■ REVIEW ARTICLE

Revision of Carcinomas in Paranasal Sinus

Juan Ramón Gras Cabrerizo,[a] Adolfo Sarandeses García,[b] Joan Ramon Montserrat i Gili,[a] and César Orús Dotú[a]
aServicio de Otorrinolaringología, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain
bServicio de Otorrinolaringología, Complejo Hospitalario Juan Canalejo, A Coruña, Spain

The annual incidence rate for paranasal sinus cancer is quite low in Europe at approximately 1 case a year per 100 000 inhabitants. The most frequent site is the maxillary sinus; in some countries such as Spain, however, carcinomas of the ethmoidal sinus complex are more prevalent. Squamous cell carcinoma is the most frequent histological type and adenocarcinoma is the one with the best prognosis.
In general terms, the association of surgery and radiotherapy continues to be the optimal therapeutic option. The inclusion of an endoscopic endonasal approach for the treatment of these lesions must be considered in very selective cases. Most authors currently accept invasion of the fat and muscles of the orbital apex and infiltration of the conjunctiva and/or sclera as an absolute indication for orbital exenteration. Lymph node involvement at diagnosis or in the course of the disease is infrequent, so prophylactic lymph node treatment would therefore not be indicated.

Key words: Carcinoma. Adenocarcinoma. Paranasal sinuses. Endoscopic surgery. Craniofacial resection. Radiotherapy. Chemotherapy.

Revisión de los carcinomas de senos paranasales
Los carcinomas de senos paranasales presentan una incidencia baja, aproximadamente un caso al año cada 100.000 habitantes entre la población europea. La localización más frecuente es el seno maxilar, aunque en algunos países como España los carcinomas de etmoides son el grupo más numeroso. El tipo histológico más frecuente es el carcinoma escamoso, y el adenocarcinoma es la variante histológica con mejor pronóstico.
En términos generales, la combinación de cirugía y radioterapia sigue siendo la modalidad terapéutica óptima. La inclusión del abordaje endonasal endoscópico en el tratamiento de estas lesiones debe considerarse en casos muy seleccionados. Actualmente, la mayoría de los autores acepta como indicaciones para llevar a cabo una exenteración orbitaria la invasión de la grasa, la musculatura y el ápex orbitario y la infiltración de la conjuntiva y/o esclerótica. La afección ganglionar en el momento del diagnóstico o durante el curso de la enfermedad es poco frecuente, lo que justificaría no tratar las cadenas ganglionares de manera profiláctica.

Palabras clave: Carcinoma. Adenocarcinoma. Senos paranasales. Cirugía endoscópica. Resección craneofacial. Radioterapia. Quimioterapia.

INTRODUCTION

Malignant tumours of the paranasal fossae and sinuses are lesions with characteristics distinguishing them from other head and neck tumours. They are infrequent, present wide histological variability, and are generally already at advanced stages at the moment of their diagnosis. All of this hinders the comparison of results and the ability to establish standardized treatment protocols.

The goal of the present study is to review the most innovative aspects with regard to the main epidemiological and aetiological characteristics of these tumours, analyze the prognosis of patients according to localization and histological type, and finally assess the different therapeutic modalities and treatment outcomes.

The review covers the most outstanding series published in the last 20 years by a search of Pub-Mediterranean using the following key words: carcinoma, adenocarcinoma, paranasal sinus, endoscopic surgery, craniofacial resection, radiotherapy, and chemotherapy, in order to obtain an up-to-date document for the management of these lesions.

The histological types included have been solely those accepted by the current classification of malignant tumours according to the International Union Against Cancer (UICC)[1]: squamous carcinoma, adenocarcinoma, adenoid cystic carcinoma, and sinonasal undifferentiated carcinoma. Furthermore, following this classification system, maxillary and ethmoidal localizations have been included. Carcinomas of the frontal and sphenoid sinuses are very infrequent and are not reflected in the TNM system. Carcinomas of the nasal vestibule have in their turn been omitted as the behaviour of these tumours is closer to that of skin tumours than to

The authors have not indicated any conflict of interest.

Correspondence: Dr. J.R. Gras Cabrerizo.
Servicio de Otorrinolaringología.
Hospital de la Santa Creu i Sant Pau.
Avda. Mas Casanovas, 90. 08041 Barcelona. España.
E-mail: jgras@hsp.santpau.es

Received April 18, 2007.
Accepted for publication April 26, 2007.

carcinomas of paranasal sinuses. All the series cited comprise carcinomas or, if not exclusively, these represented over 70% of the histologies. In some sections, data have been included from an epidemiological survey carried out in hospital centres in Spain which provided their results.

EPIDEMIOLOGY

Malignant tumours of the paranasal fossae and sinuses are infrequent, with an approximate incidence of 0.8-1 cases/100 000 inh/year among males and 0.4/100 000 inh/year among the female population.[2-4] In some Asian countries such as Japan, higher incidences have been reported (2.6/100 000 inh/year).[5]

These tumours represent 0.2%-0.8% of all malignant tumours in the body and 3%-6% of head and neck tumours.[6,7]

Most are of epithelial origin and between 57% and 68% of them are squamous, undifferentiated, or glandular carcinomas.[4,6,8,9]

Age on presentation is normally in the sixth or seventh decade of life, and there is a notable predominance of males, with a ratio of approximately 2-4:18-11. This proportion is lower than in the rest of head and neck tumours, which is probably due to the fact that the classic risk factors of tobacco and alcohol (more frequent in males) do not have such a high carcinogenic potential in the paranasal sinuses as occurs with carcinomas of the larynx, oropharynx or hypopharynx, where the male predominance is >90%.[12,13]

AETIOLOGY

The aetiopathogenic mechanism of rhinosinusal cancer is not precisely known. Different environmental carcinogens, viruses, and physical agents have been described as potentially implicated, as has the relationship between several histological types and prolonged exposure to different substances in the workplace.[14,15]

The consumption of tobacco and alcohol[16,17] has been linked to sinonasal carcinomas, although it does not present such an evident epidemiological link as in other malignant head and neck tumours.

According to a recent study, in 40% of sinonasal tumours there is a relationship with exposure to different occupational factors among the male population of Europe.[16]

For more than 30 years, there has been good documentation on the close relationship between prolonged exposure to sawdust or tanned hides and the development of a sinonasal carcinoma, particularly adenocarcinoma.[18]

Workers exposed to dust particles from hardwoods (oak and beech) are linked with adenocarcinoma, whereas squamous carcinoma is associated with prolonged exposure to particles from softer woods (fir and pine).[19-25]

This close link has led to this being considered a professional disease in some countries.[19]

In a recent case-control study[15] conducted in various countries, other substances were identified as potentially implicated in the genesis of these tumours. Specifically, evidence was found of a greater risk of the appearance of an adenocarcinoma among patients exposed to formaldehyde, textile dust or silica over a long time. Similarly, an increase in the risk of squamous carcinoma was seen with prolonged exposure to asbestos.

Several viral agents have been implicated in the aetiology of these tumours. Human papilloma viruses (HPV), basically types 16 and 18 and also, to a lesser extent, 6 and 11, have been isolated in different sinonasal carcinomas. Attempts have been made to show the involvement of HPV in the aetiology of these tumours through two main research lines: the demonstration of the malignant transformation of the inverted papilloma (associated with HPV) and the detection of HPV DNA in carcinomas using different techniques.

