Dear Editor,

Mucosal melanoma of the Eustachian tube is extremely rare. There are only 10 other case reports of mucosal melanoma of Eustachian tube origin. Here, we share our 4-year follow-up of a 55-year-old Chinese lady with right Eustachian tube melanoma. We also review other case reports of this grave condition and discuss the management options and prognoses observed.

Methods

Our patient is a 55-year old Chinese lady. She presented with right-sided conductive hearing loss of 2 months duration. Right serous otitis media was seen on otoscopy. Nasoendoscopy showed a black mass at the right Eustachian tube opening (Figure 1). A biopsy of this mass was done and histology revealed malignant melanoma.

Magnetic Resonance Imaging (MRI) of the post nasal space showed a 11 x 4 mm, hypo-enhancing, T1- and T2-weighted isointense lesion at the cartilaginous portion of the right Eustachian tube, extending to its pharyngeal orifice. This caused proximal obstruction and resultant mastoid effusion. The tumour was centered in the bony Eustachian tube, with involvement of the right torus tubarius. The tumour did not appear to extend into or beyond the middle ear orifice (Figure 2). There was no cervical lymphadenopathy seen on MRI.

Computed tomography (CT) scan of the temporal bone revealed soft tissue opacification of the right Eustachian tube. There was also opacification of the middle ear, mastoid antrum and air cells. There was no mass effect or bony erosion. There were no distant metastases.

Preoperatively, there was concern that the tumour was located close to the petrous part of the internal carotid artery. Hence, a balloon occlusion test was performed.
During balloon occlusion test of the right internal carotid artery, there was good crossover flow from the left internal carotid artery with no significant delay in the venous return compared to the baseline. Neurological assessment performed at 0, 5, 10 and 15 minutes did not reveal any focal neurological deficit.

The patient’s case was discussed at our multidisciplinary tumour board and the decision was made for surgery and adjuvant radiotherapy. She underwent infratemporal fossa Fisch B approach and open nasopharyngectomy via maxillary swing with en-bloc excision of the Eustachian tube and tumour. Figure 3 shows the maxillary swing to expose the eustachian tube opening in the nasopharynx. The eustachian tube was traced from the bony to the cartilaginous portion and removed in entirety with the tumour. The petrous carotid artery was delineated. A diamond burr was used to drill in the areas of the dura and carotid artery in order to prevent injury to these delicate areas. The nasopharyngeal defect was obliterated with a temporalis muscle flap.

Histological analysis showed tumour cells positive for human melanoma black (HMB-45) and patchily positive for Melan-A. Ki-67 staining indicated a MIB-1 index of approximately 10-15% in the tumour. No lymphovascular invasion and no perineural invasion was seen. The tumour measured up to 1.5mm thick. It did not invade the cartilage and was 1mm from the closest radial margin. Both medial and lateral resection margins were not involved by tumour. Melanin pigments were present in the acinar and ductal cell of surrounding mucinous glands.

The patient completed 60 Gy of radiation therapy (RT) in 30 fractions using a 7-field intensity modulated radiation therapy (IMRT) plan to the tumour bed only. 1-year post-treatment CT scan did not reveal any recurrence.

Results

21 months post operatively, the patient complained of right sided neck swelling. There was a 2cm right level 2 cervical lymph node on palpation. The rest of the head and neck examination was unremarkable. Fine needle aspiration of the mass confirmed malignant melanoma. Positron emission tomography-CT (PET-CT) showed an enlarged hypermetabolic right level 2 cervical lymph node measuring 2.2 x 1.5 cm with SUVmax 6.9, which was highly suspicious for nodal metastasis (Figure 4). A right modified radical neck dissection with preservation of the spinal accessory nerve, internal jugular vein and sternocleidomastoid muscle was performed. The final histology revealed 1 out of 28 lymph nodes positive for malignancy, with an enlarged blackish brown lymph node measuring 2.5cm in maximum dimension in level 2.

7 months post neck dissection, there was a subcutaneous 1-cm lump noted at the right neck level 2 region. During excision under local anaesthesia, 2 lumps were noted at the same region and histology confirmed metastatic melanoma. The patient underwent wide excision under general anaesthesia. The deep margins were consistent with metastatic deposit of malignant melanoma.

The patient’s case was discussed at the Head and Neck multidisciplinary tumour board. Tumour board suggested single modality treatment with chemotherapy, as repeat radiation therapy was not suitable since she had previously undergone radiation. The patient was not keen on chemotherapy. She subsequently deceased from pulmonary metastases, 4 years from the initial diagnosis of Eustachian tube melanoma.

Discussion

Mucosal melanomas are rare and constitute only 1.3% of all cutaneous and non-cutaneous melanomas. Non-cutaneous mucosal melanoma is most common in the head and neck with distribution as follows: head and neck
55.4%, anal/rectal 23.8%, female genital tract 18.0%, and urinary tract sites 2.8%. The nose, paranasal sinuses, and oral cavity are the most common sites of mucosal melanomas in the head and neck. Primary middle ear mucosal melanoma and eustachian tube melanoma are rare. To date, there are only 21 cases reported, with 10 cases of melanoma arising from the middle ear, and 11 cases arising from the Eustachian tube. The mean age at diagnosis was 63.7 years old, with a range of 41 to 88 years. 12 patients were female (57.1%) and 9 were male (42.9%). The most common presenting symptom of Eustachian tube melanoma was hearing loss (81.5%) and ear fullness (54.5%). Nasoendoscopy of all the patients with eustachian tube melanoma revealed a mass at the pharyngeal orifice of the Eustachian tube and 90% had serous otitis media.

