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par

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TITRE

Facteurs de risque d'échec de prise en charge de l'otite externe nécrosante :

une étude multicentrique rétrospective descriptive de 2009 à 2023

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Facteurs de risque d'échec de prise en charge de l'otite externe nécrosante :

une étude multicentrique rétrospective

Contexte : L'otite externe nécrosante est une pathologie rare et mal codifiée, de pronostic sévère (rechute de 10 à 50% des patients) retrouvée principalement chez les patients âgés diabétiques ou immunodéprimés. A ce jour, il n'existe pas de consensus sur sa prise en charge globale et plus précisément les modalités de traitement anti infectieux. L'objectif principal de cette étude est de décrire les facteurs de risque associés aux échecs à 6 mois de prise en charge de cette pathologie.

Matériel et Méthodes: Il s'agit d'une étude rétrospective descriptive multicentrique (hôpitaux du Grand Ouest en France) recueillant les données de patients majeurs présentant un diagnostic d'otite externe nécrosante entre janvier 2009 et janvier 2023. Les données démographiques, clinico-biologiques et radiologiques ont été assemblées. L'échec était défini comme réapparition des signes cliniques et/ou radiologiques, reprise d'un traitement antiinfectieux, décès dans les 6 premiers mois post traitement.

Résultats : Parmi 1119 patients screenés sur 12 centres hospitaliers, 156 patients avec un diagnostic d'otite externe nécrosante ont été inclus. Parmi ceux-là, 116 (74,4%) sont des hommes, avec un âge médian de 78 ans, et un score de Charlson médian de 3. Les patients diabétiques étaient au nombre de 108 (69,2%) et 17 (10,9%) étaient des patients immunodéprimés. Les symptômes cliniques les plus fréquemment retrouvés étaient : une otalgie pour 151 patients (96,8%), une otorrhée pour 136 patients (87,2%), un granulome du conduit auditif externe pour 90 patients (57,7%), une sténose du canal auditif externe pour 98 patients (62,8%), une atteinte des paires crâniennes pour 45 patients (28,8%), avec un délai médian diagnostic à 43 jours. La documentation microbiologique était retrouvée pour 121 patients (77,1%) dont 95 (60,5%) à *Pseudomonas aeruginosa*, 23 (14,6%) fongiques et 18 (11,5%) polymicrobiens. La durée médiane d'administration des antibiotiques est de 42 jours avec une bithérapie dans 108 cas (77,7%). Le taux d'échec à 6 mois est de 33% (48 patients). Les facteurs de risque associés significativement à l'échec sont la présence d'une paralysie faciale (20,2% vs 36,2%) ainsi qu'une perte de poids (17,4% vs 34,8%) au diagnostic et avoir reçu une radiothérapie dans la même zone (0,93% vs 8,5%).

Conclusion : L'otite externe nécrosante est une pathologie sévère à l'origine d'ostéite de la base du crâne dont le taux d'échec de prise en charge est encore majeur. La présence d'une paralysie faciale, une perte de poids et l'antécédent de radiothérapie locale sont associées à pronostic défavorable à 6 mois. Une étude prospective de grande échelle afin de valider des critères diagnostiques nous semblerait cruciale pour la conduite de futures études visant à définir les modalités optimales d'antibiothérapie.

Mots clés : Otites externes nécrosantes, otites malignes externes, ostéite de la base du crâne

Relapsing factors of necrotizing otitis externa:

An observational, retrospective, multicenter study from 2009 to 2023

ABSTRACT

Background: Necrotizing otitis externa is a rare condition, with a severe prognosis (relapse rate up to 10-50%), that mostly occurs in diabetic elderly or immunocompromised patients. Its management and specifically the duration of antimicrobial therapy have yet to be validated. This study intends to describe risk factors that may be associated with a higher failure rate at 6 months follow up, focusing on epidemiology, microbiological findings, and antimicrobial use.

Material and methods: This is a retrospective observational multicenter (Western France hospitals) study collecting data from adults presenting with a diagnosis of necrotizing otitis externa between January 2009 and January 2023. Demographic, clinical, biological, and radiographic data were collected. Failure of treatment was defined as clinical and/or radiological relapse, introduction of a new course of antimicrobial agents, or death before 6 months follow up.

Results: Among 1,119 patients screened in 12 tertiary medical centers, 156 patients were included. One hundred and sixteen (74.4%) were male, with a median age of 78 years, and a median Charlson score of 3. The number of diabetic patients was 108 (69.2%), and 17 (10.9%) patients were immunocompromised . The most frequent clinical symptoms were as followed: otalgia in 151 (98.6%) patients, otorrhea in 136 (87.2%) patients, granuloma in the external ear canal in 90 (57.7%) patients, external ear canal stenosis in 98 (62.8%) patients, cranial nerve involvement in 45 (28.8%) patients, with a median time to diagnosis of 43 days. A microorganism was identified in 121 (77.1%) cases, *Pseudomonas aeruginosa* being the most represented (60.5%), followed by fungi (14.6%), and polymicrobial culture (11.5%). Median duration of antibiotics was 42 days with a combination of two therapeutic agents in 108 (77.7%). The rate of failure at 6 months was 33% (48 patients). The factors significantly associated with a higher rate of failure were facial palsy (20.2% vs 36.2%), weight loss (17.4% vs 34.8%) on diagnosis and a history of localized radiotherapy (0,93% vs 8,5%).

