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Sinonasal mucosal melanomas in Quito, Ecuador

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ABSTRACT

Background: Head and neck mucosal melanoma account for 2 to 8% of head and neck melanomas, the majority of which arises in the nasal cavity or paranasal sinuses. The aim of this report was to review our experience on sinonasal malignant melanomas (SNMM) treated over a long period of time at a tertiary referral hospital.
Methods: Clinical records of all of the patients operated on for SNMM at the Social Security Hospital and private clinics in Quito, Ecuador, were reviewed. Nineteen patients had histologically proven diagnosis. Eleven patients were men and mean age was 64. The most common presenting symptoms were nasal obstruction and epistaxis. Most tumors were located at the nasal fossa. Extranasal extension was present in 11 patients. Twelve had stage III- IV tumors. All patients were treated by surgery. Postoperative radiotherapy was given to 7.
Results: Local recurrence (11 events) occurred in 9 cases. These 11 events were treated with surgery in 8, eventually associated to radiation therapy (RT) and chemotherapy (CT). Eight out of these 9 patients died. Five overall survival was 46%. Death was related to local disease and distant metastases. All stage I tumor patients are alive.
Conclusions: Most sinunasal melanomas have a poor prognosis, mainly attributed to initial advanced local disease, local recurrence and distant metastasis. Surgery is the mainstay treatment, followed by radiotherapy, according to the T category.

Keywords: Mucosal, Melanoma, Sinonasal

INTRODUCTION

Melanomas are tumors arising from melanocytes, which are neuroectodermal-derived cells located in the basal layers of the skin, skin adnexa, and some mucosal membranes. Common sites for skin melanomas are the lower extremities. Less common sites of involvement are oral and genital mucosa, conjunctiva, orbit, esophagus, nasal mucosa or nasopharynx, vagina, and the leptomeninges.

Primary skin melanoma of the head and neck accounts for 25-30% of all melanomas.[1] Head and neck mucosal melanoma (HNMM) is a rare and aggressive disease that makes up less than 1% of all melanoma cases in the United States and 2% to 8% of head and neck melanomas.[2,3] In a study carried out by Marcus, 452 cases of HNMM of the Surveillance, Epidemiology, and End Results (SEER) 9 registry of the United States between 1987 and 2009, were identified.[4] According to this study, the incidence of HNMM in the United States has been rising since 1987. This trend has been driven primarily by increased incidence of nasal cavity melanomas. The majority of HNMM arises in the nasal cavity or paranasal sinuses.[5,6] The nasal cavity seems to be more commonly affected than the paranasal sinuses, and the maxillary antrum is more frequently involved than the ethmoid sinuses.[7,8]

The aim of this report was to review our experience on sinonasal malignant melanomas (SNMM) treated over a long period of time at a tertiary referral hospital.

METHODS

The clinical records of all of the patients operated on for SNMM at the Social Security Hospital and private clinics in Quito, Ecuador, South America, from 1981 to 2013, were reviewed. Nineteen patients had histologically confirmed diagnosis of primary mucosal melanoma. Demographic and clinical features as well as and treatment modalities were reviewed. Actuarial survival analysis was calculated according to the Kaplan-Meier method.

Fifteeen patients were mestizo, 3 whites and one Amerindian. The sex ratio was 1,4:1 (11 men, 8 women). Mean age of presentation was 64 (range: 49 to 81). The most common presenting symptoms nasal obstruction in 12 and epistaxis in 8; other symptoms were pain in 2 and nasal secretion, swelling of the cheek, ocular proptosis and epiphora in one case, each. Mean duration of symptoms was 6 months (range: 1 to 24). Tumors were located at the nasal fossa in 13 cases, the maxillary sinus in 1 and the ethmoid sinus in one; both nasal as maxillary sinus involvement occurred in 4 patients. Extranasal extension appeared at the cheek skin in 4 patients, the cheek subcutaneous tissue in 1, the orbit in 2, the cribiform plate in 2 and the pterigo-maxillary fossa and gum in one, each. TNM distribution according to the AJCC classification system which seems to be the best staging system for patients with mucosal melanomas of the sinonasal tract appears on Table 1.[9,10] No patient had distant metastases initially.

Seven patients had stage I or II tumors whereas 12 had stage III or IV tumors. All patients were treated by surgery, performed by the senior author: initially, in our service, in 15 cases and for recurrent tumors in the other four. In the latter cases, initial surgery, mostly wide tumor resection, had been done by other oncological or ENT surgeons. Surgical modalities appear on table II. Wide tumor resection was performed in 9 patients. An extension adapted maxillectomy was performed in 8 cases (one of them associated to orbital exenteration) and a craneo-facial resection in 2 (Figure 1-3). A N1 case underwent a supraomohyoid dissection and a N2a case, a radical modified neck dissection (RMND). Postoperative radiotherapy (4800 cGy to 5800 cGy) was given to 7 patients (2 stage II, 3 stage III and 2 stage IVA).

