Current Issues in Pharmacy and Medical Sciences
Formerly ANNALES UNIVERSITATIS MARIAE CURIE-SKLODOWSKA, SECTIO DDD, PHARMACIA
https://czasopisma.umlub.pl/curipms

Navigating the uncharted territory of aggressive maxillary sinus cancer: insights from a singular case

Katarzyna Geca*, Dorota Kozaczuk, Wojciech Polkowski, Magdalena Skorzewska

Department of Surgical Oncology, Medical University of Lublin, Poland

ARTICLE INFO
Received 27 December 2023
Accepted 03 March 2025

Keywords:
maxillary sinus cancer,
MSC,
case study,
palliative chemotherapy,
CTH.

ABSTRACT

Maxillary sinus carcinoma (MSC) is a rare malignancy characterized by diagnostic and therapeutic complexity, often presenting late in its clinical course. This report details a unique and aggressive case of MSC in a 57-year-old male. Despite prompt multimodal treatment, including surgery, radiochemotherapy (RCTH) and sequential lines of palliative chemotherapy (CTH), the disease demonstrated rapid progression and resistance to standard therapies. Management was guided by a patient-centered approach, emphasizing shared decision-making in light of the patient's clinical trajectory and quality-of-life considerations. This case highlights the challenges of treating aggressive MSC and underscores the necessity for individualized care strategies in managing rare and refractory head and neck cancers.

INTRODUCTION

Maxillary sinus cancers (MSC) are infrequent and present both a diagnostic and therapeutic challenge. MSC has an annual incidence rate of one case per 100 000 individuals, accounting for roughly 3% of all head and neck malignancies [1]. The most common histological type of MSC, which makes up 60-90% of all cases, is squamous cell carcinoma [2]. The incidence rate is highest among men between the ages of 55 and 65 [3]. The development of sinonasal cancer is influenced by a multitude of recognized risk factors. Examples encompass exposure to wood, leather or coal dust, nickel compounds, formaldehyde and flour. Nevertheless, the most significant contributing factors are chronic sinusitis and a history of tobacco smoking [4-6].

MSC is typically asymptomatic during its early stages. As a result, the vast majority of patients are diagnosed at an advanced stage, where symptoms such as epistaxis, nasal obstruction and perforation of sinus walls are present [5,6]. Local invasion is evident in 70-80% of all MSC cases at the time of diagnosis, leading to classification as T3 or T4 according to the American Joint Committee on Cancer (AJCC) staging system [7]. The imaging modalities of choice for primary maxillary sinus tumors evaluation are computed tomography (CT) and magnetic resonance imaging (MRI) of the head. However, fluorine-18 fluorodeoxyglucose positron emission tomography (18F-FDG PET) is more effective for the detection of local recurrences [3,5].

* **Corresponding author**
e-mail: katarzynageca@umlub.pl

The 5-year overall survival (OS) rate for node-negative disease patients falls within a range of 34% to 49%, whereas node-positive disease patients exhibit a rate of 17% [8]. Due to the rarity of MSC and the aggressive attributes of the tumors, a postponed diagnosis has the potential to negatively affect the quality of life and contribute to a lower chance of survival [5].

The aim of this report is to present a unique case of highly aggressive squamous cell carcinoma originating from the maxillary sinus and discuss the approach to managing such cases.

Case presentation

On July 15, 2016, a suspected palatal abscess on the left side was diagnosed in a 57-year-old male patient who was admitted to the Emergency Room of the Department of Maxillo-facial Surgery, Academic Hospital of Medical University of Lublin, Poland. The patient has reported the presence a painless, enlarging mass on the left palate for five weeks that has interfered with the ability to swallow, eat and speak. The patient reported exposure to occupational pesticides, while being a non-smoker and occasional drinker. On July 18th, the patient was referred to the Maxillo-facial Surgery Outpatient Clinic, where a CT scan of the sinuses was conducted. The CT scan findings showed the existence of a homogeneously enhanced mass in the left maxillary sinus, with no involvement of cervical lymph nodes. The patient was admitted to the Department of Maxillo-facial Surgery on July 20 for an excisional biopsy. The intraoral examination indicated the

