Recurrent malignant melanoma of the palate treated successfully with gamma knife radiosurgery: a case report

Shin-ichi Yamada, DDS, PhD[a※], Souichi Yanamoto, DDS, PhD[a], Akiko Kawakita, DDS[a], Goro Kawasaki, DDS, PhD [a], Shuichi Fujita, DDS, PhD[b], Tohru Ikeda, DDS, PhD[b], Takemitsu Matsuo, DDS, PhD[c], and Masahiro Umeda, DDS, PhD[a].

Department of Clinical Oral Oncology[a] and Oral Pathology and Bone Metabolism[b] , Unit of Translational Medicine, Course of Medical and Dental Sciences, Nagasaki University Graduate School of Biomedical Sciences.

Department of Oral and Maxillofacial Surgery, Omura Municipal Hospital[c]

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*Correspondence to: Shin-ichi Yamada, DDS, PhD

Department of Clinical Oral Oncology, Nagasaki University Graduate School of Biomedical Sciences

1-7-1 Sakamoto, Nagasaki 852-8588, Japan

Email: shinshin@nagasaki-u.ac.jp

Fax: + 81 95 8197700, Tel.: + 81 95 8197698

ABSTRACT

The prognosis of oral malignant melanoma is reported to be extremely poor. In this report, a patient with recurrent oral melanoma in the skull base who was treated successfully with gamma knife radiosurgery (GKS) is described.

A 53-year-old man was referred with a chief complaint of a mass of the hard palate. Histological diagnosis of the biopsy specimen was malignant melanoma. He underwent a wide local resection with bilateral neck dissection, followed by immunochemotherapy with DAV-Feron.

At 13 months after the surgery, recurrent tumor was found in the post-lower region of the nasal septum. The patient underwent resection of the lesion followed by immunochemotherapy with DAC-Tam-Feron. However, at 9 months after the last chemotherapy, local recurrence again occurred in the skull base, and he underwent GKS. The recurrent tumor disappeared completely and he is well with no signs of recurrence or metastasis at 57 months after GKS.

Key words: malignant melanoma, skull base invasion, gamma knife radiosurgery

INTRODUCTION

Malignant melanoma of the oral cavity is a neoplasm arising from the melanocytic cells in the basal layer of the mucosa[1]. The incidence of oral melanoma is reported to be between 0.2% and 8% of all melanomas[2,3], and 0.5% of all malignant neoplasms of the oral cavity[4]. The etiology of oral melanoma is unclear, although pre-existing long-term melanosis is found in 33% to 55% of patients with mucosal melanomas of the head and neck[5]. Other possible etiological factors for this neoplasm are as follows: mechanical trauma such as denture irritation[6], use of tobacco, and exposure to formaldehyde and alcohol[7]. Most cases occur between the fourth and the seventh decade of life[8]. Apparently, malignant melanoma of the oral cavity is more common in the male gender[7].

The classification of oral melanoma has not been established[8]. It was reported that Clark's criteria for the invasion level and the prognosis of cutaneous melanoma are not applicable to oral melanoma owing to the lack of histological points of reference similar to the papillary and reticular dermis[9]. The prognosis of oral malignant melanoma has been reported to be extremely poor. According to Hicks and Flaitz[10] and Meleti et al.[11], the 5-year survival rate was 15% for all oral malignant melanomas. The Western Society of Teachers of Oral Pathology (WESTOP) stated that oral melanomas appeared to be similar to acral lentiginous melanoma (ALM) of the skin, but that the particularly poor prognosis of oral melanomas was unlike that of cutaneous lesions, and until detailed

prospective studies were completed, it would seem appropriate to classify oral lesions separately from cutaneous lesions[12]. On the other hand, Umeda et al. reported that most oral melanomas showed a radial growth phase identical to that of ALM both clinically and histologically, and that the prognosis of oral melanoma was not as poor as reported earlier, if adequate therapy was provided[13-16]. However, patients with recurrent malignant melanoma are not curable in most cases, so the therapeutic strategy for recurrent melanoma is controversial. We report a new case with recurrent oral melanoma in the skull base treated successfully with gamma knife radiosurgery (GKS).

CASE REPORT

A 53-year-old man was referred to the Department of Oral and Maxillofacial Surgery, Nagasaki University Hospital, for diagnosis and treatment of a painless, black mass of the hard palate, which had been present for 6 months. At the time of the first visit, the patient's medical history included a diagnosis of diabetes 6 years previously. Intraoral examination revealed a 45×35×15 mm, relatively well-defined, elastic hard, black, nodular and tender mass on the hard palate with surrounding brownish-black pigmented macule (Fig. 1). The overlying mucosal surface was partially ulcerated. The submandibular and cervical lymph nodes were not palpable. Computed tomography scan (CT) and magnetic resonance imaging (MRI) were performed to assess the extent of the tumor and determine possible involvement of regional lymph nodes. Enhanced CT revealed bone resorption of the palatal bone, destruction of the right floor of the nasal cavity, and enlarged lymph nodes of bilateral left level IB and bilateral level IIA (Figs. 2A and 2B). Enhanced MRI also showed the same findings. No metastases to the lung and liver were detected by CT examinations. A clinical diagnosis of malignant melanoma of the hard palate with bilateral regional lymph node metastases was made. Biopsy was performed under local anesthesia. The biopsy specimen revealed diffuse proliferation of spindle-shaped to oval cells including melanin granules in the submucosa of the palate (Fig. 3). Most tumor cells were positive for S-100 protein, HMB-45, and Melan-A, and the histological diagnosis of malignant melanoma was

made.

The patient underwent wide local resection concomitant with bilateral modified radical neck dissection (levels I-V) under general anesthesia. The whole alveolar ridge was resected, including the maxillary sinus floor and the nasal floor. The surgical margin was free of the tumor histopathologically. Three lymph node metastases were proven histologically in the left levels IB and IIA, and the right level IB. He underwent postoperative immunochemotherapy with dimethyl triazeno imidazole carboxamide (DTIC), nimustine hydrochloride (ACNU), vincristine (VCR), and interferon-β (DAV-Feron). The following administration schedule was used: DTIC, 200 mg (days 1-5); ACNU, 1 mg (day 1); vincristine, 1 mg (day 1); and interferon-β, 3,000,000 IU (days 1-5).

At 13 months after the surgery, a black recurrent lesion, 10 mm in diameter, was found in the post-lower region of the nasal septum. Axial enhanced magnetic resonance T1-weighted image revealed an enhanced recurrent mass lesion in the clivus (Fig. 4). The patient then underwent resection of the lesion under general anesthesia. Histological examination of the surgical specimen revealed proliferation of malignant melanoma cells in the deep layer of the nasal mucosa (Fig. 5). Bone invasion was also seen in the curetted bone fragments. Histological features of the tumor cells were the same as those of the palatal lesion. The lesion was diagnosed as recurrence of malignant melanoma. The surgical margin was positive for tumor cells clinically and

histopathologically. The patient underwent additional immunochemotherapy with DTIC, ACNU, VCR, cisplatinum (CDDP), tamoxifen, and IFNβ (DAC-Tam-Feron). The administration schedule was as follows: DTIC, 400 mg (days 2-4); ACNU, 109 mg (day 2); VCR, 1 mg (day 2); CDDP, 45 mg (day 2-4); tamoxifen, 20 mg (P.O. days 1-28); and interferon-β, 3,000,000 IU (days 2-6).

