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CANCER OF THE NASAL FOSSAE

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– 국문초록 –

Nasal fossae의 암이란 비강과 부비동들에서 발생하는 것으로서 환자를 가장 괴롭히며 또한 가장 믿을수 없는 악성종양들중의 하나이다. 비록 본 예수병원 암환자 등록부에 의하면 전 암환자의 2.2% 발생빈도로서 주요한 발생빈도를 보이지는 않지만, 이 부위의 암을 치유하는데는 세심하고 철저한 모든 진단적 검사와 과감한 외과 및 치료방사선의 병합치료가 요구된다. 저자들은 지난 22년간 비강 및 부비동(Nasal fossae) 에서 발생한 원발성 악성종양중 치유목적의 근치수술을 시행한 68 예를 임상고찰 하였다.

근치수술을 시행했던 68예중 91%에서 제 3 병기 또는 4 병기의 진행된 경우 이었다. 외과적 수술은 한예의 사골동 (篩骨洞) 종양적출술 및 부분上顎洞절제술 한예를 제외한 66예 모두에서 全上顎洞절제술 (total maxillectomy) 또는 확장 全上顎洞절제술 (extended total maxillectomy) 을 시행하였다.

저자들은 疫學的, 病理學的, 病期 및 치료, 재발율과 생존율들을 분석 고찰하였으며 3가지 치료형태를 서로 비교하였다. 즉 수술만 시행한 군, 수술전 방사선 치료 및 수술병합군, 수술과 수술후 방사선치료 병합 군으로 나눴다. 저자들의 예비적 (preliminary) 관찰 결과는 2 년간 무병생존율(disease-free 2-year survival)만을 볼때, 수술만 시행한 군에서 40%로써 통계학적으로는 가장 좋았으나 실제는 수술만 시행한 군에서는 단지 40%만이 제 4 病期의 진행된 경우였으나 수술전 방사선치료 또는 수술후 방사선 치료등의 병합치료에서는 제4 病期의 진행된 상태가 무려 60%나 되었다. 전체적인 재발율(Overall recurrence rate) 은 68.2%로써 무서울 정도로 높았으며 전체적인 2년 무병율은 23.7% 였다. 저자들은 이 분야에서 실패의 원인분석과 치료방법의 선택등에 대한 지침을 제시하고저 한다.

Cancer arising in the nasal fossae, that is, in the nasal cavity and paranasal sinuses, is one of the most treacherous malignant neoplasms to afflict human beings. Although not a major category (2.2% of all cancers in our registry), it demands thorough diagnostic evaluation and aggresive combined surgical and radiotherapeutic management. A review of 306 primary neoplasms arising in the nasal fossae during the past 22 years yielded 68 cases which underwent surgery with the intent to cure. Of these 68 cases, 91% were advanced Stage III or Stage IV tumors. In all but one case the surgical procedure involved maxillectomy which was total or extended total in 66 cases. This material is analyzed in terms of epidemiology, pathology, staging, management, recurrence rate and survival. Three methods of therapy employed are suitable for comparison: surgery alone; preoperative radiation followed by surgery; and surgery followed by postoperative radiation. A preliminary review indicates that the best results (40% disease-free 2-year survival) were obtained by surgery alone; however only 40% of patients in this management category had advanced Stage IV disease, whereas approximately 60% of those in the preoperative or postoperative combined therapy categories were Stage IV lesions. The recurrence rate overall was an appalling 68.2% and the overall survival at 2 years free of disease was 23.7%. An analysis of failure and guidelines for selection of the method of therapy are submitted.

Few diseases are as treacherous, painful, and stubborn as cancers of the nasal fossae, the complex mucosa-lined chambers that constitute the nasal cavity and paranasal sinuses. Although uncommon in Western countries, malignant nasal fossae tumors make up 2.2% of all cancers in Korea and are particularly prevalent among farming families in the Southwest where Presbyterian Medical Center is located.