existence of a lesion on the left hard palate and crestal bone, which extended across the midline without penetrating the soft palate. The tumor, measuring 4.5x5 cm, adhered to the underlying structures, with protruding necrotic tissue at teeth # 22-23. Upon biopsy, the tumour with a bruised-purple appearance exhibited profuse bleeding. The pathological findings revealed the existence of cancerous cells. According to the CT and biopsy results, the patient's condition was identified as locally advanced maxillary sinus carcinoma – Carcinoma planoepitheliale akeratodes (cT3N0M0). In August 2016, a total maxillectomy was performed on the patient, with the preservation of the orbital structure. Histological examination revealed planoepithelial carcinoma akeratodes at clinical stage III (pT3N1M0), according to the AJCC staging system. The resection margins were negative. Shortly after the resection (2 weeks), an irregularly shaped mass that originated from the remaining part of the left crestal bone was observed. MRI confirmed the suspicion of early recurrence. The recurrent tumor was surgically removed on October 25, 2016. Subsequently, the patient was given standard adjuvant radiochemotherapy (RCTH). Intensity Modulated Radiation Therapy (IMRT) was prescribed at a rate of 66 Gy in 2 Gy fractions to a clinical target volume (CTV) that included the surgical cavity and bilateral neck lymph nodes levels Ib-IV. The patient also received concurrent chemotherapy (CTH) in the form of cisplatin 100mg/m2 every 21 days. Upon the completion of RCTH in January 2017, tumour regrowth was observed. The tumour mass, measuring 5x8mm, was mainly present over the outer corner of the left eye and the left zygoma. The patient was evaluated for re-resection, involving enucleation/evisceration of the left eye. Despite the recommendation, the patient declined the treatment. The patient and their family opted for palliative CTH over the proposed local treatments of surgery and radiotherapy. Docetaxel monotherapy (75 mg/m2 iv one day q3w) was initiated at the Department of Clinical Oncology, Medical University of Lublin, Poland, in March 2017 (Figure 1). Despite the presence of CTCAE grade II myelotoxicity (anaemia, neutropenia), the overall

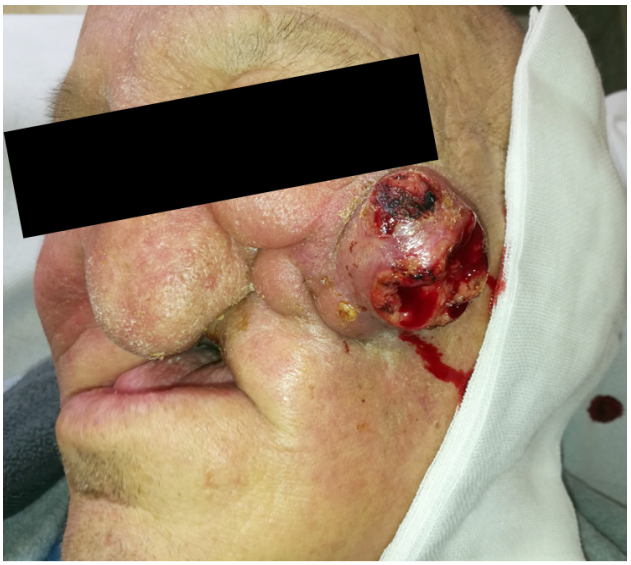

Figure 1. Cancer advancement prior to the first line of palliative CTH (March 2017)

treatment tolerance was considered acceptable. Figure 2 illustrates the clinical presentation observed during the administration of Docetaxel treatment. After five cycles of CTH, in June 2017, a CT scan revealed the presence of throat infiltration (which was confirmed with biopsy), and a clinical progression was observed (Figure 3). In July 2017, due to the excessive bleeding caused by the rapidly growing tumour mass, a gross total electroresection of the tumour was performed, following the endovascular embolization of the feeding artery (left internal carotid artery), as shown in Figure 4. The patient initiated the second-line CTH with a cisplatin and 5-fluorouracil (PF) regimen (cisplatin 100 mg/m2 1 day and 5-fluorouracil 1000 mg/m2 1-4 day q4w) in August 2017. The patient continued the regimen for four cycles until November 2017, demonstrating good tolerance.

CTH with the PF regimen was discontinued as a result of further clinical progression, as depicted in Figures 5 and 6. A secondary endovascular tumour embolization procedure (left external carotid artery) was performed (refer to Figure 7)

