Multimodality Approach to Treatment of Rhinosinusal Tumours

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The treatmentdecision for rhinosinusal tumours requires accurate knowledge of the therapeutic principles specific to each histological type and tumoral extension. Therapy strategies have been developed based on the pathophysiological knowledge and the history of these tumors. Postoperative assessment remains necessary, to establish patient-specific oncological management. The purpose of this study is the retrospective analysis of cases with rhinosinusalmalignancies, diagnosed and treated in the Otolaryngology Unit of the Spiridon Emergency Clinical Hospital in Iasi. We evaluated the characteristics of the patient group using a statistical analysis that highlights the therapeutical modalities used in multimodal treatment, surgical techniques, chemotherapy, radiotherapy, and the therapeutic protocols, all of these beeing adapted to each patient so that, their effectiveness to be maximal. Rinosinusal tumours show particular elements of severity through late diagnosis due to lack of symptomatology, thus limiting the therapeutic means and their curative potential.In order to ensure a correct and complete treatment of this disease, an interdisciplinary collaboration between the ENT surgeon, ophthalmologist, neurosurgeon, imagist, oncotherapist, anatomopathologist, OMF surgeon both preoperatively in the setting of a therapeutic and postoperative strategy is absolutely necessary.Surgery has its well-established place in multimodality complex treatment whether it is curative or palliative.

Keywords: rhinosinusal tumour, surgery, chemoterapy, radiotherapy

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Rhinosinusal cancer is a rare disease, representing 3-5% of all head and neck tumours. The annual incidence rate is 0.5-1.0 per 100,000 population [1].

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For many years, the preferred treatment for the most frequent forms of rhinosinusal tumors (squamous cell carcinoma, adenocarcinoma) is combined multimodal treatment. This approach has emerged as a need for oncological safety of postoperative radiotherapy. This causes an increased survival rate and a significant decrease in recurrence.

Until recently, standard treatment consisted of irradiation followed by about 6 weeks of surgical resection. Several authors believe that the extension of the surgery should be based on tumour volume extension and its topography. This method showed a survival rate of 5 years without recurrence in 45% cases [4].

Other researchers believe that surgery can be adapted to the residual tumor, but they did not not gavesupport for this opinion [5]. Other studies published a 5-year survival without relapse over the same period by using radiotherapy and minimally invasive surgical techniques in 29% of patients, similar to exclusive radiotherapy [6].

In the past, physicians supported postoperative irradiation [7] with 2 clear advantages:

as long as the wound healing has occurred, radiotherapy can be given at a higher total dose; it is possible to appreciate the extension of the tumour with a much higher accuracy, reducing the rate of *geographic error*.

In Houston, 1968, at M.D. Anderson Hospital and TumorInstitute, *geographic error* was responsible for 25-30% of therapeutic failures [8].

Erosion of the base of the skull, extension to the rhinopharynx, cervical and systemic metastases arecertain signs of incurability. These patients usually receive radiotherapy alone or in combination with chymiotherapy. Cervical metastases indicate an unfavorable prognosis.Although many authors consider the invasion of the base of the skull a sign of incurability, others recommend combined resections in selected cases [9-14]

In a study it was reported a 5-year survival rate of 50% for craniofacial resection [15].

The purpose of this study is the retrospective analysis of cases with rhinosinusalmalignancies, diagnosed and treated in the Otolaryngology Unit of the Spiridon Emergency Clinical Hospital in Iasi between 2004 and 2018. We evaluated the characteristics of the patient group

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using a statistical analysis that highlights the therapeutical modalities used in multimodal treatment, surgical techniques, chemotherapy, radiotherapy, and the therapeutic protocols, all of these beeing adapted to each patient so that, their effectiveness to be maximal.

Experimental part

Material and methods

The study was conducted on 108 patients (76%) of the 143 cases admitted and treated in the ENT Clinic. The 108 patients in the study group underwent surgeries: 14 as unimodal treatment - especially in the early years of the study and 92 in the multimodality, complex treatment variants.These patients, depending on the stage and location of the tumour, were treated with different curative surgical techniques.