The patient was free from the tumor clinically and radiographically for 9 months after the last chemotherapy, but then local recurrence again occurred. The recurrent tumor was black, 10 mm in diameter, located at the post-lower region, and had invaded to the clivus (Fig. 6). We considered that salvage surgery was difficult, so we performed GKS: mean tumor size, 16.1 mm^2; clinical target volume, 2.18 ml, which were defined by CT ; max. dose, 29.94 Gy; and margin dose, 20.0 Gy (Fig.7). The lesion had disappeared completely after GKS. The patient has been free from recurrence or metastasis for 57 months after GKS without developing any neurological symptoms (Fig. 8A and B), and is scheduled for careful follow-up control.

DISCUSSION

In contrast to Caucasians, Japanese people show a relatively high frequency of malignant melanoma in the oral cavity[13]. Cutaneous melanoma is classified into four major types: lentigo maligna melanoma (LMM), superficial spreading melanoma (SSM), nodular melanoma (NM), and acral lentiginous melanoma (ALM). However, the classification and treatment method for oral melanoma have not been established.

The prognosis of oral melanoma is extremely poor according to previous reports. Hicks and Flaitz reviewed oral malignant melanomas and reported a 5-year survival rate of 15% for all cases[10]. Prasad et al. reported that only 5 of 37 cases of mucosal malignant melanoma of the head and neck had survived free of disease and that no prognostic significance was found for tumor thickness or the level of invasion[4]. The most effective management for malignant melanoma is early diagnosis and removal while it is thin and the chance of metastasis is low. Induction chemo- or radiotherapy is not generally performed because it may reduce host immunity and promote metastasis. Umeda et al. reported the following treatment protocols of oral malignant melanoma: surgical resection of intraoral tumors; neck dissection for a clinically N+ patient; initiation of adjuvant immuno-chemotherapy with DTIC, ACNU, VCR, and OK-432 on the day of surgery; and no biopsy because it might promote metastasis[16]. They reported that the 5-year cumulative survival rate of 12 patients treated by their protocols was 92%, but that of 9 patients who had undergone surgical procedures (such as incision,

biopsy, or tooth extraction) before the start of treatment was significantly lower at 26%[16].

Leksell originally proposed the idea of stereotactic radiosurgery for the treatment of an intracranial lesion in 1951[17]. This was made practical when the first GKS was developed in 1967 (Elekta Instruments, Stockholm, Sweden). Today, GKS has gained considerable support as a major tool for the treatment of patients harboring intracranial metastasis, mainly because of the minimal invasiveness, the extremely low morbidity, and the excellent clinical results[18]. Malignant melanomas have traditionally been regarded as radio-resistant tumors[19]. GKS for brain metastasis of malignant melanoma has been reported to be safe and effective, and to provide a high rate of durable local control[20]. The independent predictors of survival upon GKS for metastatic malignant melanoma of the brain are single metastasis, controlled systemic disease, and a high Karnofsky performance score (KPS)[20]. Gonzalez-Martinez et al. reported that patients who receive immunotherapy and have KPS scores higher than 90 have a better prognosis after GKS than other patients[21]. With regard to cases of malignant melanoma with skull base invasion, the independent predictors of survival after GKS are uncertain. In the present case, the fact that the patient had high KPS scores and immunotherapy might have led to the good prognosis. Most tumors presenting in the skull base will be thought to require open resection[22]. Francel et al. reported that only tumors less than 3 cm in diameter and/or less than 10 cm^3 in volume should be considered for GKS alone[22].

In addition, tumors must not be exerting a significant mass effect on either eloquent or vital brain structures, such as the brainstem, basal ganglia, or visual pathways[22]. In this case, the mean tumor size was 16.1 mm in diameter and 2.18 cm^3 in volume. To add to the above predictors, tumor size and volume might also have affected the good prognosis of this case.

In conclusion, we report a case of recurrent malignant melanoma of the skull base treated successfully with GKS. The patient is free of disease 57 months after GKS and is scheduled for careful follow-up control.

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Figure legends

Fig. 1 Photograph showing a 45×35×15 mm, relatively well-defined, elastic, hard, black nodular, and tender mass on the right hard palate with adjacent brownish-black macular lesions.

Fig. 2 (A) Axial enhanced computed tomography scan revealing the bone destruction in the right hard palate (arrows) (window width: 3800, window level: 900). (B) Axial enhanced CT revealed enlarged lymph nodes in the bilateral level IIA regions (arrowheads) (window width:250, window level: 50). (C) Axial enhanced magnetic resonance T1-weighted image revealing an enhanced mass lesion in the right hard palate (arrows).

Fig. 3 Biopsy specimen. (A) Spindle-shaped or ovoid tumor cells including melanin granules diffusely proliferated in the submucosa (H-E stain, X40). (B) Melanotic tumor cells showed pleomorphism and had a pale nucleus containing distinct nucleoli (H-E stain, X400). (C) Immunohistochemical examination for S-100 protein employing AEC (3-amino-9-ethylcarbazole) as a chromogen demonstrated nuclear and cytoplasmic positivity (X400).

Fig. 4 Axial enhanced magnetic resonance T1-weighted image revealing an enhanced

recurrent mass lesion in the clivus (arrows).

Fig. 5 Surgical specimen of recurrent lesion. The melanoma (M) including melanin granules that had invaded deeply into the nasal mucosa. Arrows and asterisks indicate nasal mucosal epithelium and nasal gland, respectively (H-E stain, X25).

Fig. 6 Photograph showing recurrent lesion at the post-lower region of the nasal septum (arrows).

Fig. 7 Dose distribution of GKS: mean tumor size, 16.1 mm^2; clinical target volume, 2.18 ml; max. dose, 29.94 Gy; and margin dose, 20.0 Gy.

Fig. 8 (A) Photograph showing the no recurrence of nasal septum for 57 months after GKS. (B) Axial enhanced magnetic resonance T1-weighted image revealing no recurrence in the clivus.