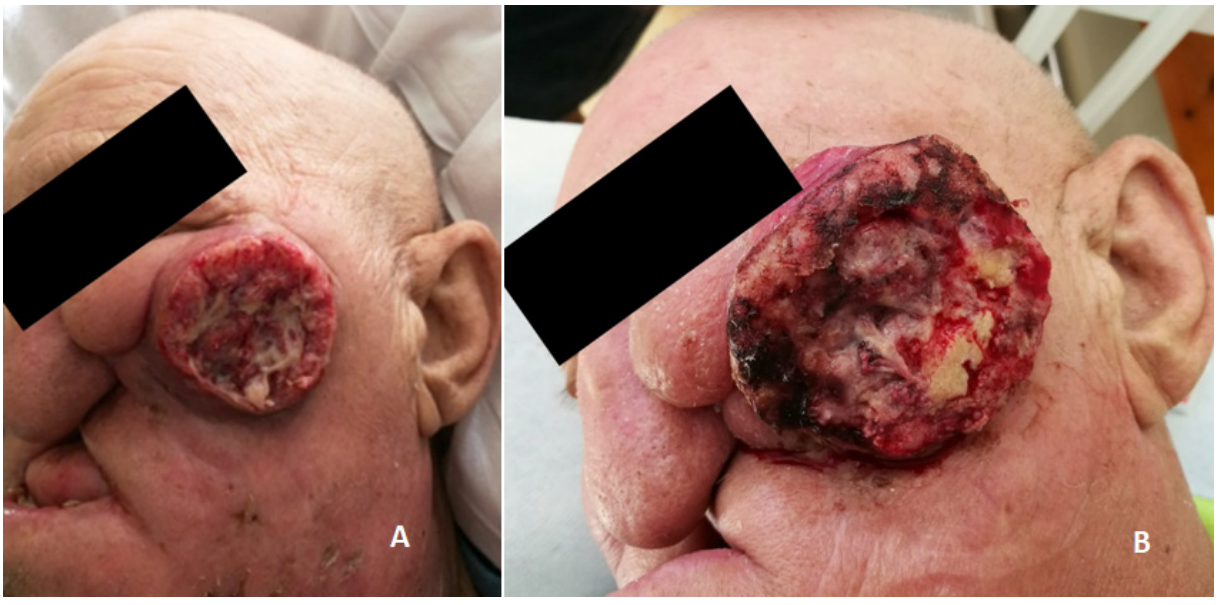

Figure 2. A – Control after cycle 1 of first line palliative CTH – Docetaxel (April 2017), B – control after cycle 2 of first line palliative CTH – Docetaxel (May 2017)

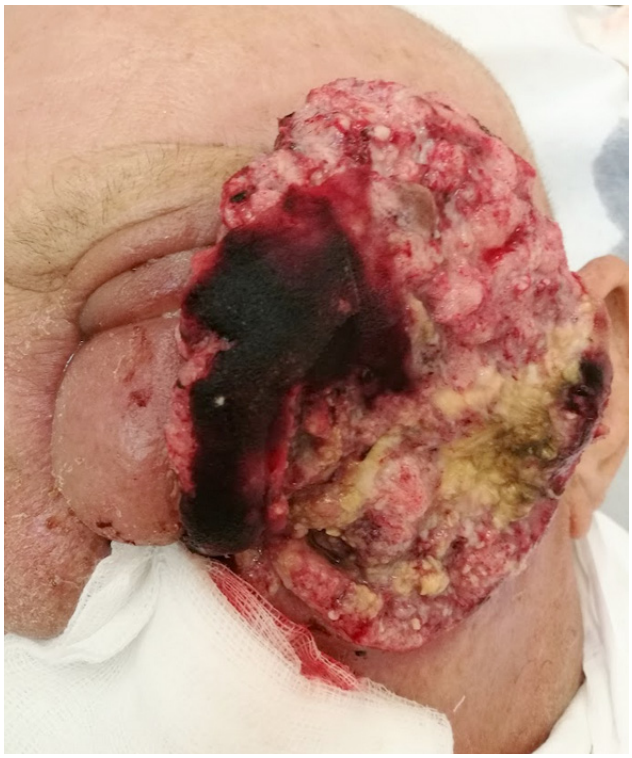

Figure 3. Control after cycle 5 of first line palliative CTH – Docetaxel (June 2017) – further clinical progression

in response to the excessive bleeding from the tumour site. The decision to pursue third-line palliative CTH was made after the CT scan showed no evidence of skull base infiltration or neck lymph node metastases and the patient's overall condition remained favorable (ECOG 2). The patient began monotherapy with methotrexate (30mg/m2 1-day q2w) in December 2017. A moderate decrease in the size of the tumor mass was observed as a clinical response following the first cycle of CTH treatment (as indicated in Figure 8).

The patient underwent a total of four cycles of methotrexate. The patient's condition, however, continued to deteriorate despite ongoing treatment (Figure 9). The lesion was bleeding heavily, and the patient was consulted for another tumour electroresection. The procedure was abandoned because of the need to resect large areas of tissues with little chance of obtaining hemostasis.

The patient displayed recurrent electrolyte imbalances (hyponatremia and hypochloremia) during the treatment course. Due to persistent anemia, the patient required blood transfusions. Hyperuricemia and a substantial increase in white blood cells (WBC) were observed as a result of tumour disintegration. The progression of the disease was accompanied by periodic elevations in CRP levels. The advancement of the tumor rendered oral feeding impossible. In November 2016, the patient underwent percutaneous endoscopic gastrostomy (PEG) tube placement, which was later replaced twice in February and April 2017. The patient continued to receive PEG feeding while at home. Massive tissue necrosis was observed alongside aggressive tumour growth. Regular resection of infected necrosis was not possible due to the extensive recurrent bleeding from the tumour. Therefore, the patient was deemed to require long-term antibiotic treatment based on the bacterial culture results.

