

## CASE REPORT

# Sinonasal undifferentiated carcinoma: Case report and short literature review

Ionut Tanase<sup>1,2</sup>, Andra Virilan<sup>1</sup>

<sup>1</sup>ENT&HNS Department, "Sfanta Maria" Hospital, Bucharest, Romania

<sup>2</sup>CESITO Centre, "Sfanta Maria" Hospital, Bucharest, Romania

## ABSTRACT

We present a case of a 48-year-old male patient who was admitted in our clinic for right nasal obstruction, antero-posterior mucopurulent rhinorrhea, recurrent right micro-epistaxis, hyposmia, cacosmia and right hemicrania. ENT findings and CT scan detects proliferative, polylobate, vascularized tumor formation occupying the right nasal nostril, with muco-purulent secretions lining the tumor formation. The tumor pushes the intersinus wall to the side and the nasal septum to the contralateral nostril. The apparent origin is at the level of the right middle nasal meatus, but we could not identify a clear limit from the nasopharynx lateral and posterior wall. Resection of the entire tumor formation was performed under endoscopic control. The histopathological outcome revealed undifferentiated carcinoma; immunohistochemical tests were performed and support the myoepithelial origins.

**KEYWORDS:** sinonasal undifferentiated carcinoma, malignant tumor, endoscopic resection.

## INTRODUCTION

Rhinosinusal tumor pathology is rare, accumulating less than 0.2-1% of all neoplasms and about 2-4% of ENT neoplasms, but of immense importance. Most rhinosinusal tumors are malignant, and the most common benign tumors are papillomas (fungiform, inverted and cylindrical cells). Inverted papilloma can turn malignant in 5-15% of cases<sup>1-3</sup>.

Undifferentiated sinonasal carcinoma is an epithelial malignancy with a high degree of aggressivity. It is characterized by rapid evolution, tendency to locoregional recurrence, distant metastases especially to the lungs and bones, and unfavourable prognosis. It originates in the superior level of the nasal mucosa derived from the Schneiderian epithelium or ectoderm<sup>4</sup>. Immunohistochemistry evaluation shows positivity for cytokeratin, epithelial membrane antigens, and possible enolase positivity, as S-100 protein and vimentin are usually negative<sup>5</sup>. Due to its aggressiveness, the sinonasal undifferentiated carcinoma tends to invade adjacent bone structures, the paranasal sinuses, the skull base, the orbit and the brain<sup>6</sup>.

The most commonly affected age groups are be-

tween 45 and 70 years, in some studies extending the maximum age to 90 years. Although about 80% of patients are in this age range, there are cases of neoplasms at a younger age, the prognosis being even more bleak in these cases. Men are more frequently affected than women (2-3 /1)<sup>1-3,5</sup>.

Rhinosinusal neoplasms have a poor prognosis. Asymptomatic at first, paranasal sinus tumors are difficult to detect in early stages and very difficult to treat in advanced stages<sup>1-5</sup>. 90% of the cases are diagnosed in stages T3 and T4. The symptoms can be very polymorphic. When the neoplasm has a sinus onset, the symptoms can appear very late, and the intrasinusal tumor growth remains undetected.

Most often, the patient goes to the doctor for nasal obstruction, epistaxis, rhinorrhea, pain or symptoms that mimic a dental abscess or other common or minor rhinosinusal pathology. There is a risk that both the patient and the doctor ignore or minimize the first signs of the disease. Late allegations include facial swelling and pain, facial numbness, exophthalmia, eyelid ptosis, motor disorders of the eyeballs, epiphora, anosmia, blindness and trismus, with treatment complications coming from important structures with vital impor-

tance such as the skull base, the orbit, the cranial nerves and the blood vessels<sup>1,4</sup>.

The positive diagnosis is based on the clinical manifestations, as well as paraclinical assessment, which include radiography of the anterior sinuses of the face (with an orienting role), CT scan, MRI, PET-CT. The definite diagnosis cannot be obtained without a biopsy and an anatomopathological analysis of the tissue fragment.