In general, the percentage of malignization of inverted papillomas, according to various series, is below 5% and the percentage of infection by HPV in sinonasal carcinomas is low, around 20%.[26] Kashima et al[27] detected a single case of HPV-18 infection in 24 squamous carcinomas analyzed and Hoffman et al[28] only isolated HPV-16 in 4 out of 20 patients with squamous carcinomas.

Epstein-Barr virus (EBV) presents a major association with nasopharyngeal undifferentiated carcinoma, but its presence in sinonasal carcinomas is anecdotal.

Hwang et al[29] proved the presence of EBV in only 2 out of 31 patients with sinusal carcinomas, whereas it was present in 100% of the biopsies from nasopharyngeal carcinomas. For all these reasons, viruses may be an aetiological factor but it is not possible to confirm this theory on the basis of current knowledge.

Advances in molecular biology are helping in the accumulation of ever better knowledge with respect to carcinogenesis and the prognosis for these lesions.

Gallo et al[30] described a relationship between the expression of oncoprotein c-erbB-2 and a worse prognosis in patients with an intestinal-type adenocarcinoma, who showed a higher number of loco-regional relapses and remote metastases.

The mutation of the gene encoding for protein p53 is one of those most studied in head and neck carcinomas. This protein plays a part in the control of the repair mechanisms for genetic material and mutations are found in 44% of intestinal-type adenocarcinomas,[31] in 43% of undifferentiated carcinomas,[32] and in 60% of carcinomas in general (squamous and adenocarcinomas).[33]

Mutated tumoural cells that do not express p53 may have an altered response to different treatments.

In a series of 30 intestinal-type adenocarcinomas, Licitra et al[34] showed that patients with mutated p53 had worse percentages in their response to chemotherapy. Investigation is currently on-going in the field of genetics. If there is any therapeutic mode that might improve the prognosis for these patients in the future, there can be no doubt that it is gene therapy.

HISTOLOGY

Squamous carcinoma is the most frequent histological type in both the maxillary and in the ethmoidal sinuses,

Table I. Distribution in Spain of Ethmoidal and Maxillary Sinonasal Carcinoma by Histology

Hospital	*Carcinomas*	*Squamous*	*Adenocarcinoma*	*Cystic Adenoid*	*Undifferentiated*
H. Juan Canalejo, A Coruña	60	35	16	4	5
H. Ramón and Cajal, Madrid	40	20	9	7	4
H.U. del Río Hortega, Valladolid	44	31	7	1	5
H. General de Alicante	28	19	2	3	4
H. Gregorio Marañón, Madrid	29	25	3	0	1
H. de Sant Pau, Barcelona	45	26	11	3	5

although it must be remembered that adenocarcinoma is practically exclusive to the ethmoidal complex.[6,10,35-38] Table 1 illustrates the distribution by histologies in a variety of Spanish hospital centres.

In general, 5-year survival for all carcinomas taken together, with different stagings and treatment regimes, is around 40%-50% in the most up-to-date series.[4,6,39-41] Many authors feel that the histological type is an important prognostic factor, as they obtain better results in patients presenting adenocarcinoma than in patients affected by a squamous carcinoma. Both of these histological types presented, in turn, better results than patients diagnosed as having sinonasal undifferentiated carcinoma, without doubt the histological type with the worst prognosis.

Dulguerov et al[6] reported specific 5-year survival rates of 78% with adenocarcinomas, 60% with squamous carcinomas and 40% with undifferentiated carcinomas in a series of 220 carcinomas.

Patients with a squamous carcinoma or an undifferentiated carcinoma presented a higher number of loco-regional and remote relapses than patients with other histologies, in a multi-variable analysis carried out by Hoppe et al.[42]

It is necessary to analyze these results with caution, as they may be influenced by several prognostic factors such as the size of the tumour, its location and the treatment used. The better therapeutic outcomes recorded with adenocarcinomas can probably be explained by their more favourable distribution in category T with respect to the rest of the histologies. The early diagnosis of these carcinomas, which is not a common occurrence, is more frequent in the ethmoidal sinus than in the case of maxillary sinus.

Twenty per cent of the carcinomas in the maxillary sinus were diagnosed in their initial stages (T1-T2) in the series by Dulguerov et al,[6] whereas 48% of the nasoethmoidal carcinomas (excluding the vestibule) were diagnosed in the same early stages. In a recent epidemiological[9] study recruiting 46 carcinomas of the paranasal sinuses, only 1 patient was diagnosed as having an early-stage carcinoma in the maxillary sinus. On the other hand, 10 patients with an ethmoidal carcinoma were classified as T2 at the moment of their diagnosis.

Nonetheless, studies performed only in the ethmoidal complex continue to show differences in tumoural histology. Cantu et al[43] reviewed 91 patients with malignant tumours of the ethmoidal sinus and found those presenting with adenocarcinomas to follow the best course. Uchida et al[44] published worse outcomes in patients with a squamous or undifferentiated carcinoma of the ethmoidal sinus than those presenting adenocarcinomas or adenoid cystic carcinoma.

Adenocarcinoma can be considered the histological type with the best prognosis among the various carcinomas of the paranasal sinuses despite the possible influence of different factors in the analysis of these results.

Adenoid cystic carcinoma tends to be located most in the maxillary sinus and characteristically presents slow growth, with the ability to progress perineurally and a considerable rate of relapse and metastases many years after the first treatment. There are excellent survival results in the early years of follow-up,[45] similar to those in squamous carcinoma in follow-up periods in excess of 5-10 years.[46] On many occasions, these are not true relapses but rather tumoural persistence that, due the slow evolution and growth along the nerve sheathes, is only diagnosed several years after the initial treatment. There are 3 histological sub-types: tubular, sieve-like (the most frequent), and solid. This last sub-type is the least frequent but the one with the greatest perineural involvement and, therefore, the worst prognosis.[47]

Frierson et al[48] and Levine et al[49] described in 1986 sinonasal undifferentiated carcinoma including a series of pathology characteristics that differentiated these from other poorly differentiated tumours (neuroendocrine carcinoma, stesioneuroblastoma, small-cell carcinoma).

This type of tumour is characterized by locally aggressive behaviour and fast growth, severe involvement of the ganglia at the moment of the diagnosis in comparison with the other histologies (10%-30%) and remote metastases in 25%-30% of cases. All these features make it the carcinoma with the worst prognosis.[50]

LOCATION

The maxillary sinus is the most frequent location for most authors.[6,9,36-38,40,46] However, in some European countries such as France,[51,52] this difference diminishes and is even turned around. In the sample of Spanish hospitals who provided data this trend is seen to be more evenly distributed over both locations (Table 2).

This is a datum that has no clear epidemiological explanation and is probably a problem of bias in the selection

Table 2. Distribution of Ethmoidal and Maxillary Carcinomas in Spain

Hospital	*Year*	*Ethmoidal*	*Maxillary*	*Total*
H. Juan Canalejo, A Coruña	1990-2006	39	21	60
H.U. del Río Hortega, Valladolid	1972-2006	23	21	44
H. General, Alicante	1975-2006	15	13	28
H. Gregorio Marañón, Madrid	1990-2004	7	27	34*
H. de Sant Pau, Barcelona	1984-2006	30	15	45

*Number of carcinomas =29.