Specific biostatistics tests and indicators have been used. The statistical conclusion addresses the issue of the distinction between random and possible systematic effects.

There is, however, a specificity of medical statistics that involves a particular study technique. We have seven distinct stages in relation to this technique: selection of the object, purpose and premises of the study, based on the most complete documentation; choice ofresearch methods and information processing; conducting the research; recording the information obtained in the research; processing the information obtained in the research; coding for statistical groupings; presenting information for analysis; statistical tables, statistical indicators system, graphical presentation; analysis and synthesis of the study and evaluation, using mathematical analysis (multifactorial, discriminatory, segmentation, logistics, etc.).

Results and discussions

It has been found that in some cases the exclusive application of radiotherapy did not significantly alter the survival rate. Thus, current treatment guidelines seek to extend surgical techniques also to cases that years ago were classified as inoperable.

According to current theories, in giant tumors that are out of operative resources, surgical techniques of tumor reduction are practiced to achieve a higher survival rate, even if it does not reach oncological limits, followed by radiotherapy. It was observed that the survival rate in these patients could increase on average by approximately 6-12 months (table 1, table 2).

In order to optimize the treatment of rhinosinusal malignant tumours in the last 6-7 years, we have been implementing more laborious surgical techniques in our country that found to be beneficial for the patient. They are thus approaching the survival rates of patients with rhinosinusal malignant tumors in advanced countries.

In the first 7 years, surgery was reduced to tumor excision by lateral rhinotomy, by Rouge-Denker technique, and rarely by sub-or supraorbital prolonged lateral rhinotomy (Weber-Fergusson). Over the past 7 years, larger interventions have been performed using the Labayle incision or a lateral rhinotomy with bilateral supraorbital extension through which a much wider tumour approach has been achieved. In many cases tumour ablation has been achieved within the oncologycal limits.

In a few cases, where the invasion of rhinobasis was found, it was intervened in the complex team (neuro-surgeon - ENT surgeon) through which the tumour process was fully lifted.

We exemplify a few cases presenting the tumour extension, its stage, the intervention that has been practiced and the subsequent evolution of the tumor in figures 1, 2 and 3.

TYPE OF THERAPY	NUMBER OF PACIENTS	PERCENT OF PATIENTS
UNIMODAL	49	35 (24.48%) RADIOTHERAPY
		14 (9.79%) SURGERY
MULTIMODAL	94	65.73%

Table 1
TREATMENT IN RHINOSINUSAL MALIGNANCIES

THERAPY	NUMBER OF PATIENTS	PERCENT
Chimiotherapy	0	0.00%
COMPLEX THERAPY		
Surger +Radiotherapy	75	52.45%
Chimiotherapy+Surgery	5	3.50%
Chimiotherapy + Radiotherapy	0	0.00%
Chimiotherapy+ Radiotherapy +Surgery	8	5.59%
Radiotherapy +Emergency Surgery	6	4.20%

Table 2
THERAPY IN RHINOSINUSAL MALIGNANCIES

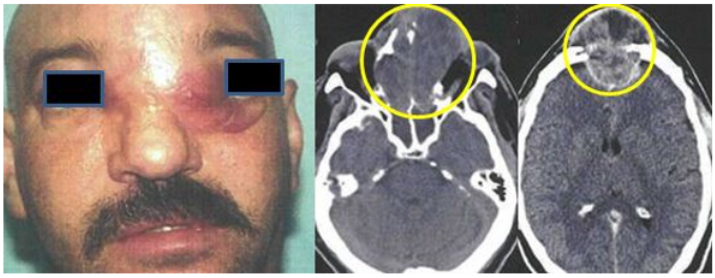

Fig. 1. CT - a tumor extended in the nasal passages (nasal septal destruction), the entire maxillary sinus, and partly the left maxillary sinus (destruction of the bilateral interstitial-nasal wall), the sphenoidal sinuses, the bilateral orbit invasion, the frontal sinuses with the destruction of their anterior and posterior walls.

