinophils, lymphocytes, histiocytes). The overlying epithelium was pseudostratified, being composed of ciliated columnar cells and presenting areas of squamous metaplasia. At this point, the diagnosis on histological grounds was Schneiderian papilloma with area of squamous metaplasia. Serial sections revealed areas of malignant epithelioid cells, with eosinophilic cytoplasm and vesicular nucleus containing prominent nucleolus. The cells were disposed in sheets and originated from squamous metaplasia, being surrounded by fibrous connective stroma (Figures 2 and 3).

Moreover, as precursor lesion, at transition site between normal epithelium and malignant tumor, was noted severe dysplasia (Figure 4).

The final histopathological diagnosis was consistent with a non-keratinizing squamous sinonasal carcinoma arising in a Schneiderian polyp with fibro-glandular core and concomitant severe epithelial dysplasia, as a precursor lesion. The excisional edges were free of malignant invasion. The tumor was classified as a pT4 lesion.

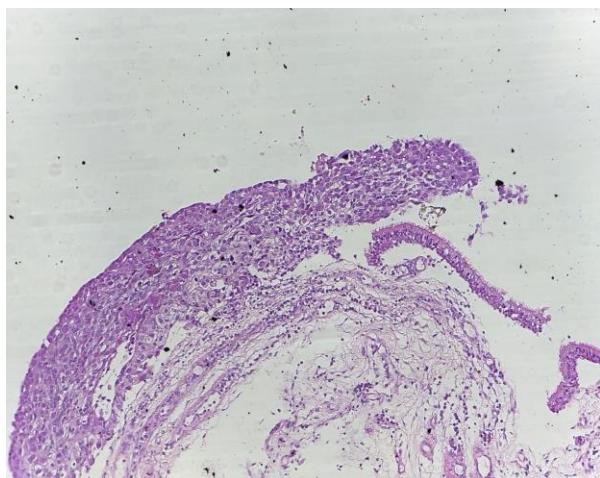


Fig. 2. Malignant cells originated from area of squamous metaplasia (left side), normal columnar ciliated pseudostratified epithelium of nasal cavity (right side), HE stain, ob. 4\*

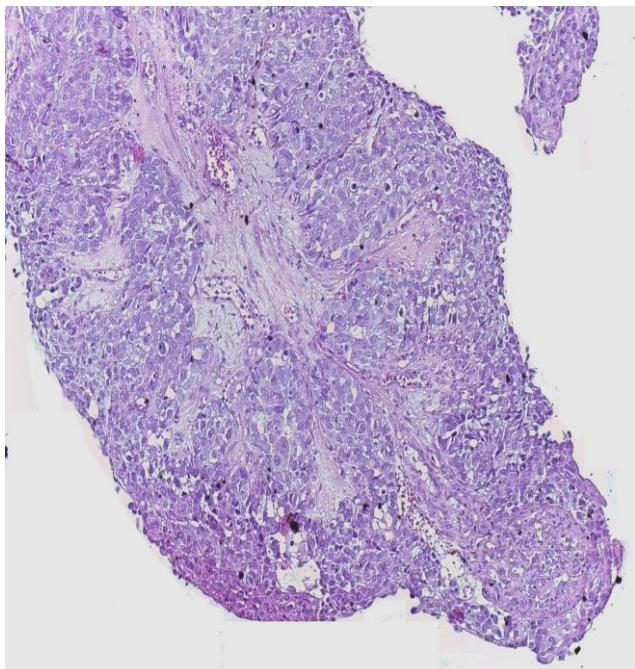


Fig. 3. Non-keratinizing squamous cell carcinoma of nasal cavity, HE stain, ob. 10\*