This report is a candid account of our experience with 306 patients proved histologically to have new primary cancers of the nasal fossae from 1963 to 1984. Although the successful results are meager, we have gained information worth sharing in this difficult struggle during the past 22 years, during which period the policies of management have been modified both in terms of selection and of technic.

Table 1. Observed incidence AT PMC*

	Registered	Surgical Management
Ethmoid	2	0
Nasal Cavity	80	22
Maxillary Antrum	224	46
Total	306	68

*PMC= Presbyterian medical center, chonju, korea.

Table 2. Epidemiologic characteristics

A. Sex ratio	Male	Female	Ratio	
Ethmoid	1	-	-	
Nasal cavity	15	7	2.1 : 1	
Maxillary antrum	43	12	3.6 : 1	
B. Age incidence	Below 40	40–49	50–59	Over 60
Ethmoid	1	-	-	-
Nasal cavity	4	9	5	4
Maxillary antrum	8	13	14	10
C. Age range and median age		Range		Median
Nasal cavity		22–72		49
Maxillary antrum		30–70		50

Table. 3. Pathology of surgical cases

	Ethmoid	Nasal Cavity	Maxillary Antrum
Epidermoid	1	14	37
Transitional	—	—	2
Papillary	—	3	—
Adenoid cystic	—	4	1
Mucoepidermoid	—	—	1
Undifferentiated	—	1	2

INCIDENCE AND EPIDEMIOLOGY

Of the 306 cases registered, 224 or 73% were cancers arising in the maxillary antrum, while 80 or 26% arose in the nasal cavity. There were only two cancers whose primary site was in the ethmoid sinus, and none were found to have arisen in the frontal or sphenoid sinuses primarily. Of these 306 cases 68 were subjected to greater scrutiny because they underwent treatment with curative purpose. The male: female ratio was 2.6:1 overall, but the male preponderance was 3.6:1 in cancers of the maxillary antrum. There was no appreciable difference in the age range nor in the median age at presentation for the two principal categories(See Tables 1 and 2).

PATHOLOGY

By far the largest proportion of tumors arising in the nasal fossae are squamous cell(epidermoid) carcinomas, which comprised over 75% of this series. There were five adenoid cystic carcinomas, most of these in the nasal cavity and three papillary carcinomas, all in the nasal cavity(See Table 3).

DIAGNOSIS

In the early part of the 22-year period comprising this report our diagnostic methods were confined to clinical findings, conventional radiographs of the paranasal sinus areas and biopsy, either through the nostril or via a Caldwell-Luc approach. Ten years ago, as we sought to select patients for preoperative radiotherapy whose tumors extended to or near the margins of feasible resection, tomograms of the paranasal sinuses and maxillae became an important instrument for staging and treatment planning. In the past four years computerized tomography has virtually replaced the coventional tomogram, providing information of greater accuracy as to the extent of disease and as to the indications for preoperative irradiation.

In addition to the assessment of the extent of tumor in the primary site, examination of the lymphatics of the neck and standard preoperative work-up are carried out, including peripheral blood counts, chest x-rays, electrocardiograms, urinalysis and blood chemistries.

STAGING

The "Manual for Staging of Cancer" of the American Joint Committee on Cancer is employed with modifications to include the nasal cavity[1]. This modified TNM System is as follows:

- T_1 Tumor confined to the antral mucosa infrastructure or to a single site in the nasal cavity measuring 2 cm or less.
- T_2 Tumor confined to the suprastructure mucosa of antrum or to the infrastructure with destruction of medial or inferior bony walls only; or to a single site in the nasal cavity which measures 2-4 cm but without ethmoid, sphenoid or frontal invasion.
- T_3 More extensive tumor invading skin of cheek, orbit, anterior ethmoid sinuses, or pterygoid muscle; and in the case of nasal cavity tumors, not extending beyond the sphenoethmoidal recess nor invading the cribriform plate.
- T_4 Massive tumor with invasion of cribriform plate, posterior ethmoids, sphenoid, nasopharynx, pterygoid plates or base of skull.

The remainer of the AJC Staging System is

employed without Change.