Table III. Treatment Outcomes by Location

Authors	*n*	*Years*	*Location*	*Survival*
Jiang et al[56]	34	1969-1993	Ethmoidal	63%*
Cantu et al[43]	91	1987-1994	Ethmoidal	47%†
Tiwari et al[57]	50		Ethmoidal	63%†
Bhattacharyya et al[58]	180	1988-1998	Ethmoidal	40%†
Claus et al[59]	47	1985-2001	Ethmoidal	60%†
Stoll et al[60]	76	1975-2000	Ethmoidal	80%†
Lietin et al[61]	60	1985-2005	Ethmoidal	47%†
St. Pierre et al[62]	66	1983	Maxillary	27%*
Jiang et al[63]	73	1969-1985	Maxillary	51%‡
Waldron et al[64]	110	1976-1993	Maxillary	43%*
Paulino et al[65]	48	1969-1995	Maxillary	42%‡
Lee et al[66]	97	1959-1996	Maxillary	34%†
Qureshi et al[67]	62	1994-1999	Maxillary	35%†

*Specific. †Total. ‡Disease-free according to TNM.

of patients according to the different countries or regions considered.

The survival outcomes for tumours located in the ethmoidal complex are slightly higher than those obtained in the maxillary sinus in most of the series published. the specific 5-year survival was 45% with maxillary carcinomas versus 51% with carcinomas located in the ethmoidal area in a meta-analysis carried out in the nineteen-nineties.[6]

Five year survival with ethmoidal carcinomas varies with some exceptions in general between 40% and 60%, whereas those with maxillary sinus involvement is a little lower, at 30%-50%. Table 3 shows the 5-year survival values in the most recent series by ethmoidal or maxillary location.[43,56-67]

The percentages of survival in the maxillary sinus have not seen any notable improvement in the last few decades.

The same is not the case in the ethmoidal sinus, where the approach via craniofacial resection has enabled treatment of ethmoidal carcinomas that were considered non-resectable years ago. O´Malley et al[53] reported that there has been an increase of 20% in the survival values over the last few decades in the treatment of carcinomas and sarcomas of the paranasal sinuses. This increase is attributable to the developments in surgery of the skull base.

Over a period of 10 years, Howard´s group[54,55] studied the treatment of different malignant tumours of the paranasal sinuses involving the skull base, namely carcinomas located in the ethmoid in over half of the cases. That study found an increase of 15% in the loco-regional survival values.

Therefore, craniofacial resection has allowed a substantial improvement in the prognosis for these tumours, basically those located in the nasoethmoidal complex.

STAGING

The first attempt as classification of these tumours is from 1906, when Sebileau[68] divided the facial mass into 3 segments (superstructure, mesostructure, and infrastructure) and observed a worse prognosis as the tumour reached a higher structure.

Ohgren[69] classified the tumours of the maxillary sinus in 1933 based on a line running between the internal edge of the eye and the angle jaw. Tumours located anterior to this line corresponded to a better prognosis than those located posteriorly. The first time the location of "paranasal sinuses" (specifically the maxillary sinus) appeared in a universally

accepted classification is the fourth edition of the TNM UICC (revised in 1982).[70]

The publication of the fifth edition[71] in 1997 redefined the location by reference to the maxillary sinus and the "ethmoidal sinus" location appears for the first time. The most outstanding contributions of the sixth edition[1] are the independent classifications for the nasal fossa and the ethmoidal complex and differentiation in 2 sub-groups of patients classified as T4: a first sub-group T4a, comprising locally advanced tumours and considered "respectable," and another sub-group T4b comprising locally advanced "non-resectable" tumours. This division allows the differentiation between a sample of patients with low survival (T4a), as corresponds to these advanced tumours, and a sub-group also included in this category T4, but with worse survival (T4b).

However, the classification of tumours in terms of their "resectability" is confusing in the latest edition. The concept of resectability is subjective and exposed to some controversy depending on the centre or the medical team dealing with the patient.

O´Sullivan et al[72] attempted to explain this concept by considering those included in group T4a (resectable) as "potentially curable" patients and those classified as T4b (non-resectable) as "doubtfully curable." Finally, incurable tumours (M1) would be classified as stage IVc according to these authors.

There can be no doubt that these definitions will improve in subsequent editions.

For the time being, it seems to us to be useful from a prognostic standpoint to sub-divide this very heterogeneous category T4 in 2 different populations.

Table 4 describes the main innovations included in the sixth edition of the TNM.

TREATMENT

It is currently difficult to achieve consensus on the optimal treatment of carcinomas in the paranasal sinuses for different reasons: the small number of patients; the wide histological variety, which has on occasions caused the published results to include multiple types; the anatomical complexity of the region, which hinders the precise definition of the site of origin and, as a result, the use of excessively general terms such as tumours of the nasal fossae or ethmoidal-maxillary tumours, and the recent changes introduced into the latest edition of TNM that do not facilitate the comparison of results with preceding series.

Table IV. Main Novelties in the Sixth Edition With Respect to the Fifth According to the TNM-UICC System

1. Inclusion of the nasal fossa location as independent of the ethmoidal complex. In its turn, the nasal fossa is divided into 4 sub-locations: septum, floor, vestibule, and lateral wall
2. Revision of the upper T categories of the ethmoidal complex. Carcinomas invading the medial wall and the floor of the eye socket are classified as T3. On the other hand, if they affect the anterior content or the apex of the socket, they will be considered as T4a and T4b respectively. There is also a specification of the involvement of the lamina cribosa as T3, whereas such an invasion in the maxillary sinus would represent T4a
3. Division of category T4 into T4a and T4b for both the maxillary sinus and the ethmoidal sinus

In general terms, the association of surgery and radiotherapy continues to be the optimal therapeutic modality. However, from the surgical standpoint, 2 conceptually different treatment lines have emerged in the last few years. One aims to apply wider external approaches, basically at skull base level, so as to achieve better control over the lesion, and the other is endoscopic surgery, less aggressive, with the advantage of minimal morbility and a better quality of life for patients, although only feasible in very select cases.

The surgical approach will depend on the location and extension of the tumour, the possibilities of reconstruction and the risks and morbility in each case.

External Approaches

The surgical procedure used in carcinomas of the maxillary sinus is maxillectomy. Various modalities have been described, which has created some confusion as there is no standardized nomenclature. Spiro et al[73] proposed the following distribution into 3 groups:

- Limited maxillectomy: resection of 1 wall of the maxillary sinus. In most cases, the wall involved is the medial wall, so in many cases we will be referring to this group as medial maxillectomies.
- Sub-total maxillectomy: resection of at least 2 walls of the maxillary sinus including always the inferior wall
- Total maxillectomy: resection of all the walls in the maxillary sinus. In most cases this approach will require exenteration of the eye socket.

In our experience, we prefer to use the following classification:

- Radical maxillectomy: exeresis of all bone walls of the maxillary sinus including the pterygoid apophyses and the contents of the pterygoid fossa, if any.
- Total maxillectomy: exeresis of all bone walls of the maxillary sinus with conservation of the pterygoid apophyses, the neurovascular package and musculature, through a posterior osteotomy at this level.
- Sub-total maxillectomy: despite the confusion that might be caused by the concept of sub-total, it seams reasonable to apply this manoeuvre to the resection of all bony walls except for the floor of the eye socket; it may be necessary from time to time to perform exeresis of the pterygoid apophyses or the neurovascular content of the pterygoid fossa.
- Any other manoeuvre may be described as a limited maxillectomy and the surgeon must specify which wall(s) to resect. It is customary to perform medial

maxillectomy with resection of the intersinonasal wall in ethmoidal tumours which do not extend to the mesostructure.

