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Ear canal and middle-ear tumors: a single-institution series of 87 patients

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ABSTRACT

Background: Ear canal and middle ear tumors are rare and exhibit variability in histology and clinical manifestation. Surgical resection remains the treatment of choice, but individualized approach is needed to preserve function when possible.

Aims/objectives: To review the management and outcome of ear canal and middle ear tumors at an academic referral center.

Materials and methods: Helsinki University Hospital (HUS) patient files were searched for clinically and histologically confirmed ear canal and middle ear tumors over a 14-year period. The minimum follow-up time was 2 years.

Results: Eighty-seven patients with 88 tumors were identified. There were 20 (23%) benign external auditory canal (EAC), 36 (41%) benign middle ear space (MES), 29 (33%) malignant EAC, and 3 (3%) malignant MES tumors. Most (92%) tumors were managed with primary resection. Thirty-five percent of the operatively managed patients had a residual or a recurrent tumor.

Conclusions and significance: EAC and MES tumors show great diagnostic and histologic heterogeneity with need for individualized investigative and treatment approaches. In benign tumors, we advocate aggressive local surgical control without sacrificing vital structures. In malignant tumors, we recommend local surgical control with or without adjunct RT.

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Malignancy; neoplasm; middle ear; ear canal; treatment; surgery; radiotherapy

Introduction

Ear canal and middle ear tumors form rare entities that exhibit considerable variability in histology and clinical manifestation. Both conditions may present as primary tumors, or as tumors of adjacent structures extending to the external auditory canal (EAC) or the middle ear space (MES). Osteomas and exostoses are the prevailing primary benign EAC lesions [1]. In the MES paragangliomas (PGs) along with middle ear adenomas in adults and hemangiomas in children dominate [2]. Squamous cell carcinoma (SCC) followed by basal cell carcinoma (BCC) and adenoid cystic carcinoma (AdCC) are the most common primary malignant EAC tumors [3,4]. Primary tumors may extend from the EAC and MES into the temporal bone, the skull base, or intracranially. Even benign tumors e.g. ceruminoma, can be locally destructive. Metastases from other cancers to EAC or MES are infrequent but possible.

While imaging, most often computed tomography (CT) and magnetic resonance imaging (MRI), is customarily used to evaluate the extension of these tumors, histological examination is often needed for a definite diagnosis. Surgical resection remains the treatment of choice for most of these tumors. Due to the number of both benign and malignant entities in EAC and MES, no clear data exist for clinical guidance. While primary surgical resection can be a fully efficacious treatment for isolated benign or malignant tumors, surviving advanced SCC is still infrequent [5]. This polarity highlights the versatility within these entities and the need for individualized treatment.

The purpose of this study was to review the contemporary management and outcome of patients diagnosed with a clinically and histologically confirmed EAC or MES tumor at a tertiary care hospital over a 14-year period with a 2-year minimum follow-up time. We discuss management of these versatile tumors.

Materials and methods

We retrospectively reviewed the Helsinki University Hospital (HUS) patient files of all patients with a clinically

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confirmed EAC or MES tumor over a 14-year period (1 January 2005–31 December 2018). All solid tumors, including metastatic tumors, that extended from neighboring structures to EAC/MES were included in the study. Cholesteatomas, benign bony lesions (osteomas and exostoses), meningoceles, encephaloceles, and all tumors restricted to mastoid were excluded from the study. At the time of this study, the HUS catchment area covered a population of approximately 1.6 million people in Finland. Our hospital is the only institute within the catchment area where these tumors are treated. Data were recorded on demographics, symptoms, time of diagnosis, tumor location and stage, histological diagnosis, smoking status, and management including imaging, analysis of operative techniques, and follow-up. Carcinomas were staged using the 8th edition of TNM Classification for Malignant Tumors [6]. Macroscopic or microscopic evidence of tumor at the end of primary surgery was regarded as residual tumor in this study. All macroscopic residuals also had microscopic evidence of residual at the edge of the resection margin. In this study, tumors that were discovered after 6 months post primary treatment were regarded as recurrent tumors, and those detected within 6 months as residuals. Survival status was updated in January 2022 using the HUS electronic patient record system. Statistical analyses were carried out using a computerized software package (SPSS, version 25.0, Chicago, IL). The study was approved by the HUS Research Ethics Board, and an institutional research permission was granted.