MANAGEMENT POLICIES

Cancer arising in the sphenoid and frontal sinuses is fortunately rare. The ethmoid sinus is also an uncommon primary site but two cases were identified in this review. In this paper we will tabulate results of patients treated by surgery alone and by the combination of surgery and radiation, in which the radiotherapy was administered preperatively or postoperatively. However, this should not suggest that there was either random selection or historical grouping of patients into these three subsets for the purpose of comparison. In earlier years the decision as to resectability was essentially clinical, and was often made at the time of surgical exploration(bimanual palplation of the space between nasopharynx and pterygomaxillary fossa was found to provide a rough index as to the amount of tumor at the base of the skull). During recent years we have been able to make the decision as to resectability on the basis of tomography in most cases, thus, avoiding the possibility of retreating after embarking upon surgical resection. When the margins have been found to be inadequate, preoperative radiotherapy is employed. The specific indications we have employed are as follows:

a) Destruction of the pterygoid plates
b) Destruction of the orbital floor
c) Involvement of superior or posterior ethmoids
d) Extension to cribriform plate
e) Extension to sphenoethmoidal recess.

Surgery is planned for 5 weeks after a tumor dose of 5000 rads has been delivered, and 6 or more weeks after dosages of 6000 rads.

Postoperative radiation has been reserved for patients in which unexpectedly close or positive margins were found. If this situation occurs in a patient in which preoperative radiotherapy has not been employed, full course radiation will be prescribed. If, on the other hand, preoperative therapy had been employed, a Cesium 137 application to the point of concern is used.

Radiotherapy to primary site recurrences is nearly always a palliative excercise in our experience. On the other hand, metastasis to the neck may be amenable to radical neck dissection and metastasis to the parotid lymph node justifies parotidectomy.

Our experience with temporal artery cannulation for intraarterial chemotherapy infusion has been substantial but of limited value except as inductive chemotherapy combined with preoperative radiation. The internal maxillary artery which serves as the principal conduit for such regional chemotherapy is not distributed to the entire cancer-bearing area in most cases. The advent of multiagent chemotherapy protocols which include cisplatinum appear to offer a higher degree of reponse than single-agent programs.

TECHNIC OF MAXILLECTOMY

The basic procedure is a total maxillectomy, which may be extended in several ways as dictated by the anatomical extent of the lesion. Involvement of the nasal cavity requires that a nasal cavity exenteration be performed, removing the septum and the ethmoid sinuses as needed as far back as the nasopharynx and sphenoid sinus when necessary. Involvement of the zygoma requires its resection, laterally to the arch of the bone and including the inferior part of the lateral orbital wall if necessary. Invasion of the orbit floor does not automatically require orbit exenteration, but if orbit soft tissue is invaded the orbit contents must be removed. The anatomical scope of total maxillectomy and extended total maxillectomy are shown in Fig. 1 and 2.

A Weber-Fergusson incision is employed, marking the line of the canthal fold so that symmetrical repair of the eyelids may be accomplished later. The thickness of the cheek flap depends on whether anterior maxillary wall has been invaded; often a major part of the facial musculature must be sacrificed. The plane between the orbicularis oculi and the orbit fat must be followed in order

