American Journal of Otolaryngology and Head and Neck Surgery

Research Article
Published: 24 Sep, 2018

Endoscopic Surgery Followed by Postoperative Radiation for T3/T4a Nasal Malignant Mucosal Melanoma

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Abstract

Objective: To report the results of endoscopic endonasal surgery with segmental resection followed by postoperative radiation for T3/T4aN0M0 nasal mucosal malignant melanoma, and to identify future issues in the treatment of nasal mucosal malignant melanoma.

Methods: This was a retrospective study in one institute. Six patients with T3/T4aN0M0 nasal malignant mucosal melanoma between March 2009 and June 2013 were analyzed. A surgical procedure, endoscopic endonasal surgery with segmental resection, with curative intent was performed that was followed by postoperative radiation.

Results: Two patients were alive without disease. One patient had local recurrence and was salvaged by resection. The other three patients had distant metastases. Aggressive treatments that consisted of surgery, irradiation, chemotherapy, and nivolumab administration for distant metastases were performed. Median disease-free survival was 1017 days (207 to 2807 days), and median overall survival was 1754 days (207 to 2807 days).

Conclusion: Endoscopic endonasal segmental resection with minimum safety margins that was followed by postoperative radiation produced good local control. Despite distant metastases, aggressive treatments for distant metastases may provide good overall survival rates. Endoscopic endonasal segmental resection followed by postoperative irradiation is useful for nasal malignant melanoma.

Keywords: Endoscopic endonasal surgery; Segmental resection; Postoperative radiation; Nasal mucosal malignant melanoma

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Received Date: *12 Sep 2018*
Accepted Date: *21 Sep 2018*
Published Date: *24 Sep 2018*

Citation:
Takanosawa M, Nagatomo T, Nishino H, Yamauchi T. Endoscopic Surgery Followed by Postoperative Radiation for T3/T4a Nasal Malignant Mucosal Melanoma. Am J Otolaryngol Head Neck Surg. 2018; 1(4): 1020.

Introduction

Nasal mucosal malignant melanoma is a rare disease, reported as accounting for less than 1% of all melanic tumors and 2% to 8% of all cancers of the nasal cavity and sinuses [1]. Because of its rarity, we have limited experience treating nasal mucosal malignant melanoma, so that when we need to treat patients with nasal mucosal malignant melanoma, we refer to the treatment strategy for skin malignant melanoma. For skin malignant melanoma, wide safety surgical margins and en bloc resection are recommended. If we choose the same treatment strategy with wide safety margins and en bloc resection, we must perform total maxillectomy with orbital exenteration and facial skin resection, but such surgery would reduce a patient's quality of life. Recently, endoscopic endonasal surgical procedures have often been performed for not only nasal benign tumors, but also nasal malignant tumors. If we choose endoscopic endonasal surgical procedures, minimally invasive surgical outcomes are expected. On the other hand, when we choose endoscopic endonasal surgical procedures, we are not able to obtain a sufficient surgical view and working space or a clear margin >5 mm because of various anatomical issues. To get a sufficient surgical view and working space, we have recently performed endoscopic endonasal surgery with segmental resection for T3/T4a nasal malignant mucosal melanoma. When massive tumor occupied the nasal cavity, we resected segmentally to obtain a sufficient surgical view and working space. These procedures were followed by postoperative radiation. The purpose of this article is to report our results of endoscopic endonasal surgery with segmental resection followed by postoperative radiation for T3/T4aN0M0 nasal mucosal malignant melanoma and to compare the results of this treatment strategy with the past treatment strategy with wide, en bloc resection. Future issues in the treatment of nasal mucosal malignant melanoma are also identified for further consideration.