Undifferentiated sinonasal carcinoma is a tumor with high aggressiveness that cannot be completely eradicated and responds poorly to radiation therapy. In case of advanced tumors, a combination of radiotherapy and chemotherapy (cisplatin and etoposide) can be recommended, while the presence of metastases indicates chemotherapy. Unfortunately, loco-regional and distant metastases are cited by some authors in proportion of 63%, respectively 50% two years after treatment<sup>6</sup>.

According to Sebileau, maxillary neoplasms can be divided into superstructure tumors, involving the ethmoid, mesostructured, with maxillary sinus location, and infrastructure, with the invasion of the upper dental arch<sup>7</sup>.

The treatment must be individualized according to the tumor extension, the factors of prognosis, histological type, the result of imaging investigations, the experience of the team surgeons, as well as the possibility of combining radiotherapy or chemotherapy<sup>8</sup>.

At the time of diagnosis, many cases are at an advanced stage, so the surgical option may involve major risks and the results may be unsatisfactory. In this case, the major therapeutic decision must be made between curative and palliative surgery<sup>8</sup>. In general, there must be a clear delimitation between the curative and palliative treatment. The surgical approach can be external, endonasal or combined<sup>9</sup>.

Another important factor is the experience of the surgical team in preventing or treating complications such as intraorbital hematoma, cerebrospinal fluid (CSF) fistulas, massive haemorrhages. Concluding, the keystone of surgical treatment is considered by many authors to choose the right approach depending on the type and extent of the tumor<sup>9</sup>. There is an agreement on major predictive factors, such as the histological grade of the tumor and orbital, sphenoid or transdural extension. The nasopharyngeal extension does not represent a limiting factor of surgery. There are critical structures such as the brain substance or dura mater but, in the case of intracerebral invasion, the purpose of surgery is to obtain a good cleavage plane between the tumor formation and the frontal lobe. The main limiting factor is represented by the extension of the tumor at the level of the cavernous

sinus and the infratemporal fossa. The most serious situation, described by several surgeons, is the infiltration of the internal carotid artery wall from the base of the skull. Remote metastases always indicate a poor prognosis and, by definition, these patients are considered incurable. Skin extension is not a contraindication for surgical treatment, the affected areas can be excised and reconstructed with freely vascularized or rotating flaps.

Regarding the external approach versus the endoscopic approach, the results after endoscopic procedures are as good as those obtained externally, but with a shorter functional recovery time and a clearly superior quality of life<sup>10</sup>.

However, there are important limitations related to tumor invasion. Multidisciplinary teams with a special training can choose for endoscopic approach to the detriment of the classic procedures (resection of the bony portion of the skull base, dura mater, periorbital and their reconstruction within the same intervention).

The optimal therapeutic management is not yet a consensus. Most authors and guidelines indicate surgery associated with radio and chemotherapy. Optimally, the therapeutic decision is made in a multidisciplinary team: ENT surgeon, radiologist, oncologist, radiotherapist, plastic surgeon, neurosurgeon, vascular surgeon, OMF surgeon.