Results

Patients and tumor diagnostics

Eighty-seven patients with 88 EAC or MES tumors were identified. The population-based annual occurrence of this select group of EAC/MES tumors was 0.5 per 100,000 inhabitants. There were 41 (47%) men and 46 (53%) women with a median age of 57 (range, 1–90) years, of which 35 (40%) patients were considered elderly (≥65 years of age). The median age of the patients with benign and malignant tumors was 55 (range, 1–84) and 60 (range, 1–90), respectively. Thirty (34%) patients had no past medical history to report.

There were 56 (64%) benign and 32 (36%) malignant tumors. Table 1 shows the breakdown of EAC/MES tumors. EAC was the first place of metastatic manifestation for acute myeloblastic leukemia, and myeloid sarcoma. The main presenting complaints are outlined in Figure 1. Up to three presenting complaints were recorded per patient. The median delay from symptom onset to diagnosis was 17 months (range, 2–38) for SCC, 11 (range, 7–25) for BCC, 24 (range, 8–65) for AdCC, four for mucoepidermoid carcinoma, three for carcinoma ex pleomorphic adenoma (Ca ex PA), and three (range, 2–5) months for the metastatic tumors. In contrary, the median diagnostic delay was on average 8 months (range, 0.25–65) for benign tumors, the delay being longest for PGs and meningiomas. Thirteen (41%) patients with a malignant tumor and nine (16%) with a benign tumor reported to being current or ex-smokers ($p < .00001$). Two patients with AdCC had had previous radiotherapy (RT) to the head and neck area, one patient (with EAC AdCC) to the neck and mediastinum for a suspected nasal cavity Hodgkin's disease 30 years prior to presentation, and the other to the ipsilateral MES in 1980 (Table 4).

Radiological imaging

Pre-operative radiological imaging was used in 80% of patients with a benign, and in 90% of patients with a malignant tumor. Combination imaging with high-resolution CT and MRI with contrast agent was utilized in 21% of benign, and in 44% of malignant tumors. Separate CT and MRI scans were used equally often to diagnose benign tumors (21% versus 21%), while CT and MRI were used in 28% versus 13% of malignant tumors. Of the other imaging combinations, CT + MRI + magnetic imaging angiography (MRA), CT + MRA, or ultrasound (US) scan + CT + MRI were the preferred imaging choices in 12% of benign tumors, and US + MRI, or positron emission tomography (PET) + CT + MRI in 6% of malignant tumors.

Management

Eighty-one (92%) tumors were managed with curative and 3 (3%) with palliative intent. Four (5%) patients, all with a benign tumor, were observed without treatment.

Of the 56 benign tumors, 50 (89%) received primary resection, 4 (7%) were followed up without active treatment, and 2 (4%) received primary RT (meningioma and PG). Of the conservatively treated patients, one had EAC vascular malformation, two MES meningiomas (extensions to MES from middle cranial fossa, and sigmoid sinus/jugular foramen), and one a vestibular schwannoma with an extension to MES.

Of the 32 malignant tumors, 27 (84%) received primary resection, and 1 (3%) primary RT. Three (9%) EAC metastases were followed up with palliative intent. One (3%) patient received palliative RT (EAC metastasis). Table 2 reviews the surgical approaches. CNVII was sacrificed in three extensive, malignant tumors (BCC, MES metastasis, and Ca ex PA). EAC was closed as part of lateral temporal bone resection (LTBR), and subtotal temporal bone resection (STBR), as well as in three widespread tumors (two BCCs and MES metastasis). Five meningiomas were debulked in collaboration with a neurosurgeon. There were no major intraoperative complications or intraoperative deaths in this study.

There was no set departmental guideline for the timing or number of follow-up visits. Due to the large variety of histological entities, varying tumor sizes, and a plethora of treatment modalities, the follow-up was always individually tailored. The median follow-up time was 46 (range, 1–192) months for benign, and 42 (range, 1–192) months for malignant tumors. Of the benign tumors, meningiomas had the longest follow-up time, while the follow-up was the

Table 1. The breakdown of tumors to benign and malignant in the order of prevalence.