In tumours limited to 1 wall, in which a limited maxillectomy is performed, an external approach may be avoided and this procedure can be carried out through a sub-labial incision or an endonasal approach. In the rest of the cases, the access route will be a transfacial incision. A Weber-Ferguson incision is the standard incision allowing us to approach the medial wall and the palatodental plane as well as the ethmoids if necessary. Should the carcinoma require an approach to the floor of the eye socket, the incision will be extended following the inferior palpebral sulcus, a manoeuvre habitually causing post-operative palpebral oedema. Should the approach be through the frontal sinus or exenteration of the socket be performed, this will be extended superiorly following the upper edge of the eye socket or the superior palpebral sulcus, respectively.

The technical difficulty in the approach to these tumours lies in the involvement of the posterior wall of the maxillary sinus and invasion of the pterigomaxillary fossa. In these cases a total maxillectomy may not be sufficient, with tumoural remains in the posterosuperior margin of the sinus; in these cases it is recommendable to perform a radical maxillectomy including the resection of the pterygoid apophysis and the pterygoid muscles. This approach may be combined with a lateral approach in order to obtain better visualization of the pterigomaxillary fossa and the infratemporal fossa. Generally, these lateral routes are used in the treatment of benign tumours. Classically, malignant lesions infiltrating this region were considered incurable, due to the extreme difficulty in obtaining oncologically safe margins and the high morbility and mortality associated with this surgical approach. Some centres currently treat malignant tumours affecting this region despite the high risk of local relapse. The number of patients treated is small to be able to make an evaluation of the results. On the other hand, the current edition of the TNM-UICC considers maxillary and ethmoidal carcinomas invading the infratemporal fossa or infiltrating the pterygoid apophysis as resectable and potentially curable lesions (T4a).[1]

These tumours may also be approached through midfacial degloving so as to allow a degree of exposure similar to that of transfacial approaches, with the possibility of carrying out bilateral surgery and the absence of scars caused by facial incisions, although all of this entails a slightly greater surgery time.

Degloving allows the nasomaxillary complex to be approached bilaterally, achieving a wide opening of the maxillary sinus, visualizing the pyriform opening, the septum, the anteroposterior ethmoid, the sphenoid, the cavum and even, in modified approaches, the anterior skull base.

In the case of cutaneous or orbital involvement, the use of this approach would not be useful. The most common complications are the anaesthesia or hypoaesthesia of the infraorbital nerve and stenosis of the nasal vestibule.

Most of the series uses this approach in the treatment of benign tumours, basically inverted papillomas and angiofibromas. Nonetheless, certain centres also use it in malignant tumours, albeit in highly selective cases.[74,75]

In ethmoidal carcinomas, the same transfacial incisions are used to approach the ethmoidal complex. Bearing in mind the considerable percentage of the ethmoidal carcinomas that invade the anterior skull base, approximately 40%,[76,77] craniofacial resection has become a fundamental element when there is infiltration of the lamina cribosa or the roof of the ethmoid.

The technique of choice in the context of craniofacial resection is Raveh´s subfrontal approach. Through a bicoronal incision that allows the anterior frontal diploe to be extracted together with the bony vault of the nasal pyramid, it is possible to access the nasal fossa, ethmoid, sphenoid and all of the skull base. Through this opening, good control is achieved over the tumoural lesion and the adjacent territories. It allows good repair of the structures at the skull base and minimizes the traction of the frontal lobe during the operation, all related with lower amounts of aesthetic impact. At the end of the operation, the frontonasal bony segment extracted previously is put back in place.

According to a recent multi-centric review[78] analyzing different histological types of malignant tumours, perioperative mortality was 4.7% with a complications rate of 36%. Infection of the surgical wound, fistulae of cerebrospinal fluid (CSF), meningitis, and pneumoencephalus were the most frequent. These complications mainly occurred in territories irradiated previously and in lesions affecting the dura mater and/or the contents of the brain.

Endoscopic Approach

The number of publications on the resection of malignant tumours using the endonasal endoscopic approach has increased greatly in recent years.[79-82]

Evidently, this provides patients with a lower surgical morbility and an improved post-operative quality of life than with external approaches. However, despite the excellent outcomes reported by some centres, similar on occasion to external approaches, we must be very cautious in the indications and in the selection of these patients.

Without a doubt, the greatest problem lies in the extreme difficulty in achieving *en bloc* resection with oncologically satisfactory margins. External approaches provide improved visualization and control of the operating field, with greater accessibility to the skull base, lachrymal route, frontal sinus, and eye socket.

Stammberger et al[83] understood that the involvement of the dura mater should not be considered a contraindication for the endoscopic approach and they effected resections of up to a maximum size of 1 cm^2 on the surface. Patients subjected to larger resections or with invasion of the brain´s contents are candidates for a craniofacial approach providing that the tumour is resectable.

The indication for this approach will in many cases depend on the centre and the surgeon´s expertise but it is usually applied to carcinomas of the nasoethmoidal complex without involvement of the lamina cribosa and the roof of the ethmoid

(T1-T2) and as palliative treatment for non-resectable tumours. It may be extended to larger carcinomas. Lund et al[82] performed resections of the bone at the level of the skull base, including the dura mater when the tumour was close to it, as well as resections of the periorbital area at the level of the orbital complex, with excellent oncological outcomes. They published 5-year disease-free survival rate of 72% in 15 adenocarcinomas (T1-T3) operated on with endoscopic control. We will however need longer series to be able to define clearly the absolute indications for this technique in the treatment of sinonasal carcinomas.

The locations which are generally assumed to be inaccessible for an endoscopic approach in the treatment of these carcinomas are[80,82]: the involvement of the frontal sinus, especially if the lateral and/or posterior wall is/are affected; the necessity of orbital exenteration; massive bilateral involvement, and the infiltration of soft tissues on the facial plane.

Some authors consider certain histological types, such as adenoid cystic carcinoma, as an unfavourable situation for performing an endoscopic approach due to perineural growth.[82]

Another important element that must be considered is the precarious nature of the sealing and the reconstruction of the skull base in the endonasal approach vis-à-vis transfacial approaches when the impairment is severe.

RADIOTHERAPY AND CHEMOTHERAPY

Practically all carcinomas receive radiotherapy as a complement to surgery due to the difficulty in performing *en bloc* extirpations and achieving safe resection margins due to the proximity of the eye socket and the anterior skull base, the results obtained with radiotherapy as the sole treatment manoeuvre are poor with some exceptions.[84,85] Most of the centres use radiotherapy as a post-surgical treatment, but it can also be used as a primary technique in order to reserve surgery as a salvage option. The published results are similar to those obtained with post-operative radiotherapy, albeit the difficulty is greater through having to work on an irradiated field.

Waldron et al[86] published specific 5-year survival percentages of 58% in 29 ethmoidal carcinomas using this therapeutic sequence. The same authors confirmed their good results in an extensive series of 110 carcinomas located in the maxillary, with a survival rate of 43%.[64]

Some authors[87] have used pre-operative radiotherapy as a useful therapeutic option for the conservation of the eye socket, by reducing the size of the tumour and, as in consequence, the extension of surgery.

The introduction of new radiotherapy techniques (stereotactic, hyperfractioned, intensity modulation) has allowed the irradiation of more complex areas with application of low doses to healthy surrounding tissues. These have improved the effects of radiotherapy for treating these tumours in combination with the other therapies.

Chemotherapy has traditionally been used as a palliative treatment. However there is some evidence, according to recent publications,[88] that the use of concomitant chemotherapy and radiotherapy in treatment protocols may improve the outcomes. It has been demonstrated that the use of chemoradiotherapy is better than neoadjuvant chemotherapy plus radiotherapy in the treatment of advanced carcinomas in different head and neck locations.[89]

Unfortunately, carcinomas of the paranasal sinuses in these meta-analyses represent a negligible percentage in order to be able to extrapolate the results to this location.