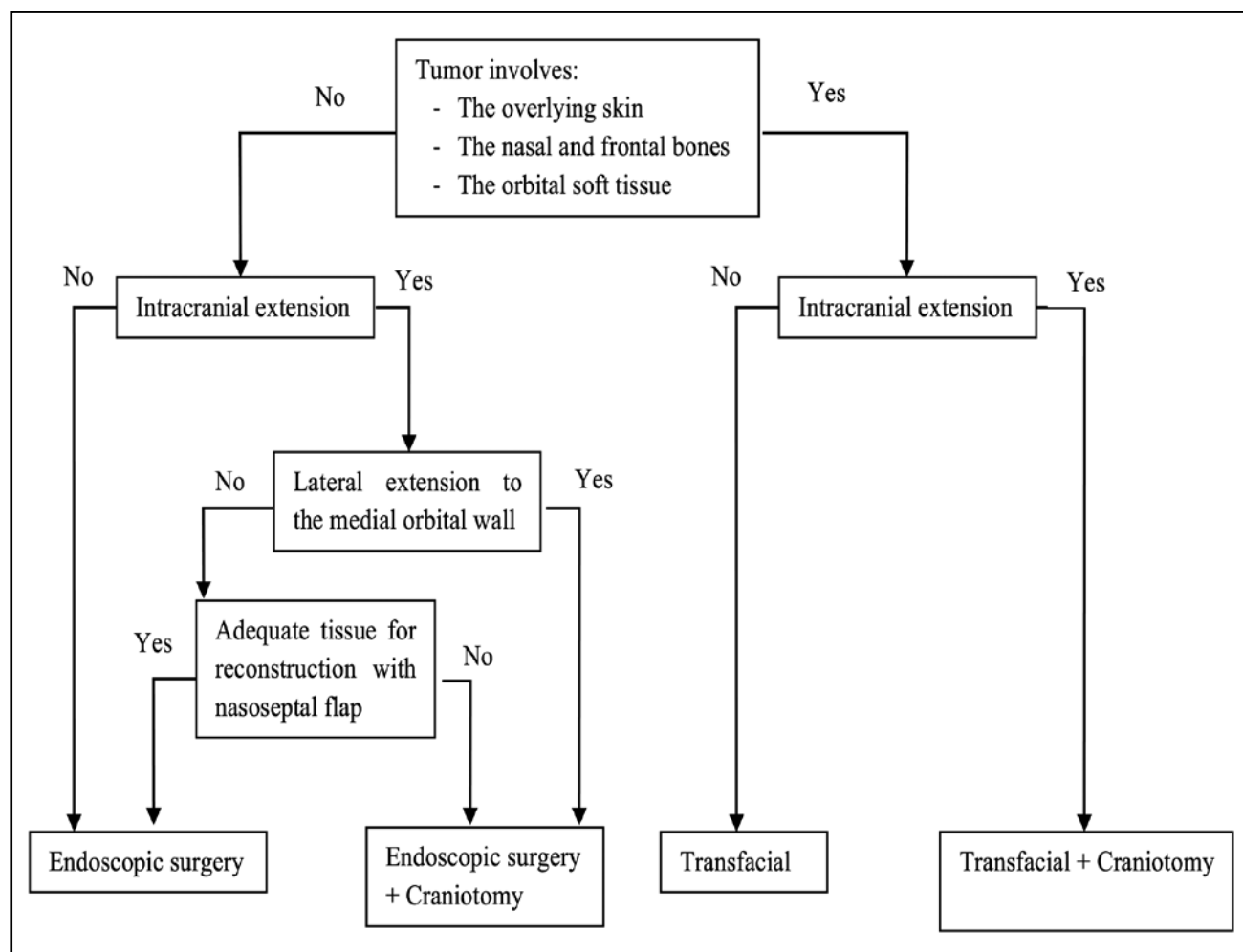
A study on a group of 25 patients with malignant tumors of the anterior skull base compared the results after traditional craniofacial resection with those after minimally invasive endoscopic resection<sup>11</sup>. In both groups, in terms of anatomical structures interested, patients had a similar degree of tumor extension. There were no significant differences from a statistical point of view on survival or recurrence. There were also no major differences between the duration of operation, blood loss, length of hospitalization or transfer to the intensive care unit, although a superiority of these may be noted for the group that was treated endoscopically.

In the literature, there are no data on the benefits of block excision in comparison with piecemeal resection in terms of the goal of performing and completing the ablation of the tumor<sup>12</sup>.

Paolo Castelnuovo<sup>13</sup> sets out the major exclusion criteria for craniofacial endoscopic surgery as follows:

1. Tumors affecting the tear duct;
2. Tumors that infiltrate the hard palate;
3. Tumors affecting the posterior wall of the sphenoid sinus;
4. Tumor invasion of all walls of the maxillary sinus except the medial one.

The establishment of the surgical plan should also include the evaluation of the structure of the



**Figure 1.** Criteria for the endoscopic endonasal approach on sinonasal malignant tumors after Naunheim et al.<sup>15</sup>.

bone tissues and soft tissues to be included in the block resection, with oncological safety margins.

The surgical approach must ensure adequate exposure and, at the same time, the functions and cosmetic integrity should be maintained whenever possible. Reconstruction includes prosthesis or free tissue transplantation when necessary.