MRI has better soft tissue resolution than CT and is currently the best imaging technique for Eustachian tube melanomas, giving information on both the primary lesion and cervical lymph nodes. Melanin is paramagnetic and hence, the higher the melanin content in the tumour, the more intense the signal on T₁-weighted image, and the lower the signal intensity on T₂-weighted image. Amelanotic melanoma will display converse properties with hypointensity on T₁-weighted and hyperintensity on T₂-weighted images. However, our patient showed a hypo-enhancing, T₁- and T₂-weighted isointense lesion even though it was a melanotic melanoma (Figure 2).

The position of the Eustachian tube makes it a challenging area for surgical resection. We combined the maxillary swing and Fisch B infratemporal approaches to excise the tumour and Eustachian tube en-bloc. The Fisch B approach allows good exposure of the carotid artery and this was essential as the preoperative imaging showed close proximity of the tumour to the carotid artery. Hence, exposure of the vessel would allow quick vascular control in the event of inadvertent injury to the vessel.

The role of elective neck dissection for mucosal melanoma of the head and neck is undetermined. The lymphatic drainage of the Eustachian tube is to the parotid, retropharyngeal and cervical lymph nodes. Bachar et al found regional recurrence rate of 19.7%. This significant proportion of recurrence coupled with the aggressive and high mortality rate of recurrent disease, should compel the surgeon to consider an elective neck dissection, especially since the surgery for the primary tumour is a major surgery intended to cure. In our case, the patient subsequently had cervical lymph node metastases, illustrating this point. In particular, level 2 should be addressed in the elective neck dissection.

Fig. 4. (A) Positron Emission Tomography and (B) Computed Tomography images show a very FDG avid (SUV_{max}) 6.9 and enlarged right cervical level 1b lymph node, that is suspicious for nodal recurrence.
Sentinel lymph node biopsy is performed in cutaneous melanoma to determine the regional lymph node status in early stage disease as lymph node involvement is an important prognostic indicator. Mucosal melanoma is different from cutaneous melanoma, as most patients will develop distant metastases independent of lymph node status. At present, there is insufficient information on the accuracy or clinical utility of sentinel lymph node biopsy in mucosal melanoma.

The role of radiotherapy in mucosal melanoma of the head and neck is favoured as adjuvant treatment rather than primary therapy. The mainstay treatment is radical surgical resection and adjuvant radiotherapy in select patients with high-risk features. In spite of multimodality local treatment, the outcomes for mucosal melanoma remain poor. The 5-year overall survival of head and neck mucosal melanomas is poor at less than 30% in most series. In a review of the 11 cases of Eustachian tube mucosal melanoma available in the literature, only 4 patients had no evidence of disease at the time of reporting. 1 patient died, 3 had distance metastasis, 2 had local recurrence and 1 had partial response. The follow-up period of the patients with no evidence of disease was low and ranged from 8 to 15 months. With longer follow-up, the prognosis of this condition may be grimmer. Of the 10 cases available in the literature of Eustachian tube melanoma, ours provides the longest follow up available.

Michel et al. compared 3 staging systems for sinonasal mucosal melanomas – Ballantyne/Prasad staging, AJCC staging systems, and AJCC carcinoma TNM. In their retrospective study of 35 patients with sinonasal mucosal melanoma, they found that only the AJCC carcinoma TNM was significantly correlated with overall survival. We wonder if this finding is applicable to Eustachian tube mucosal melanomas, as although the Eustachian tube is not a direct component of the sinonasal tract, the mucous membrane of the Eustachian tube and sinonasal tract is similar and in continuity. Based on Ballantyne/Prasad staging, our patient’s tumour was stage 1 level 2 as the tumour was localized and did not invade the cartilage. Based on the 8th edition AJCC staging of head and neck mucosal melanomas, our patient’s tumour was T3N0MO. There is no prognostic stage grouping in AJCC for head and neck mucosal melanomas.

Precision medicine and immunotherapy has a growing role in cancer management. Tumour genome sequencing and molecular pathology are increasingly used to tailor therapy, and immune checkpoint inhibitors has led to long remissions of more than 10 years for advanced malignant melanoma. Frequently altered genes such as KIT, BRAF, N-RAS and GNAQ, and molecular pathways like PI3K-Akt-mTOR in mucosal melanoma are being studied. Research on the use of c-KIT inhibitors such as imatinib in melanomas with c-KIT alterations is on-going. However, implementing these advances in research is challenging due to the rarity of head and neck mucosal melanomas, and high cost. C-kit mutation analysis and BRAF sequencing for our patient did not detect any mutation.

Conclusions

Mucosal melanoma of the Eustachian tube is a rare condition. Majority of patients present with localised disease, without nodal metastases. Surgical excision is challenging due to the deep-seated nature of the Eustachian tube from the nasopharynx to the middle ear, and close proximity to critical structures such as the internal carotid artery and facial nerve. Although the role of elective neck dissection is undetermined in the literature, we recommend performing based on current limited evidence. Despite multimodality treatment, outcomes remain poor with a high rate of mortality.

REFERENCES


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