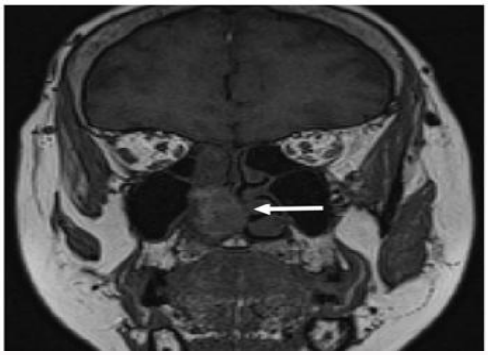

Figure 1: Magnetic Resonance Image T1 weighted image. White arrow: the massive tumor in the right nasal cavity disturbed en block resection and getting working space. Therefore, segmental resection was performed as a debulking procedure to reveal the base of the tumor and obtain a wide working space.

Materials and Methods

Study design

This was a retrospective study in one institute, involving six patients. This study was carried out after receiving approval from the Ethics Board of Jichi Medical University Hospital.

Patients

Between March 2009 and June 2013, six patients with T3/T4aN0M0 nasal malignant mucosal melanoma were identified. All patients were female, with a median age of 75 years. Median observation period was 1754 days. The tumor was located at the nasal lateral wall in five patients and at the septum in one patient. T category (UICC TNM Classification of Malignant Tumours 8th Edition) was T3 in two patients and T4a in four patients (Table 1). All patients had no neck lymph node metastases and no distant metastases at the time of diagnosis. All cases were diagnosed as melanotic melanoma.

Treatments

A surgical procedure with curative intent was performed. The surgical procedure was done under endoscopic endonasal technique. Of course, en bloc resection is recommended for resection of malignant melanoma, but this could not be done in all cases because of the massive tumor in the nasal cavity (Figure 1). Therefore; segmental resection was performed as a debulking procedure to reveal the base of the tumor and obtain a wide working space. Finally, the tumor was respected with safety surgical horizontal margins of a few millimeters. After surgery, postoperative radiation was added. Irradiation doses ranged from 40 Gy to 60 Gy. The method of irradiation was conventional irradiation in two patients and hyper fractionated irradiation in four patients.

Statistical analysis

Survival curves were calculated by the Kaplan-Meier method. Statistical software was Prism 6 for Mac OS X (Graph Pad Software Inc, San Diego CA, USA).

Results

All patients underwent endoscopic endonasal segmental resection, and negative surgical margins were achieved in all cases. All patients received postoperative irradiation. The median observation period was 1754 days (207 to 2807 days). Two patients were alive without disease. The other four patients developed recurrences. One patient had local recurrence at a choanal region. This recurrent tumor was resected under endoscopic endonasal technique. Five years after this salvage surgery, this patient was alive without disease. Three patients developed distant metastases. One patient with axillary lymph node metastases was administered Dacarbazine/1-(4-Amino-2-Methyl-5-Pyrimidiny) Methyl-3-(2-Chloroethl)-3-Nitrosourea Hydrochloride/Vincristine Sulfate (DTIC/ACNU/VCR). The axillary lymph node metastases were not controlled, and the patient died due to distant metastases. One patient developed vertebral and breast metastases. After palliative irradiation to the vertebra to control pain, the patient was administered nivolumab, and stable disease was maintained for six months after administration of nivolumab. The other patient developed a single lung metastasis and a single brain metastasis. The single lung metastasis was resected by thoracoscopic surgery, and X-knife surgery was performed for the single brain metastasis. After these salvage treatments, the patient was still alive without disease at one year (Table 2).

The median disease-free survival was 1017 days (207 to 2807 days) (Figure 2a). A 5 year overall survival rate was over 75%, and the median overall survival was 1754 days (207 to 2625 days) (Figure 2b).

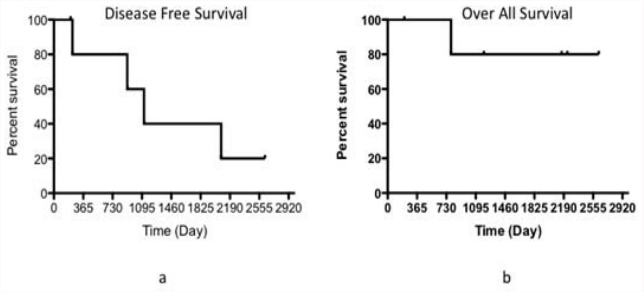

Figure 2: Disease-Free Survival (DFS) and Overall Survival (OS). (a) DFS: median DFS is 1017 days (207 to 2807 days); (b) OS: median OS is 1754 days (207 to 2625 days).

