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ORIGINAL ARTICLE

Cancer of the external auditory canal

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KEYWORDS
Squamous cell carcinoma;
External auditory canal;
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Radiotherapy

Summary
Introduction: Cancer of the external auditory canal is a rare tumour with an annual incidence of one per one million inhabitants. The objective of this study was to evaluate the 5-year overall survival and disease-free survival rates in a series of patients with carcinoma of the external auditory canal and to compare our results concerning the clinical presentation, management and survival with those of the literature.
Patients and method: Ten patients were included in this retrospective, single-centre study over a 20-year period. Data concerning age, symptoms, imaging, TNM stage according to the Pittsburgh classification, histology, management, sequelae, recurrences and survival were recorded.
Results: The mean age of the patients of this series was 60.7 years. Seven patients had a squamous cell carcinoma. The other histological types were undifferentiated carcinoma, adenoid cystic carcinoma and neuroendocrine carcinoma. Staging was based on the Pittsburgh classification with one stage I, one stage III and eight stage IV tumours. Five-year overall survival rates were 100%, 50% and 0%, respectively. The mean 5-year overall survival rate was 35% and the mean 5-year disease-free survival rate was 24%.
Conclusion: Carcinoma of the external auditory canal is a difficult diagnosis when the tumour does not present as a fungating mass protruding from the external auditory canal. The Pittsburgh classification was used for TNM staging of these tumours, allowing comparison of our results with those of the literature. The clinical findings and survival rates observed in this study are comparable to those reported in the literature. These tumours are associated with a poor prognosis on the basis of our results and published data.

Introduction

Cancer of the external auditory canal (EAC) is a rare tumour, representing less than 0.2% of all head and neck cancers [1]. Only 4% of cancers of the outer ear are confined to the EAC. The annual incidence of carcinoma of the EAC is estimated to be between one to six per million inhabitants [2] and the prevalence is one per million inhabitants [3,4], which explains the small sample sizes of the series published in the literature.

These tumours must be diagnosed at an early stage to avoid the mutilating surgery required at advanced stages. Otoscopy usually allows easy diagnosis of these tumours by providing direct vision of the lesion. In clinical practice, the

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lesion is usually superinfected, invasive and can be confused with chronic otitis externa [5]. When the lesion is not correctly diagnosed, it can spread locally to the middle ear and invade vital structures present in the temporal bone (internal carotid artery, facial canal, cochlea, vestibule).

There is no consensus at the present time concerning TNM staging of these tumours by the Union Internationale Contre Le Cancer (UICC) or the American Joint Committee on Cancer (AJCC). However, since the beginning of the 1990s, the Pittsburgh radioclinical classification of carcinoma of the EAC [6] has become widely used in the international literature and has been demonstrated to be reliable and reproducible [1,7].

The reference treatment for cancer of the EAC is surgery [8], which is often mutilating due to the anatomical site of these tumours. These operations were reputed to be associated with severe postoperative morbidity. However, progress in general anaesthesia, aseptic techniques and intensive care has allowed an improvement of postoperative survival following radical surgical procedures. The progress provided by new technologies, such as surgical navigation and intraoperative facial nerve monitoring, have allowed an improvement of the quality of otological tumour resection and improvement of the patient's quality of life by reducing the risks of sequelae. Despite these improvements, advanced tumours (stages III—IV) are associated with a poor prognosis with low disease-free survival and overall survival rates.

The most common histological type of carcinoma of the EAC is squamous cell carcinoma. The other histological types are basal cell carcinoma, malignant melanoma, Merkel cell carcinoma, angiosarcoma, adnexal carcinoma, including ceruminous adenocarcinoma and adenoid cystic carcinoma, and lymphoma [9]. The prognosis depends on the histological type [9].

The primary objective of this study was to evaluate the overall survival and disease-free survival rates of patients with a malignant tumour of the external auditory canal with metastatic potential. The results of this study are discussed in the light of the literature.

Patients and methods

This retrospective, single-centre study was based on review of the medical charts of a consecutive series of patients with a malignant tumour of the EAC managed between 1991 and 2011 in our otorhinolaryngology department.