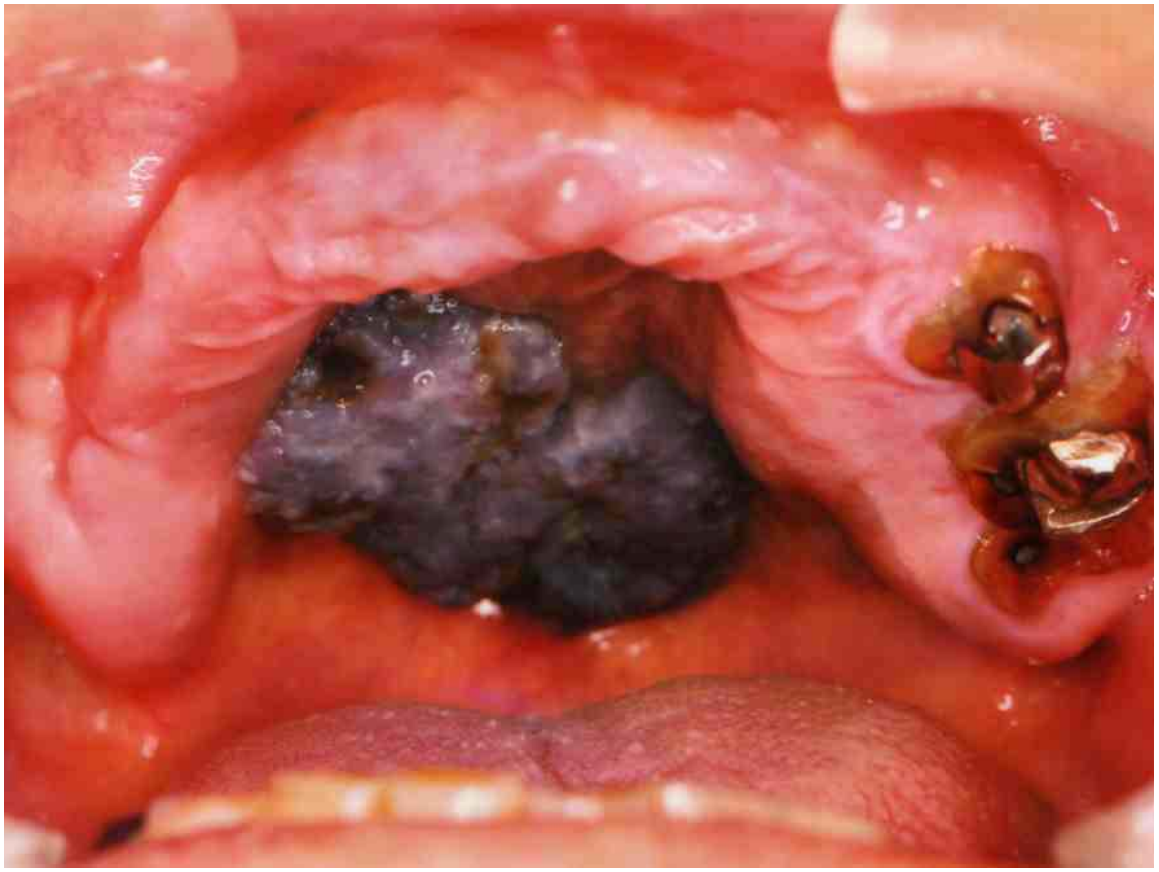

Fig. 1

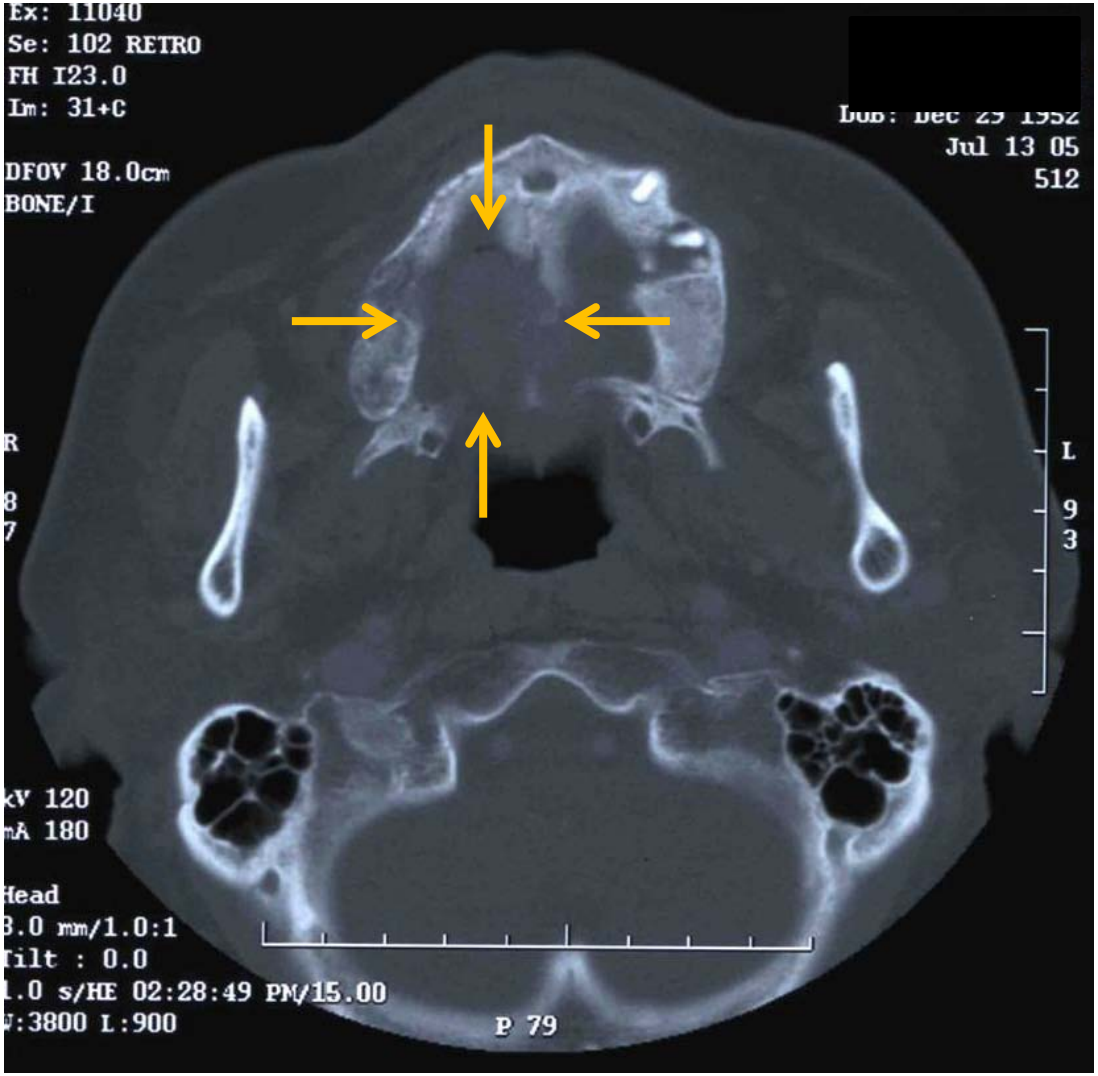
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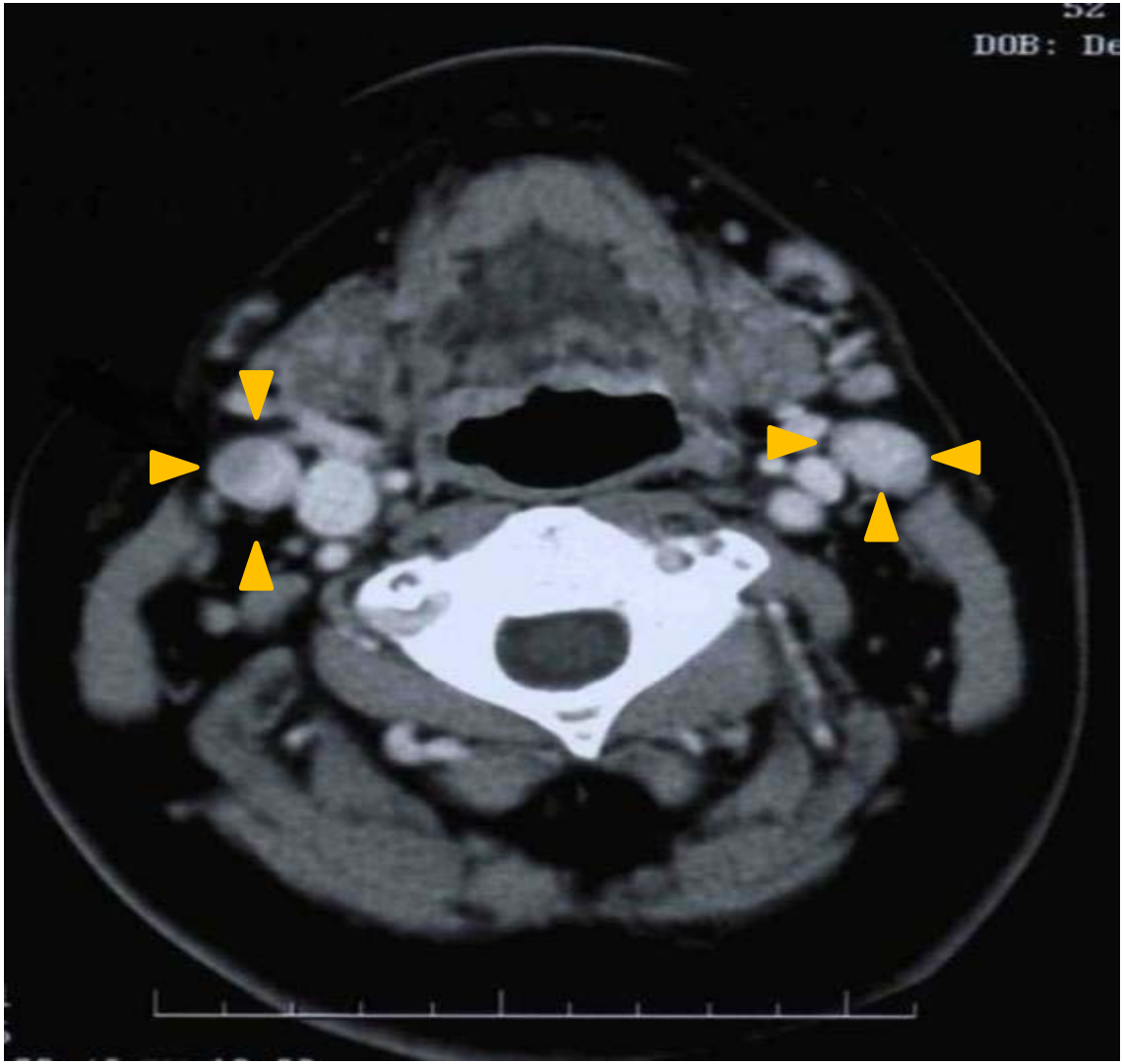
Fig. 2A