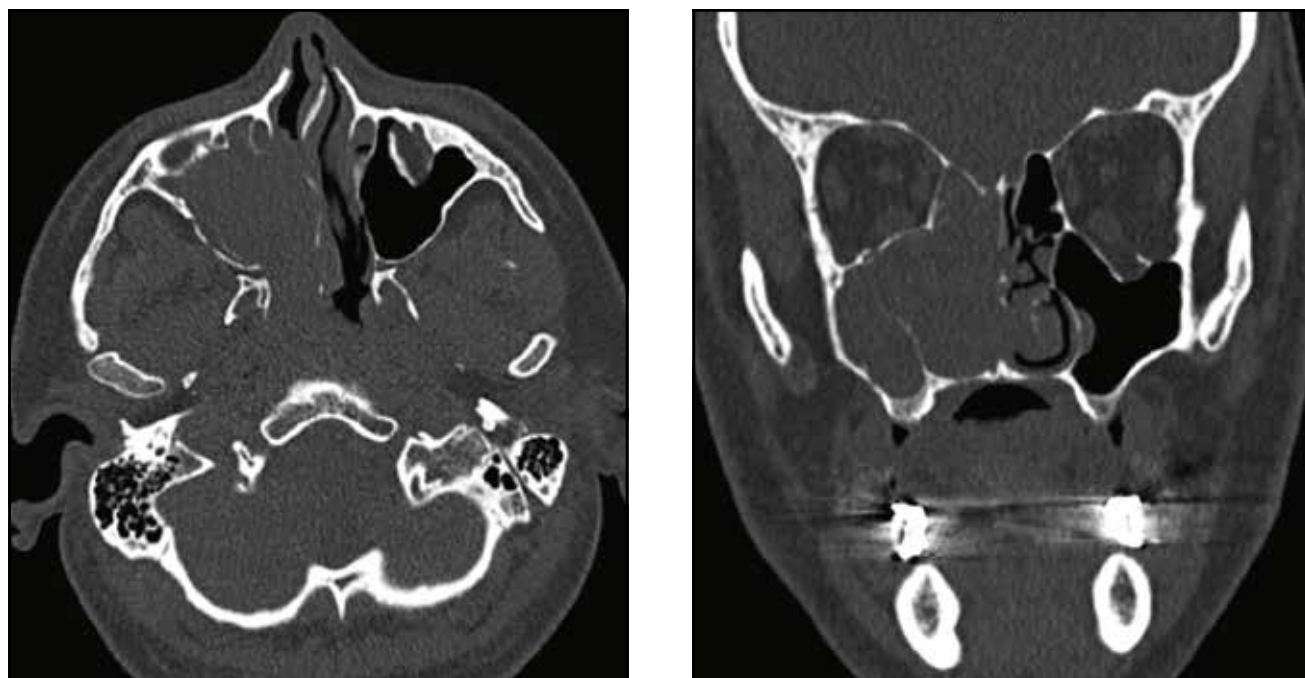
There are several staging systems except TNM staging, which is reserved for the maxillary, ethmoidal sinuses or for the nasal fossae, like the system of staging belonging to Kadish, modified by Morita<sup>14</sup>, originally used for esthesioneuroblastoma that can also be used to make decisions about the treatment of midline tumors. The characteristics of Morita staging are:

- A. Tumor limited to the nostrils;
- B. Tumor extending to the nostrils and paranasal sinuses;
- C. Tumor extension beyond the paranasal sinus cavities;
- D. Tumor with loco-regional or distant metastases.

Naunheim et al. published a study highlighting the surgical experience in sinus cancers in a group of 67 patients who underwent both endoscopic surgery and open surgical techniques (13 patients, representing 19.4%, with sinonasal undifferentiated carcinoma). They did not show any difference in the survival rate at 5 years, or intracranial complications (meningitis, CSF fistula, etc.) or orbital complications (diplopia, epiphora, blindness). However, he established some criteria for the application of sinus endoscopic surgery in such cases depending on the local characteristics of the tumor (Figure 1)<sup>15</sup>.