Clinical data concerning age, gender, otological history, date and mode of diagnosis, site, histological type, management, and survival were recorded for each patient included. The date of diagnosis corresponded to the date of the first biopsy that confirmed the malignant nature of the lesion. Tumour site, lymph node status (cervical and parotid) and the presence of metastases were determined from clinical findings, computed tomography (CT) and/or magnetic resonance imaging (MRI) imaging and the operation report. Tumour stage was established according to the university of Pittsburgh Tumor, Node and Metastasis (TNM) classification for squamous cell carcinomas of the EAC [1,8] (Table 1).

The type of therapeutic management and the length of postoperative hospital stay in surgically treated patients were recorded. The histology reports for the operative specimens indicated the surgical margins, revised surgical margins, bone and cartilage invasion and the presence of lymph node invasion on lymph node dissection specimens.

Table 1 University of Pittsburgh TNM staging system for carcinomas of the external auditory canal (EAC) [1,6].

T
T1: tumour limited to the EAC without bony erosion or evidence of soft tissue involvement
T2: tumour with limited external auditory canal bone erosion (not full thickness) or limited (< 0.5 cm) soft tissue involvement
T3: tumour eroding the osseous bone EAC (full thickness) with limited (< 0.5 cm) soft tissue involvement or tumour involving the middle ear and/or mastoid
T4: tumour eroding the cochlea, petrous apex, medial wall of the middle ear, carotid canal, jugular foramen, or dura, or with extensive soft tissue involvement (> 0.5 cm), or evidence of facial paresis
N
N0: no regional lymph node metastasis
N1: a single regional metastatic lymph node < 3 cm
N2a: a single ipsilateral metastatic lymph node measuring 3—6 cm
N2b: several ipsilateral metastatic lymph nodes < 6 cm
N2c: contralateral metastatic lymph node
N3: metastatic lymph node > 6 cm
M: distant metastasis
Stages
Stage I
Stage II
Stage III
Stage IV: T4N0 or T × N+

Each case was discussed at a multidisciplinary consultation meeting. Surgical resection was systematically proposed except for locally advanced tumours with extension to the posterior cranial fossa, internal carotid artery or middle cranial fossa, in the presence of contraindications to general anaesthesia related to comorbidities or in the case of metastatic disease. Adjuvant radiotherapy was systematically proposed after surgical resection. Chemotherapy was considered in cases with positive surgical margins, local recurrence or distant metastases.

Post-treatment sequelae (peripheral facial nerve palsy, sensorineural hearing loss) and cosmetic sequelae (poor healing, amputation of the outer ear) were also recorded. The 5-year overall survival and disease-free survival rates were evaluated according to the Kaplan—Meier method.

Results

Ten patients with a mean age of 60.7 years (±7.2) and a sex ratio of 1 were included. Two patients had been followed for cholesteatoma. The presenting symptoms and signs were non-specific. Six (60%) patients reported otorrhoea and three of them (30%) had been followed for persistent

Table 2 Clinical findings, TNM stage and therapeutic management of the 10 patients of this series.

#	Age	Gender	Symptoms	FNP	Otoscopy	Histo	Pittsburgh TNM	pTNM	Stage	Treatment	Follow-up (months)	Status
1	61	M	Otalgia	N		SCC	T4N0M0	—	IV	—	0	D
2	69	M	Otorrhoea Loss of balance	Y		SCC	T4N0M0	T4N0M0	IV	TP EBR	7	D
3	55	M	Otalgia Otorrhoea	N		SCC	T4N0M0	T4N0M0	IV	PP EBR CT	10	D
4	57	F	None	Y		NEC	T4N0M0	T4N1M0	IV	PP + OER + NPD CT	10	D
5	65	F	Otalgia Otorrhoea	N		SCC	T4N0M0	T4N0M0	IV	EBR CT	17	D
6	70	F	Otorrhoea Bleeding	N		SCC	T3N1M0	T3N1M0	IV	EACR + NPD EBR	113	D
7	67	M	Otorrhoea	N		SCC	T4N0M0	T4N0M0	IV	PP + OER + NPD EBR	4	A
8	52	M	Bleeding Otorrhoea	N		SCC	T4N0M0	T4N0M0	IV	TP + OER + NPD EBR + CT	12	A
9	62	F	Pruritus	N		SCC	T3N0M0	T3N0M0	III	PP + OER + NPD EBR	7	A
10	49	F	Unknown	N		ACC	T1N0M0	T1N0M0	I	EACR + NPD EBR	62	A