RESULTS

Mean follow-up was 35 (range: 2-214) months. Three patients were lost to follow up. Local recurrence occurred in 9 cases: one recurrence in 7 and 2 recurrences in 2 patients. These 11 events were treated with surgery in 8 cases (3 patients refused treatment), associated to radiation therapy (RT) in 2 patients and chemotherapy (CT) in another. Eight out of these 9 patients with local recurrence died (2 for local disease, 5 for additional metastases and one with not related disease) and only one is currently alive. Neck recurrence occurred in 2 patients in association to local recurrence: they were treated with a RMND in one case and a parotidectomy and RMND in the other. Distant metastases during follow up occurred in 9 patients and they were located in the liver in 5, the brain in 4, the lungs in 2, the bone in 2, the bone marrow in 2 and the spleen in 1. All of them died. Five-year overall survival was 46%. Twelve patients died during follow up. Death was related to tumor progression in 2 patients, distant metastases in 7, both local disease and distant metastases in 2 and not related disease in one (Table 3). No patient with stage I tumor died with disease.

Table 1: TNM and stage distribution.

	N0	N1	N2a	N2b	Total	Stage	
T1	3	0	0	0	3	I	3
T2	4	0	0	0	4	II	4
T3	4	1	0	0	5	III	5
T4A	5	0	1	1	7	IVA	7
Total	**16**	**1**	**1**	**1**	**19**	**Total**	**19**

Table 2: Initial surgical procedures performed in our institution.

Type of surgery	Number of cases
Wide local excision	9
Lateronasal approach	3
Denker	3
Degloving, vestibular or endoscopic	3
Extension adapted maxillectomy	7
Total maxillectomy + orbit exenteration	1
Craneo-facial resection	2

Table 3: Cause of death according to stage.

Stage	Local disease	Metastases	Local and metastatic disease	Not related disease	Total
I	-	-		1	1/3
II	1	2		-	3/4
III	-	3		-	3/5
IVA	2	1	2	-	4/7*

*2 lost to follow up

Figure 1: Patient with a left-sided T3 tumor extending to the subcutaneous tissue of the cheek.

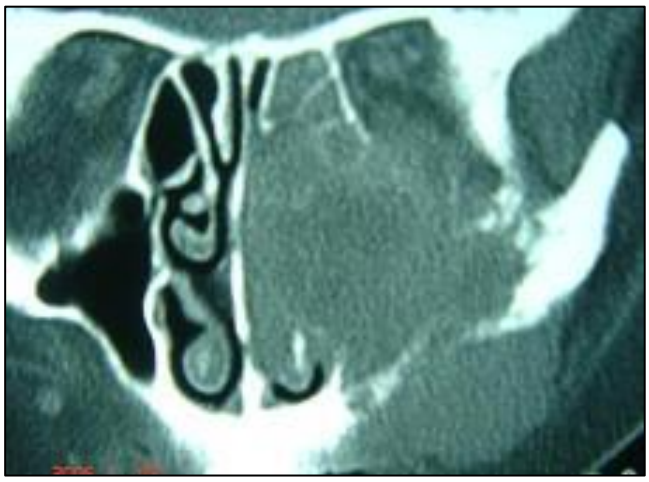

Figure 2: CT scan of the same patient.

Figure 3: Surgical specimen of an extension adapted maxillectomy of the same patient.

DISCUSSION

Among the cancers that arise in nasal cavity and paranasal sinuses, mucosal melanomas are rare in comparison to squamous cell carcinomas. Case reports have been commonly published and most series have included a limited number of cases (Table 4).

Peak incidence has been reported to be between the fifth and eighth decade.[11,12] Mean age in our patients was 64. In the study of Marcus with patients of SEER 9 registry (4), 237 (52.4%) patients were female, and 215 (47.6%) were male. In other smaller series and in ours, a slightly more common presentation in males than in females was found.[11-15]

The presentation depends on the size and site of the lesion. At initial presentation, these tumors can be fairly advanced, due to the ample space available to accommodate their growth in the nasal cavities and sinuses. Twelve of our 19 patients presented with advanced lesions, T3 and T4a, and duration of symptoms was certainly long before the first consultation. The majority of the patients present with epistaxis and progressively increasing nasal obstruction.[13] However, other less common symptoms such as pain, nasal secretion, swelling of the cheek, ocular proptosis and epiphora can be present as in our series.

Surgery has been the mainstay of the treatment of these tumors, provided they are resectable.[16] The modality of the surgical procedure must be adapted to the extension of the disease. The tumor must be excised completely even if a one block resection may be not always usually feasible.