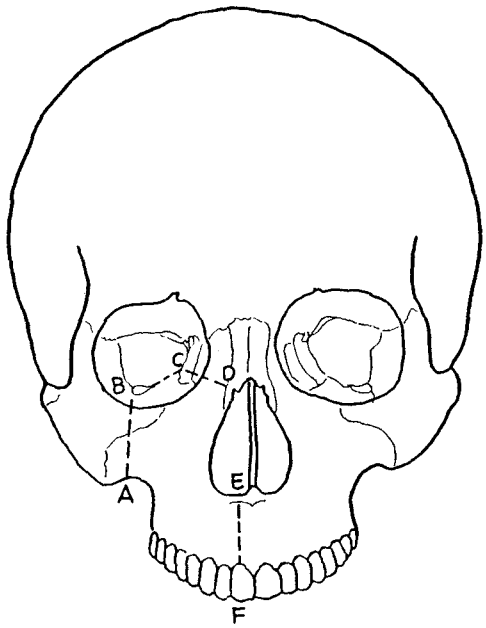

Fig. 1. Extent of resection in standard total maxillectomy. Point A : Undersuface of zygomatic arch. Point B : Inferior orbital fissure. Point C : Apex of maxillary bone forming orbital floor. Point D : Edge of nasal bone at the anterior nasal aperture. Point E : Nasal cavity floor at posterior edge of bony hard palate. Point F : Lower edge of maxilla at socket of extracted ipsilateral incisor. The procedure is accomplished by using a Gigli saw from A to B ; a fine osteotome from B to C ; Gigli saw from D to the lamina papyracea of the ethmoid bone and osteotome to the apex at C ; and Gigli saw around the posterior edge of hard palate and across the alveolar ridge, E to F.

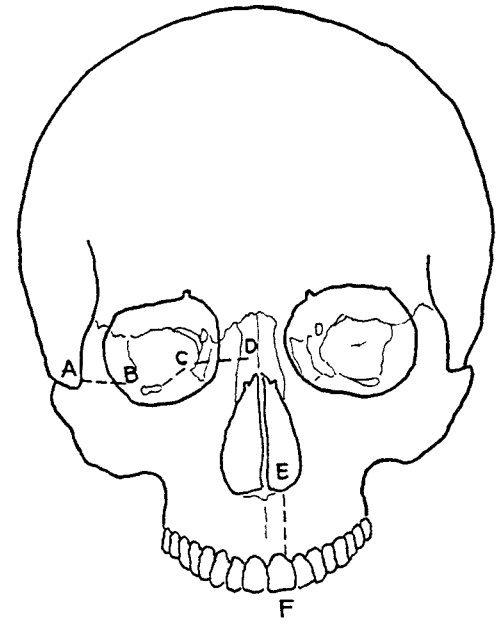

Fig. 2. Types of extended total maxillectomy. Point A : Lateral surface of the frontal process of the zygomatic bone. Point B: Inferior orbital fissure. Point C : Apex of maxillary bone forming orbital floor. Point D : Midline between nasal bones iust below level of frontal sinus (below cribriform plate). Point E : Contralateral nasal cavity floor at posterior edge of bony hard palate Point F : Lower edge of maxilla at socket of extracted contralateral incisor. Extended maxillectomies are of four types plus combinations thereof ; resection of zygoma with maxilla ; resection of lower haif of ethmoid with maxilla; resection of contralateral nasal cavity floor with maxilla, or even contralateral partial maxillectomy ; and orbit exenteration with maxillectomy. Procedures are accomplished using electric bone saw from A to B ; fine osteotome from B to C ; osteotome and electric saw from C to D ; and Gigli saw from E to F.

to preserve this muscle. The inferior oblique muscle of the eye is generally divided at its attachment and tagged for later repair, thus avoiding postoperative diplopia. The bony maxillary antrum should be removed as an intact box. In order to do this Gigli saws should be used as much as possible in that they do not collapse the box as will occur if chisels and osteotomes are used extensively. The first Gigli saw goes under the zygoma emerging in the lateral orbital fissure. The second goes through the upper reaches of the nasal cavity through ethmoid and emerges through the lamina papyracea of the Ethmoid bone; when ethmoid is involved we must generally use an electric or compressed air bone saw in order to obtain a rectangular cut sufficiently high in the medial orbital wall. The third Gigli saw is placed through the nasal cavity and emerges in the palate behind the bony hard palate; if the

Table 4. Management

	Ethmoid	Nasal cavity	Maxillary antrum
Preoperative radiation & surgery	-	8	19
Surgery alone	-	6	10
Surgery and post-operative radiation	1	8	16

Table 5. Stage of disease

	T_{2D}	T_3	T_4
Ethmoid	-	-	1
Nasal cavity	3	9	10
Maxillary antrum	3	14	28
All sites	6(9%)	23(34%)	39(57%)