Table 1: Patients' characteristics.

Characters of Six patients	
Sex	All Female
Median age	75 years old (46 years old to 81 years old)
Median observation period	1754 days (207 days to 2807 days)
Sites	
Nasal latral wall	5
Septum	1
T category	
T3	2
T4a	4

Table 2: Results.

Results		**Salvage Treatments**	
No recurrence	2		
Local recurrence	1 Choanal lesion	Resection	AWOD
Distant metastasis	1 Vertebra, Mammary gland	Palliative RT, Nivolumab	AWD
	1 Lung, Brain	Thoracoscopic surgery, X-Knife	AWOD
	1 Axilla LN	DAV	Dead

LN: Lymph Node; RT: Radiation; DAV: DTIC/ACNU/VCR; AWOD: Alive Without Disease; AWD: Alive With Disease

Discussion

Since nasal mucosal malignant melanoma is rare, we have limited experience in its treatment. Because of this limited experience, we have only low-level evidence treatment strategies. It is generally said that the prognosis of mucosal malignant melanoma is worse than that of skin malignant melanoma [2,3]. The treatment results of 16 patients with malignant melanoma of the nasal cavity including 14 patients with or without irradiation and/or chemotherapy were reported, with 2 year and 5 year actuarial survival rates of 63.6% and 31.8%, respectively [4]. Wide surgical resection followed by postoperative radiation is recommended in NCCN Guidelines Version 2.2017. However, for nasal mucosal malignant melanoma, it is difficult to obtain wide surgical safety margins because of anatomical issues. If we perform total maxillectomy with resection of facial skin, palate, or the orbital complex to obtain wide surgical safety margins, there are cosmetic and functional issues, such as with nasal breathing, mastication, swallowing, and visual acuity. The quality of life of patients may deteriorate after such aggressive surgery.

To maintain patient's quality of life, minimally invasive surgical procedures are needed. Of course, such minimally invasive surgical procedures must provide a good prognosis. A case of nasal malignant melanoma involving the septum, nasal turbinates, and nasopharynx, which was approached by lateral rhinotomy combined with an anterior transantral approach with excision of the septum and the lateral wall of the nasal cavity, was reported as providing wide exposure of the tumor. Using this technique, complete surgical resection of a large nasal malignant melanoma was achieved with minimal morbidity and good aesthetic results [5]. Currently, endoscopic endonasal surgical procedures are often performed for not only sinonasal benign tumors, but also sinonasal malignant tumors [6,7]. In a retrospective study of nine patients who underwent endoscopic endonasal resection of sinonasal mucosal melanoma, comparable outcomes were achieved to the open approach [8]. Negative surgical margins were achieved in all patients. The 5-year overall survival rate was 53.3%, and the 5-year disease-free survival rate was 55.6%, similar to the open approach. In another retrospective study, in which the majority of patients received adjuvant radiotherapy, rates of local recurrence and rates of distant metastases were similar in the endoscopic endonasal surgery group and the open approach group [9]. In the above study, the open approach group and the endoscopic endonasal approach group had rates of local recurrence of 23% and 8%, respectively, and rates of distant metastases of 15% and 25%, respectively; these were not significantly different. While performing an endoscopic endonasal surgical procedure, it is often difficult to get a good surgical view and maintain sufficient working space because of the narrow nasal cavity occupied by intranasal tumor. When we could not get a good surgical view and maintain sufficient working space, we segmentally resected the nasal tumor. After the majority of the intranasal tumor was resected, a good surgical view and enough working space were obtained to achieve complete resection with good detection of the base of the tumor. In most cases, the surgical margins were within a few millimeters in the present series. It is a major concern that segmental resection may cause a high rate of distant metastases in patients with malignant melanoma. In the present series, the rate of distant metastases was 50%.