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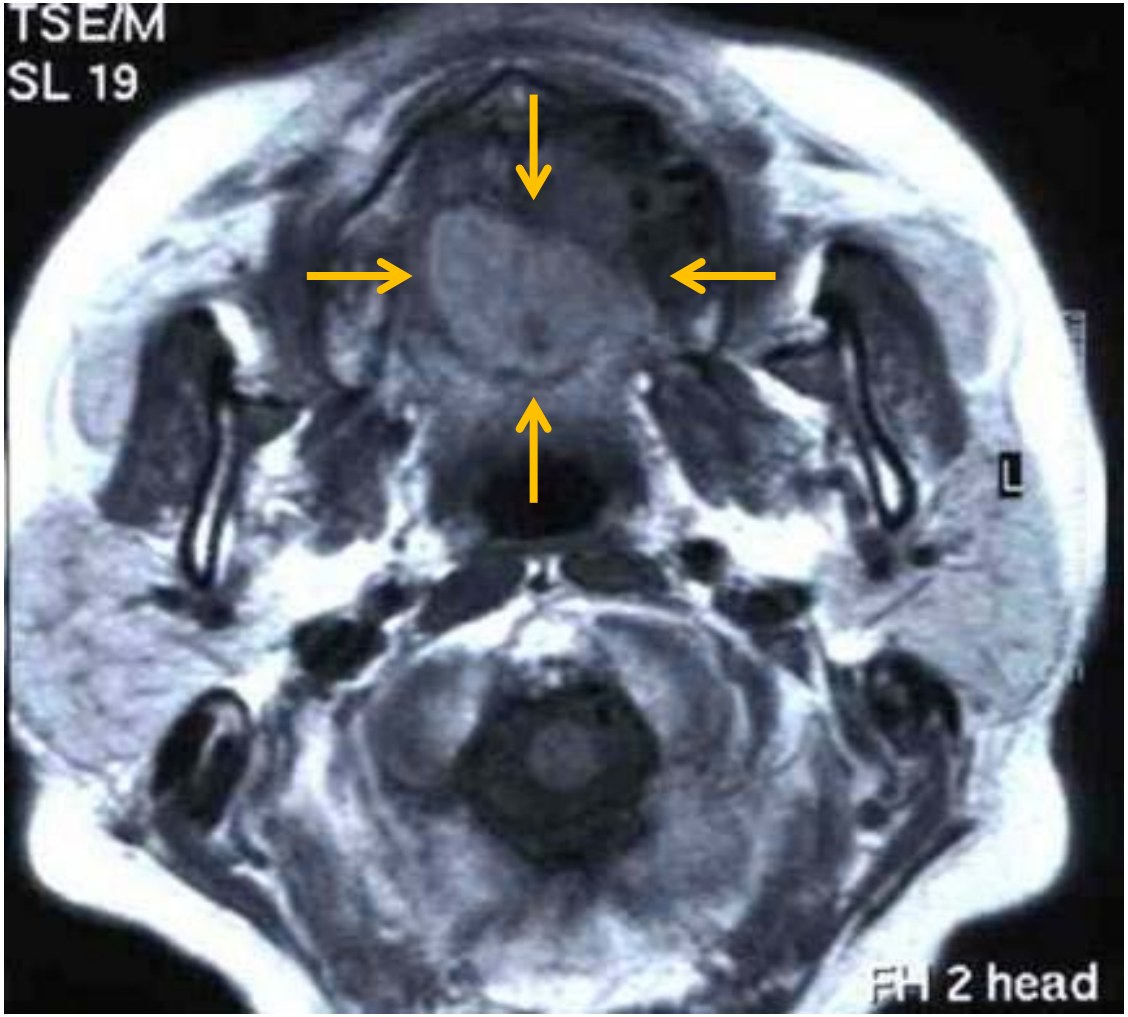