In smaller studies, Lee et al[90] showed excellent results in local control and survival with locally advanced carcinomas of the paranasal sinuses (mostly stage IV), treated with chemotherapy followed by surgery and concomitant post-operative chemotherapy, with 10-year survival rates of 56%. Samant et al[91] used radiochemotherapy as a curative therapy followed by surgery in 19 patients with different carcinomas of the paranasal sinuses, with a total 5-year survival over 50%. In some histologies such as sinonasal undifferentiated carcinoma, good response to chemotherapy has been shown to have promising results using induction chemotherapy followed by chemoradiotherapy in some series.[92]

It has also been shown that the use of induction chemotherapy reduces in high percentages the size of the tumour, limits surgery and achieves conservation of the contents of the eye socket. In this sense, Papadimitrakopoulou et al[40] obtained a 2-year disease-free survival rate of 61%, and preserved the contents of the eye socket in 88% of 23 carcinomas in advanced stages treated with intra-arterial cisplatin and intravenous paclitaxel-ifosfamide. In future, the publication of results with a larger number of patients may confirm these promising results with non-surgical therapies.

RESULTS BY TREATMENT APPLIED

The best results that have been published in both ethmoidal and maxillary cases are from series using surgical treatment associated with post-operative radiotherapy.

Tiwari et al[93] showed higher percentages of survival in the surgical group than in the group of patients treated with chemoradiotherapy on an intend-to-treat basis in 35 patients with carcinomas in the maxillary sinus (64% and 37%). Paulino et al[65] obtained better local control of the disease (59%) in the surgical group than in the group that received radiotherapy (23%) in 48 patients with carcinomas located in the maxillary area.

Lee et al compared 35 patients treated with radiotherapy and 61 patients treated with surgery plus post-surgical radiotherapy and obtained a 5-year survival rate of 0% in the first group and 38% in the second.

Similar conclusions were obtained by Lee et al[94] in a multivariable survival analysis in which they showed that the initial treatment is an important and independent prognostic factor in favour surgery plus radiotherapy (relative risk [RR], 0.52) with respect to radiotherapy as the only therapeutic manoeuvre.

Other studies[6,39] analyzed the role of the surgery as the sole treatment in the handling of these patients. They have

compared the results obtained in the use of surgical treatment against the rest of the therapeutic modalities and obtain better survival values with surgery, without any evidence of improved local control through the use of post-operative radiotherapy.[95]

All these results must be valued with caution, basically due to the considerable bias in patient selection. These publications do not randomly compare treatment groups but are retrospective studies in which, generally speaking, the tumours treated with surgery are tumours with better expectations of radicality than those which do not include surgical treatment in their therapeutic sequence. Patients treated solely with surgery without post-surgical radiotherapy mostly present lesions in the initial stages, and it is reasonable that they should obtain better outcomes than the rest.

In conclusion, treatment of carcinomas in paranasal sinuses should include surgical treatment in association with radiotherapy in a large majority of patients. Should any of these lesions be identified in early stages, particularly carcinomas classified as T1, it might be possible to assess the use of surgery as the sole therapy. Unfortunately, this is an infrequent situation in carcinomas of the paranasal sinuses.

MANAGEMENT OF THE EYE SOCKET

Involvement of the eye socket is a possibility in the course of ethmoidal carcinomas and maxillary carcinomas.

The percentage of orbital invasion is extremely variable depending on the different series, mainly because of the wide spectrum covered by the expression "orbital invasion," which ranges from the minimal erosion of the lamina papyracea to the involvement of the eye itself.

Ianneti et al[96] analyzed orbital invasion in a series of 29 malignant ethmoidal tumours. Of these, 82% had invasion of the eye socket; in 24% of cases, infiltrating only the medial wall and in the remaining 58%, invading the fat, muscle or orbital cone.

Carrau et al[97] found that 36% of squamous carcinomas located in the paranasal sinuses penetrates the bony plane with or without invasion of the anterior orbital content.

Blanch et al,[95] in a series of 125 malignant tumours, mostly carcinomas of the paranasal sinuses, observed 25% of orbital involvement at the moment of the diagnosis, and 7% had invasion of the eyeball. The indications for orbital exenteration have evolved notably in the last few decades. Most authors currently accept the following situations as absolute indications peforming exeresis: the involvement of orbital fat or muscle, the invasion of the orbital cone and the infiltration of the conjunctiva or the sclerotic vein.

More controversial is which surgical manoeuvre to use when the periorbital area is infiltrated. As with the dura mater at the skull base, the periorbital area is an effective barrier against invasion of the orbital content by the carcinoma. Nonetheless, Scott-McCary et al[87] showed that the orbital periosteum is not the last anatomical barrier, there is another thin fascia around the periocular fat other than the periorbital area. In their studies, they confirmed that, when this periocular fascia was not infiltrated, the conservation of the socket was justified despite the involvement of the periorbital area.

In 66 patients with sinonasal carcinomas, Imola et al[98] showed that the group of patients presenting infiltration of the periorbital area and whose orbital content was conserved did not have more recurrences than the group whose eye was subjected to exenteration due to involvement of the fat or muscle of the eye socket (30% and 33%); they only had 1% of non-functional eyes as a consequence of surgery or treatment with coadjuvant radiotherapy. Different authors have confirmed these results in their series.[97,99]

Despite the evident improvement in radiodiagnostic techniques, these are still limited when it comes to determining precisely if the carcinoma infiltrates the periorbital area or is merely in contact with it. This often entails a decision that needs to be taken in the operating room after intra-operative confirmation.

MANAGEMENT OF THE GANGLIA

The presence of adenopathies at the moment of diagnosis is low, between 2% and 12%,[6,9,93,100,101] and generally occurs in squamous carcinomas or undifferentiated carcinomas located in the maxillary sinus. Regional recurrence is also low and varies from 5% to 15%.[6,101-104]

Therefore, in view of these data, most centres do not perform prophylactic treatment of the gangliar chains. Nonetheless, in some series of patients with squamous or undifferentiated carcinomas of the maxillary sinus, clearly higher percentages have been published.[63,105] They report between 29% and 38% of gangliar relapses in untreated N0 patients and recommend, in consequence, prophylactic gangliar treatment, especially in certain circumstances such as involvement of the alveola, infiltration of soft tissues in the cheek or in histologically poorly differentiated tumours that invade the nasopharynx.[103]

Albeit infrequent, the appearance of gangliar involvement entails a considerable worsening of the prognosis.

Most series present loco-regional 5-year survival values of less than 15% if there is gangliar involvement at the moment of the diagnosis. In an analysis of 97 patients with carcinomas located in the maxillary area, Lee et al[100] detected a total 5-year survival rate of 40% in the group of patients with regional control versus 8% of the group with gangliar involvement at the moment of diagnosis or after a relapse involving the ganglia.

In conclusion, gangliar involvement at the moment of diagnosis or in the course of the disease is infrequent in the vast majority of the series published, thus justifying not treating gangliar chains prophylactically.

Acknowledgements

The authors would like to express their gratitude to the following institutions for their collaboration through providing epidemiological data: the Juan Canalejo Hospital in A Coruña, the Ramón y Cajal Hospital in Madrid, the del Río Hortega Hospital in Valladolid, the General Hospital in Alicante, and the Gregorio Marañón Hospital in Madrid.

