PATHOLOGICA 2024;116:144-152;
DOI: 10.32074/1591-951X-980

Review

Melanoma of the external auditory canal: case report and systematic literature review

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Summary

Melanoma of the external auditory canal (EAC) is particularly rare and poorly understood, with limited available data on management and survival. This systematic review aims to analyze existing data and provide insights into the management and prognosis the beginning of EAC melanoma. It is conducted using Pubmed and Scopus databases from inception to July 2023 and it follows the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 guidelines. Searches are performed using the search string "(melanoma) AND (external auditory canal)".

The review includes a total of 30 patients diagnosed with EAC melanoma, supplemented by an additional case from the authors' clinical experience. The role of Breslow thickness as a determining factor for the choice of surgery remains inconclusive due to limited available data. Sentinel lymph node biopsy and adjuvant therapy are sparingly employed, indicating the need for standardized guidelines. Patients in the study demonstrate a 50% overall survival rate at 5 years.

EAC Melanoma is a rare and aggressive malignancy with limited therapeutic guidelines. Surgical interventions, including wide local excision and lateral temporal bone resection, are the primary treatment options for patients without distant metastases.

Key words: melanoma, external auditory canal, ear's melanoma, surgery for melanoma, skull base surgery

Received: February 4, 2024
Accepted: May 3, 2024

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How to cite this article: Demattè M, Liberale C, Bonsembiante A. Melanoma of the external auditory canal: case report and systematic literature review. Pathologica 2024;116:1-4. https://doi.org/10.32074/1591-951X-980

Introduction

Invasive melanoma constitutes about 1% of all skin cancers, but it still remains one of the most deadly types of cancer [1]. In the last 30 years, the incidence of melanoma has been steadily increasing [2]. According to the latest evidence in the literature, melanoma of the ear comprises approximately 1% of all melanomas and represents approximately 7% to 17% of melanomas found on the head and neck district [2,3]. EAC melanoma is a rare entity and to date only a few cases have been reported in the literature. While sun exposure is a well-established risk factor for cutaneous melanoma [4], it does not appear to play a significant role in the development of melanoma in the external auditory canal, due to its location. Because of its rarity, EAC melanoma is poorly characterized, and there is a lack of extensive data about its management and overall survival. In our systematic literature review we include one additional case from our direct clinical experience, making it the largest case series of EAC melanoma reported to date.

Given the scarcity of cases, the available literature may provide limited insights into the best management strategies and prognosis of EAC mel-

anoma. Our aim is to analyze all available data to gain a comprehensive overview of this rare condition, especially with regards to treatment and overall survival. The main goal is to collect relevant data to improve clinical decision-making and patient outcomes, with a special focus on recent discoveries such as the role of the sentinel lymph node or the latest systemic therapy.

Case report

A 44-year-old woman presented to our clinic with complaints of persistent left ear fullness following a bout of flu. Upon physical examination the left external auditory canal was observed to be filled with inflammatory material and exhibited easy bleeding. The patient underwent a CT scan of the ear bone, which showed a polypoid formation measuring 9 mm adherent to the anterior wall of the external auditory canal, without any evidence of bone erosion (Fig. 1). Then the patient underwent an MRI with contrast, which revealed the presence of a solid neoformation with contrast-enhancement measuring approximately 12 mm at the level of the left external auditory canal, with no associated bone changes (Fig. 2). Subsequently multiple biopsies of the mass were taken and the result was fragments of intradermal melanocytic nevus.

Considering the histological examination and CT and MRI reports, the patient was recommended to under-

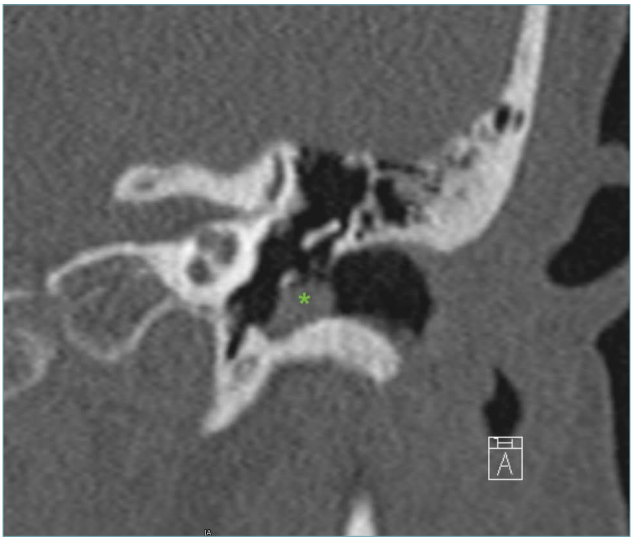

Figure 1. Coronal CT scan showing a polypoid formation (*) measuring 9 mm adherent to the anterior wall of the external auditory canal, without any evidence of bone erosion.