Fig. 2C

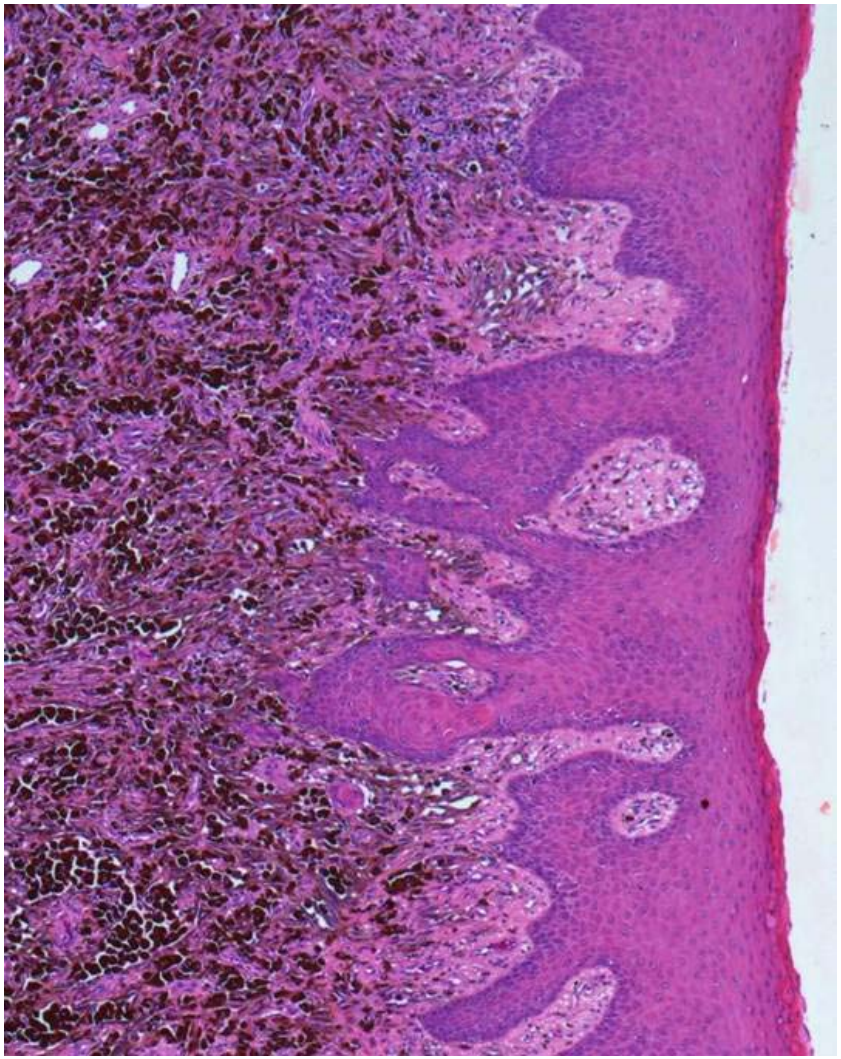


Fig. 3A

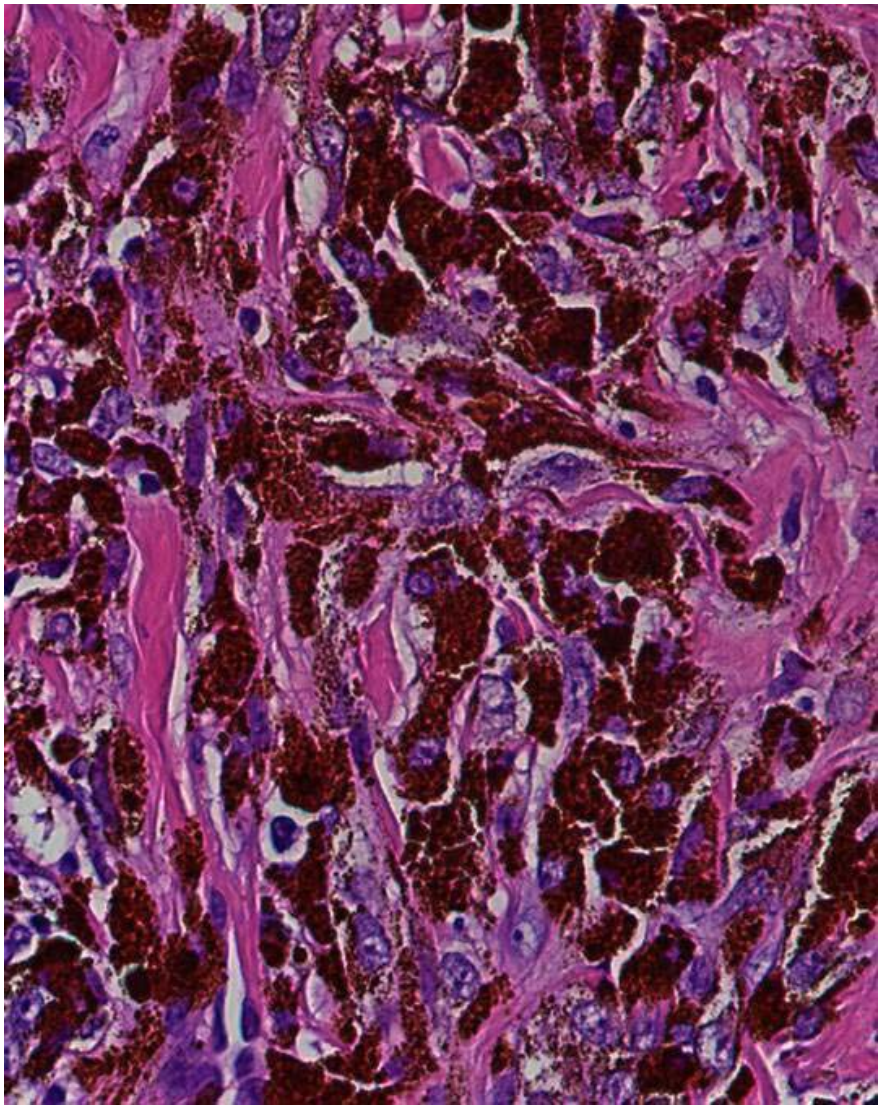
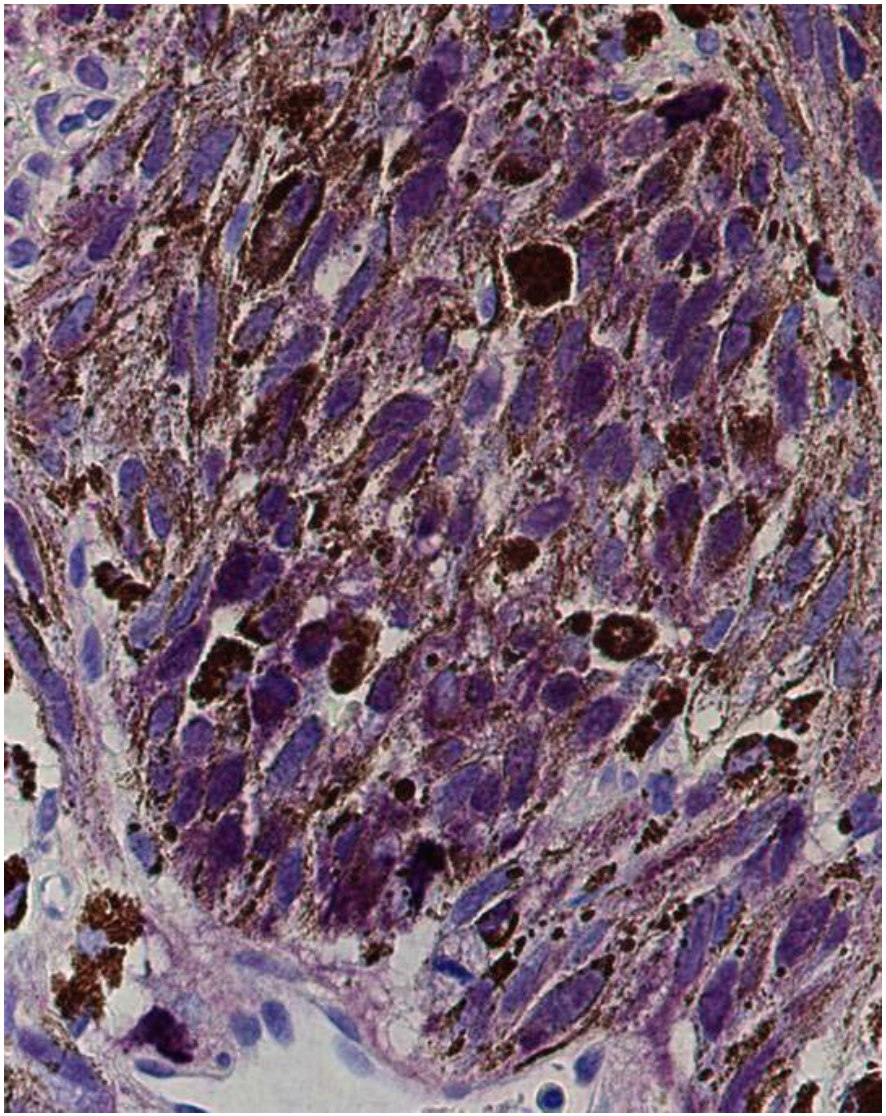