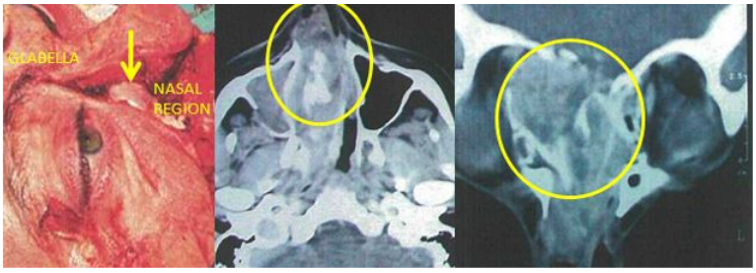

Fig. 2. CT -a tumor extended in the nasal passages(nasal septum *blown* and lysed in the upper part), right choana, right maxillary sinus, bilateral ethomidal cells with overlapping horizontal ethmoid lamina, invasion at the tip of right orbit, extension in frontal and sphenoidal sinuses

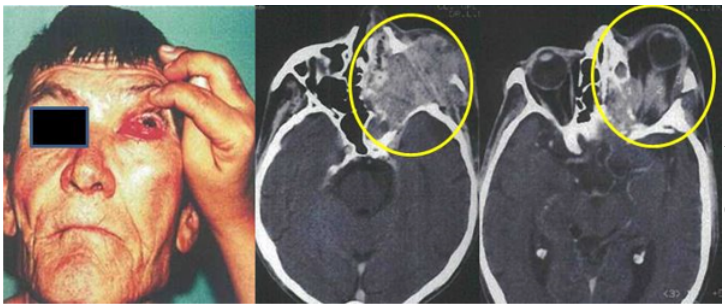

Fig. 3. The CT performed revealed a gigantic expansive tumour, non-homogeneous with multi-calcification inside, causing osteolytic changes in the left upper hemimaxillar and invasion into the left nostril, fully filling the maxillary sinus with bone destruction of the walls, invasion of left etmoid, left sphenoid sinus, left orbit - with destruction of internal and external bone walls - zygomatic apophysis and inclusion of the intraorbital structures and left anterior sinus. There are no changes in the cerebral hemispheres, symmetric ventricular system

Modern treatment of a neoplasm should be considered as a therapeutic protocol (multimodal treatment) established by a complex team (surgeon, radiologist, oncologist, etc.) where each treatment method (chemotherapy, surgery, radiotherapy, hormone therapy, bone marrow transplantation) have to find their place based on various factors and their chronology [16-18].

From this point of view, chemotherapy can be:initial (induction), adjuvant (after RT and surgery), neoadjuvant (preoperative), regional, palliative.

Studies have been conducted on intra-arterial chemotherapy by Japanese investigators who have catheterized the superficial temporal artery by administering Cisplatin and Bleomycin along with surgery and radiotherapy. This approach minimizes the toxic effects on surrounding healthy tissues.

Thus, a response rate of 23% was obtained in those who received chemotherapy alone. If radiotherapy and surgery were added, the response rate was 63%, in 61% of cases.

In our study, chemotherapy was used in 13 cases (9%), always in combination with surgery andexternal radiotherapy as 4 ABVD cycles: Adriamicin 25mg / m^2; Bleomycin 10mg / m^2; Vinblastine 6mg / m^2; Dacarbazine 375mg / m^2 or in combination with VPDVinblastine 25mg / m^2; Doxorubicin 300mg / m^2 or Cisplatin and 5-Fluorouracil (4 cycles) followed by Cisplatin and Gemzar with RC (another 6 cycles) if the patient tolerates therapy.

In the case of the study group, chemotherapy was reserved for very sensitive anatomopathological varieties, giant tumours that go beyond surgical limits and tumour recurrences.