The patient's last visit to the Department of Clinical Oncology ended on February 12, 2018, after he received supportive treatment and was subsequently discharged to his residence. Due to the general condition's deterioration and increased tumour bleeding, the patient was relocated to an inpatient hospice. A head CT scan was performed during the hospice stay, which revealed infiltration of the skull base. Progressive cerebral oedema led to a sudden deterioration in the patient's condition, and ultimately caused his death on February 17, 2018.

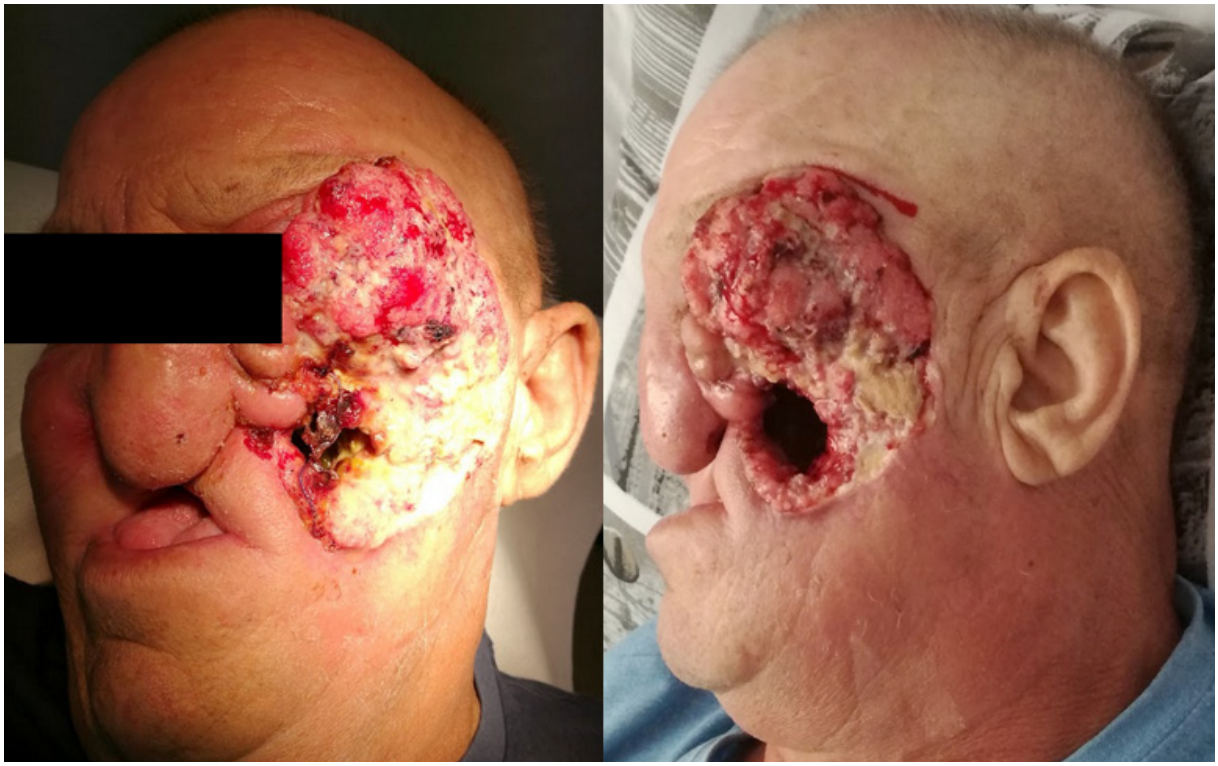

Figure 4. Control after first electroresection (July 2017)

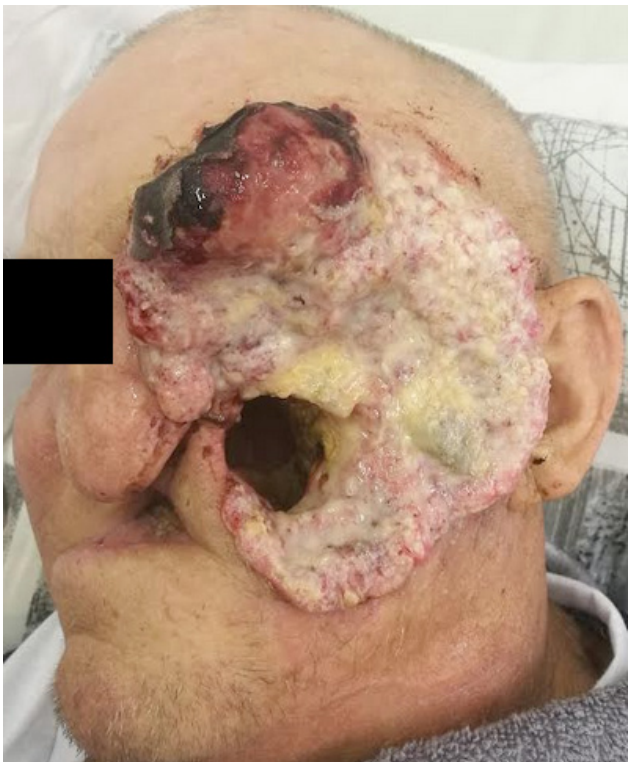

Figure 5. Control after cycle 3 of second line palliative CTH – PF (October 2017)