Benign 56 (64%)		Malignant 32 (36%)	
EAC 20 (23%)	MES 36 (41%)	EAC 29 (33%)	MES 3 (3%)
Hemangioma 5 (6%)	PG 16 (18%) • TPG 10 (10%) • JTPG 5 (6%) • JPG 1 (2%)	SCC 10 (11%) • T1N0M0 ($n = 4$) • T2N0M0 ($n = 2$) • T3N0M0 ($n = 1$) • T3N2M1 ($n = 1$) • T4N0M0 ($n = 1$) • T4N1M0 ($n = 1$)	Metastasis from parotid cancer 1 (1%) • T0N3M0
Ceruminoma 3 (3%)	Meningioma 12 (14%) • Sigmoid sinus/jugular foramen 5 (6%) • Intraosseus 3 (3%) • Skull base/jugular foramen 2 (2%) • CPA 1 (1%) • middle fossa 1 (1%)	Metastasis: 6 (7%) • Lung cancer 1 (1%) • ccRCC 1 (1%) • Myeloid sarcoma 1(1%) • AML 1 (1%)[d] • ALL 1 (1%)[d] • Melanoma 1 (1%)[a]	AdCC 1(1%)[c] • T1N0M0
Syringocystadenoma 2 (2%)	Schwannoma 5 (6%) • Vestibular 3 (3%) • Facial nerve 2 (2%)	AdCC 6 (7%) • T1N0M0 ($n = 3$) • T3N0M0 ($n = 1$) • T4N0M0 ($n = 2$)	Malignant PG 1 (1%)[c] • Grade II
Neurofibroma 2 (2%) • 1 (1%) plexiform	Neurofibroma 1 (1%)		
Dermoid cyst 2 (2%) Hemangiopericytoma 1 (1%) Sebaceous adenoma 1 (1%) Squamous cell papilloma 1 (1%) Amyloidosis 1 (%) Myxoma 1 (1%) Vascular malformation 1 (1%)	Adenoma 1 (1%) GCT 1 (1%)	BCC (nodular) 5 (6%)[a] MEC 1 (1%) • T1N0M0 Ca ex PA 1(1%)[b] • T2NxM1	

Percentages as of total number of tumors. TNM classification at presentation. AdCC: adenoid cystic carcinoma; ALL: acute lymphoblastic leukemia; AML: acute myeloblastic leukemia; Ca ex PA: carcinoma ex pleomorphic adenoma; ccRCC: clear cell renal cell carcinoma; CPA: cerebellopontine angle; EAC: external auditory canal; GCT: giant cell tumor; JPG: jugular paraganglioma; JTPG: jugulotympanic paraganglioma; MEC: mucoepidermoid carcinoma; MES: middle ear space; PG: paraganglioma; TPG: tympanic paraganglioma.
[a]Also in the MES.
[b]Extension from a parotid gland primary.
[c]Two tumors in the same patient.
[d]Detected as tissue lesions.