Fig. 3B



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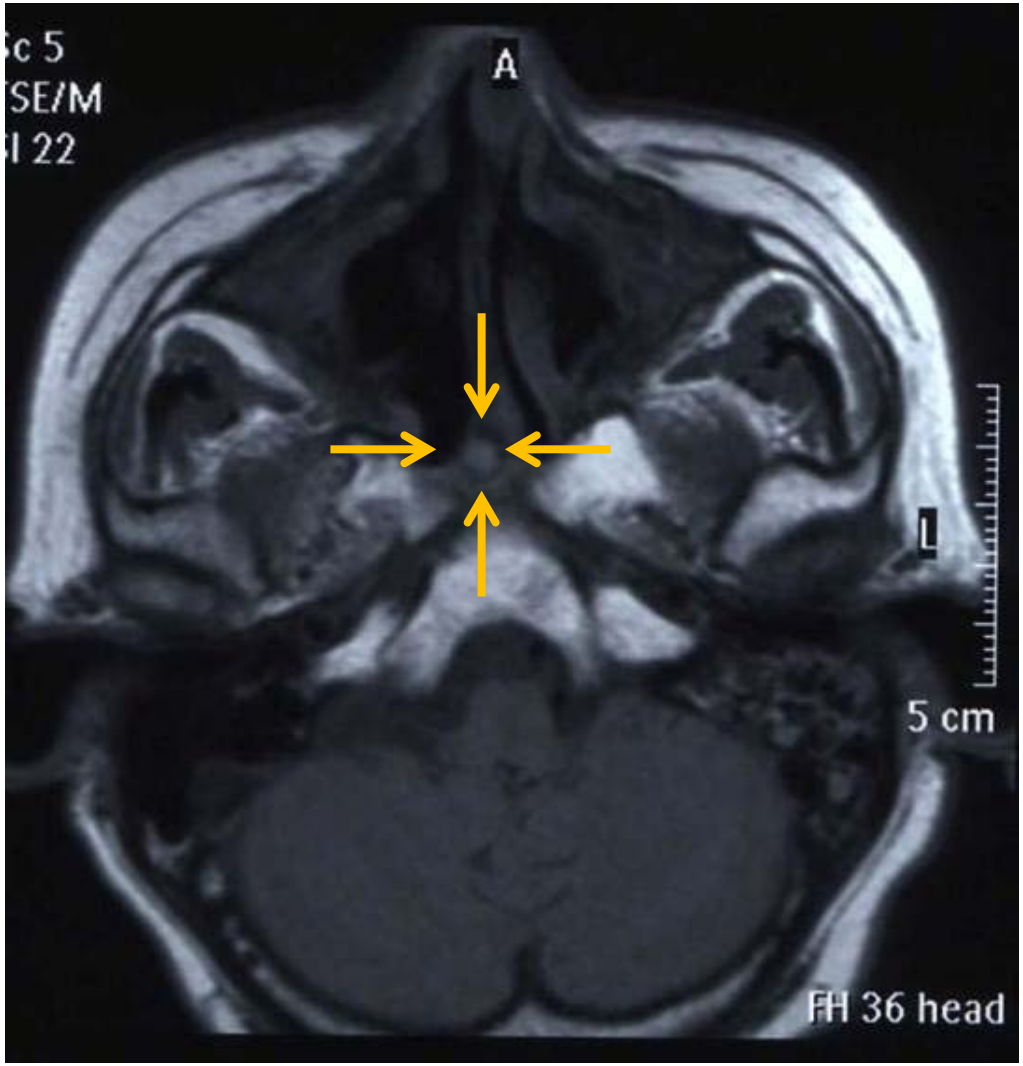