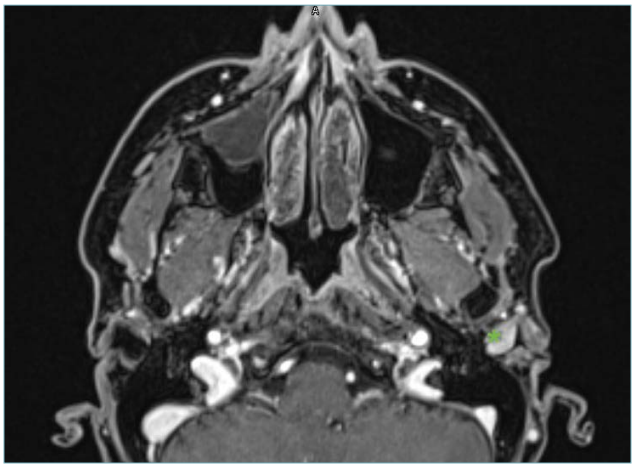

Figure 2. Axial MRI with contrast, showing a solid neoformation with contrast-enhancement (*) measuring approximately 12 mm at the level of the left external auditory canal, with no associated bone changes.

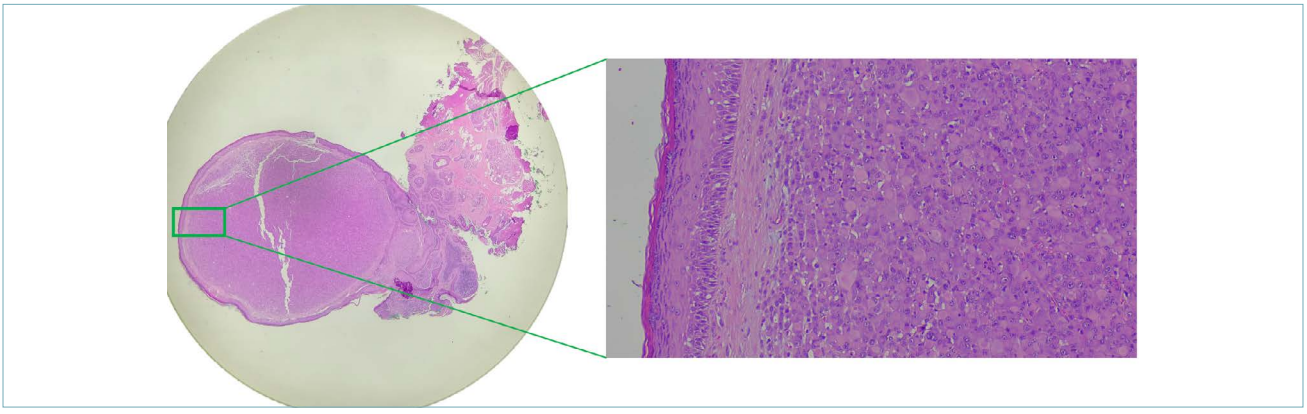

Figure 3. Histologic report showing nodular melanoma arising in dermal nevus, consisting of large pleomorphic atypical cells (on the left side). The neoplastic nodule has a maximum depth of 5 mm in the dermis. Epidermal surface appears normal (on the right side).

go wide locale excision (WLE) under general anesthesia. The patient underwent surgery and the histological reports revealed nodular melanoma in composite melanocytic nevus of congenital type. The microscopic examination of the lesion showed absent ulceration, a maximum diameter of 5 mm, Breslow thickness of 6.8 mm, Clark level III with no vascular and perineural invasion. Excision margins were unharmed (Fig. 3). Moreover, the immunohistochemistry showed positivity for proteins S100, SOX10, BRAF-V600E, INI1, and negativity for p16, HMB45, MelanA. The expression of BAP1 appeared preserved; the lesion did not fall within BAP-mutated melanocytic neoplasms.
The disease was staged as cutaneous melanoma of the EAC pT4a according with the 8th Edition of TNM. After a multidisciplinary discussion, the patient was referred for a brain MRI and PET-CT scan to detect any metastasis. The results of both exams were negative (staging: cN0 M0, following the 8th Edition of TNM). The patient then returned to her hometown continuing follow-up there. After 3 months of follow-up, the patient was alive without any relapse of disease.

Materials and methods

This review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 guidelines [5]. The research was carried out using the Pubmed and Scopus databases with the following search string: (melanoma) AND (external auditory canal). All articles found with this search string were included without any period restriction. According to the databases, the most recent research was conducted in July 2023. Duplicate articles in the two databases were eliminated at the beginning. The inclusion criteria for the first phase of abstract reading selection were: availability of abstracts and articles about the disease of the external auditory canal. The exclusion criteria for this phase were: no abstract available or incongruous articles. Following the initial abstract-based selection, a full-text reading was performed using additional criteria. The inclusion criteria for the second selection phase were: case reports or case series as study designs, full text availability and articles concerning EAC melanoma. The exclusion criteria were full-text unavailability, articles with data missing and melanoma of other ear districts. Four articles were included from other sources. The selected articles were analysed in-depth and data on the following topics were extracted: study design and year of publication, age and gender of the patients, imaging, and histologic reports of the first disease and its metastasis, type of treatment and treatment's result, potential recurrence and related treatment, as well as the follow-up status.