## CASE REPORT

A 48-year-old male patient presents for right nasal obstruction, a symptomatology that began several years ago, which was progressively accentuated, being later accompanied by right hemicrania, cacosmia, hy-



**Figure 2.** Cranio-facial CT scan (axial and coronal slices). Complete opacification of the right nasal fossa, maxillary sinus, ethmoidal cells and the frontal recess. The tumoral mass is extended up to the nasopharynx. Also, the orbital complex is pushed laterally by the tumor volume, without infiltrating its structures.

posmia and intermittent muco-purulent, antero-posterior rhinorrhea and epistaxis on the right side.

The cranio-facial computer assisted tomography (CT scan) revealed a large mass occupying almost entirely the right nostril, right maxillary sinus and right ethmoid region, with destruction of the lateral wall of the right nasal fossa (Figure 2).

No metastatic cervical or submandibular lymph nodes were detected by radioimaging investigations.

As surgical approach, we chose the nasal endoscopic surgery. A medial maxillectomy under endoscopic control was performed, with the ablation of the tumor in a piece-meal manner. The apparent origin of the tumor was at the level of the inferior nasal turbinate and of the right intersinuso-nasal wall (maxillary sinus); the nasal septum was deviated towards the left nasal fossa but without detecting macroscopic tumor infiltration. The right maxillary sinus, the right anterior ethmoid cells and the right sphenoid sinus were occupied by purulent secretions.

The histopathological appearance was suggestive for sinonasal undifferentiated carcinoma (SNUC) and immunohistochemical tests were recommended for differential diagnosis. The immunohistochemical examination supported the diagnosis of myoepithelial carcinoma.

The postoperative evolution of the patient under antibiotic treatment, anti-inflammatory and daily nasal toilet was favourable.

Oncological evaluation was recommended, and the patient performed radio-chemotherapy. We mention that the type of radiotherapy chosen was intensity-modulated radiotherapy (IMRT) at a prescribed dose of 74Gy delivered in 36 fractions over almost 6 weeks and the chemotherapy was an association between Cisplatin, Docetaxel and Etoposide on six cycles.

A systematic follow-up was performed at 3, 6 and 9 months. The endoscopic imaging (Figure 3) and MRI examination (Figure 4) 9 months after surgery revealed cavities without tumor residue.

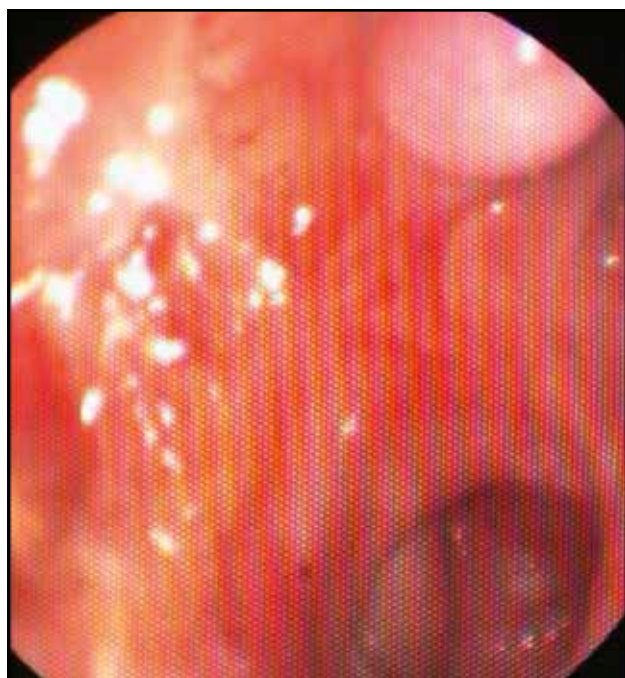
## DISCUSSIONS

Maxillary tumors surgery, depending on the tumor extension, may be represented by partial maxillectomy techniques, total maxillectomy and extended maxillectomy.

It is well known that the maxillary sinus neoplasm has been treated differently in various studies, with surgery, radiation therapy and chemotherapy or an association between them, but there is still a worldwide controversy over the most proper treatment protocol. However, 5-year survival and recurrence rate of the disease is at comparable values.