Fig. 4

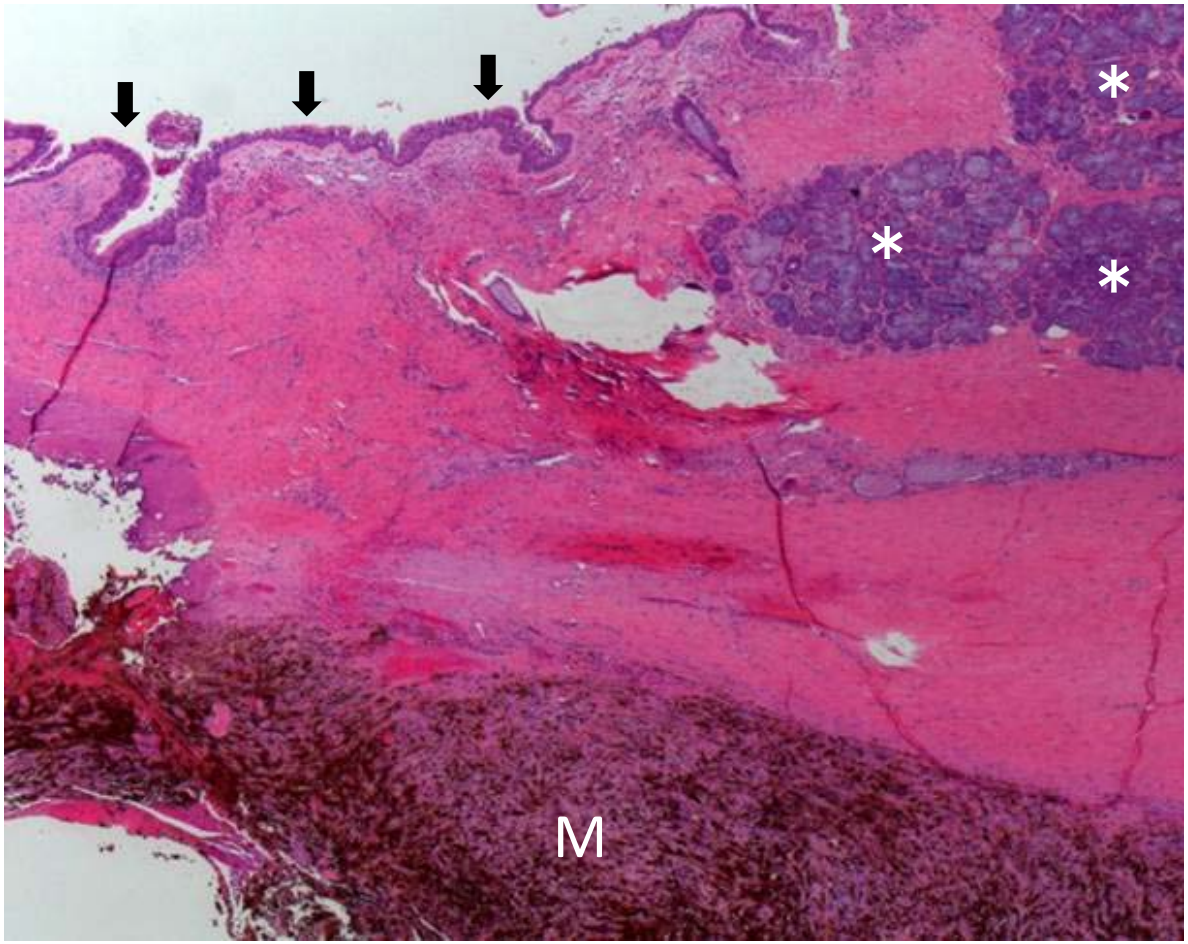

Fig. 5

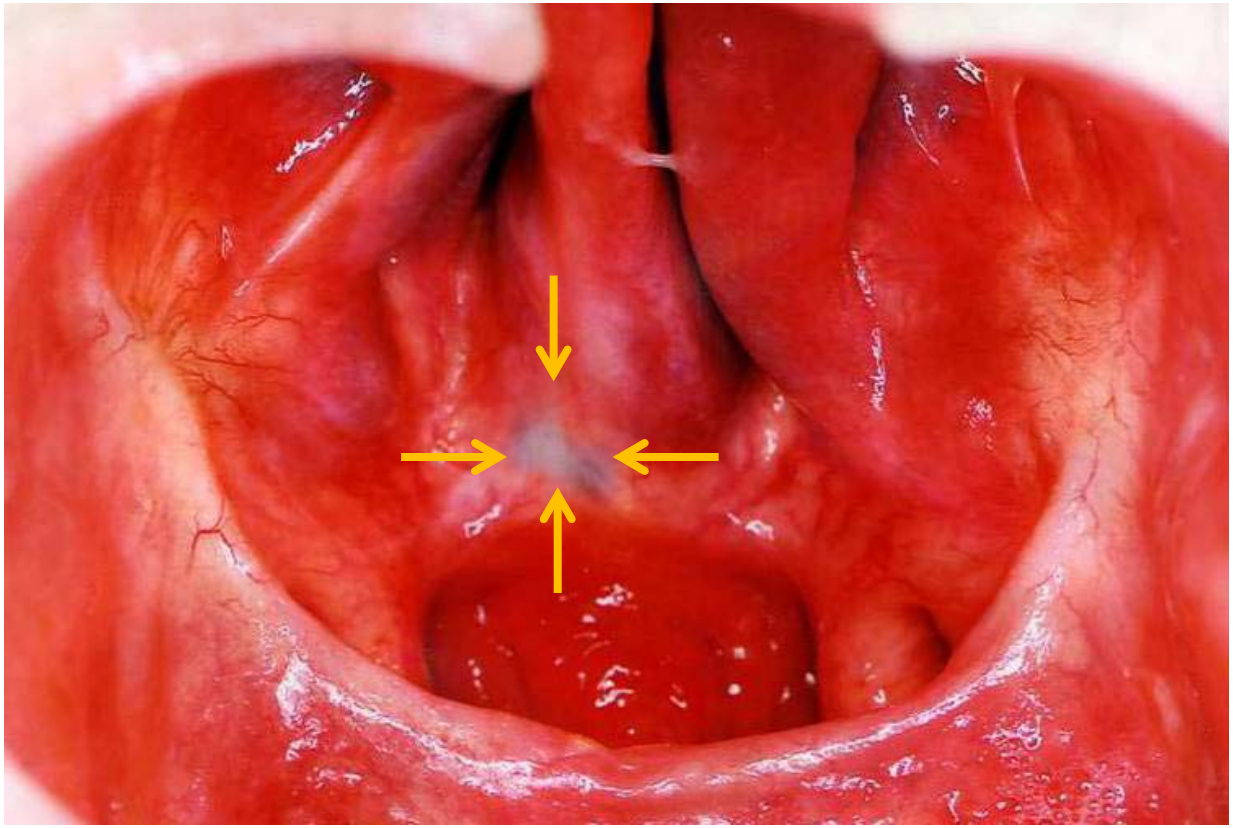

Fig. 6

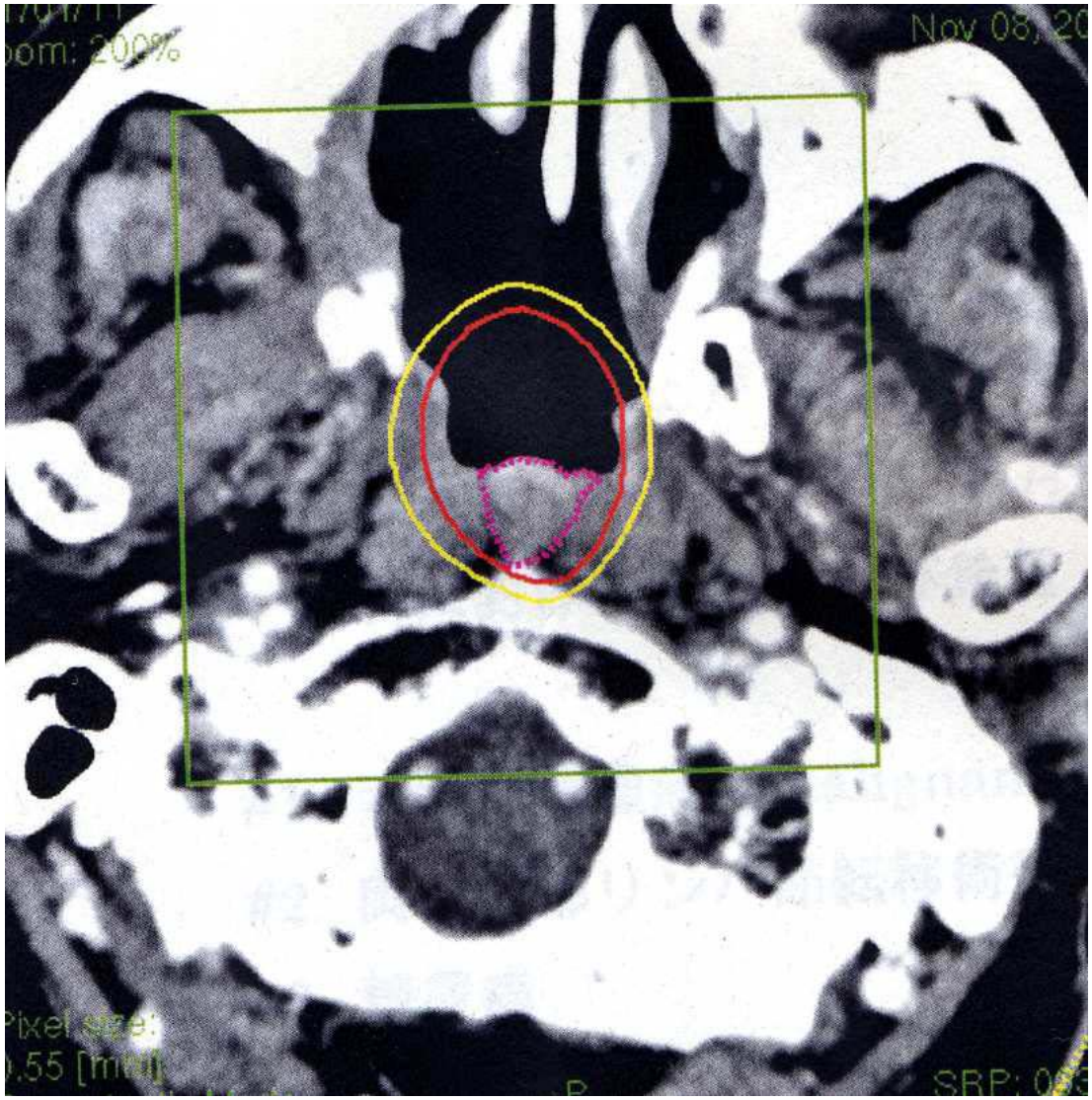