Results

Using our search string, we initially identified a total of 173 articles. After removing 51 duplicate articles, we performed an abstract reading selection based on the inclusion criteria and chose 34 articles. Subsequently, we conducted a further exclusion reading of full-length papers, resulting in 16 articles that met the pre-established criteria. Four articles were added from other sources, due to their relevance. The process of literature selection, following the PRISMA statement guidelines [5], is depicted in Figure 4.
A total of 31 patients were included in the selected papers, with the uthors adding the treated case to perform a comprehensive analysis. The details of the 31 patients are presented in Table I.
There were 13 men and 12 women (for 6 patients, data regarding gender was not available). The mean age at the diagnosis of melanoma of the EAC was 57.06 years (range 11-80 years). The disease was in the left external auditory canal in 10 cases and in the right one in 7 cases. In the remaining 14 cases this data was not available.
The clinical presentation of EAC melanoma showed a wide variability. Several patients report multiple symptoms at the first visit. In fact, 8 patients complained of pain, 8 referred bleeding or otorrhea from the affected ear, 7 patients reported hearing loss or deafness, 4 patients referred ear fullness, and only 3 patients complained of swelling in the auricular region.
For the diagnosis, several radiological examinations were performed: 12 patients underwent CT scans, 5 patients MRI, and 4 PET CT. Some patients underwent more than one exam, but there is no data regarding diagnostic radiology for 16 patients.
All 31 patients had a histological diagnosis of malignant mucosal EAC melanoma. Specific data about Clark level and Breslow thickness was available for 14 patients (Tab. I for details). In immunohistochemistry, four patients showed positivity for HMB-45, and another four patients show positivity for protein S100.
The treatment of EAC melanoma differed according to the stage of the disease and the patients' conditions. Two patients undergo lateral temporal bone resection and 11 lateral temporal bone resection, superficial parotidectomy and selective neck dissection. Eleven patients underwent WLE and one of them also had selective neck dissection. Four patients undergo surgery, but details of the surgery were not available. Only one patient underwent radiotherapy and another