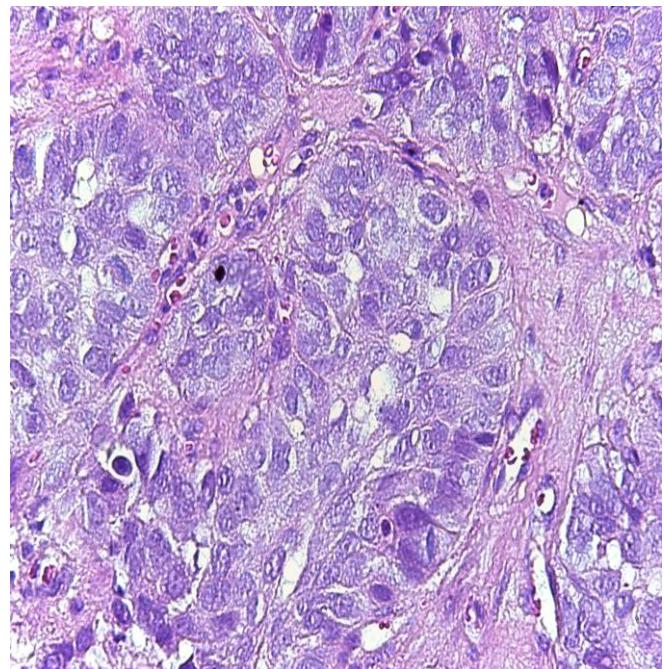


Fig. 4. Islands of malignant squamous cells with ample eosinophilic cytoplasm and vesicular nuclei, HE stain, ob. 40\*

### Discussions

The maxillary sinus (about 60%), the nasal cavity (about 22%), ethmoid sinus (about 15%) and frontal and sphenoid sinuses (<3%) are the most commonly sites affected by a sinonasal carcinoma. Unlike squamous cell carcinoma from other sites of head and neck region as nasopharynx, squamous cell carcinoma has a male predilection (2:1), with the highest incidence in the sixth – seventh decade of life (7)

Epistaxis is not uncommon and develops when the mucosa is ulcerated and the tumor extends to the medial sinus wall. Purulent and mucoid nasal discharge is also common due to secondary infection. Restriction of eye motility, diplopia or loss of vision and proptosis are present when the tumor affects the ethmoid, maxillary or frontal sinuses. Epiphora appears when the tumor affects the lacrimal sac or duct, cranial nerve involvement may also appear (1, 2, 3, 4, 5)

Late manifestations such as facial swelling and cheek paraesthesia, resulting from anterior maxillary extension into the soft tissue and infraorbital nerve involvement, are also common. Extension into the oral cavity forms a visible mass in the hard palate or alveolar ridge. Trismus can be caused by posterior extension, from the invasion of the pterygoid muscle. Auricular symptoms such as recurrent otitis media suggest possible involvement of the nasopharynx, eustachian tube and pterygoid plates. Extension into the skull base may lead to cranial nerve involvement, dura mater and intracranial invasion. It is rare to find cervical lymph node metastasis in early stages (1, 3, 4, 5)

The histopathological evaluation of excised specimen frequently reveals a squamous cell carcinoma either

keratinizing or not. Other variants of squamous cell carcinoma as verrucous, papillary, basaloid cells, spindle cells, adenosquamous or acantholytic carcinomas are quite rare encountered in sinonasal region. The tumors are similar with their more frequent counterpart from the other sites of the body and can be well, moderately and poorly differentiated. The tumor cells are large, with eosinophilic cytoplasm and vesicular, nucleolated nuclei. Keratinization, were present, is observed at extracellular or intracellular level (dyskeratotic cells). The tumor cells are disposed in islands or small groups and, except for acantholytic subtype, are stabilized each to other with intercellular bridges. Frequently the tumor presents desmoplastic stroma. The tumor invades underlining tissues with cellular malignant strands (1)

As in our case, the tumor sometimes develops in a schneiderian papilloma or in area of squamous metaplasia, but precursor lesions for sinonasal carcinoma are by far less well defined as for oral or laryngeal counterpart. This feature is found in 10% of cases (1, 9)

Involvement of cervical lymph node appears in up to 20% of patients. Distant metastases are rare (1, 5).

If the sinonasal carcinoma is localized in the nasal cavity, the 5- and 10 year survival rates are as high as 80%, but extension to the paranasal sinus significantly lowers the survival rates (1, 3, 4, 10) Moreover, factors that predict a worse prognosis are advanced local disease and keratinizing histological subtype.

Treatment options include combination modalities of surgery, radiotherapy, and chemotherapy. Due to the low incidence and diverse histopathologic types it is difficult for a department to gain enough experience in the sinonasal tumors treatment (15).

Treatment failures mainly are related either to an advanced disease (T3 and T4) or to a tumor recurrence in areas difficult to access (skull base, dura and brain) (1).

M. H. Jakobsen et al. (11) do not support the advantages of combined treatment modality over a single treatment modality of RT or S.