Despite negative surgical margins, mucosal malignant melanoma has a poor prognosis, and most deaths are due to distant metastases [10]. After surgery, adding radiotherapy has been recommended. Adding radiotherapy to surgery was also our treatment strategy. Some studies have shown that postoperative irradiation improves local control in mucosal malignant melanoma patients [11,12]. However, postoperative radiation has not been shown to improve overall survival [11,13,14]. Because of the high frequency of distant metastases, adjuvant radiotherapy to local disease did not affect overall survival rates. Based on our experience with six patients, adjuvant radiotherapy to local disease may reduce local recurrence, but there was a high rate of distant metastases, and distant metastases were observed in the early period after initial treatment. Whether segmental resection may induce distant metastases is debatable. In the present study, 3 of 6 patients showed distant metastases. In 14 head and neck mucosal melanoma patients, including 12 patients who underwent surgery with or without postoperative radiation and two patients who received palliative chemotherapy, distant metastases were observed in six patients [12]. Another study in which the treatment strategy was resection with an open approach or endoscopic resection with postoperative radiation showed that metastatic disease were observed in 10 of 25 patients [11]. Our segmental resection may increase the risk of distant metastases, but further study is needed to resolve this issue.

Despite the high rates of distant metastases, overall survival rates were relatively good, because the distant metastases were treated aggressively in the present series. In patients with metastatic lesions, resection or radiation was performed, and nivolumab was administered. Due to these treatments, the patients were alive with or without disease. Nivolumab was especially effective for metastatic lesions. It is said that malignant melanoma induces the host immune response. In the past, Lymphokine-Activated Killer (LAK) cell therapy was administered to patients as adjunctive immunotherapy after the initial treatment course [15]. Good results of LAK cell therapy were reported, but the process of LAK cell treatment was complicated, and limited improvements of outcomes were observed. LAK cell therapy is not now usually performed. Recently, good results of blockade of Programmed Death 1 (PD-1) were reported [16]. For the anti-tumor host immune system, PD-1 is an inhibitory receptor on the T cell surface. In this series, one patient was administered nivolumab as an anti-PD-1 antibody to treat distant metastases, and stable disease was observed for six months after administration.

This study has some limitations because there were only six cases, all of which were melanotic melanoma. Some cases of nasal malignant melanoma are amelanotic melanomas, and the prognosis of patients with amelanotic mucosal melanoma is poorer than that of patients with melanotic mucosal melanoma. Amelanotic mucosal melanoma tends to have a high incidence of metastases, recurrence, and ultimately death [17]. The present cases were all diagnosed pathologically as melanotic mucosal melanoma. Because of rarity of the disease, number of patients was limited. But we strongly explain that accumulated such as this report with small number is important to improve quality of patients.

Conclusion

Since nasal mucosal malignant melanoma is a rare disease, we have limited experience in its treatment. The NCCN guidelines recommend wide surgical resection with postoperative radiation. Indeed, local control rates were improved, but overall survival was not improved because of distant metastases. We performed endoscopic endonasal segmental resection with minimum safety margins followed by postoperative radiation, and good local control was achieved. Despite

distant metastases, aggressive treatment of distant metastases may provide good overall survival. Endoscopic endonasal resection with segmental resection followed by postoperative radiation resulted in complete resection and showed good local control. Since segmental resection may lead to distant metastases, further study is needed. In the present series, endoscopic endonasal segmental resection followed by postoperative irradiation for nasal malignant melanoma was found to be useful. The main issue in the treatment of nasal malignant melanoma that still needs to be resolved is the treatment of distant metastases. Aggressive treatments, including radiation, chemotherapy, and immunotherapy, are considered effective for metastatic lesions.