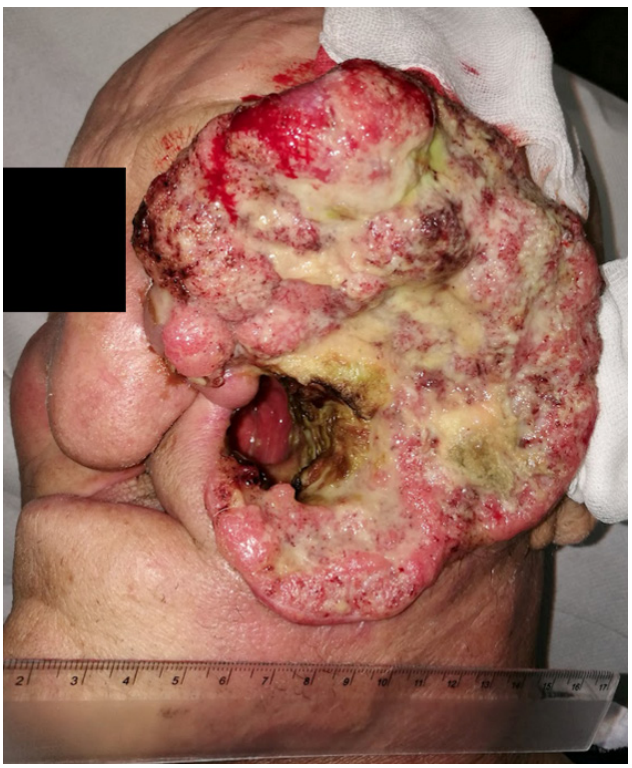

Figure 6. Control after cycle 4 of second line palliative CTH – PF (November 2017) – Further clinical progression

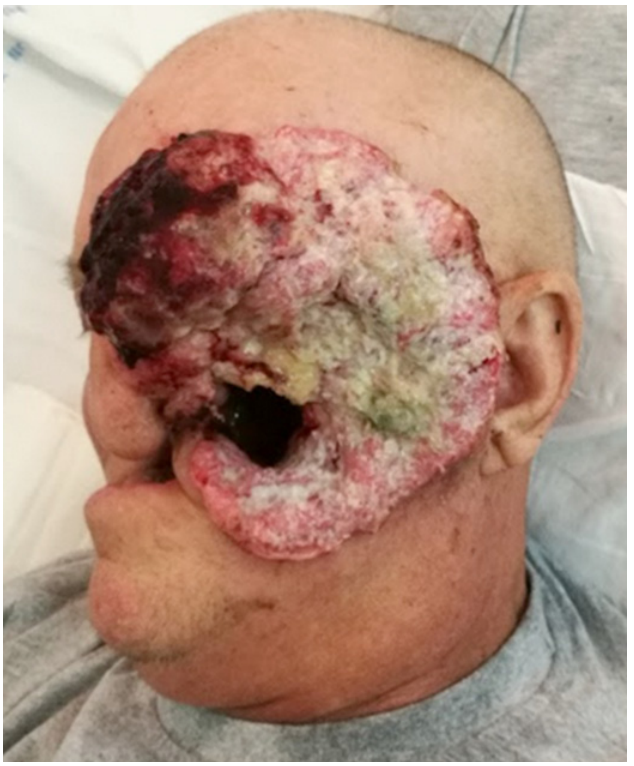

Figure 7. Control after second electroresection (November 2017)