If, initially, the sinus endoscopic surgical techniques had as addressability only the inflammatory



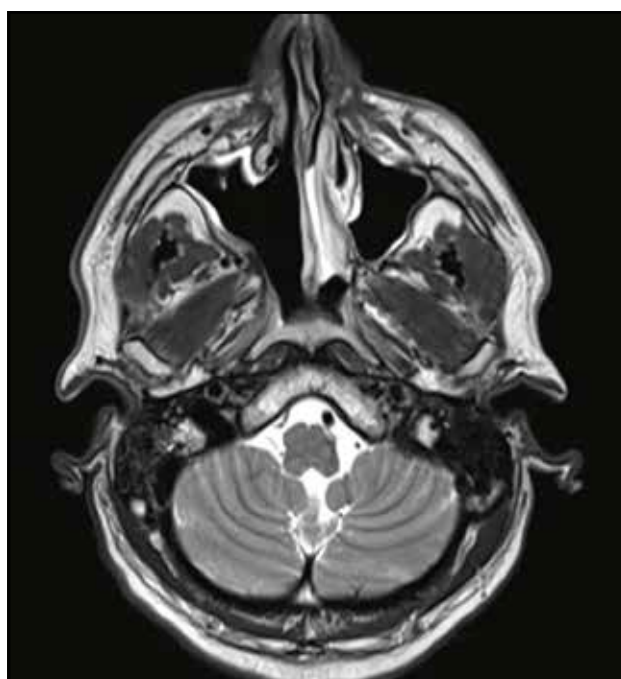
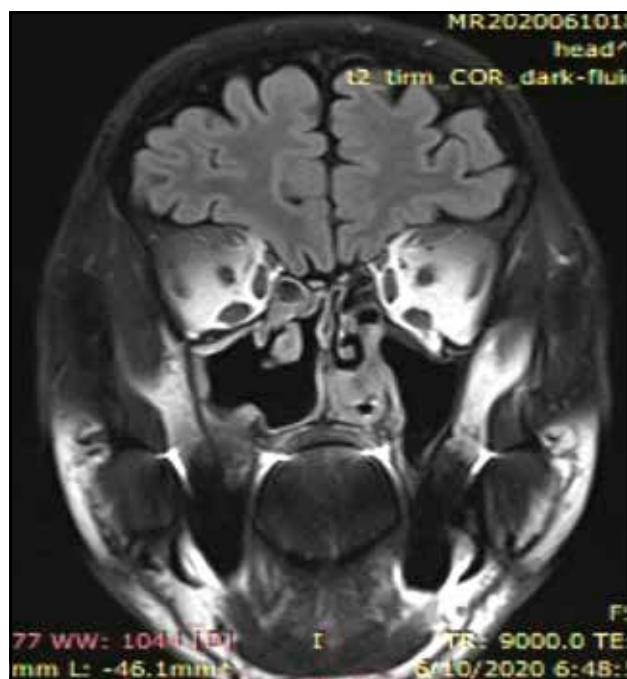


**Figure 3.** Endoscopic aspect - without remaining or areas of tumoral mass in the maxillary sinus, the nasal fossa, ethmoidal cells or spheno-ethmoidal recess; also, the free choanal arch can be observed.

pathology, with the experimentation of the surgical teams, the surgical indications have become more extensive. In the last century, combined surgical techniques or only solitary endoscopic surgery have been successfully applied in the treatment of malignant paranasal tumors<sup>16,17</sup>.

Mainly, the degree of tumor invasion at the time of diagnosis, and less the applied therapeutic strategy, dictates the patient's evolution.

Functional endoscopic extended sinus surgery (FESS) is not a contraindication for performing operations in malignant pathologies and the sur-



**Figure 4.** Cranio-facial MRI (coronal and axial slices). Absence of the medial wall of the maxillary sinus, without MRI sings of tumor areas in the right maxillary sinus, ethmoidal cells or nasal fossa. Normal aspect of the orbital contents.

geon's experience, a very good knowledge of local anatomy and a multidisciplinary team can manage most of skull tumors. FEES dedicated to nasal and sinus neoplasms brings many benefits, including the lack of facial incisions, better visualization of the surgical field, minimal trauma, shorter hospitalization and reduced costs<sup>18</sup>.