Table 6. Surgical procedures employed

Transcranial resection of ethmoid tumor	1
Partial maxillectomy	1
Total maxillectomy	25
Extended total maxillectomy	22
Maxillectomy, nasal cavity exenteration	15
Maxillectomy, orbit exenteration	4
Total	68

situation demands, resection through the opposite nasal cavity floor may be required, but care must be taken to avoid injury to the nasotracheal intubation which is the patient's anesthesia lifeline. When all three Gigli saws have been placed, they are cut and rapid completion of the resection is carried out to minimize blood loss. The chisel is used on the pterygoid plates toward the pterygoid fissure, laterally. A find chisel or osteotome is used to complete the division of the orbit floor from the point of Gigli saw sections toward the apex of the maxilla, with care to avoid injury to the orbit contents which are retracted. At this point the maxilla can be pushed downward, and loosened, and the remaining soft tissue attachments are cut with heavy scissors. The internal maxillary artery will be divided at this point and must be secured. The specimen is checked for margins and frozen section of suspicious areas is

Table 7. Analysis by policy periods

Year	No Recurrence	2-yr NED Survival
1963-1968	18.2%	25 %
1969-1973	16.7%	16 %
1974-1978	43.5%	28 %
1979-1983	36.4%	33.3%

performed. After irrigation and glove and instrument change, repair is carried out with a split thickness skin graft to line the maxillary cavity. The inferior bolique muscle is repaired, suturing to available soft tissue medially. The skin graft is made into an envelope sutured at the buccal mucosa and packed tightly with gauze; care must be taken to prevent this graft from intruding between the orbicularis oculi and the orbit fat which can cause ectropion of the lower lid later. In repairing the cheek flap accurate approximation of the underlying musculature is essential for cosmetic repair and avoidance of fistulas.

RESULTS

Table 4 shows the treatment modalities employed in the 68 cases treated surgically with curative intent. In 67 cases maxillectomy was performed; in one case only was a transcranial resection of a tumor primary in the ethmoid attempted on the neurosurgical survice. It must be noted that 91% of these tumors were advanced lesions (Table 5). There were only 6 patients who could be classified as T_2 and there were no T_1 cases. This must be borne in mind in considering the rather poor survival results. Table 6 describes the various surgical techniques employed. The majority of the maxillextomies were extended procedures (61%) if nasal cavity exen-

teration and orbit exenteration are included.

Results are evaluated in terms or recurrence and survival (Table 7~11). Unfortunately, it is difficult in Korea to obtain long-term survival information despite strong efforts to communicate with our patients, and to follow them through Tumor Clinic. However, in as much as most cancers of the head and neck which recur will do so within two years, two-year survival data is useful. (An exception to this statement must be made for adenoid cystic carcinoma which has an indolent course.) Comparison of results by 5-year period shows mild improvement in the 1979-1983 period as compared with previous experience (Fig. 3).

As mentioned earlier, it is not the purpose of this paper to compare combined therapy with surgical resection alone; nor is it to compare preoperative with postoperative radiotherapy. The management policies in this paper have evolved over a period of time and many factors have changed along the way so that a meaningful statistical comparison is not possible. The recurrence rates are very high, 68.2% over all (Table 8). The lower recurrence rate when surgery alone was used relates to the fact that only 40% or patients who had surgery alone had Stage IV disease (Table 9). The poor results with preoperative radiation were reanalyzed due to the fact that many patients were treated in earlier years with inadequate doses of radiation. When all patients whose delivered radiotherapy dosage was