FNP: facial nerve palsy; Histo: histopathology; SCC: squamous cell carcinoma; ACC: adenoid cystic carcinoma; NEC: neuroendocrine carcinoma; TP: total petrectomy; PP: partial petrectomy; EBR: external beam radiotherapy; CT: chemotherapy; EACR: EAC resection; OER: outer ear resection; NPD: neck and parotid dissection; A: alive; D: dead; N: no; Y: yes.

otitis externa (# 2, # 5, # 6) for more 1 year. Three patients complained of otalgia (30% of cases) (# 1, # 3, # 5), and two reported bleeding from the external auditory canal (20%) (# 6, # 8). One patient (# 2) complained of loss of balance (10%) and another patient reported pruritus of the external auditory canal (10%) (# 9). The mean interval between onset of the first symptoms and diagnosis was 10 months (±8) with a mean interval of 14 months for patients with a stage IV tumour (±8).

Otoscopic findings are presented in Table 2. Otoscopy revealed a fungating tumour in seven cases and an invasive tumour of the EAC in three cases (# 3, # 5, # 8). Complete peripheral facial nerve palsy was present in two patients (20%) (# 2, # 4). Extension to the outer ear was reported for three patients (# 4, # 7, # 9) (30%). Pretreatment audiometry demonstrated profound deafness in two patients (20%) (# 2, # 7). Three patients (30%) presented mixed hearing loss (# 1, # 3, # 8) on the side of the tumour. Five patients (50%) did not present any audiometric signs related to the tumour (# 4, # 5, # 6, # 9, # 10).

Histological examination revealed squamous cell carcinoma for seven patients (70%) (Fig. 1), while the other