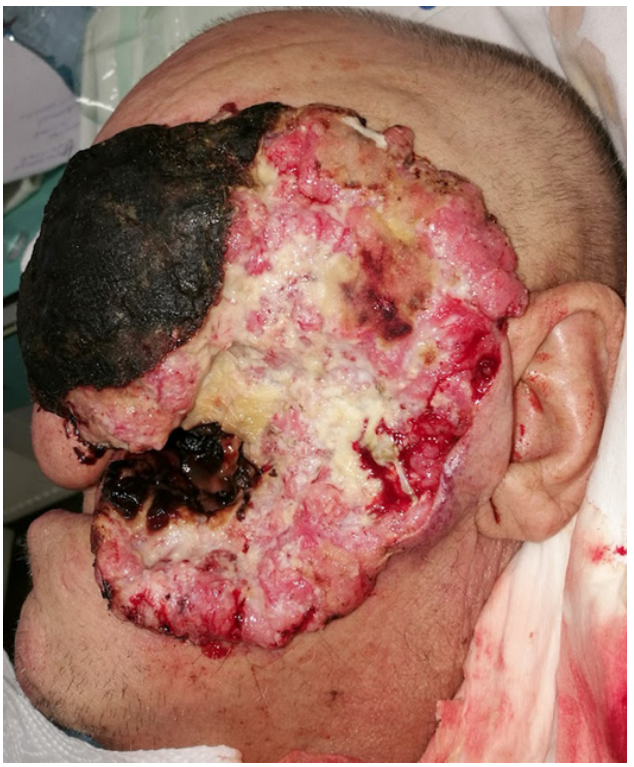

Figure 8. Control after cycle 1 of third line palliative CTH – MTX (December 2017)

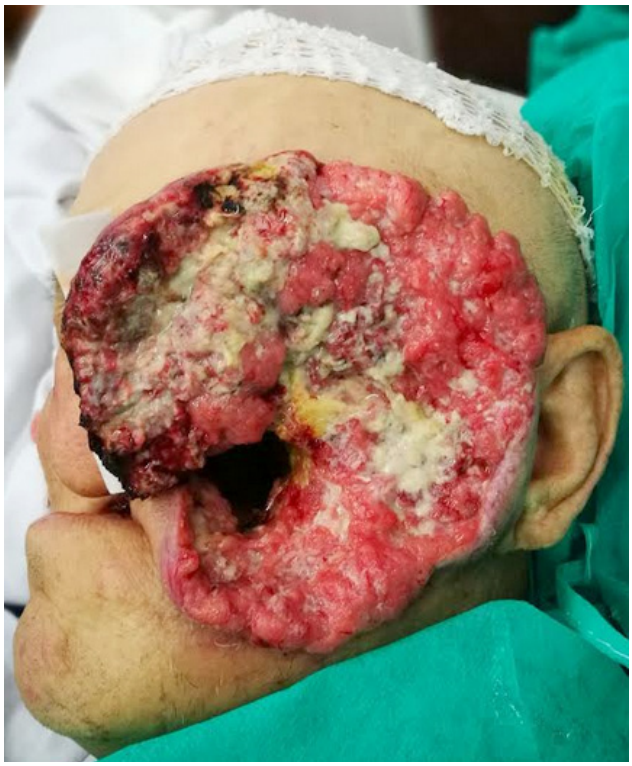

Figure 9. Control after cycle 4 of third line palliative CTH – MTX (February 2018) – further clinical progression

DISCUSSION

Since MSCs are rare, prospective multi-institutional studies still need to be included. The consequence is a considerable uncertainty about the fundamental aspects of the management of these tumors. Thus, every clinical case provides valuable information regarding the treatment of MSCs.

MSCs are a significant challenge for head and neck surgeons, radiotherapists and clinical oncologists due to their rarity. The reason for this is that they are connected to unsatisfactory treatment results and considerable morbidity associated with both tumour and treatment [9]. The advanced stage at diagnosis and complex anatomic relationships with the contents of the orbital and base of skull make the treatment of carcinomas of paranasal sinuses a significant therapeutic dilemma.

This paper outlines a case report of MSC that was extremely aggressive and required multiple therapeutic interventions. Despite the prompt diagnosis and treatment administered to the patient within a month, it proved insufficient to halt the cancer progression. Although implementing surgical treatment, RCTH, and palliative CTH, the patient's survival was only 20 months.

Surgical intervention, radiotherapy (RT), or a combination of both are the principal treatment methods for MSC [7]. However, the application of surgery and radiation therapy is confined to advanced stages of MSC [10]. Incomplete resection is a significant contributor to treatment failure and local disease recurrence, mainly because of the intricate regional anatomy and the tumours' proximity to the skull base [5]. The effectiveness of induction CTH has been demonstrated for locally advanced and technically unresectable MSC, resulting in successful surgical outcomes in numerous patients [11].

The OS is typically unfavorable after single-modality therapy for MSC. In the study by Amendola et al., a total of 39 MSC patients who underwent treatment with curative intent, either through resection or definitive RT, were analysed [12]. The results showed no statistically significant difference in OS at 3 or 5 years after treatment, with a 5-year survival rate of 31% and 35% for resection and RT, respectively [12]. The objective of the multimodal approach is to optimize the treatment of locally advanced MSC, improve the tumour control rate, and reduce functional impairment. The assessment of the superiority between combined modality therapy (CMT) and single modality therapy was conducted by St.-Pierre and Baker [13]. Of the 61 patients treated with curative intent, 10 (16%) received resection alone, 32 (53%) underwent definitive RT and 19 (31%) received CMT. The outcomes revealed an improved survival in patients who underwent both surgery and RT [13]. Paulino et al. reported similar findings. Eleven (23%) of the 48 patients having MSC were treated with RT alone, while 37 (77%) were managed with surgery and RT. The results showed statistically significant improvement in local control and disease-specific survival rate at 5 years [14].