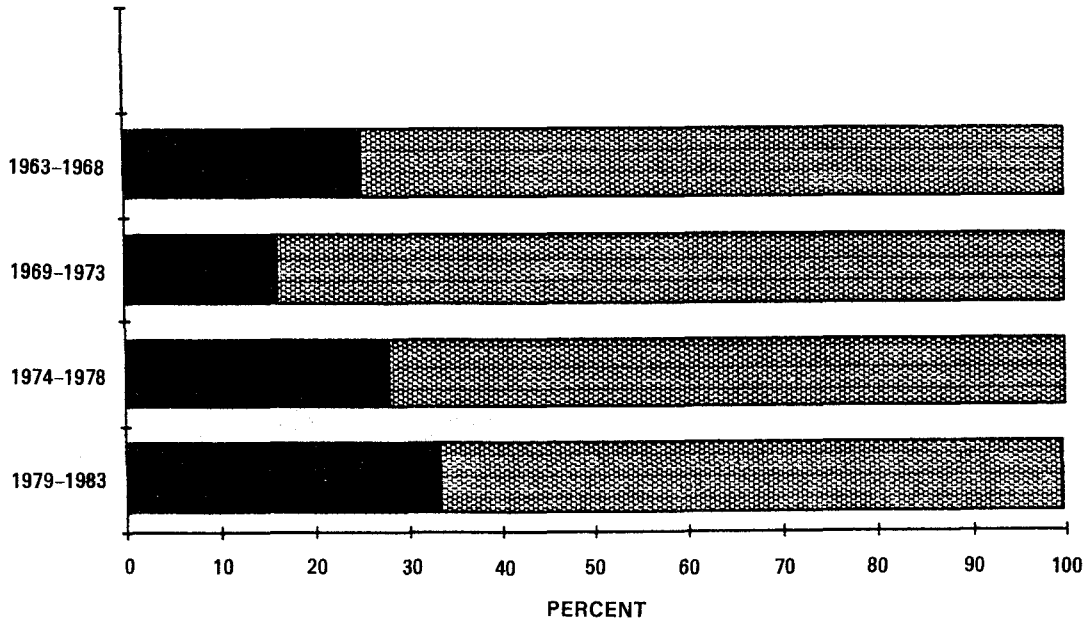

Fig. 3. 2-year ned survival analysis by policy periods.

Table 8. Recurrence rates according to treatment methods

	Nasal Cavity	Maxillary Antrum	Overall
Preoperative radiation	42.9 %	76.2 %	71.4 %
Surgery alone	50.0 %	70.0 %	62.5 %
Postoperative radiation	77.8 %	71.4 %	73.9 %
Recurrence rate for all methods	57.5 %	73.3%	68.2 %

Table 9. Analysis of treatment methods

	Recurrence rate	2-yr NED* Surval
Preoperative radiation	71.4 %	14.8 %
Surgery alone	67.5 %	40.0 %
Postoperative radiation	73.9 %	23.0 %
Overall	68.2 %	23.7 %

*NED=No evidence of disease

Table 10. Analysis of treatment adjusted for adequacy of radiation

	Recurrence rate	2-yr NED Survival
Preoperative radiation	60.0 %	33.3 %
Surgery alone	67.5 %	40.0 %
Postoperative radiation	70.1 %	29.4 %
Overall	65.5 %	33.3 %

less then 5000 rads tumor dose were excluded, the two-year disease-free survival for patients who received preoperative radiation followed by adequate surgery increased to 33.3% (Tabe 10). Elimination of T_4 lesions from the satistics would undoubtedly increase the survival rates further.

DISCUSSION

The importance of cancers of the nasal fossae in Korea relates to the relatively higher incidence than in Western countries. According to Batsakis these tumors comprise between 0.2% and 0.8% of all cancers in the United States. At our hospital it is 2.2% of all cases placed in the Cancer Registry, i. e., between 2.5 and 10 times the incidence in America. Batsakis states that "Perhaps more so that other neoplasms in the head and neck, cancers of the nose and paranasal sinuses present more unresolved problems for both surgeons and radiotherapists." He mentions three factors responsible for the poor prognosis:

1) the advanced stage of disease at time of diagnosis;
2) the complex anatomy of the region; and
3) the reluctance of surgeons to pursue aggressive treatment.

In our situation the third reason is not relevant but a more important factor is psychological acceptance, given the limited degree of patient cooperation for economic, cultural and educational reasons. Any complex form of therapy which extends over a period of months will be associated with a high drop-out rate in rural Korea.