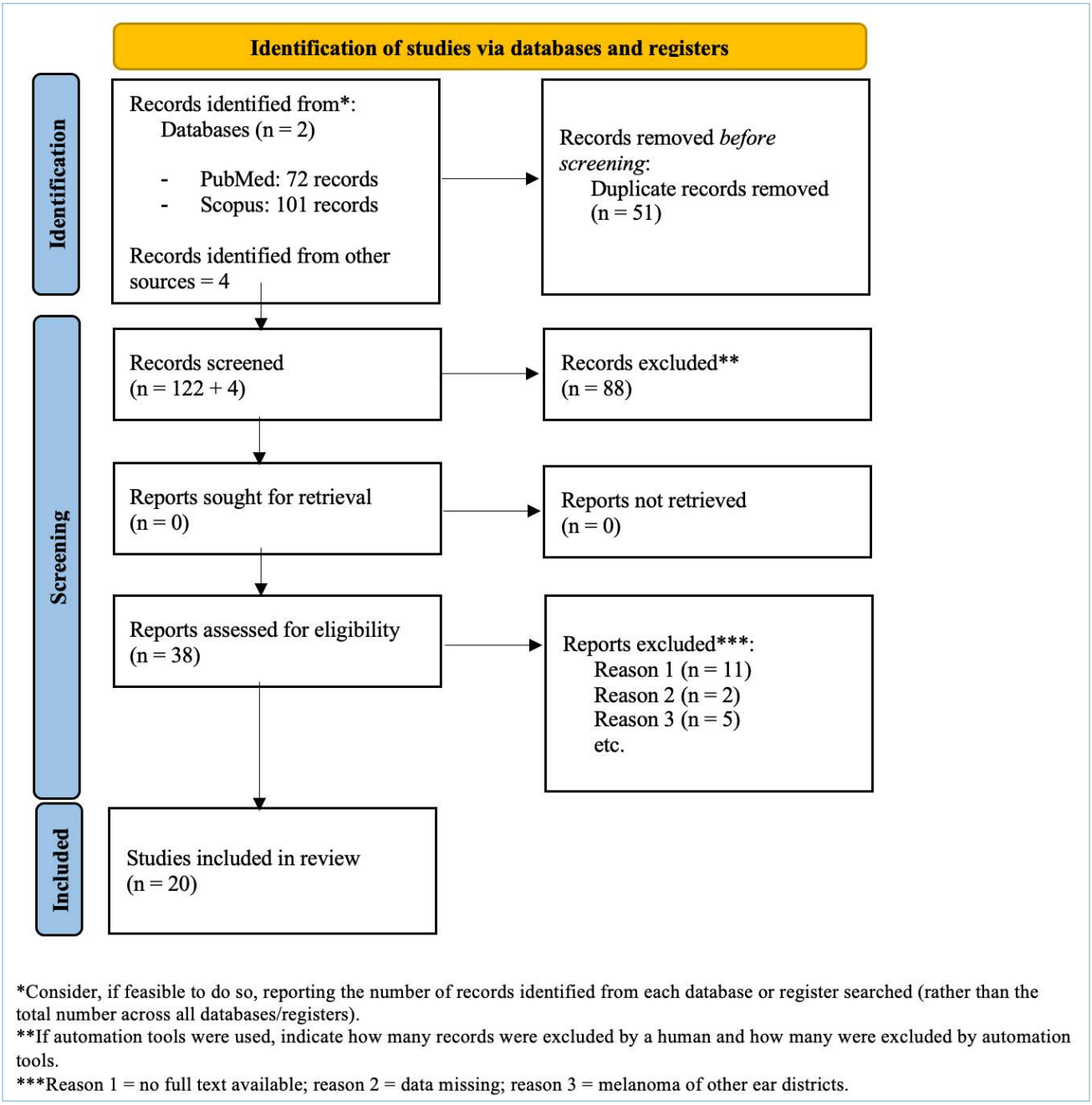

Figure 4. Paper selection process.

one chemotherapy with nivolumab (Tab. II). Only 4 patients underwent a sentinel lymph node biopsy.

After the first treatment, 13 patients had adjuvant radiotherapy, and only two of them also underwent adjuvant chemotherapy.

Only three patients developed local recurrence. One underwent, one receives chemotherapy, and there was no available data for the last one.

Fourteen patients (45.16%) developed metastasis. Some patients had metastasis in more than one site. The sites of metastasis are listed in Table III. The most frequent site of metastasis was the lung (7 patients), followed by lymph nodes (4 patients), the brain (3 patients) and the spine and the liver (2 patients each).

The average follow-up time for patients is 17.59 months

Table I. Details of the 31 patients.

Author	Year	N.	Sex	Age	Primary treatment	Histology details	Breslow thickness	Clark level	Sentinel lymph node biopsy	MTX	FU time (months)	FU status
Friedman et al.*[6]	1954	1	F	68	WLE	NA	NA	NA	NA	Brain	12	DOD
Lederman*[7]	1965	3	NA	NA	WLE	NA	NA	NA	NA	NA	NA	DOD
Conley et al.*[8]	1976	3	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sambe et al.[9]	1985	1	F	39	WLE	NA	NA	NA	NA	lungs	3	DOO
Shih et al.*[10]	1990	1	F	68	LTBR + P + SND	NA	NA	NA	NA	-	18	AND
Kang et al.[11]	1992	1	F	58	LTBR + P + SND	NA	NA	NA	NA	-	4	AND
Banerjee et al.[12]	1993	1	M	76	WLE	NA	6 mm	NA	NA	Lungs + spine	16	DOD
Langman et al.[13]	1996	1	F	43	LTBR + P + SND	NA	1.37-2.17 mm	III	NA	-	36	AND
Milbrath et al.[14]	1998	1	M	75	LTBR + P + SND	NA	17 mm	IV-V	NA	Lymph nodes + lungs	13	DOD
Ayadi et al.[15]	2002	1	M	65	WLE + SND	NA	NA	NA	NA	Lymph nodes + brain	6	DOD
Amando Garcìa et al.[16]	2003	1	M	59	LTBR + P + SND	NA	10 mm	V	NA	-	9	AND
Hannan[17]	2006	1	M	40	LTBR + P + SND	NA	NA	NA	NA	Lymph nodes	NA	NA
Lin et al.[18]	2009	1	M	52	LTBR	HMB45, S100	NA	NA	Yes	Lungs	36	AD
Gowthami et al.[19]	2014	1	F	11	surgery	HMB45, S100	NA	NA	NA	local	9	DOD
Khonglah et al.[20]	2017	1	M	50	WLE	HMB45	15 mm	V	NA	Parotid + lymph nodes	9	AD
Landau et al.[21]	2018	1	M	86	WLE	NA	3 mm	IV	NA	brain, peritoneum, liver	7	DOD
Komatsuda et al.[22]	2020	1	F	80	CT	NA	NA	NA	NA	-	60	AD
Li et al.[23]	2021	1	F	57	RT	NA	NA	NA	NA	liver	8	DOD
Appelbaum et al.[2]	2021	7	3 M, 4 F	52 (average)	LTBR + P + SND	NA	NA	NA	NA	-	135	AND
					LTBR + P + SND	NA	1.8 mm	IV	Yes	Yes	8	DOD
					LTBR	NA	5.5 mm	IV	NA	Yes	136	AD
					LTBR + P + SND	NA	3 mm	IV	NA	-	15	AND
					LTBR + P + SND	NA	5.1 mm	V	Yes	Yes	21	DOD
					WLE	NA	In situ	I	NA	-	27	AND
					LTBR + P + SND	NA	2.8 mm	IV	Yes	-	22	AND
Liu et al.[24]	2023	1	M	56	NA	HMB45, melanA, S100	NA	NA	NA	lungs	NA	NA
Dematte et al.	2023	1	F	44	WLE	S100	6,8 mm	III	NA	-	3	AND