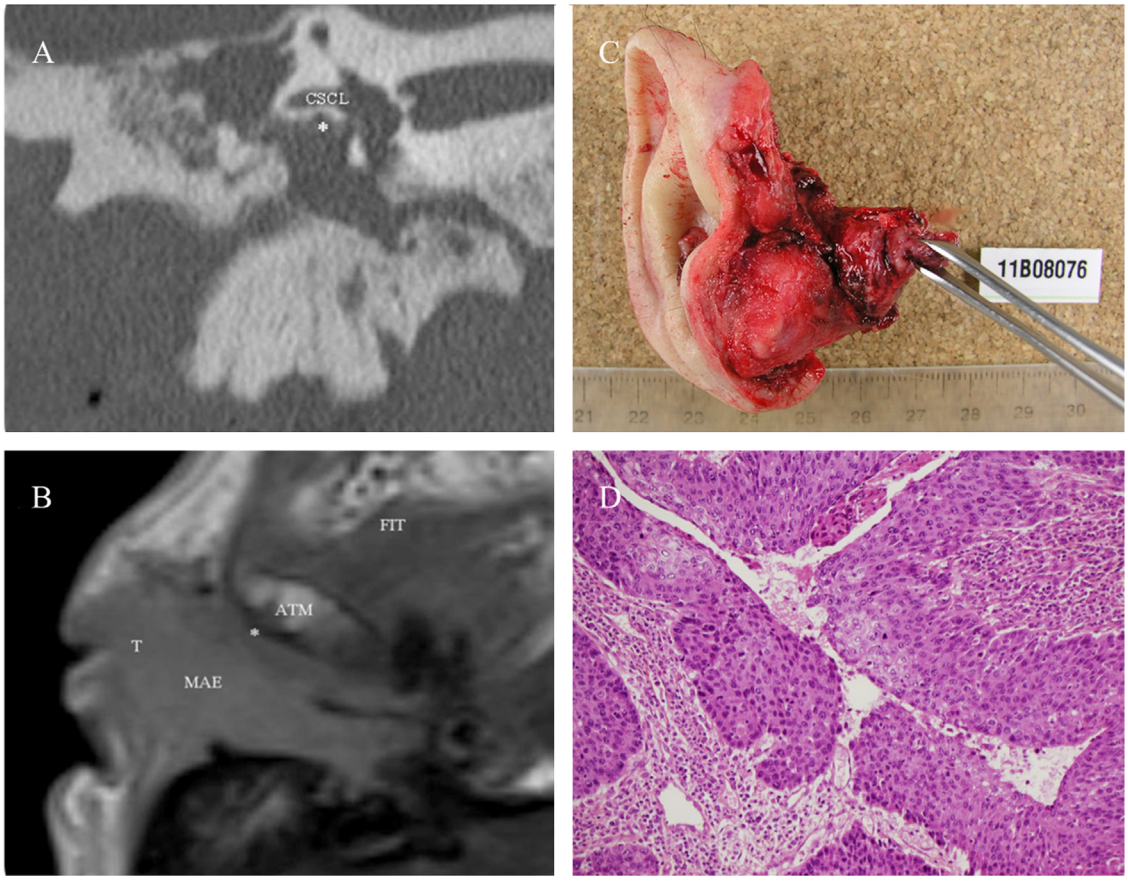

Figure 1 Imaging assessment (CT and MRI), operative specimen and histology of a patient (# 7) with squamous cell carcinoma of the right external auditory canal. A. CT scan of petrous temporal bones, coronal reconstruction showing middle ear and facial canal involvement (*). CSCL: lateral semicircular canal. B. MRI, axial T1-weighted sequence showing tumour extension to subcutaneous soft tissues and erosion (*) of the anterior wall of the right external auditory canal. FIT: infratemporal fossa; ATM: temporomandibular joint; MAE: external auditory canal. C. Operative specimen with *en bloc* resection of the outer ear, external auditory canal (cartilaginous and bony) and tympanic membrane. D. Histological section (HES stain) of a squamous cell carcinoma of the external auditory canal (magnification × 10).

histological types were undifferentiated carcinoma (10%), adenoid cystic carcinoma (10%) and a neuroendocrine carcinoma comprising skin cells (10%).

CT scan of the petrous temporal bones and CT scans looking for lymph node and lung metastases were systematically performed. Head and neck MRI was performed in six patients. Imaging assessment demonstrated invasion of the tympanic cavity and mastoid in six patients (60%), erosion of the EAC in five cases (50%), suspected invasion of the temporal dura mater in four cases (40%), invasion of the facial canal in four cases (40%), parotid gland involvement in four cases (40%), erosion of the lateral semicircular canal in three cases (30%), erosion of the atlas in one case (10%) and extension to the temporal lobe in one case (10%). Metastatic cervical lymphadenopathy was demonstrated in one patient (10%). No metastatic disease was detected prior to treatment.

The TNM stage was determined on the basis of this pretreatment clinical and radiological work-up according to the Pittsburgh classification, revealing six stage T4 tumours (60%), three stage T3 tumours (30%) and one stage T1 tumour (10%). Only one patient was classified as N1. The tumour was classified as stage IV for eight patients (80%), stage III for one patient (10%) and stage I for another patient (10%).

Two patients were not treated surgically. One patient died from pulmonary embolism before starting treatment (# 1) and the other patient presented deterioration of his general status associated with intracerebral extension excluding surgical control of the cancer (# 5).

Eight patients (80%) were treated surgically, by total or subtotal petrectomy with resection of the dura mater in two cases (25% of operated patients) (# 2, # 8) and partial petrectomy in four cases (50% of operated patients) (# 3, # 4, # 7, # 9). Two patients (25% of operated patients) (# 7, # 10) underwent radical resection of the EAC and the vertical segment of the facial nerve was resected in two cases (25% of operated patients) (# 2, # 4). Surgical resection removed all of the outer ear in three patients (46.9% of operated patients) (# 4, # 7, # 8) (Fig. 1), while partial resection of the outer ear was necessary in another case (# 9). Reconstruction of the defect after total amputation of the outer ear used a pectoralis major flap in two cases (# 7, # 8) and a temporalis muscle flap with secondary healing in the other case (# 4). Tumour resection was complete (negative surgical margins)