REFERENCES

1. Sobin LH, Wittekind. TNM Classification of Malignant Tumours, 6th ed. New York: John Wiley & Sons; 2002.
2. Gotte K, Hormann K. Sinonasal malignancy: what´s new? ORL J Otorhinolaryngol Relat Spec. 2004;66:85-97.
3. Barbieri PG, Lombardi S, Candela A, Festa R, Miligi L. Epithelial nasosinusal cancer incidence and the role of work in 100 cases diagnosed in the Province of Brescia (northern Italy), in the period 1978-2002. Med Lav. 2005;96:42-51.
4. Svane-Knudsen V, Jorgensen KE, Hansen O, Lindgren A, Marker P. Cancer of the nasal cavity and paranasal sinuses: a series of 115 patients. Rhinology. 1998;36:12-4.
5. Muir CS, Nectoux J. Descriptive epidemiology of malignant neoplasms of nose, nasal cavities, middle ear and accessory sinuses. Clin Otolaryngol Allied Sci. 1980;5:195-211.
6. Dulguerov P, Jacobsen MS, Allal AS, Lehmann W, Calcaterra T. Nasal and paranasal sinus carcinoma: are we making progress? A series of 220 patients and a systematic review. Cancer. 2001;92:3012-29.
7. Osguthorpe JD. Sinus neoplasia. Arch Otolaryngol Head Neck Surg. 1994;120:19-25.
8. Porceddu S, Martin J, Shanker G, Weih L, Russell C, Rischin D, et al. Paranasal sinus tumors: Peter MacCallum Cancer Institute experience. Head Neck. 2004;26:322-30.
9. Gras Cabrerizo JR, Orus Dotu C, Montserrat Gili JR, Fabra Llopis JM, Leon Vintro X, de Juan Beltran J. Epidemiologic analysis of 72 carcinomas of the nasal cavity and paranasal sinuses. Acta Otorrinolaringol Esp. 2006;57:359-63.
10. Norlander T, Frodin JE, Silfversward C, Anggard A. Decreasing incidence of malignant tumors of the paranasal sinuses in Sweden. An analysis of 141 consecutive cases at Karolinska Hospital from 1960 to 1980. Ann Otol Rhinol Laryngol. 2003;112:236-41.
11. Alvarez I, Suarez C, Rodrigo JP, Nunez F, Caminero MJ. Prognostic factors in paranasal sinus cancer. J Otolaryngol. 1995;16:109-14.
12. Quer M, León X, Orús C, Recher K, Gras JR. Analysis of 2,500 squamous cell carcinomas of the head and neck. Acta Otorrinolaringol Esp. 2001;52: 201-5.
13. Hoffman HT, Karnell LH, Funk GF, Robinson RA, Menck HR. The National Cancer Data Base report on cancer of the head and neck. Arch Otolaryngol Head Neck Surg. 1998;124:951-62.
14. Holt GR. Sinonasal neoplasms and inhaled air toxics. Otolaryngol Head Neck Surg. 1994;111:12-4.
15. Luce D, Leclerc A, Begin D, Demers PA, Gerin M, Orlowski E, et al. Sinonasal cancer and occupational exposures: a pooled analysis of 12 case-control studies. Cancer Causes Control. 2002;13:147-57.
16. 't Mannetje A, Kogevinas M, Luce D, Demers PA, Begin D, Bolm-Audorff U, et al. Sinonasal cancer, occupation, and tobacco smoking in European women and men. Am J Ind Med. 1999;36:101-7.
17. Zheng W, McLaughlin JK, Chow WH, Chien HT, Blot WJ. Risk factors for cancers of the nasal cavity and paranasal sinuses among white men in the United States. Am J Epidemiol. 1993;138:965-72.
18. Acheson ED, Cowdell RH, Hadfield E, Macbeth RG. Nasal cancer in woodworkers in the furniture industry. Br Med J. 1968;2:587-96.
19. Wolf J, Schmezer P, Fengel D, Schroeder HG, Scheithauer H, Woeste P. The role of combination effects on the etiology of malignant nasal tumours in the wood-working industry. Acta Otolaryngol Suppl. 1998;535:1-16.
20. Demers PA, Kogevinas M, Boffetta P, Leclerc A, Luce D, Gerin M, et al. Wood dust and sino-nasal cancer: pooled reanalysis of twelve case-control studies. Am J Ind Med. 1995;28:151-66.
21. Vaughan TL, Davis S. Wood dust exposure and squamous cell cancers of the upper respiratory tract. Am J Epidemiol. 1991;133:560-4.
22. Voss R, Stenersen T, Roald Oppedal B, Boysen M. Sinonasal cancer and exposure to softwood. Acta Otolaryngol. 1985;99:172-8.
23. Viladot J, Alejo M, Droguet M, Garcia P, Esteller E, Leon J. Adenocarcinoma of the nose and paranasal sinuses. Presentation of 3 cases. Acta Otorrinolaringol Esp. 1990;41:405-8.
24. Morales Angulo C, Megia Lopez R, del Valle Zapico A, Acinas O, Rama J. Nasal sinus adenocarcinoma in patients exposed to wood dust in the Community of Cantabria, Spain. Acta Otorrinolaringol Esp. 1997;48:620-4.
25. Klintenberg C, Olofsson J, Hellquist H, Sokjer H. Adenocarcinoma of the ethmoid sinuses. A review of 28 cases with special reference to wood dust exposure. Cancer. 1984;54:482-8.
26. Syrjanen KJ. HPV infections in benign and malignant sinonasal lesions. J Clin Pathol. 2003;56:174-81.
27. Kashima HK, Kessis T, Hruban RH, Wu TC, Zinreich SJ, Shah KV. Human papillomavirus in sinonasal papillomas and squamous cell carcinoma. Laryngoscope. 1992;102:973-6.
28. Hoffmann M, Klose N, Gottschlich S, Gorogh T, Fazel A, Lohrey C, et al. Detection of human papillomavirus DNA in benign and malignant sinonasal neoplasms. Cancer Lett. 2006;239:64-70.
29. Hwang TZ, Jin YT, Tsai ST. EBER in situ hybridization differentiates carcinomas originating from the sinonasal region and the nasopharynx. Anticancer Res. 1998;18:4581-4.