NA = not available; RT = radiotherapy; LTBR = lateral temporal bone resection; P = parotidectomy; SND = selective neck dissection; WLE = wide local excision; DOD = dead for disease; AD = alive with disease; AND = alive without disease. *articles included from other sources (i.e. not PubMed nor Scopus).

Table II. Treatments in detail.

Type of treatment	Number of patients
Wide local excision	10
Wide local excision, selective neck dissection	1
Lateral temporal bone resection	2
Lateral temporal bone resection, superficial parotidectomy, selective neck dissection	11
Surgery (not specified)	1
CT	1
RT	1
NA	4
	31

Table III. Sites of metastasis of EAC melanoma.

Site of metastasis	Number of patients
Lymph nodes	1
Lungs	3
Liver	1
Brain	1
Contralateral EAC, lungs and brain	1
Lymph nodes and brain	1
Brain, peritoneum, liver, subcutaneous metastasis	1
Lungs and spine	2
Lungs and lymph nodes	1
Chest wall, liver and skin of the back	1
Parotid gland and lymph nodes	1
	14

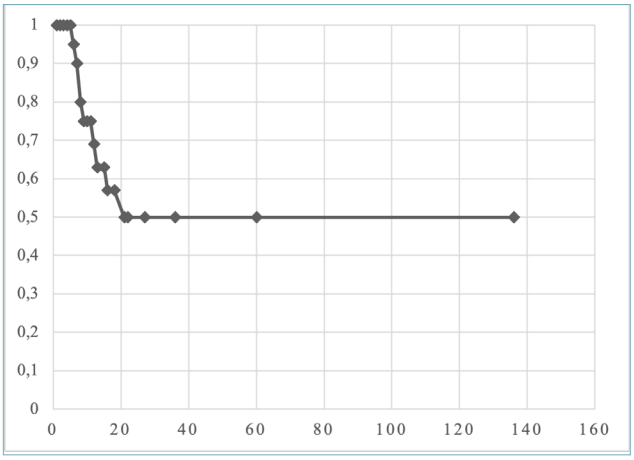

Figure 5. Kaplan-Meier survival curve.

(range 1-136 months) and data was not available for 8 patients. The follow-up status is not available for 5 patients. Out of the available data, 4 patients are alive with disease (AD), 9 patients alive without disease (AND) and 13 patients deceased from the disease (DOD).

Figure 5 displays the Kaplan-Meier survival curve generated from the data of 23 patients. Our findings indicate that the mean survival rate for individuals with melanoma of the EAC was 50% after 5 years (60 months).

Discussion

According to the latest statistical evidence, the incidence rate for cutaneous melanoma continues to increase. It is projected to reach 7% among men and 4% among women of estimated new cancer cases in the coming years [25]. As previously stated, melanoma is a rare cancer, constituting only 1% of all skin cancers [1] and EAC melanoma is even rarer [2]. To our knowledge, this is the systematic review with the largest number of patients diagnosed with EAC melanoma (31 patients). The treatment of skin melanomas is primarily surgical and the specific surgical approach depends on the location of the disease. Ethun et al. collected various national guidelines to determine the appropriate surgical margins required to achieve oncological radicality in cutaneous melanoma excision [26]. The extent of surgical margins primarily correlates with the depth of melanoma invasion; deeper melanomas necessitate wider resection margins [26]. Breslow thickness, which measures the depth of melanoma from the skin's surface down to the deepest point of the tumor, plays a fundamental role in the decision-making process for managing melanoma. Unfortunately, to date, there is still no established cutoff value for Breslow thickness that dictates the need for more extensive surgery in external auditory canal (EAC) melanoma. In our dataset, Breslow thickness data is available for only 12 out of 31 patients. Among them, eight underwent lateral temporal bone resection with a range of Breslow thickness between 1.37 mm and 17 mm, along with superficial parotidectomy and selective neck dissection, while four patients had WLE surgery with a Breslow thickness ranging from 3 mm to 15 mm. Our analysis suggests that Breslow thickness does not yet appear to be a determining factor in the choice of surgery type.