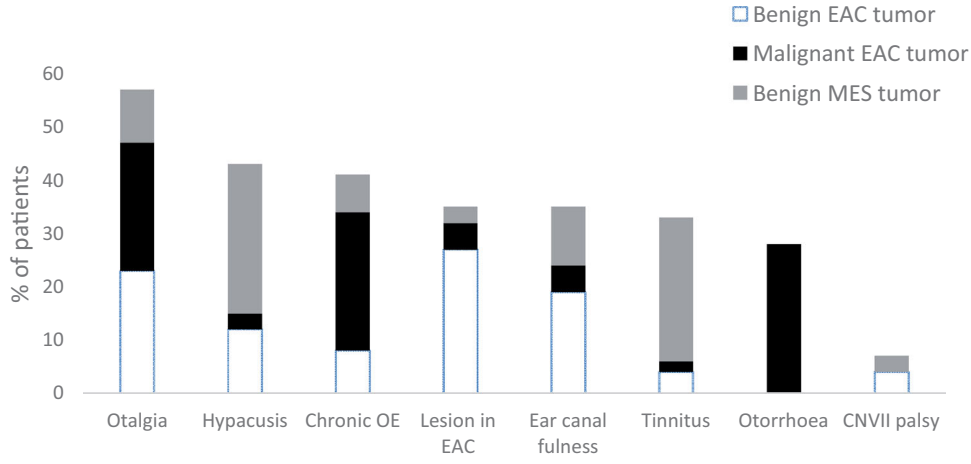

Figure 1. Presenting symptoms of patients with benign ($n = 56$) and malignant ($n = 32$) tumors in the external auditory canal and the middle ear space. CNVII: facial nerve; EAC: external auditory canal; MES: middle ear space; OE: otitis externa. Two patients with altogether three malignant MES tumors were under specialist surveillance when their tumors were discovered, one patient presented with a neck lump and the other with headache.

longest for AdCCs in the malignant group. Small cutaneous carcinomas were generally followed up for 3 years (excluding completely excised BCCs that received shorter follow-up), SCCs for 5 years, and AdCCs for a minimum of 10 years. Meningiomas, schwannomas, and PGs were commonly imaged with CT and/or MRI 6–12 months post-operatively, then yearly, and if no growth was seen, every 2–3 years thereafter. While post-operative CT and/or MRI were the preferred imaging modalities also in patients with a malignant tumor, post-operative imaging depended on the

Table 2. Primary operative approaches and post-operative complications.

Benign EAC (*n*)	Operative technique (*n*)	Post-operative complications	Malignant EAC (*n*)	Operative technique (*n*)	Post-operative complications
Haemangioma (5)	• Local excision (4) • EA (1)		SCC (10) • T1N0M0 (4) • T2N0M0 (2) • T3N0M0 (1) • T3N2M1 (1) • T4N0M0 (1) • T4N1M0 (1)	• T1N0M0: EA; EA w/skin graft; LTBR + skin graft; LTBR + ND II + skin graft • T2N0M0: LTBR + PP + ND II-III; LTBR + temporal muscle flap • T3N0M0: Mastoidectomy + PP + ND IIa–IIb + temporal muscle flap • T3N2M1: STBR + TP + mastoidectomy + ND IIA-IIB, III, Va + free fat & skin graft • T4N0M0: LTBR + PP + ND II-III + skin graft & temporal muscle flap • T4N1M0: LTBR + TP + ND II-V + skin graft & temporal muscle flap	**Short-term:** • LTBR + PP + ND II-III (T2N0M0): CNVII weakness • LTBR + TP + ND II-V (T4N1M0): CNVII weakness • EA (T1N0M0): bleeding from EAC **Long-term:** • LTBR (T2N0M0): CNVII palsy • Mastoidectomy + PP + ND IIa–IIb (T3N0M0): CNVII palsy • LTBR + TP + ND II-V (T4N1M0): minor Frey syndrome
Ceruminoma (3)	• Local excision (1) • EA (1), EA with skin graft (1)				
Syringocystadenoma (2)	Local excision (2)				
Neurofibroma	• Local excision (1) • EA (1)				
	EA (2)				
Haemangiopericytoma (1)	RA				
Sebaceous adenoma (1)	Local excision		Metastases (6)	• Lung cancer, palliative RT; AML: RT • Renal cancer, myeloid sarcoma, ALL: Palliative care • Melanoma: TrM	
Squamous cell papilloma (1)	Local excision		AdCC (6) • T1N0M0 (3) • T3N0M0 (1) • T4N0M0 (2)	• T1N0M0: STBR + PP + ND II + skin graft[14]; TrM; LTBR + ND II • T3N0M0: LTBR + PP + skin graft • T4N0M0: STBR + PP + ND II-III + skin graft; LTBR + PP + free fat and skin graft	**Short-term:** • STBR + PP + ND II-III (T4N0M0): CNVII weakness, FBS • LTBR + PP (T4N0M0): CNXII weakness • LTBR + PP (T3N0M0): dizziness, CNVII weakness **Long-term:** • LTBR + ND II (T1N0M0): CNVII palsy, tinnitus • STBR + PP + ND II (T1N0M0) shoulder and TMJ pain • STBR + PP + ND II-III (T4N0M0): sensation loss around ear, TMJ pain
Amyloidosis (1)	Conservative management		BCC (5)	• Local excision + skin graft (2) /+PP (1) • LTBR + PP + EAC closure; LTBR + PP + SP + CNVII sacrifice + EAC closure	**Short-term**: Local excision + PP: CNVII weakness **Long-term**: LTBR + PP + SP: CNVII palsy
Myxoma (1)	Local excision		MEC (T1N0M0)	Local excision + superficial parotidectomy	
Vascular malformation (1)	Conservative management		Ca ex PA (T2NxM1)	TP + ND (I-V), CNVII sacrifice, mandibular resection + gold weight to eyelid	

(Continued).