30. Gallo O, Franchi A, Fini-Storchi I, Cilento G, Boddi V, Boccuzzi S, et al. Prognostic significance of c-erbB-2 oncoprotein expression in intestinal type adenocarcinoma of the sinonasal tract. Head Neck. 1998;20:224-31.
31. Perrone F, Oggionni M, Birindelli S, Suardi S, Tabano S, Romano R, et al. TP53, p14ARF, p16INK4a and H-ras gene molecular analysis in intestinal-type adenocarcinoma of the nasal cavity and paranasal sinuses. Int J Cancer. 2003;105:196-203.
32. Shinokuma A, Hirakawa N, Tamiya S, Oda Y, Komiyama S, Tsuneyoshi M. Evaluation of Epstein-Barr virus infection in sinonasal small round cell tumors. J Cancer Res Clin Oncol. 2000;126:12-8.
33. Fang SY, Yan JJ, Ohyama M. Immunohistochemistry of p53 in sinonasal inverted papilloma and associated squamous cell carcinoma. Am J Rhinol. 1998;12:119-24.
34. Licitra L, Suardi S, Bossi P, Locati LD, Mariani L, Quattrone P, et al. Prediction of TP53 status for primary cisplatin, fluorouracil, and leucovorin chemotherapy in ethmoid sinus intestinal-type adenocarcinoma. J Clin Oncol. 2004;22:4901-6.
35. Menaches Guardiola MI, Sancho Mestre M, Burgos Sanchez A, Gras Albert JR, Aranda I. Twenty years of retrospective study of malignant paranasal sinus tumors. Acta Otorrinolaringol Esp. 1998;49:289-92.
36. Myers LL, Nussenbaum B, Bradford CR, Teknos TN, Esclamado RM, Wolf GT. Paranasal sinus malignancies: an 18-year single institution experience. Laryngoscope. 2002;112:1964-9.
37. Tufano RP, Mokadam NA, Montone KT, Weinstein GS, Chalian AA, Wolf PF, et al. Malignant tumors of the nose and paranasal sinuses: hospital of the University of Pennsylvania experience 1990-1997. Am J Rhinol. 1999;13:117-23.
38. Grau C, Jakobsen MH, Harbo G, Svane-Knudsen V, Wedervang K, Larsen SK, et al. Sino-nasal cancer in Denmark 1982-1991–a nationwide survey. Acta Oncol. 2001;40:19-23.
39. Guntinas-Lichius O, Kreppel MP, Stuetzer H, Semrau R, Eckel HE, Mueller RP. Single modality and multimodality treatment of nasal and paranasal sinuses cancer: a single institution experience of 229 patients. Eur J Surg Oncol. 2007;33:222-8.
40. Papadimitrakopoulou VA, Ginsberg LE, Garden AS, Kies MS, Glisson BS, Diaz EM Jr, et al. Intraarterial cisplatin with intravenous paclitaxel and ifosfamide as an organ-preservation approach in patients with paranasal sinus carcinoma. Cancer. 2003;98:2214-23.
41. Sisson GA Sr, Toriumi DM, Atiyah RA. Paranasal sinus malignancy: a comprehensive update. Laryngoscope. 1989;99:143-50.
42. Hoppe BS, Stegman LD, Zelefsky MJ, Rosenzweig KE, Wolden SL, Patel SG, et al. Treatment of nasal cavity and paranasal sinus cancer with modern radiotherapy techniques in the postoperative setting – the MSKCC experience. Int J Radiat Oncol Biol Phys. 2007;67:691-702.
43. Cantu G, Solero CL, Mariani L, Salvatori P, Mattavelli F, Pizzi N, et al. Anterior craniofacial resection for malignant ethmoid tumors – a series of 91 patients. Head Neck. 1999;21:185-91.
44. Uchida D, Shirato H, Onimaru R, Endou H, Aoyama H, Tsuchiya K, et al. Long-term results of ethmoid squamous cell or undifferentiated carcinoma treated with radiotherapy with or without surgery. Cancer J. 2005;11: 152-6.
45. Harbo G, Grau C, Bundgaard T, Overgaard M, Elbrond O, Sogaard H, et al. Cancer of the nasal cavity and paranasal sinuses. A clinico-pathological study of 277 patients. Acta Oncol. 1997;36:45-50.
46. Waldron J, Witterick I. Paranasal Sinus Cancer: Caveats and Controversies. World J Surg. 2003;27:849-55.
47. Rhee CS, Won TB, Lee CH, Min YG, Sung MW, Kim KH, et al. Adenoid cystic carcinoma of the sinonasal tract: treatment results. Laryngoscope. 2006;116:982-6.
48. Frierson HF Jr, Mills SE, Fechner RE, Taxy JB, Levine PA. Sinonasal undifferentiated carcinoma. An aggressive neoplasm derived from schneiderian epithelium and distinct from olfactory neuroblastoma. Am J Surg Pathol. 1986;10:771-9.
49. Levine PA, Frierson HF Jr, Stewart FM, Mills SE, Fechner RE, Cantrell RW. Sinonasal undifferentiated carcinoma: a distinctive and highly aggressive neoplasm. Laryngoscope. 1987;97:905-8.
50. Mendenhall WM, Mendenhall CM, Riggs CE Jr, Villaret DB, Mendenhall NP. Sinonasal undifferentiated carcinoma. Am J Clin Oncol. 2006;29:27-31.
51. Knegt PP, de Jong PC, van Andel JG, de Boer MF, Eykenboom W, van der Schans E. Carcinoma of the paranasal sinuses. Results of a prospective pilot study. Cancer. 1985;56:57-62.
52. Simon C, Toussaint B, Coffinet L. Tumeurs malignes des cavités nasales et paranasales. Encyclopédie Med Chirur. 1997;405:A10.
53. O´Malley BW Jr, Janecka IP. Evolution of outcomes in cranial base surgery. Semin Surg Oncol. 1995;11:221-7.
54. Howard DJ, Lund VJ, Wei WI. Craniofacial resection for tumors of the nasal cavity and paranasal sinuses: a 25-year experience. Head Neck. 2006;28:867-73.
55. Lund VJ, Howard DJ, Wei WI, Cheesman AD. Craniofacial resection for tumors of the nasal cavity and paranasal sinuses–a 17-year experience. Head Neck. 1998;20:97-105.
56. Jiang GL, Morrison WH, Garden AS, Geara F, Callender D, Goepfert H, et al. Ethmoid sinus carcinomas: natural history and treatment results. Radiother Oncol. 1998;49:21-7.