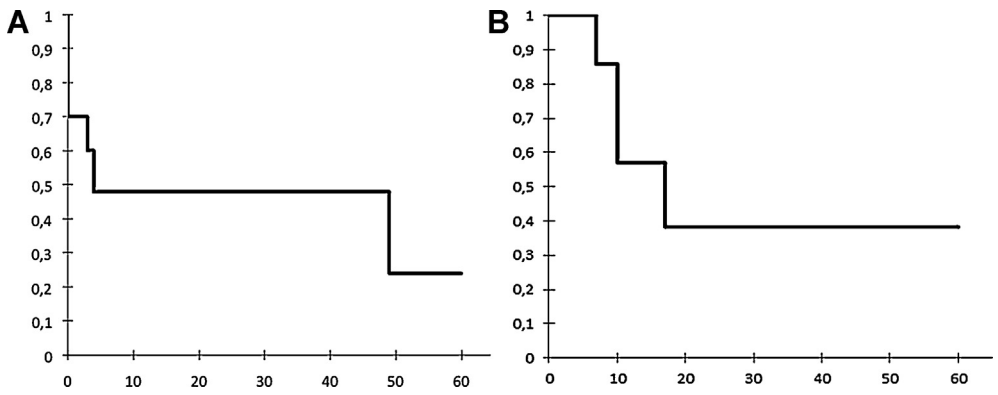

Figure 2 Five-year disease-free survival and overall survival rates for patients with carcinoma of the external auditory canal (EAC). A. Five-year disease-free survival rate. B. Five-year overall survival rate.

in five patients (62.5% of operated patients) (and positive margins were reported for three patients) with positive surgical margins for three patients (37.5% of operated patients) (# 4, # 7, # 8).

Neck and parotid dissection was performed in six cases and a modified radical neck and parotid dissection (with resection of the sternocleidomastoid muscle and internal jugular vein) was performed in one case (# 6). Histological examination revealed lymph node invasion in two patients (# 4 and # 6), i.e. 33% of the patients in whom lymph node dissection was performed. Selective neck dissection was performed in patient # 2 in a context of ipsilateral metastatic level V lymph node involvement 4 months after the initial resection. The mean length of postoperative hospital stay was 22.3 days (±16.7).

Radiotherapy was performed in eight cases (80%). Radiotherapy was not performed in two cases: one patient died before treatment (# 1) and one patient developed lung metastases before healing (# 4). Radiotherapy consisted of conventional radiotherapy to the tumour bed and lymph node areas with a prophylactic dose of 40—55 Gy and a curative dose of 66—75 Gy and corresponded to adjuvant radiotherapy in seven cases (87.5% of irradiated patients), while one patient received first-line radiotherapy (# 5).

Chemotherapy was administered to four patients. Two patients (20%) (# 5, # 8) received cisplatin-based chemotherapy concomitant to radiotherapy: due to positive surgical margins in case # 8 and as primary treatment in patient # 5, who was not treated surgically. One patient (10%) was treated by cisplatin and 5-fluorouracil chemotherapy followed by paclitaxel chemotherapy after radiotherapy for a local recurrence (# 3) and one patient with lung metastases was treated with cisplatin VP-16 (# 4).

The mean disease-free survival was 13.1 months (±22.1) with a 5-year disease-free survival rate of 24% (0.188) all stages combined. The mean 5-year overall survival was 18.7 months (±22.2). The mean overall survival was 62 months for early stage disease (stage I) and 19.4 months (±37.7) for advanced stages (III—IV). The mean overall survival was 28.1 months in the absence of peripheral facial nerve palsy versus 8.5 months in the presence of peripheral facial nerve palsy. The 5-year overall survival rate was 35% (±0.185) all stages combined according to the Kaplan—Meier method (Fig. 2): 100% early stage disease (stage I) and 22.9% (0.187) for advanced stages (III—IV).

Four patients (# 2, # 3, # 7, # 8) presented profound postoperative hearing loss (50% of operated patients). Peripheral facial nerve palsy was observed in five patients (# 2, # 3, # 4, # 7, # 8) (55.6% of treated patients), corresponding to grade V facial nerve palsy of the House—Brackmann score for three patients (# 2, # 3, # 4), grade IV for one patient (# 8) and grade III for one patient (# 7). Delayed healing was observed in three patients (37.5% of operated patients) (# 4, # 7, # 8) in whom complete resection of the outer ear was necessary.

Discussion

Cancer of the EAC is a rare disease. Several case series have been reported in the literature, but no randomized controlled study has yet been published. The mean age of the patients in the present study was 61.5 years with a sex ratio of 1, as described in the literature [2,6,7,10,11].