Prior studies have indicated that the incorporation of neoadjuvant CTH in multimodal treatment can improve operability by decreasing tumor volume and enhancing patient outcomes [4, 15, 16]. Additionally, a favorable response to the induction CTH was linked to a heightened survival rate and a greater possibility of preserving the organ [16]. Despite its potential efficacy, systemic CTH may cause severe side effects, such as mucositis, bone marrow suppression and performance difficulties in patients with poor overall condition. Several studies have been undertaken to alleviate these adverse effects through the application of intra-arterial CTH in combination with multimodal treatment in MSCs [17, 18]. According to a recent study conducted by Keun-Ik et al., regional CTH has been proven to be more effective than systemic CTH in reducing tumour volume for treating locally advanced MSC [16].

Immunotherapy (ITH) has also been proposed as a treatment for MSC. The use of immune checkpoint inhibitors has become a promising treatment option. Ongoing studies are examining several anti-PD-1 and anti-PD-L1 antibodies, two of which (nivolumab and pembrolizumab) were granted Food and Drug Administration (FDA) approval in 2016 for sinus cancers [19]. Several studies have investigated the effect of ITH and RT in MSC [20, 21]. Nonetheless, there is no provision for reimbursement of such treatment in Poland. The patient was ineligible to participate in clinical trials, as the advanced stage of the disease and prior treatment did not meet the inclusion criteria.

The comparative analysis of our case is challenging owing to the patient's refusal of the proposed local treatment. An individualised treatment approach was the result of this. The recurrence of the tumor was observed shortly after the completion of re-resection and RCTH. A subsequent re-resection procedure, which may involve the enucleation or evisceration of the left eye and additional RT, has been proposed. The patient refused the recommended

treatment due to concerns about the impact it might have on his quality of life. Palliative systemic CTH was the sole treatment option he accepted. As a consequence, the treatment provided was not optimal. The treatment that followed relied entirely on systemic CTH, which did not suppress the rapid progression. The presence of necrotic tumour tissues could have significantly limited the penetration of CTH, leading to a poor response. The tumour grew back rapidly, despite the regular removal of necrotic tissue.

Reviews of case-control studies suggest an association between pesticides and morbidity from head and neck cancer [22,23]. The patient had been exposed to pesticides for a minimum of ten consecutive years due to his occupation. The patient stated that the use of personal protective equipment during pesticide handling was mainly insufficient. The disease's treatment-resistant and highly aggressive course may be connected to this.

CONCLUSION

The report presents a unique case of rapidly progressing MSC that was treated utilizing an individualized approach according to a communication model focused on partnership. The patient had a fundamental influence on therapeutic decisions, which could significantly affect the success of the therapy. However, given the patient's peculiar clinical course and unfavorable prognosis, this treatment seems justified. The patient's clinical course suggests that local treatment would not be effective in improving their condition. Furthermore, such treatment would lead to further mutilation, which was unacceptable to the patient and this family.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Informed consent for participation has been obtained from the patient.

CONSENT FOR PUBLICATION

Informed consent for publication has been obtained from the patient.

FUNDING

This research received no external funding.

COMPETING INTERESTS

The authors declare no competing interests.

ORCID iDs

Katarzyna Gęca https://orcid.org/0000-0001-5024-2559
Wojciech Polkowski https://orcid.org/0000-0001-6455-563
Magdalena Skórzewska https://orcid.org/0000-0002-5004-9940