Table 2. Continued.

Benign MES (*n*)	Operative technique (*n*)	Post-op complications	Malignant MES (*n*)	Operative technique (*n*)	Post-operative complications
Paraganglioma (16) • TPG (10) • JTPG (5) • JPG (1)	• TPG: EA (9), TT + tympanoplasty (1) • JPG: RT (1) • JTPG: EA (1), TT (2); ITF (1), STBR (1)	**Short-term:** • EA: TM perforation (1), dysphonia (1) **Long-term:** • EA: TM perforation	Metastasis (1)	TrM, + TP + ND I-V, pectoralis flap + CNVII sacrifice gold weight to eyelid + tracheotomy	**Short-term:** haematemesis (gastroscopy: bleeding duodenal ulcer detected & treated) **Long-term:** CNVII palsy
Meningioma (12)	• Conservative management (2) • RT (1) • Tympanomastoidectomy (2), CMFTM + SOC (5), SOC (2)	**Short-term:** • *: CSF leak • **: dizziness; CNIX palsy • **: CNVII weakness	AdCC (1)	See Table 4 for operative details	
Schwannoma (5) • Vestibular (3) • Facial nerve (2)	• Vestibular: Local excision; CMFTM; Conservative • Facial nerve: STBR; ATM + tympanoplasty	**Long-term:** • CMFTM: CNVII palsy • ATM + tympanoplasty: CNVII palsy	Malignant PG (1)	See Table 4 for operative details	
Neurofibroma (1)	• EA				
Adenoma (1)	• RA + fascial reconstruction + bone transfer				
Giant cell tumor (1)	• TT, superficial parotidectomy, mandibular reconstruction				

AdCC: adenoid cystic carcinoma; ALL: acute lymphoblastic leukemia; AML: acute myeloblastic leukemia; ATM: atticotympanomastoidectomy; BCC: basal cell carcinoma; Ca ex PA: carcinoma ex pleomorphic adenoma; CMFTM: combined middle fossa transmastoid; CN: cranial nerve; CSF: cerebrospinal fluid; EA: endaural; EAC: external auditory canal; FBS: first bite syndrome; ITF: infratemporal fossa; JPG: jugular paraganglioma; JTPG: jugulotympanic paraganglioma; LTBR: lateral temporal bone resection; MEC: mucoepidermoid carcinoma; MES: middle ear space; *n*, number; ND: neck dissection; PP: partial parotidectomy; RA: retroauricular; RT: radiotherapy; SCC: squamous cell carcinoma; SOC: suboccipital craniotomy; SP: subtotal petrosectomy; STBR: subtotal temporal bone resection; TM: tympanic membrane; TMJ: temporomandibular joint; TP: total parotidectomy; TPG: tympanic paraganglioma, TrM: transmastoid; TT: transtemporal. Underlined complications denote persisting symptoms.

Table 3. Residual tumors post primary surgery, treatment approaches, and outcome.