The clinical presentation is non-specific. Otorrhoea is the most common symptom and may be suggestive of chronic otitis externa [7]. Otalgia disproportionate to the otoscopy findings is highly suggestive of the diagnosis of EAC tumour, particularly adenoid cystic carcinoma [12]. The presence of peripheral facial nerve palsy is a major clinical finding, as it suggests a locally advanced tumour [13]. Facial nerve palsy was present at diagnosis in 20% of cases in this series, a rate comparable to that reported in the literature [14]. Twenty percent of patients had a history of multi-operated cholesteatoma for more than 10 years. Several cases of squamous cell carcinoma of the EAC secondary to cholesteatoma have been reported in the literature [15,16]. However, the role of cholesteatoma in carcinoma of the EAC remains controversial, as some authors consider cholesteatoma to be a risk factor for carcinoma of the EAC [17], while others do not [18].

In the presence of non-specific clinical features and doubtful otoscopic findings (especially invasive forms), biopsy must be performed, preferably in the operating room to ensure good quality biopsy samples for histological examination.

Most published studies have concerned squamous cell carcinoma, which is the most common histological type [19], as confirmed in our study (70%). No cases of basal cell carcinoma of the EAC were observed in this study, although

Table 3 Survival rates for carcinoma of the external auditory canal (EAC) reported in the literature.

Author	Sample size	Types	Survival
Gurgel et al., 2009 [29]	215	SCC (62.8%) ADC (18.2%) OC (13%) NCT (6%)	Five-year SCC (23.9%) ADC (65%) OC (60%) NCT (38.6%)
Yin et al., 2006 [11]	95	SCC (100%)	Five-year Stage I et II (100%) Stage III (67.2%) Stage IV (29.5%)
Ogawa et al., 2007 [26]	87	SCC (100%)	Five-year 55% all stages
Zhang et al., 1998 [27]	33	SCC (100%)	Five-year 51.7% all stages Stage I and II (100%) Stage III (68.8%) Stage IV (19.6%)
Moody et al., 2000 [1]	32	SCC (100%)	Two-year SCC T1 (100%) SCC T2 (80%) SCC T3 (50%) SCC T4 (7%)
Pfreundner et al., 1999 [28]	27	SCC (71.5%) ADC (9.5%) OC (19%)	Five-year 61% all stages T1 et T2 (86%) T3 (50%) T4 (41%)
Nakagawa et al., 2006 [30]	12	SCC (100%)	Five-year SCC T3 (85%) SCC T4 (35%)
Present study 2012	10	SCC (60%) OC (20%) ACC (10%)	Five-year 35% all stages Stage III—IV (22.9%)

SCC: squamous cell carcinoma; ADC: adenocarcinoma; OC: other carcinomas; NCT: other non-carcinomatous malignant tumours; BCC: basal cell carcinoma; ACC: adenoid cystic carcinoma.

it constitutes the second most common histological type encountered. No studies concerning the other histological types have been published.

The Pittsburgh classification, based on clinical and radiological findings, is used for TNM staging of squamous cell carcinoma of the EAC. No classification is specifically devoted to the other types. Like other authors [20,21], we extrapolated this classification to all histological types. CT scan allows reliable detection of bony erosion of the EAC and invasion of the facial canal. The findings of preoperative CT of the petrous temporal bones are correlated with histological findings [6]. In our study, comparison between imaging and histological and preoperative findings validated the use of this classification. However, there are a number of limitations to the use of CT for evaluation of soft tissue involvement (parotid and infratemporal fossa). The TNM staging based exclusively on CT was accurate in 90% of cases for local extension, while parotid gland invasion was only demonstrated by MRI in 10% of cases. In 40% of cases, MRI raised the suspicion of invasion of the temporal dura mater allowing planned dura mater resection. Although MRI findings have little impact on the TNM staging based on CT, it can be used to evaluate parotid, soft tissue, infratemporal fossa and temporal dura mater involvement [6,22]. This information is essential for the management of invasive EAC tumours, especially in the case of adenoid cystic carcinoma, for which clinical staging assessment is particularly difficult. These findings therefore suggest that MRI should be systematically performed for local staging of carcinoma of the EAC. The place of PET-CT has yet to be defined, as no study has evaluated this imaging modality, although it is used in specific indications for squamous cell carcinomas of the larynx and hypopharynx. No study has been published concerning the use of PET-CT in malignant tumours of the EAC.