The incidence of regional lymph node metastasis on admission is approximately 5-15%.[11] Eleven per cent in the current series .The submandibular lymph nodes are the most commonly involved. A comprehensive neck dissection must be performed in case of regional disease.

Historically, mucosal melanoma was characterized as a radioresistant disease, but recent observations suggest that radiotherapy has a significant role in their treatment. Adjuvant RT is usually well-tolerated and should be used for patients with either large bulky primary disease or regional metastases. It reduces the likelihood of local-regional failure but probably does not enhance survival.[15-19] However, some authors have reported improved survival is selected groups with postoperative RT.[20-22]

Patients with unresectable local disease or that cannot be operated for medical reasons or those who do not agree for surgery should be considered for radiotherapy alone as a definitive management, whereas chemotherapy should be reserved for patients with systemic disease. Long-term survival for patients treated with RT alone remains uncertain.[22,23] Christopherson of the University of Florida in Gainesville in recent report of 21 cases of

MMHN concluded that the prognosis for patients treated with definitive RT is less promising than for those who receive surgery and postoperative RT.[18] Bonner demonstrated the usefulness of concomitant chemoradiotherapy in squamous cell carcinomas of the head and neck region, and indicated a possible role of primary concomitant chemoradiation in mucosal melanomas as well.[24]

Table 4: Recent series on nasal and paranasal region melanomas.

Institution	Years	Number of cases
University of Campinas, Piracicaba, São Paulo, Brazil (14)		12
Institut Gustave Roussy, Villejuif, France (20)	1979-1997	46
Finish Nationwide Study, Finland (27)	1990-2004	50
The University of Texas M. D. Anderson Cancer Center, Houston, USA (15)	1993-2004	58
Shantou Central Hospital of Sun-Yat-Sen University, Shantou, China (28)	1980-2005	34
Chang Gung Memorial Hospital, Tao-Yuan, Taiwan (13)	1994-2005	15
Fachklinik Hornheide, Westfälische Wilhelms University of Münster, Münster, Germany (30)	1971-2006	40
Centre Antoine-Lacassagne, University Nice Sophia-Antipolis, Nice, France (29)	1991-2006	23
University of Miami, Miami, USA (21)	1990-2007	11
Memorial Sloan-Kettering Cancer Center, New York, USA (17)	1992-2007	24
Huriez Hospital, University of Lille, France. (26)	1991-2008	25
Yokohama City University School of Medicine, Kanagawa, Japan (7)	1992-2010	13
La Timone Universitary Hospital Center, Aix-Marseille, France (10)	1995-2010	35
Present series	1981-2013	19

Several new biologic and immunomodulatory treatments are currently being investigated for use in patients with mucosal melanoma. KIT and BRAF mutations, which are accessible for present targeted therapies, are only rarely present in SNMMs, whereas NRAS mutations seem to be relatively more frequent.[25] Newer radiotherapy modalities like intensity-modulated radiotherapy (IMRT) and three-dimensional conformal radiotherapy (3-D-CRT) are being investigated and show some promise for use in treating these tumors in the future.

The natural course is marked by early local recurrences, metastasis to lymph nodes and distant metastases. The likelihood of local recurrence after resection for HNMM is approximately 50%.[19] In a series of 69 HNMM patients treated at the Gustave Roussy Institut (IGR), thirty-seven patients (54%) experienced local disease recurrence and 47 patients (68%) developed distant metastasis at the IGR.[20]

The 5-year survival rates for HNMM vary from approximately 20 to 50%, although the median time to relapse is roughly 1 year or less (19). Overall survival for HNMM has ranged between 49.5% and 64.7% at 2 years and between 20% and 51.5% at 5 years in the most recent series.[13,16,20,21,26-30] HNMM, and particularly SNMM, are primarily impacted by advanced T stage and the presence of regional metastases.[15,19,21,28] Additionally, the presence of distant metastasis at the time of diagnosis is also a bad prognostic factor. The patients treated at the IGR with advanced T classification and pN > 0 stage had a earlier distant metastasis, disease-free and overall survival compared with patients with early T-classification and pN < 0 stage.[20]

Tumor extension to the sphenoid sinus had a significant negative impact on survival in the Finnish Nationwide Study.[27] Initial surgery with en bloc resection, has been reported as a prognostic factor on outcomes for local control and survival.[24,25] Histological features such as pigmentation and pseudopapillary architecture are associated with worse outcome.[15] It seems that other factors such as age and sex do not affect the prognosis.[11,12,30]

In conclusion, a high index of suspicion is required to make an early diagnosis, particularly by ENT surgeons who may have problems in diagnosing this disease owing to its rarity. However, advanced disease can be easily diagnosed clinically.

As a rule, patients with localized disease should undergo surgery followed by postoperative radiotherapy for better local control of the disease, according to the T category. Poor prognosis may be attributed mainly to initial advanced local disease, local recurrence and distant metastasis.

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