Tumors (TNM)	Age/gender	Location	Primary surgical treatment	Residual	Residual treatment	F/u time, years	Status at last f/u
Benign							
Meningioma	64/M	MES	CMFTM + SOC	Macro	Resection	6.3	AWD
Meningioma	40/F	MES	SOC	Macro	Resection	10.5	AWD
Meningioma	65/F	MES	CMFTM + SOC	Macro	F/u with imaging (MRI)	14	AWD
Meningioma	48/F	MES	CMFTM + SOC	Macro	Resection + RT	15.5	AWD
Meningioma	64/F	MES	Tympanomastoidectomy	Macro	F/u with imaging (MRI)	15.5	AWD
Meningioma	43/F	MES	Tympanomastoidectomy	Macro	resection	17.5	AWD
JTPG	72/F	MES	STBR	Micro	F/u with imaging (MRI)	3.5	AWD
JTPG	31/F	MES	TT	Micro	F/u with imaging (MRI)	7	AWD
JTPG	53/F	MES	ITF	Macro	2 × resection + RT	5	AWD
Schwannoma (facial nerve)	69/M	MES	ATM + tympanoplasty	Macro	Resection	1	AWD
Neurofibroma	39/M	EAC	EA	Micro	Resection	0.1	NED
Neurofibroma (PNF)	76/M	EAC	EA	Micro	Resection	2.3	AWD
Malignant							
AdCC (T3N0M0)	62/F	EAC	LTBR + PP	Micro	RT	4.3	AWD
AdCC (T1N0M0)	75/M	EAC	LTBR + ND II	Micro	RT	4.7	AWD
AdCC (T4N0M0)	31/F	EAC	STBR + PP + ND II-III	Micro	RT	11	NED
AdCC (T4N0M0)	52/M	EAC	LTBR + PP	Micro	Resection + RT	5.5	AWD
AdCC (T1N0M0)	49/M	EAC	TrM	Micro	Resection + RT	16.5	AWD
SCC (T2N0M0)	68/M	EAC	LTBR	Micro	RT	1.5	DOD
SCC (T4N0M0)	58/M	EAC	LTBR + PP + ND II-III	Micro	RT	6	NED
SCC (T4N1M0)	72/F	EAC	LTBR + TP + ND II-V	Micro	RT	9	DWND
SCC (T3N0M0)	78/M	EAC	Mastoidectomy + PP + ND IIa-IIb	Macro	2 × resection + RT	2.8	DWND
SCC (T3N2M1)	64/M	EAC	STBR + TP + ND IIa-IIb, III, V	Macro	Chemo + palliative RT	0.5	DOD
Metastasis (T0N3M0)	83/M	MES	TrM, TP, ND I-V	Macro	RT	0.1	DOD
Ca ex PA (T2NxM1)	67/M	EAC	TP + ND I-V	Micro	Chemo + palliative RT	0.1	DOD

Age at the time of primary surgery. All macroscopic residuals also contained microscopic evidence of tumor. Shaded boxes denote ongoing follow-up. AdCC: adenoid cystic carcinoma; AWD: alive with disease; Ca ex PA: carcinoma ex pleomorphic adenoma; chemo: chemotherapy; CMFTM/SOC: combined middle fossa transmastoid; DOD: dead of disease; DWD: dead with disease; DWND: dead with no evidence of disease; EAC: external auditory canal; F: female; f/u: follow-up; JTPG: jugulotympanic paraganglioma; LTBR: lateral temporal bone resection; macro: macroscopic; M: male; MES: middle ear space; micro: microscopic; MRI: magnetic resonance imaging; ND: neck dissection; NED: no evidence of disease; PNF: plexiform neurofibroma; PP: partial parotidectomy; RT: radiotherapy; SCC: squamous cell carcinoma; SOC: suboccipital craniotomy; STBR: subtotal temporal bone resection; TP: total parotidectomy; TrM: transmastoid.
Shaded boxes denote ongoing follow-up.

type of tumor, and the treatment given. If benign or malignant tumor growth was clinically suspected or seen in imaging, prompt follow-up imaging was arranged. By January 2022, patients with a benign tumor had had 0–33, and patients with a malignant tumor 4–41 post-operative visits that included 7–37 visits for those who underwent LTBR/STBR.

Outcome

Six (12%) patients with a benign tumor, and eight (25%) with a malignant tumor experienced short-term complications. Conversely, three (6%) patients with a benign tumor and eight (25%) with a malignant tumor experienced long-term complications. CNVII palsy, present mainly in those who had undergone LTBR/STBR and parotidectomy, was the most frequent short-term and long-term complication. Post-operative hearing status was not routinely quantified even if maximal post-operative conductive hearing loss was expected in patients who had undergone EAC closure. Two major post-operative complications were recorded. One patient, who had undergone removal of a sigmoid sinus/jugular foramen meningioma through a combined middle fossa transmastoid resection and suboccipital craniotomy, experienced CNIX palsy on the first post-operative day. A 4-day treatment with tracheostomy ensued during which CNIX regained its normal function. Another patient with MES metastasis developed hematemesis post-operatively. Gastroscopy revealed a bleeding duodenal ulcer which was treated. At the end of follow-up, three (6%) patients with a benign tumor suffered from TM perforation ($n = 1$), and CNVII palsy ($n = 2$). Four of the eight patients with a malignant tumor had deceased by the end of follow-up. The long-term symptoms had resolved for the other three patients, while one patient suffered from CNVII palsy because of its sacrifice. Table 2 reviews the short-term (lasting < 6 months) and long-term (lasting > 6 months) minor and major post-operative complications.