All patients in this series were treated surgically by partial or total petrectomy in 60% of cases. Despite extensive

surgery, the resection was incomplete in more than one-third of operated patients (37.5%), which is comparable to the data of the literature [21], as *en bloc* surgical resection comprising safety margins is difficult to perform in the small bone volume of the petrous apex. Assessment of the quality of resection by the pathologist is complicated by resection in multiple fragments. Positive surgical margins are synonymous with progressive disease [23]. Progressive disease was observed in one half of cases, leading to death within 1 year in 80% of cases. A low lymph node invasion rate (20%) was observed compared to the high rate of local extension (T4 in 60% of cases). Distant metastases during the course of the disease were observed in 10% of cases. Various studies [7,21] suggest that early aggressive surgical management is associated with improved survival. Some authors therefore recommend petrectomy associated with *en bloc* superficial parotidectomy for squamous cell carcinoma of the EAC [21]. Facial nerve involvement does not constitute a contraindication to surgical management [24]. In the presence of parotid involvement, with tumour adjacent to the vertical segment of the facial nerve, the patient must be informed about the possibility of facial nerve resection and postoperative facial palsy [24]. Like other authors, we perform limited dura mater resection when this tissue is invaded. Dural extension does not appear to constitute a contraindication to surgery. However, surgery is contraindicated in the presence of posterior fossa, middle fossa, or internal carotid artery involvement [25]. Resections did not exceed 2 cm^2 in the present series.

This approach was confirmed by the conclusions of a meta-analysis [8] based on 26 publications that recommended subtotal petrectomy followed by external beam radiotherapy in the presence of middle ear involvement. However, this meta-analysis also concluded on the absence of any significant survival difference between EAC resection and subtotal petrectomy in patients with tumours confined to the EAC.

The role of adjuvant radiotherapy remains controversial, as no study has formally demonstrated a survival benefit [8,14]. Until this controversy has been resolved, we, like other authors [21,26], continue to propose adjuvant radiotherapy. Some authors suggest that small lesions without bony erosion can be treated by radiotherapy alone [8,13]. In our study, 10% of patients, whose general status was not compatible with surgery, were treated by first-line radiotherapy. Conformal radiotherapy was delivered at a prophylactic dose of 50 Gy and a curative dose of 70 Gy in the presence of residual tumour.

The poor 5-year overall survival rate (35% all stages) observed in this series can be explained by the fact that most patients presented advanced disease (stages III and IV). In the literature, the 5-year overall survival rate ranges from 80 to 100% for stages I and II carcinoma of the EAC [1,11,27] and from 50 to 20% for stages III and IV [1,11,28] depending on the series, hence the importance of early diagnosis. The present series comprised a smaller proportion of stages I and II tumours compared to other published series (33—54%) [7,14]. The 5-year overall survival rate for stages III and IV disease was 22.9%, comparable to the rates reported in the literature (Table 3). This lower survival rate for advanced stages confirms the validity of the Pittsburgh classification.

Prognostic factors for carcinoma of the EAC are TNM stage, bony erosion of the EAC, positive surgical margins, extratemporal locoregional invasion (parotid, cervical), middle ear involvement and the presence of peripheral facial nerve palsy [6,7,21,24,31]. In this study, the mean survival of the 20% of patients with peripheral facial nerve palsy at diagnosis was 8.5 months (7 and 10 months, respectively) versus 28.13 months in the absence of facial nerve palsy. Middle ear involvement corresponds to stage III of the Pittsburgh classification. Patients presenting retrotympanic involvement on otoscopy and/or audiometric abnormalities (often related to middle ear involvement) presented a lower survival, thereby validating the Pittsburgh classification. The histological type also constitutes a prognostic factor. Patients with basal cell carcinoma had a better survival than patients with other histological types. Squamous cell carcinoma of the EAC is the most common histological type and is associated with the poorest prognosis.

Conclusion

Cancer of the EAC is a difficult diagnosis in the presence of chronic otitis externa or invasive forms. The Pittsburgh classification has been validated and should be used for staging of these tumours. Clinical examination and imaging (CT and MRI) can demonstrate the main prognostic factors: peripheral facial nerve palsy, soft tissue (parotid) involvement, middle ear involvement and lymph node involvement. Management consists of a combination of radical surgery and radiotherapy and the prognosis is related to local tumour control. This aggressive treatment is almost always responsible for sequelae. Diagnosis and treatment need to be improved in order to improve patient survival associated with fewer sequelae. Modern imaging techniques (PET-CT scan) and new radiotherapy techniques (cyberknife, IMRT) must be evaluated.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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