Cervical lymph node metastases are generally associated with poor survival and high recurrence rate (12, 13, 14, 15, 16), being considered to be the most important survival prognostic parameter in squamous cell carcinoma group (11) and anemia in neonates (1). Improving

educational opportunities, health-related behavior and access to health care (13) could reduce the risks and not ultimately different inequalities in health in the EU countries for instance (13).

### Conclusions

The patient underwent radiotherapy for both sinonasal tumor area and bilateral cervical area, followed by chemotherapy. At 12 months after treatment there were no recurrence noted.

### References

1. Pilch BZ, Bouquot J, Thompson LDR. Squamous cell carcinoma. In: Barnes EL, Eveson JW, Reichart P, Sidransky D, editors. Pathology and genetics of head and neck tumours. (Kleihues P, Sobin LH, series editors. World Health Organization classification of tumours.) Lyon, France: IARC Press; 2005. p. 15–17
2. Luce D, Leclerc A, Begin D, et al. Sinonasal cancer and occupational exposures: a pooled analysis of 12 case-control studies. *Cancer Causes Control* 2002; 13: 147–57
3. McNicoll W, Hopkin N, Dalley VM, et al. Cancer of the paranasal sinuses and nasal cavities. Part II. Results of treatment. *J Laryngol Otol* 1984; 98: 707–18
4. Hopkin N, McNicoll W, Dalley VM, et al. Cancer of the paranasal sinuses and nasal cavities. Part I. Clinical features. *J Laryngol Otol* 1984; 98: 585–95
5. Jackson RT, Fitz-Hugh GS, Constable WC. Malignant neoplasms of the nasal cavities and paranasal sinuses: (a retrospective study). *Laryngoscope* 1977; 87: 726–36
6. Budu V, Bulescu I, Mogoanta CA, Particular aspects in endoscopic surgery for juvenile nasopharyngeal angiomas. Case reports and review of literature, Rom J Morphol Embryol 2013, 54 (3 Suppl): 867–870
7. Boia ER, Boia M, Balica NC, Rusu LC, Mazilu O, Solovan C, Baderca F, Non-keratinizing undifferentiated carcinoma of the nasopharynx, Rom J Morphol Embryol 2013, 54 (3 Suppl): 839–843
8. Khademi B, Moradi A, Hoseini S, Mohammadianpanah M. Malignant neoplasms of the sinonasal tract: report of 71 patients and literature review and analysis. *Oral Maxillofac Surg* 2009; 13:191–199
9. Clarke SR, Amedee RG. Schneiderian papilloma. *J La State Med Soc*.1997; 149(9):310-5
10. Carrau RL, Segas J, Nuss DW, et al. Squamous cell carcinoma of the sinonasal tract invading the orbit. *Laryngoscope* 1999; 109: 230 –5
11. Jakobsen MH, Larsen SK, Kirkegaard J, Hansen HS, Cancer of the Nasal Cavity and Paranasal Sinuses Prognosis and Outcome of Treatment *Acta Oncologica* 1997, 36, 1: 27 - 31
12. Stern J, Goepfert H, Byers R, Kian Ang K, El-Naggar AK, Wolf P. Squamous cell carcinoma of the maxillary sinus. *Arch Otolaryngol Head Neck Surg* 1993; 119: 964-9
13. Larsson LG, Mirtensson G. Carcinoma of the paranasal sinuses and the nasal cavities. *Acta Radiol* 1954; 42: 149- 72
14. Flores AD, Anderson DW, Doyle PJ, Jackson SM, Morrison MD. Paranasal sinus malignancy-a retrospective analysis of treatment methods. *J Otolaryngol* 1984; 13: 141 -6
15. Giri SPG, Reddy EK, Gemer LS, Krishnan L, Smalley SR, Evans RG. Management of advanced squamous cell carcinomas of the maxillary sinus. *Cancer* 1992; 69: 657-61
16. Penzer RD, Moss WT, TongD, Blasko JC, Griffin TW. Cervical lymph node metastasis in patients with squamous cell carcinoma of the maxillary antrum: the role of the elective irradiation of the clinically negative neck. *Int J Radiat Biol Phys* 1979; 5: 1977-80.

### Correspondence to:

Eugen Radu Boia, MD  
"Victor Babeș" University of Medicine and Pharmacy  
ENT Department,  
Piata Eftimie Murgu nr. 2  
300041, Timisoara, Timis, Romania  
Phone: 0040745977531  
Email: eugen\_boia@yahoo.com