Twenty-four (31%) of the 77 patients that underwent surgery with curative intent had a tumor residual. Twelve (50%) of the 24 residuals were benign tumors (six meningiomas, three PGs, one schwannoma, and two neurofibromas), and 12 (50%) malignant (five AdCCs, five SCCs, one MES metastasis from unknown primary, and 1 carcinoma ex pleomorphic adenoma) tumors. Both benign tumors (PG and meningioma) that were treated with primary RT had a residual tumor. The meningioma residual was later resected while the patient with PG refused further treatment or follow-up. Table 3 overviews the residual tumors, the treatment approaches, and outcome after primary surgery.

During follow-up, three patients experienced tumor recurrence: one patient with a giant cell tumor (GCT) and two patients with a malignant tumor (one AdCC, and another AdCC + malignant PG), bringing the combined residual and recurrence rate to 35%. The GCT recurrence was detected 19 months after primary surgery and treated

Table 4. Treatment approaches for a patient with AdCC + malignant PG.

Year	Treatment approach/recurrence	Treatment modality	Resection radical/sparing	Histology	Outcome/notable
1979	Primary	Resection	Radical	AdCC	
1980	Post-operative RT	Cobalt therapy 28/2 Gy		AdCC	
2001	Recurrence	Resection		Middle ear adenoma/AdCC	
2007	Recurrence	Resection	Radical	Middle ear adenoma/AdCC	Affected ear deafened
2011	Recurrence	Resection (craniotomy) + post-p RT 45/1.8 Gy	Sparing	Malignant PG	
2014	Recurrence	Resection (transtemporal + subtemporal)	Radical	Malignant PG	Somatostatin-PET CT: intake in ipsilateral temporal bone
2015	Post-operative chemotherapy	Sandostatin once a month for 33 months		Malignant PG	No treatment response. Residual near foramen ovale ipsilaterally + in base of skull bilaterally, grown in F/U
2017	Recurrence	Resection (subtemporal re-craniotomy: intracranial part resected)	Sparing	Malignant PG	Resection of extracranial part not possible through craniotomy
2019	Recurrence	PRRT with lutetium octreotate × 4 (7.4 GBq)		Malignant PG	Metastases in pelvis and ribs

AdCC: adenoid cystic carcinoma; CT: computed tomography; F/U: follow-up; GBq: gigabecquerels; Gy: gray; PET: positron emission tomography; PG: paraganglioma; PRRT: peptide receptor nuclide therapy; RT: radiotherapy.

with resection. The multidisciplinary treatment of this challengingly located benign tumor has been published as a case report [7]. Of the two malignant recurrences, the patient with AdCC developed a recurrence 8 years after primary treatment. The recurrence was resected, followed by post-operative RT. The other patient with a malignant recurrence (AdCC + malignant PG) underwent numerous treatments to multiple tumor recurrences over several decades (Table 4). For clarity, these two tumors have been regarded as separate entities in this study.

Twenty (23%) patients had died by the end of the follow-up period. Fifteen (43%) of the deceased patients had had a malignant tumor (seven metastatic EAC/MES tumors, and eight primary EAC tumors (five SCCs, two BCCs, and one Ca ex PA)). All patients with a metastatic EAC/MES tumor as well as two patients with EAC SCC had died of the disease. The two SCCs lead to death within 2 and 12 months of discovery, respectively (Table 3). Five (9%) patients with a benign tumor (one meningioma, one schwannoma, one PG, one syringocystadenoma, and one adenoma) had died by the end of the follow-up period.