Additional considerations come into play when dealing with head and neck melanoma (HNM). HNM involves anatomical regions rich in structures that require a more conservative approach (such as eyes, mouth, and ears) while still aiming for oncological radicality. Excessively wide resection margins in this sensitive area can result in significant esthetic and functional consequences. Due to the emphasis on minimizing in-

vasiveness in the head and neck region, several studies have highlighted higher recurrence rates and poorer survival outcomes for head and neck melanoma (HNM) in comparison to other anatomical regions [27,28]. As noted by Appelbaum et al. [2], the unique nature of the head and neck region poses challenges in selecting the most suitable treatment. Furthermore, there is limited evidence available for head and neck melanoma, particularly concerning melanomas of the external auditory canal.

In our review, the majority of patients (11) underwent lateral temporal bone resection, superficial parotidectomy, and selective neck dissection, while 10 patients underwent WLE and one patient WLE with neck dissection. Various studies have shown that local T resection, when performed correctly, enables accurate disease staging and can achieve high rates of local control [2]. It is important to emphasize that these surgical indications are based on data from other types of cancers, such as squamous cell and basal cell carcinomas, because there is a lack of literature on HNM [29,30]. Currently, the gold standard treatment for EAC melanoma involves surgical excision with clear margins. However, there are no strict guidelines, as demonstrated by our data, such as tumor size, tumor Breslow thickness or Clark level, to definitively determine the optimal surgical approach between WLE or extended resection to other regions, such as LTBR. The surgical choice still primarily depends on the surgeon's decision and patient characteristics.

According to our review, only four patients underwent sentinel lymph node biopsy (SLNB). The current evidence concerning the role of SLNB in head and neck cases remains controversial. While lymph drainage in trunk, arms, and leg regions is well-established and reproducible, head and neck lymph drainage is recognized to be highly complex and variable[31]. In a recent study, Adigbli et al investigated the role of SLNB in HNM [32].The authors discovered that patients with HNM had significantly more positive LN hotspots and LN groups detected on lymphoscintigraphy, compared to other body regions. Additionally, they found that patients with a higher number of positive LN hotspots experienced significantly higher recurrence rates and lower median survival time. Kesmodel et al conducted an investigation to determine whether there is a difference in overall survival between patients with HNM who underwent SLNB and those who did not [33]. They found that there was no difference in overall survival between the two groups. Therefore, there are still no strict indications for performing SLNB in patients with EAC melanoma.

Another topic of significant interest in the management of HNM is the role of adjuvant therapy, such as radiotherapy (RT). Although melanoma has been demonstrated to be radioresistant, some studies recommend adjuvant radiotherapy for patients with risk factors such as tumor location where achieving negative margins may be challenging, desmoplastic tumor type, tumor thickness, satellitosis, ulceration and positive or uncertain margin status [34]. RT appears to have a consistent role in preventing locoregional recurrence. Adjuvant RT is recommended for patients with high-risk factors for regional recurrence, including extracapsular extension and the number and size of affected lymph nodes [2]. Before the approval of systemic therapy (ST) for stage III melanoma, studies suggested adjuvant RT for patients with extra-nodal extension (ENE), lymph nodes larger than 3 cm, involvement of multiple lymph nodes, recurrent disease or those who have undergone therapeutic neck dissection [35]. According to evidence presented by Mansour et al, adjuvant RT may still play a significant role in enhancing regional control in stage III melanoma [36]. As of now, the decision to recommend RT should be based on individual patient assessments, taking into account their specific risk factors for local or regional disease relapse.

Nowadays, systemic therapy involving immune checkpoint inhibitors is gaining much popularity through adjuvant treatment for HNM. Currently, ipilimumab, nivolumab and pembrolizumab have gained FDA approval for adjuvant therapy for stage III and greater melanoma. They are checkpoints inhibitors and they activate the immune system to treat melanoma [37]. As systemic therapies, these recent molecules are designed not only to control metastatic disease but also to enhance overall survival for patients, even in advanced conditions. When analyzing our patient population, it is worth noting that only two patients [2] undergo adjuvant immunotherapy. This limited utilization can be attributed first to its recent development and then to relatively short follow-up period available for most patients.

Based on the data collected, the rare entity of EAC melanoma has shown an overall survival rate of 50% within 5 years. It is essential to note that this condition is exceptionally rare and the available data are quite heterogeneous, often relying on old case reports. Therefore, it is crucial to interpret the estimated overall survival within the historical context specific to each case. Over the years, surgical and medical knowledge has evolved, leading to significant improvements in patient care and overall survival for this rare but lethal disease.