References

1. Ciolofan S, Ionita E, Mogoanta CA, Popescu FC, Anghelina F, Chiutu L, et al. Malignant melanoma of nasal cavity. Rom J Morphol Embryol. 2011;52(2):679-84.
2. Uysal IO, Misir M, Polat K, Altuntas EE, Atalar MH, Tuncer E, et al. Primary malignant melanoma of the nasal cavity. J Craniofac Surg. 2012;23(1):2-5.
3. Clifton N, Harrison L, Bradley PJ, Jones NS. Malignant melanoma of nasal cavity and paranasal sinuses: report of 24 patients and literature review. J Laryngol Otol. 2011;125(5):479-85.
4. Nakaya M, Mochiki M, Takeuchi S, Yuge T, Nakao K, Nakamura N, et al. Malignant melanoma of nasal cavity: report of 16 Japanese patients. Auris Nasus Larynx. 2004;31(3):233-7.
5. Gonzalez-Garcia R, Ruiz-Laza L, Roman-Romero L. Lateral rhinotomy combined with anterior transantral approach for the treatment of large malignant melanoma of the nasal cavity involving the nasopharynx. J Craniomaxillofac Surg. 2012;40(3):266-70.
6. Roth TN, Gengler C, Huber GF, Holzmann D. Outcome of sinonasal melanoma: clinical experience and review of the literature. Head Neck. 2010;32(10):1385-92.
7. Hanna E, DeMonte F, Ibrahim S, Roberts D, Levine N, Kupferman M. Endoscopic resection of sinonasal cancers with and without craniotomy: oncologic results. Arch Otolaryngol Head Neck Surg. 2009;135(12):1219-24.
8. Migiani A, Patel SH, Kosiorek HE, Hinni ML, Hayden RE, Lal D. Endoscopic resection of sinonasal mucosal melanoma has comparable outcomes to open approaches. Am J Rhinol Allergy. 2017;31(3):200-4.
9. Swegal W, Koyfman S, Scharpf J, Sindwani R, Greskovich J, Borden E, et al. Endoscopic and open surgical approaches to locally advanced sinonasal melanoma: comparing the therapeutic benefits. JAMA Otolaryngol Head Neck Surg. 2014;140(9):840-5.
10. Breik O, Sim F, Wong T, Nastri A, Iseli TA, Wiesenfeld D. Survival Outcomes of Mucosal Melanoma in the Head and Neck: Case Series and Review of Current Treatment Guidelines. J Oral Maxillofac Surg. 2016;74(9):1859-71.
11. Benlyazid A, Thariat J, Temam S, Mallard O, Fluoresce C, Choosy O, et al. Postoperative radiotherapy in head and neck mucosal melanoma: A GETTEC study. Arch Otolaryngol Head Neck Surg. 2010;136(12):1219-25.
12. Wushou A, Hou J, Zhao YJ, Miao XC. Postoperative adjuvant radiotherapy improves loco-regional recurrence of head and neck mucosal melanoma. J Cranio Maxillofac. 2015;43(4):553-8.
13. Krengli M, Machine L, Kanders JHAM, Mango P, Oei SB, Zouhair A, et al. Radiotherapy in the treatment of mucosal melanoma of the upper aerodigestive tract: Analysis of 74 cases. A rare cancer network study. Int J Radiat Oncol Biol Phys. 2006;65(3):751-9.
14. Meleti M, Leemans CR, de Bree R, Vescovl P, Sesenna E, van der Wall I. Head and neck mucosal melanoma: Experience with 42 patients, with emphasis on the role of postoperative radiotherapy. Head Neck. 2008;30(12):1543-51.
15. Kanetaka S, Tsukuda M, Takahashi M, Komatsu M, Niho T, Horiuchi C, et al. Mucosal melanoma of the head and neck. Exp Ther Med. 2011;2(5):907-10.
16. Topalian SL, Hodi FS, Brahmer JR, Gettinger SN, Smith DC, McDermott DF, et al. Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. N Engl J Med. 2012;366(26):2443-54.
17. Paulo LF, Servato JP, Rosa RR, Oliveira MT, Faria PR, Silva SJ, et al. Primary amelanotic mucosal melanoma of the oronasal region: report of two new cases and literature review. Oral Maxillofac Surg. 2015;19(4):333-9.