In our case, we used the endoscopic approach despite the bulky tumor, because it did not infiltrate the orbital contents and had no endocranial extension, which brought solid arguments for this type of surgery. No significant complications were recorded both during the operation and postoperatively.

In any case, solitary surgery is not a viable solution, it will always be accompanied by the oncological treatment represented by radio- and chemotherapy<sup>19,20</sup>. Al-Magnani et al. compared IMRT with conventional radiotherapy, the first one being associated with a significantly lower toxicity (14% versus 57%), and with less complications rate, such as blindness (0% versus 29%)<sup>21</sup>.

Analysing the literature, we find a study published by Gamez et al. which shows a 60% improvement in the 5-year survival rate in the use of IMRT versus conventional radiation therapy, also associated with low toxicity and absence of serious complications<sup>22</sup>.

The use of chemotherapy is very common, not as solitary therapy but in association with surgery and radiotherapy. Mourad et al. demonstrated, in a group of 18 patients diagnosed with SNUC, that trimodality therapy, which includes cisplatin, docetaxel (TPF) and 5-FU, provides better control of tumor reduction than conventional chemotherapy (83% versus 50%) and a low degree of associated systemic complications (92 versus 33%)<sup>23</sup>. In our patient, the association of endoscopic extended sinus surgery, IMRT (74 Gy) and chemotherapy (Cisplatin, Docetaxel and Etoposide) resulted in complete remission of the tumor and the absence of local or regional recurrences 1 year after treatment.

## CONCLUSIONS

According to the available data from the specialty literature and from our own experience, endoscopic surgery for nasal and paranasal sinuses carcinoma seems to be a more safe and also more effective treatment than the open approach technique in selected cases.

The association between surgical treatment, radiotherapy and chemotherapy shows encouraging results.

**Conflict of interest:** The authors have no conflict of interest to disclose.

**Contribution of authors:** All authors have equally contributed to this work.

## REFERENCES

- Chalian AA, Litman D. Neoplasms of the nose and paranasal sinuses. In: Snow JB, Ballenger JJ (eds.). Ballenger's Otorhinolaryngology Head and Neck Surgery, 16th Edition. Ed. BC Decker Inc, Hamilton, Ontario; 2003, p.807-27.
- Popović D, Milisavljević D. Malignant tumors of the maxillary sinus. A ten-year experience. *Medicine and Biology*. 2004;11(1):31-4.
- National Cancer Institute. Paranasal Sinus and Nasal Cavity Cancer Treatment (Adult) (PDQ®) – Health Professional. [Internet]. [updated August 22, 2019]. Available from: <https://www.cancer.gov/types/head-and-neck/hp/adult/paranasal-sinus-treatment-pdq>.
- Gorelick J, Ross D, Martenette L, Blaivas M. Sinonasal undifferentiated carcinoma: case series and review of the literature. *Neurosurgery*. 2000;47(3):750-4; discussion 754-5. DOI: 10.1097/00006123-200009000-00045.
- Klem C. Malignant tumors of the sinuses treatment & management. [Internet]. Medscape [updated Mar 31, 2020]. Available from: <https://emedicine.medscape.com/article/847189-treatment>.
- Musy PY, Reibel JF, Levine PA. Sinonasal undifferentiated carcinoma: the search for a better outcome. *Laryngoscope*. 2002;112(8 Pt 1):1450-5. DOI: 10.1097/00005537-200208000-00023.
- Garbea St. Patologie ORL. Ed II. Ed. Didactica si Pedagogica, Bucuresti; 1980, p.166-71.
- Committee for Head and Neck Surgery and Oncology; American Academy of Otolaryngology – Head and Neck Surgery; Neck dissection classification committee; American Head and Neck Society; Deschler DG, Day T (eds.); Sharma AK, Kies MS (primary contributors). Pocket guide to neck dissection classification and TNM staging of head and neck cancer. – 3rd ed. American Academy of Otolaryngology – Head and Neck Surgery Foundation, Inc.; 2008.
- McCaffrey TV, Olsen KD, Yohanan JM, Lewis JE, Ebersold MJ, Piepgras DG. Factors affecting survival of patients with tumors of the anterior skull base. *Laryngoscope*. 1994;104(8 Pt 1):940-5. DOI : 10.1288/00005537-199408000-00006.
- Nicolai P, Battaglia P, Bignami M, Bolzoni Villaret A, Delu G, Khrais T. et al. Endoscopic surgery for malignant tumors of the sinonasal tract and adjacent skull base: a 10-year experience. *Am J Rhinol*. 2008;22(3):308-16. DOI: 10.2500/ajr.2008.22.3170.
- Batra PS, Citardi MJ, Worley S, Lee J, Lanza DC. Resection of anterior skull base tumors: comparison of combined traditional and endoscopic techniques. *Am J of Rhinol*. 2005;19(5):521-2.
- Shipchandler TZ, Batra PS, Citardi MJ, Bolger WE, Lanza DC. Outcomes for endoscopic resection of sinonasal squamous cell carcinoma. *Laryngoscope*. 2005;115(11):1983-7. DOI: 10.1097/01.mlg.0000178330.09881.6b.
- Castellnuovo PG, Belli E, Bignami M, Battaglia P, Sberze F, Tomei G. Endoscopic nasal and anterior craniotomy resection for malignant nasosphenoid tumors involving the anterior skull base. *Skull Base*. 2006;16(1):15-8. DOI: 10.1055/s-2005-922095.
- Morita A, Ebersold MJ, Olsen KD, Foote RL, Lewis JE, Quast LM. Esthesioneuroblastoma: prognosis and management. *Neurosurgery*. 1993;32(5):706-14; discussion 714-5.
- Naunheim MR, Goyal N, Dedmon MM, Chambers KJ, Sedaghat AR, Bleier BS, et al. An algorithm for surgical approach to the anterior skull base. *J Neurol Surg B Skull Base*. 2016;77(4):364-70. DOI: 10.1055/s-0036-1580598.