The largest case series available for EAC melanoma is the one by Appelbaum et al. [2], which includes 7 patients. In the future, it is advisable to gather data from larger and more homogeneous cohorts to gain deeper

insights and a better understanding of this condition. As of now, with the currently available knowledge, the primary treatment options for EAC melanoma are based on surgery, with adjuvant radiotherapy or immunotherapy considered for advanced and selected cases with high-risk features. It is important to keep in mind the aforementioned limitations when considering the estimated overall survival rate of 50% at 5 years.

Conclusions

EAC melanoma is an extremely rare malignant tumor with limited evidence regarding the best available therapeutic options. Surgical procedures such as WLE or lateral temporal bone resection, including the resection of surrounding structures like the parotid gland for larger lesions, followed by nodal dissection, should be considered for all patients without distant metastases. This approach is essential for accurate disease staging. Close and comprehensive follow-up, including clinical and radiological assessments, is crucial due to the high incidence of distant metastases.
As per the current state of knowledge, the overall survival rate remains quite low. EAC melanoma is characterized by its aggressiveness and invasiveness, posing a high risk of recurrence and distant spread, which is further complicated by the complex anatomical region it involves.

Conflicts of interest

The authors declare no conflict of interest.

Funding

None.

Authors' contributions

Both the first two authors made equal contributions to the work.

Ethical consideration

Approval from the Ethical Committee was not obtained as our Institution does not require it for literature reviews and case reports.
The research was conducted ethically, with all study procedures being performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki.
Written informed consent was obtained from each patient for study participation and data publication.

References

1 PDQ Adult Treatment Editorial Board. Melanoma treatment (PDQ®): health professional version. PDQ Cancer Information Summaries. Bethesda, MD: National Cancer Institute; 2002 Available at: http://www.ncbi.nlm.nih.gov/books/NBK66034/. Accessed March 7, 2019.

2 Appelbaum EN, Gross ND, Diab A, et al. Melanoma of the External Auditory Canal: A Review of Seven Cases at a Tertiary Care Referral Center. Laryngoscope. 2021;131(1):165-172. https://doi.org/10.1002/lary.28548.

3 Byers RM, Smith JL, Russell N, et al. Malignant melanoma of the external ear. Review of 102 cases. Am J Surg 1980;140:518-521.

4 Hawkes JE, Truong A, Meyer LJ. Genetic predisposition to melanoma. Semin Oncol 2016;43:591-597.

5 Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021 Mar 29;372:n71. https://doi.org/10.1136/bmj.n71.

6 Friedmann I, Radcliffe A. Otosclerosis associated with malignant melanoma of the ear. J Laryngol Otol. 1954;68(2):114-9. https://doi.org/10.1017/s0022215100049434

7 Lederman M. Malignant tumours of the ear. J Laryngol Otol. 1965:79:85-119. https://doi.org/10.1017/s0022215100063465.

8 Conley J, Schuller DE. Malignancies of the ear. Laryngoscope. 1976;86(8):1147-63. https://doi.org/10.1288/00005537-197608000-00007.

9 Sambe S, Kobayashi K, Asakura K, et al. [A case of malignant melanoma in the external auditory canal followed by systemic vasculitis]. Nihon Jibiinkoka Gakkai Kaiho. 1985;88(4):455-62. Japanese. https://doi.org/10.3950/jibiinkoka.88.455

10 Shih L, Crabtree JA. Carcinoma of the external auditory canal: an update. Laryngoscope. 1990;100(11):1215-8. https://doi.org/10.1288/00005537-199011000-00016

11 Kang S, Barnhill RL, Graeme-Cook F, et al. Primary malignant melanoma of the external auditory canal: a case report with presentation as an aural polyp. Am J Otol. 1992;13(2):194-6

12 Banerjee AR, Meikle D, Dawes PJ, et al. Malignant melanoma of the external auditory meatus. Clin Oncol (R Coll Radiol). 1993;5(4):255-6. https://doi.org/10.1016/s0936-6555(05)80241-9

13 Langman A, Yarington T, Patterson SD. Malignant melanoma of the external auditory canal. Otolaryngol Head Neck Surg. 1996;114(4):645-8. https://doi.org/10.1016/S0194-59989670262-0.

14 Milbrath MM, Campbell BH, Madiedo G, et al. Malignant melanoma of the external auditory canal. Am J Clin Oncol. 1998;21(1):28-30. https://doi.org/10.1097/00000421-199802000-00006.

15 Ayadi K, Wachuku E, Letaief H, et al. Primary malignant melanoma of the external auditory canal: CT features. Ann Saudi Med. 2002;22(3-4):221-3. https://doi.org/10.5144/0256-4947.2002.221.

16 Amando García L, Suárez Nieto C, Madrigal Rubiales B, et al. Melanoma de conducto auditivo externo [External ear melanoma]. Acta Otorrinolaringol Esp. 2003;54(2):89-93. Spanish. https://doi.org/10.1016/s0001-6519(03)78388-5.