One aspect worth noting is the succession of chemotherapy and radiotherapy. In the past years oncologists opted for initial radiotherapy followed by surgery and then chemotherapy, but histology studies dismantled this theory demonstrating that after radiotherapy the fibrosis of irradiated tissues with local hypoperfusion, do not allow chemotherapy drugs to penetratethe remaining tumour tissue [19-22].

Thus, modern protocols of multimodality therapy recommend the use of radiotherapy only after exhaustion of chemotherapy and surgical treatment.

As we can see from our statistics there is a difference between the patients treated in the first 7 years of the interval and those in the last 7 years, from the point of view of the survival rate.

The comparative analysis of the survival rate over the first 7 years of the study with the survival rate calculated for the last 7 years of the study and according to the tumour stage leads to the conclusion that in the last seven the survival rate of patients has increased significantly. This increase in survival rate is also noticeable for advanced tumour stages.

We synthesized a set of aspects that we believe should be taken into account in establishing the therapeutic course: an anaplastic tumour in a young patient will not be surgically treated, most often resulting in the patient's mutilation with large incisions of facial parts; if we are dealing with an aggressive tumour variety, then an aggressive radiotherapy and chemotherapy protocol should be applied, which will ultimately result in major disfigurement of the patient; the case must always be discussed with the anatomopathologist. Nowhere, in the head and neck, there is such a large variety of malignant tumors with an equally wide variety of therapeutic possibilities.Lately, a new technique has emerged in rhinology - craniofacial resection. From all published studies, it emerges that unimodal treatment (radiotherapy or single surgery) yields far worse results than their combined use. There is no conclusive evidence that radiotherapy is more appropriate pre or postoperatively, and therefore we believe that the decision should be made after consulting the radiotherapist in the team.All cases should be discussed before surgery and with the dental technician, as there are often cases when, moreover, paradoxically, a larger incision will create better support for the prosthesis to be applied.Eye management in rinosinusal tumours treatment has always raised difficulties, it is widely recognized that a conservative orbital approach is incorrect but on the other hand it is very difficult to remove the content of an almost normal orbit [23-26].

Our study shows that in advanced cases a non-curative excision is indicated because the patient is more likely to have a more comfortable life in the last period of his life. It is important, therefore, to recognize the exceptional cases where palliative radiotherapy is more appropriate.

The surgical approach of a rhinosinusal neoplasm is based on histology, dimensions, and location relative to orbit, skull base, and internal carotid artery. Anatomo-pathological examination, whether determined by biopsy, cytology of sinus aspirated or intraoperative, establishes the diagnosis.The clinical examination determines cranial

nerve invasion, orbital and extrasinusal dissemination (trismus, palatal ulceration, etc.) [27-29]. Prior to the emergence of the cranio-facial resection technique, it was almost impossible to resect a tumor in oncological limits, a tumor that invaded the posterior etmoid and the cribriform lamina, and often due to the proximity of the tumor to the orbit, the eyeball was unjustifiably sacrificed. Therefore, it is absolutely essential that the modern imaging technique (CT, MRI) be used to fully appreciate the tumor.

Conclusions

Rinosinusal tumours show particular elements of severity through late diagnosis due to lack of symptomatology, thus limiting the therapeutic means and their curative potential.In order to ensure a correct and complete treatment of this disease, an interdisciplinary collaboration between the ENT surgeon, ophthalmologist, neurosurgeon, imagist, oncotherapist, anatomopathologist, OMF surgeon both preoperatively in the setting of a therapeutic and postoperative strategy is absolutely necessary.Surgery has its well-established place in multimodality complex treatment whether it is curative or palliative. Radiotherapy in recent years tends to be used postoperatively to sterilize the preoperative tumour location or palliative preoperatively. The role of chemotherapy is not well established although there are studies that, in some anatomo-pathological forms, demonstrate an increase in survival rates in patients receiving initial induction chemotherapy.

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