16. Banhiran W, Casiano RR. Endoscopic sinus surgery for benign and malignant nasal and sinus neoplasm. *Curr Opin Otolaryngol Head Neck Surg.* 2005;13(1):50-4.
17. Buchmann L, Larsen C, Pollack A, Tawfik O, Sykes K, Hoover LA. Endoscopic techniques in resection of anterior skull base/paranasal sinus malignancies. *Laryngoscope.* 2006;116(10):1749-54.
18. Devaiah AK, Lee MK. Endoscopic skull base/sinonasal adenocarcinoma surgery: what evidence exists? *Am J Rhinol Allergy.* 2010;24(2):156-60. DOI: 10.2500/ajra.2010.24.3449.
19. van der Laan TP, Iepma R, Witjes MJ, van der Laan BFAM, Plaat BEC, Halmos GB. Meta-analysis of 701 published cases of sinonasal neuroendocrine carcinoma: The importance of differentiation grade in determining treatment strategy. *Oral Oncol.* 2016;63:1-9. DOI: 10.1016/j.oraloncology.2016.10.002.
20. Kuan EC, Arshi A, Mallen-St Clair J, Tajudeen BA, Abemayor E, St John MA. Significance of tumor stage in sinonasal undifferentiated carcinoma survival: a population-based analysis. *Otolaryngol Head Neck Surg.* 2016;154(4):667-73. DOI: 10.1177/0194599816629649.
21. Al-Mamgani A, van Rooij P, Mehilal R, Tans L, Levendag PC. Combined-modality treatment improved outcome in sinonasal undifferentiated carcinoma: single-institutional experience of 21 patients and review of the literature. *Eur Arch Otorhinolaryngol.* 2013;270(1):293-9. DOI: 10.1007/s00405-012-2008-5.
22. Gamez ME, Lal D, Halyard MY, Wong WW, Vargas C, Ma D, et al. Outcomes and patterns of failure for sinonasal undifferentiated carcinoma (SNUC): the Mayo Clinic Experience. *Head Neck.* 2017;39(9):1819-24. DOI: 10.1002/hed.24834.
23. Mourad WF, Hauerstock D, Shourbaji RA, Hu KS, Culliney B, Li Z, et al. Trimodality management of sinonasal undifferentiated carcinoma and review of the literature. *Am J Clin Oncol.* 2013;36(6):584-8. DOI: 10.1097/COC.0b013e31825eb3a5.