Fig. 7

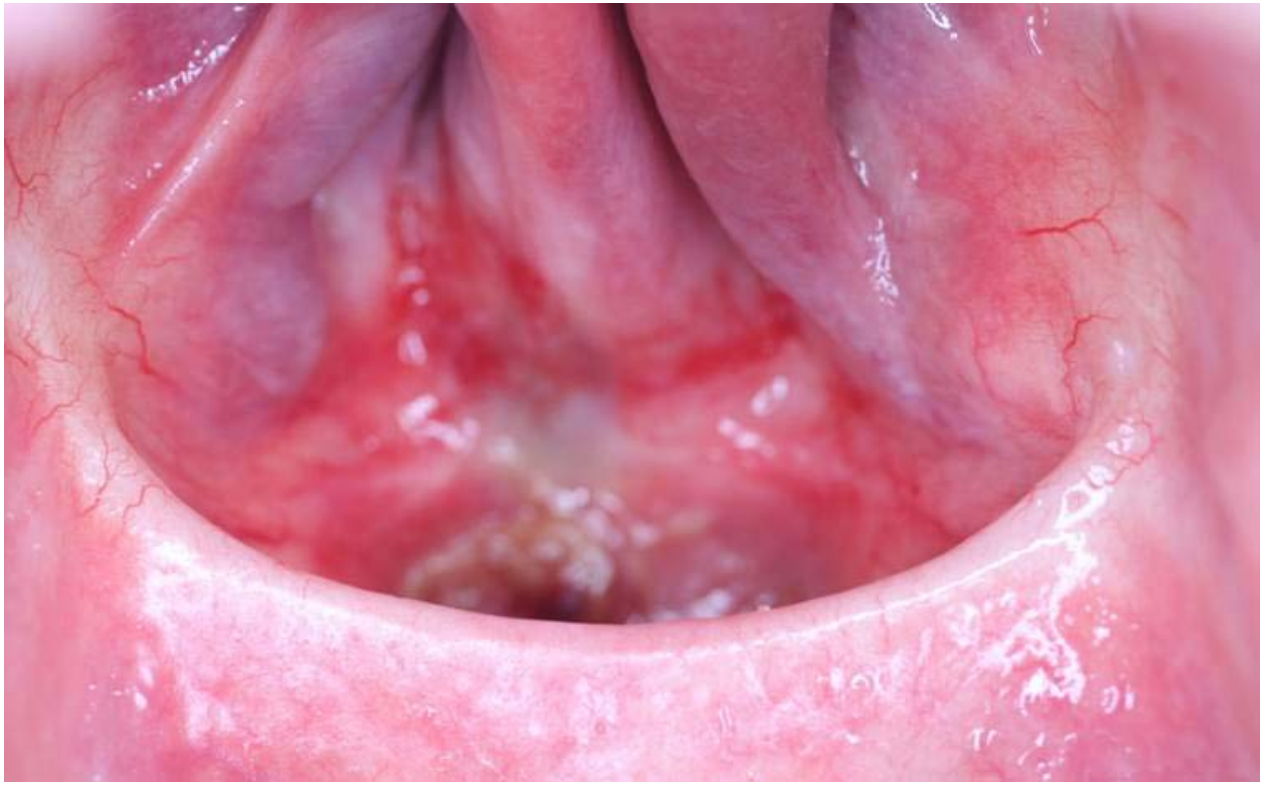

Fig. 8A

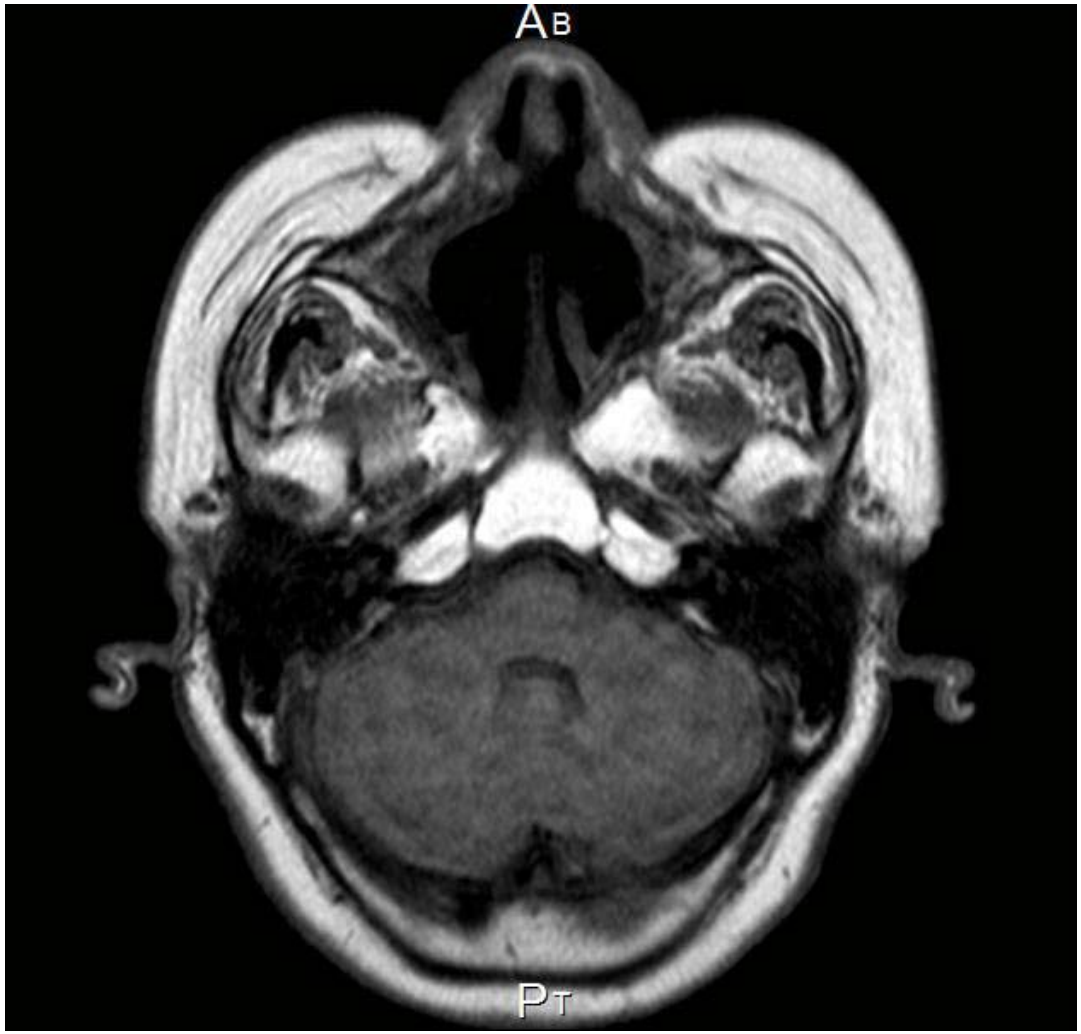

Fig. 8B