Historically the first resection of the upper jaw was performed by Lizars[3] in 1826. In 1888 Parsons[3] reported destruction of a tumor of the sinuses by the use of the hot cautery, a method which was still employed during my surgical residence in the early 1950s. The advent of radiotherapy brought in various combined approaches to the problem; irradiation and electrosurgery; electrodessication and radium implantation; and radical surgery combined with orthovoltage.

Cooperation between surgeon and radiotherapist remains a central concept in attempting to reduce the lethal effects of tumors of nasal fossae today. Previously it was stated that whether preoperative radiation or postoperative radiation were employed the results were essentially similar. Previously it was also stated that invasion of the orbital floor required orbital exenteration. It is now being shows that preoperative radiotherapy delivered to an adequate dosage of 6000 rads or more to the tumor is superior to postoperative radiotherapy in most cases, and that such treatment generally (though not always) mades orbital exenteration

Table 11. Preliminary survival rates at two years

	Survival > 2years	
	Nasal cavity	Maxillary antrum
Preoperative radiation	2/9	2/18
Surgery alone	1/4	3/6
Postoperative radiation	2/8	4/18
Overall	5/17	9/42

Note : 7patients are free of disease for less than 2 years.

unnecessary for invasion of the orbit floor (Sisson)[3].

Batsakis[2] points out that although the maxillary antrum is involved in 80% of cases, it is limited to the antrum in only 25%, and that bone destruction occurs in 70-80% of patients. In our series the figure was 91%. This again reemphasizes the necessity of adequate preoperative radiotherapy. Extension of the cancer beyond the maxillary antrum, expecially into the pterygoid space, ethmoids and orbit, requires that the peripheral edges of advancing tumor be destroyed if adequate surgical margins are to be obtained. In nasal cavity cancer the same applies to extension into the posterior ethmoids, the sphenoethmoidal recess and the cribriform plate.

In terms of management policy we feel that the use of the criteria for preoperative radiation and the delivery of adequate dosage are the cornerstone factors for improving results. Sisson has developed a program of management where by an exploratory antrostomy is performed for staging; T_1 and T_2 lesions are resected immediately; and T_3 and T_4 lesions are debulked at the time of the antrostomy followed by 6000 rads cobalt teletherapy. Following radiotherapy at 4-5 weeks exploratory antrostomy is again performed and decision is- made relative to ablative surgery.

We prefer to rely on clinical examination and the computerized tomography for the staging and to proceed accordingly. We agree that all T_3 and T_4 lesions should receive adequate preoperative radiotherapy. However, we repeat the CT Scan and decide upon resection on this basis. We dislike the idea of "debulking" because is may spread tumor and violates the principle of keeping the maxillary antrum as an intact box.

Our overall results are relatively poor, but are presented despite the fact that many patients were treated berfore Cobalt teletherapy was available and before the necessity of an adequate preoperative dose was appreciated. Cobalt teletherapy, introduced at our hospital in 1972, was available for only the last 41 patients in this 68 case series. When adequacy of preoperative therapy was used as a criterion, the two-year disease-free survival increased to 33.3% for preoperative radiation. Only 13 patients received over 6000 rads. Of these two are lost to follow up, one died of aspiration pneumonia, and one is free of disease for 1 year. Of nine patients who thus received 6000 rads and are suitable for evaluation, four are disease-free beyond two years, i. e., 44.4% (Table 11). This encourages us to continue with our present policies.

In Batsakis review the over all 5-year survival as reported by 15 authors varied from 13 to 18.5%. Sisson reports 33% 3-year survival for T_3 lesions involving the orbit floor treated by preoperative radiation. Jesse's [4] over all results are 35% at 5 years for T_3 and T_4 lesions.

CONCLUSIONS

Cancer of the nasal fossae requires aggressive but carefully planned therapeutic effort. In patients whose tumors extend to or near the levels of planned resection, preoperative radiotherapy in adequate dosage is indicated, followed by surgical resection which has been designed to meet each

anatomical situation. Never combinations of chemotherapeutic agents delivered as inductive therapy may also have a role in improving the chances for long-term disease-free survival.

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