Discussion

This retrospective single-center study presents data on patients with a clinically and histologically confirmed EAC or MES tumor over a 14-year period with a 2-year minimum follow-up time. Eighty-seven patients with 88 tumors were included to investigate treatment details.

In this study, there was an unacceptably long diagnostic delay for SCC, AdCC, and BCC. All patients with EAC SCC presented with prolonged symptoms of otorrhea/otitis externa (OE) with up to a 38-month delay from presentation to diagnosis. Patients had commonly received multiple treatments for OE with or without otitis media (OM) without routine control appointments in the primary sector, which added most to the diagnostic delay. In the literature, SCC is hypothesized to be related to chronic infection and inflammation [8]. Hearing loss, otorrhea, and bleeding from EAC along with concurrent OM/OE are the other common presenting symptoms of EAC and temporal bone malignancies [4,9]. There were significantly more smokers among patients with a malignant tumor in the current study, which is in line with a recent meta-analysis that associates current or heavy smoking and higher risk of SCC [10]. Otalgia, especially if disproportionate to clinical findings, has been reported to be suggestive of an EAC tumor, particularly of AdCC [11]. In this study, one patient with EAC AdCC presented with over a 5-year history of otalgia, before the diagnosis was confirmed on imaging and histology. We recommend that all patients (regardless of age) with persisting otalgia, otorrhea, and/or symptoms of prolonged OE/OM are referred for urgent consideration of diagnostic imaging and tissue biopsy.

CT, MRI, or their combination was successfully used to diagnose most benign tumors in this study. Combination imaging with CT and MRI was the preferred imaging choice for malignant tumors. We recommend using high resolution CT and contrast-enhanced MRI for pre-operative planning and staging of suspected malignant EAC/MES tumors; this is in line with previous recommendations [4,12].

In this study, the surgical approaches depended on pre-operative radiological extension of the tumor, and on intra-operative findings. Benign EAC tumors received local excision and reported no post-operative complications. Six SCCs and five AdCCs were resected through LTBR or STBR, which we recommend for appropriate tumors. Although most of the 11 patients suffered from short or long-term post-operative CNVII palsy, the nerve regained its function as long as it was not sacrificed. Importantly, permanent post-operative complications were rare even if the operative techniques were, on occasion, radical. Thirty-

five percent of the surgically treated patients had a residual (31%), or recurrent (4%) tumor, which is in line with previous studies [5,13]. The relatively high residual tumor rate may be partly explained by the contemporary increase in non-invasive treatment of benign EAC and MES tumors [14], that our department also employs. The follow-up times were the longest for meningiomas, and PGs because of the intentional subtotal resections to preserve vital structures of anatomically challenging tumors.

In this study, detailed survival analyses were not done because of the large number of different histological EAC and MES entities, and because of incomplete survival data. Interestingly, however, all six patients with an AdCC were alive at the end of follow-up despite five patients having a microscopic residual post primary surgery and one patient experiencing a recurrence eight years into follow-up. This may be because all AdCCs received RT for the residual and were under active follow-up. A recent study advocates long-term follow-up for middle ear adenomatous neuroendocrine tumors because the tumors' high tendency for recurrence and because of their malignant potential [15]. In our experience, the follow-up of EAC/MES AdCC should include regular imaging and continue for a minimum of 10 years, which is in line with a previous study's recommendations [16]. In a study by Matoba et al., the outcome of surgically treated EAC and MES SCC was better than that of patients who received only RT even in advanced disease [17]. Lechner et al. [18] furthermore note that differentiation of SCC and its staging at presentation appears to have the greatest influence on 5-year survival rates. While five of the ten patients with SCC received post-operative RT in this study, this nor the primary TNM status of the tumor seemed to significantly affect survival. Shortening the diagnostic delay would be the easiest way to improve outcome for patients. Centralization of the management of this patient population to multidisciplinary head and neck centers could, furthermore, improve treatment outcomes.

Conclusions

EAC and MES tumors show great diagnostic and histologic heterogenicity. Investigative and treatment approaches as well as follow-up time must be individualized to each tumor in question. Shortening the diagnostic delay is the easiest way to improve outcome for patients.

Disclosure statement

The authors have no conflicts of interest to disclose.

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