REFERENCES

1. Sakashita T, Homma A, Hatakeyama H, Kano S, Mizumachi T, Furusawa J, et al. Salvage operations for patients with persistent or recurrent cancer of the maxillary sinus after superselective intra-arterial infusion of cisplatin with concurrent radiotherapy. *Br J Oral Maxillofac Surg.* 2014;52(4):323-8.
2. Kosugi Y, Suzuki M, Fujimaki M, Ohba S, Matsumoto F, Muramoto Y, et al Radiologic criteria of retropharyngeal lymph node metastasis in maxillary sinus cancer. *Radiat Oncol.* 2021;16:1-6.
3. d'Errico A, Pasian S, Baratti A, Zanelli R, Alfonzo S, Gilardi L, et al. A case-control study on occupational risk factors for sino-nasal cancer. *OEM.* 2009;66(7):448-55.
4. Won HS, Chun SH, Kim B-S, Chung SR, Yoo IR, Jung C-K,et al. Treatment outcome of maxillary sinus cancer. *Rare Tumors.* 2009; 1(2):110-4.
5. Santos MRM, Servato JPS, Cardoso SV, de Faria PR, Eisenberg ALA, Dias FL, Loyola AM. Squamous cell carcinoma at maxillary sinus: clinicopathologic data in a single Brazilian institution with review of literature. *Int J Clin Exp Pathol.* 2014;7(12):8823.
6. Ramachamparambathu AK, Vengal M, Mufeed A, Siyo N, Ahmed A. Carcinoma of maxillary sinus masquerading as odontogenic infection. *JCDR.* 2016;10(9):ZD11.
7. Kuo Y-H, Lin C-S. Regression of advanced maxillary sinus cancer with orbital invasion by combined chemotherapy and immunotherapy: A one-year follow-up case report. *Mol Clin Oncol.* 2022;16(4):94.
8. Rho H-J, Kim S-J, Nam H, Kim B, Kim I, Kim Y-K, et al. Detection and prediction of local recurrence of maxillary sinus cancer using F-18 FDG PET/CT. *EJSO.* 2010;36(2):214-20.
9. Blanco AI, Chao KC, Ozyigit G, Adli M, Thorstad WL, Simpson JR, et al. Carcinoma of paranasal sinuses: long-term outcomes with radiotherapy. *Int J Radiat Oncol Biol Phys.* 2004;59(1):51-8.
10. Ashraf M, Biswas J, Dam A, Bhowmick A, Sing V, Nayak S. Results of treatment of squamous cell carcinoma of maxillary sinus: a 26-year experience. *World J Oncol.* 2010;1(1):28.
11. Noronha V, Patil VM, Joshi A, Krishna MV, Dhumal S, Juvekar S, et al. Induction chemotherapy in technically unresectable locally advanced carcinoma of maxillary sinus. *Chemother Res Pract.* 2014;2014(1):487872.
12. Amendola BE, Eisert D, Hazra TA, King ER. Carcinoma of the maxillary antrum: surgery or radiation therapy? *Int J Radiat Oncol Biol Phys.* 1981;7(6):743-6.
13. St.-Pierre S, Baker SR. Squamous cell carcinoma of the maxillary sinus: analysis of 66 cases. *Otolaryngol Head Neck Surg.* 1983; 5(6):508-13.
14. Paulino AC, Marks JE, Bricker P, Melian E, Reddy SP, Emami B. Results of treatment of patients with maxillary sinus carcinoma. *Cancer.* 1998;83(3):457-65.
15. Hanna EY, Cardenas AD, DeMonte F, Roberts D, Kupferman M, Weber R, et al. Induction chemotherapy for advanced squamous cell carcinoma of the paranasal sinuses. *Arch Otolaryngol Head Neck Surg.* 2011;137(1):78-81.
16. Kim WT, Nam J, Ki YK, Lee JH, Kim DH, Park D, et al. Neoadjuvant intra-arterial chemotherapy combined with radiotherapy and surgery in patients with advanced maxillary sinus cancer. *Radiat Oncol J.* 2013;31(3):118.
17. Shiga K, Yokoyama J, Hashimoto S, Saijo S, Tateda M, Ogawa T, et al. Combined therapy after superselective arterial cisplatin infusion to treat maxillary squamous cell carcinoma. *Otolaryngol Head Neck Surg.* 2007;136(6):1003-9.
18. Yi KI, Kim SD, Mun SJ, Roh HJ, Cho KS. Therapeutic efficacy of regional and systemic chemotherapy in advanced maxillary sinus cancer. *Head Neck Pathol.* 2019;41(8):2732-40.
19. Xiang JJ, Uy NF, Minja FJ, Verter EE, Burtness BA. Hyperprogression after one dose of nivolumab in sinonasal cancer: a case report. *Laryngoscope.* 2020;130(4):907-10.
20. Yazici G, Gullu I, Cengiz M, Elmali A, Yilmaz MT, Aksoy S, et al.The synergistic effect of immune checkpoint blockade and radiotherapy in recurrent/metastatic sinonasal cancer. *Cureus.* 2018;10(10).
21. Guram K, Nunez M, Einck J, Mell LK, Cohen E, Sanders PD, et al. Radiation therapy combined with checkpoint blockade immunotherapy for metastatic undifferentiated pleomorphic sarcoma of the maxillary sinus with a complete response. *Front Oncol.* 2018;8:435.
22. da Silva Leonel ACL, Bonan RF, Pinto MBR, Kowalski LP, da Cruz Perez DE. The pesticides use and the risk for head and neck cancer: A review of case-control studies. *Medicina Oral, Patología Oral y Cirugía Bucal.* 2020;26(1):e56.
23. Amizadeh M, Safari-Kamalabadi M, Askari-Saryazdi G, Amizadeh M, Reihani-Kermani H. Pesticide exposure and head and neck cancers: a case-control study in an agricultural region. *Iran J Otorhinolaryngol.* 2017;29(94):275.