17 Hannan SA, Parikh A. Malignant melanoma of the external ear canal. Lancet. 2006;368(9548):1680. https://doi.org/10.1016/S0140-6736(06)69702-X.

18 Lin CH, Tu TY, Chu PY, et al. Malignant Melanoma of the External Auditory Canal. Tzu Chi Medical Journal. 2009;21(3):244-247. https://doi.org/10.1016/S1016-3190(09)60047-1

19 Gowthami C, Kumar P, Ravikumar A, et al. Malignant melanoma of the external auditory canal. J Clin Diagn Res. 2014;8(8):FD04-6. https://doi.org/10.7860/JCDR/2014/8841.4719.

20 Khonglah Y, Das N, Raphael V, et al. Malignant Melanoma of the External Auditory Canal: A Rare Entity. Iran J Otorhinolaryngol. 2018;30(97):107-111.

21 Landau DC, Caruso Territoriale A, et al. Melanoma in external auditory canal: regarding a case report [Melanoma en conducto

auditivo externo. A propósito de un caso]. Medicina cutánea iberolatino-americana. 2018;46(2):120-123

[22] Komatsuda H, Kumai T, Ueda S, et al. Response to PD-1 blockade in a patient with mucosal melanoma of the middle ear: Case report. Clin Case Rep. 2020;8(12):3468-3471. https://doi.org/10.1002/ccr3.3424

[23] Li L, London NR, Chen X. Malignant Mucosal Melanoma of the Eustachian Tube With Extension Into the Ipsilateral External Ear Canal: A Case Report and Review of the Literature. Ear Nose Throat J. 2021;100(5_suppl):730S-733S. https://doi.org/10.1177/0145561320904813.

[24] Liu Y, Ding H, Wan Z, et al. Malignant Melanoma of the External Auditory Canal on 68 Ga-FAPI PET/CT. Clin Nucl Med. 2023;48(6):532-533. https://doi.org/10.1097/RLU.0000000000004658.

[25] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin. 2019;69(1):7-34. https://doi.org/10.3322/caac.21551.

[26] Ethun CG, Delman KA. The importance of surgical margins in melanoma. J Surg Oncol. 2016;113(3):339-45. https://doi.org/10.1002/jso.24111.

[27] Fadaki N, Li R, Parrett B, et al. Is head and neck melanoma different from trunk and extremity melanomas with respect to sentinel lymph node status and clinical outcome? Ann Surg Oncol 2013;20:3089-3097.

[28] Hudson LE, Maithel SK, Carlson GW, et al. 1 or 2 cm margins of excision for T2 melanomas: Do they impact recurrence or survival? Ann Surg Oncol 2013;20:346-351.

[29] Gidley PW, Roberts DB, Sturgis EM. Squamous cell carcinoma of the tem- poral bone. Laryngoscope 2010;120:1144-1151.

[30] Breen JT, Roberts DB, Gidley PW. Basal cell carcinoma of the temporal bone and external auditory canal. Laryngoscope 2018;128:1425-1430.

[31] Lavelli V, Ferrari C, Santo G, et al. The lymphoscintigraphic study of unpredictable head and neck cutaneous melanoma lymphatic drainage. Biomedicines. 2020;8(4):70. doi:10. 3390/biomedicines8040070

[32] Adigbli G, Woolley L, Issa F. Complex Lymphatic Drainage in Head and Neck Cutaneous Melanoma and SLNB Outcomes. JAMA Otolaryngol Head Neck Surg. 2023;149(9):853-854. https://doi.org/10.1001/jamaoto.2023.1584.

[33] Kesmodel SB, Kronenfeld JP, Zhao W, et al. Omission of Completion Lymph Node Dissection in Sentinel Node Biopsy Positive Head and Neck Cutaneous Melanoma Patients. Ann Surg Oncol. 2023 Aug 28. https://doi.org/10.1245/s10434-023-14036-8.

[34] Li W, Yu Y, Wang H, et al. Evaluation of the prognostic impact of postoperative adjuvant radiotherapy on head and neck mucosal melanoma: a meta-analysis. BMC Cancer 2015;15:758.

[35] Ballo MT, Bonnen MD, Garden AS, et al. Adjuvant irradiation for cervicallymph node metastases from melanoma. Cancer 2003;97:1789-1796.https://doi.org/10.1002/cncr.11243

[36] Mansour J, Asarkar A, Pang J, Nathan CO. What Is the Role of Adjuvant Radiotherapy in Head and Neck Melanoma in the Era of Systemic Therapy? Laryngoscope. 2022;132(11):2085-2086. https://doi.org/10.1002/lary.30048

[37] Wehbe J, Jaikaransingh D, Walker A. Immunotherapy as a treatment modality for mucosal melanoma of the head and neck: A systematic review. Medicine (Baltimore). 2022;101(31):e29979. https://doi.org/10.1097/MD.0000000000029979.