57. Tiwari R, Hardillo JA, Tobi H, Mehta D, Karim AB, Snow G. Carcinoma of the ethmoid: results of treatment with conventional surgery and post-operative radiotherapy. Eur J Surg Oncol. 1999;25:401-5.
58. Bhattacharyya N. Factors predicting survival for cancer of the ethmoid sinus. Am J Rhinol. 2002;16:281-6.
59. Claus F, Boterberg T, Ost P, Huys J, Vermeersch H, Braems S, et al. Postoperative radiotherapy for adenocarcinoma of the ethmoid sinuses: treatment results for 47 patients. Int J Radiat Oncol Biol Phys. 2002;54:1089-94.
60. Stoll D, Bebear JP, Truilhe Y, Darrouzet V, David N. Ethmoid adenocarcinomas: retrospective study of 76 patients. Rev Laryngol Otol Rhinol (Bord). 2001;122:21-9.
61. Lietin B, Mom T, Avan P, Llompart X, Kemeny JL, Chazal J, et al. Adenocarcinomas of the ethmoid sinus: retrospective analysis of prognostic factors. Ann Otolaryngol Chir Cervicofac. 2006;123:211-20.
62. St-Pierre S, Baker SR. Squamous cell carcinoma of the maxillary sinus: analysis of 66 cases. Head Neck Surg. 1983;5:508-13.
63. Jiang GL, Ang KK, Peters LJ, Wendt CD, Oswald MJ, Goepfert H. Maxillary sinus carcinomas: natural history and results of postoperative radiotherapy. Radiother Oncol. 1991;21:193-200.
64. Waldron JN, O´Sullivan B, Gullane P, Witterick IJ, Liu FF, Payne D, et al. Carcinoma of the maxillary antrum: a retrospective analysis of 110 cases. Radiother Oncol. 2000;57:167-73.
65. Paulino AC, Marks JE, Bricker P, Melian E, Reddy SP, Emami B. Results of treatment of patients with maxillary sinus carcinoma. Cancer. 1998;83: 457-65.
66. Le QT, Fu KK, Kaplan M, Terris DJ, Fee WE, Goffinet DR. Treatment of maxillary sinus carcinoma: a comparison of the 1997 and 1977 American Joint Committee on cancer staging systems. Cancer. 1999;86:1700-11.
67. Qureshi SS, Chaukar DA, Talole SD, D´Cruz AK. Squamous cell carcinoma of the maxillary sinus: a Tata Memorial Hospital experience. Indian J Cancer. 2006;43:26-9.
68. Sebileau P. Les formes cliniques du cancer du sinus maxillaire. Ann Maladies d´Oreille Larynx Pharynx. 1906;32:430-50.
69. Spiessl B. TNW Atlas. 3rd ed. New York: Springer; 1992.
70. Hermanek P, Sobin LH, editores. TNM classification of malignant tumours, 4th ed [revised 1992]. New York: Springer-Verlag; 1987.
71. Sobin LH, Wittekind C, editors. TNM classification of malignant tumors, 5th ed. New York: Wiley-Liss; 1997.
72. O´Sullivan B, Shah J. New TNM staging criteria for head and neck tumors. Semin Surg Oncol. 2003;21:30-42.
73. Spiro RH, Strong EW, Shah JP. Maxillectomy and its classification. Head Neck. 1997;19:309-14.
74. Howard DJ, Lund VJ. The role of midfacial degloving in modern rhinological practice. J Laryngol Otol. 1999;113:885-7.
75. Eze NN, Wyatt ME, Bray D, Bailey CM, Hartley BE. The midfacial degloving approach to sinonasal tumours in children. Rhinology. 2006;44: 36-8.
76. Knegt PP, Ah-See KW, van der Velden LA, Kerrebijn J. Adenocarcinoma of the ethmoidal sinus complex: surgical debulking and topical fluorouracil may be the optimal treatment. Arch Otolaryngol Head Neck Surg. 2001;127:141-6.
77. Nuñez F, Suarez C, Alvarez I, Losa JL, Barthe P, Fresno M. Sino-nasal adenocarcinoma: epidemiological and clinico-pathological study of 34 cases. J Otolaryngol. 1993;22:86-90.
78. Ganly I, Patel SG, Singh B, Kraus DH, Bridger PG, Cantu G, et al. Complications of craniofacial resection for malignant tumors of the skull base: report of an International Collaborative Study. Head Neck. 2005;27: 445-51.
79. Roh HJ, Batra PS, Citardi MJ, Lee J, Bolger WE, Lanza DC. Endoscopic resection of sinonasal malignancies: a preliminary report. Am J Rhinol. 2004;18:239-46.
80. Shipchandler TZ, Batra PS, Citardi MJ, Bolger WE, Lanza DC. Outcomes for endoscopic resection of sinonasal squamous cell carcinoma. Laryngoscope. 2005;115:1983-7.
81. Castelnuovo PG, Belli E, Bignami M, Battaglia P, Sberze F, Tomei G. Endoscopic nasal and anterior craniotomy resection for malignant nasoethmoid tumors involving the anterior skull base. Skull Base. 2006;16:15-8.
82. Lund V, Howard DJ, Wei WI. Endoscopic resection of malignant tumors of the nose and sinuses. Am J Rhinol. 2007;21:89-94.
83. Stammberger H, Anderhuber W, Walch C, Papaefthymiou G. Possibilities and limitations of endoscopic management of nasal and paranasal sinus malignancies. Acta Otorhinolaryngol Belg. 1999;53:199-205.
84. Dulguerov P, Allal AS. Nasal and paranasal sinus carcinoma: how can we continue to make progress? Head Neck Surg. 2006;14:67-72.
85. Maghami E, Kraus DH. Cancer of the nasal cavity and paranasal sinuses. Expert Rev Anticancer Ther. 2004;4:411-24.
86. Waldron JN, O´Sullivan B, Warde P, Gullane P, Lui FF, Payne D, et al. Ethmoid sinus cancer: twenty-nine cases managed with primary radiation therapy. Int J Radiat Oncol Biol Phys. 1998;41:361-9.
87. McCary WS, Levine PA, Cantrell RW. Preservation of the eye in the treatment of sinonasal malignant neoplasms with orbital involvement. A confirmation of the original treatise. Arch Otolaryngol Head Neck Surg. 1996;122:657-9.
88. Bernier J, Pfister DG, Cooper JS. Adjuvant chemo-and radiotherapy for poor prognosis head and neck squamous cell carcinomas. Crit Rev Oncol Hematol. 2005;56:353-64.
89. Pignon JP, Bourhis J, Domenge C, Designe L. Chemotherapy added to locoregional treatment for head and neck squamous-cell carcinoma: three meta-analyses of updated individual data. MACH-NC Collaborative Group. Meta-Analysis of Chemotherapy on Head and Neck Cancer. Lancet. 2000;355:949-55.
90. Lee MM, Vokes EE, Rosen A, Witt ME, Weichselbaum RR, Haraf DJ. Multimodality therapy in advanced paranasal sinus carcinoma: superior long-term results. Cancer J Sci Am. 1999;5:219-23.
91. Samant S, Robbins KT, Vang M, Wan J, Robertson J. Intra-arterial cisplatin and concomitant radiation therapy followed by surgery for advanced paranasal sinus cancer. Arch Otolaryngol Head Neck Surg. 2004;130: 948-55.
92. Rischin D, Porceddu S, Peters L, Martin J, Corry J, Weih L. Promising results with chemoradiation in patients with sinonasal undifferentiated carcinoma. Head Neck. 2004;26:435-41.
93. Tiwari R, Hardillo JA, Mehta D, Slotman B, Tobi H, Croonenburg E, et al. Squamous cell carcinoma of maxillary sinus. Head Neck. 2000;22:164-9.
94. Lee F, Ogura JH. Maxillary sinus carcinoma. Laryngoscope. 1981;91:133-9.
95. Blanch JL, Ruiz AM, Alos L, Traserra-Coderch J, Bernal-Sprekelsen M. Treatment of 125 sinonasal tumors: prognostic factors, outcome, and follow-up. Otolaryngol Head Neck Surg. 2004;131:973-6.
96. Iannetti G, Valentini V, Rinna C, Ventucci E, Marianetti TM. Ethmoido-orbital tumors: our experience. Craniofac Surg. 2005;16:1085-91.
97. Carrau RL, Segas J, Nuss DW, Snyderman CH, Janecka IP, Myers EN, et al. Squamous cell carcinoma of the sinonasal tract invading the orbit. Laryngoscope. 1999;109:230-5.
98. Imola MJ, Schramm VL Jr. Orbital preservation in surgical management of sinonasal malignancy. Laryngoscope. 2002;112:1357-65.
99. Suárez C, Llorente JL, Fernandez de Leon R, Maseda E, Lopez A. Prognostic factors in sinonasal tumors involving the anterior skull base. Head Neck. 2004;26:136-44.
100. Le QT, Fu KK, Kaplan MJ, Terris DJ, Fee WE, Goffinet DR. Lymph node metastasis in maxillary sinus carcinoma. Int J Radiat Oncol Biol Phys. 2000;46:541-9.
101. Kim GE, Chung EJ, Lim JJ, Keum KC, Lee SW, Cho JH, et al. Clinical significance of neck node metastasis in squamous cell carcinoma of the maxillary antrum. Am J Otolaryngol. 1999;20:383-90.
102. Logue JP, Slevin NJ. Carcinoma of the nasal cavity and paranasal sinuses: an analysis of radical radiotherapy. Clin Oncol. 1991;3:84-9.
103. Katz TS, Mendenhall WM, Morris CG, Amdur RJ, Hinerman RW, Villaret DB. Malignant tumors of the nasal cavity and paranasal sinuses. Head Neck. 2002;24:821-9.
104. Giri SP, 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.
105. Paulino AC, Fisher SG, Marks JE. Is prophylactic neck irradiation indicated in patients with squamous cell carcinoma of the maxillary sinus? Int J Radiat Oncol Biol Phys. 1997;39:283-9.