Conclusion: Necrotizing otitis externa is a rare and severe pathology with a major risk of relapse. Findings such as facial palsy and weight loss on diagnosis as well as a history of localized radiotherapy may be associated with a poor prognosis. Prospective studies validating proper diagnostic criteria are necessary to ultimately define optimal antimicrobial management of necrotizing otitis externa.

Keywords: Necrotizing otitis externa, Malignant otitis externa, Skull base osteomyelitis

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SERMENT D'HIPPOCRATE

En présence des enseignants et enseignantes
de cette Faculté,
de mes chers condisciples
et selon la tradition d'Hippocrate,
je promets et je jure d'être fidèle aux lois de l'honneur
et de la probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuits aux indigents,
et n'exigerai jamais un salaire au-dessus de mon travail.

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yeux ne verront pas ce qui s'y passe, ma
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les secrets qui me seront confiés et mon état ne servira
pas à corrompre les mœurs ni à favoriser le crime.

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Table des matières

Abréviations

- NOE : necrotizing otitis externa
- EAC : External auditory canal
- CNS : Central Nervous System
- ENT : Ear Nose Throat
- BMI : Body Mass Index
- IQR : InterQuartile Range
- CKD : Chronic Kidney Disease
- PMSI : Programme de Médicalisation des Systèmes d'Information
- CRP : C Reactive Protein
- TDM : Tomodensitometry
- MRI : Magnetic Resonance Imaging
- PETscan : Positron Emission Tomography

INTRODUCTION:

Defined as an invasive infection of the external auditory canal (EAC), necrotizing otitis externa is a rare and not fully understood condition.

A combination of clinical symptoms such as otorrhea and otalgia, resistance to local treatment and radiological abnormalities showing extension to adjacent structures has initially been proposed as diagnostic criteria (1).

Throughout the last decades, various studies have outlined demographic trends in this pathology: it tends to occur in elderly diabetic or immunocompromised patients (2) and evolves towards cranial base osteomyelitis responsible for neurologic and hearing defects (3–5). The most common pathogen known to cause this particular disease is *Pseudomonas aeruginosa*, followed by *Staphylococcus aureus* and fungi (4,6).

Treatment remains challenging, and, although the numbers are heterogenous, relapse rate is still high (10-50%) (7,8). In fact, there is neither consensus over the use of monotherapy vs bitherapy, oral vs intraveinous therapy, nor duration of antibiotic course although one recent study shows a benefit from a longer duration of treatment (9).

Studies aiming at improving its management are limited by their poor recruitment and therefore have difficulty establishing prognostic factors in order to anticipate potential relapse, fatal issue, or neurological sequelae(6,10,11).

This study aims to highlight factors linked to a higher rate of relapse, factors that should raise clinician awareness for close subsequent follow up.

MATERIAL AND METHODS

Study design: We conducted a retrospective, observational, and multicentered study from January 2009 to January 2023. The primary outcome focuses on revealing and analyzing some of the predictive factors for treatment failure among patients with necrotizing otitis externa (NOE) at 6 months follow up. Secondarily, it intends to describe the population characteristics, the mortality rate and the sequelae up to one year follow up.

Population: We included patients over 18 years of age, with a diagnosis of necrotizing external otitis. We defined NOE as followed: clinical signs of external otitis (at least three signs among

otalgia, otorrhea, inflammatory external auditory canal, granuloma in the EAC for at least 1 week, resistant to local antibiotherapy plus radiological evidence consistent with cranial base osteomyelitis (local cortical erosion and/or local infiltration of soft tissues surrounding the external ear canal). Were excluded from our analysis patients with lack of data >40% and the ones that were unable to consent.

Outcome:

Primary outcome: Treatment failure included disease relapse and death. Criteria for relapse were decided as followed: recurrence of pain, discharge, new Central Nervous System (CNS) involvement, imaging progression and/or initiation of a new course of antimicrobial therapy. We divided our population into 2 groups (with or without treatment failure at 6 months) and compared their characteristics and disease history.

Secondary outcomes: (i) Description of the population, (ii) mortality rate, (iii) sequelae.

Data source: Data in the tertiary care university hospital of Tours were collected using eHOP, a software of clinical data warehouse including electronic medical records produced by the hospital information system. A research algorithm was built, with the ability to detect the following combinations of keywords “malignant external otitis”, “necrotizing otitis externa” and “skull base osteomyelitis” (each combination of words being spaced maximum by 5 words) in medical charts. The PMSI (Programme de Médicalisation des Systèmes d’Information) was used in the absence of eHOP to extract the list of patients (Appendix).

Ethics: A letter of information was sent to all participants to signify their inclusion in the article and remind them of their right to decline participation. The study protocol was reviewed and approved by the CNIL (F20220203153003) and was conducted according to the MR004 process.

Statistics: The primary outcome was assessed as a binomial variable. Using the Chi2 and t-student test, we compared the characteristics of the failing vs non failing group allowing us to identify potential prognostic factors. We used the Kaplan-Meyer method to obtain survival curves. A p value inferior to 0.05 was considered as statistically significant. Analysis was conducted on Excel 2016 and R (3.1 version).

RESULTS

From 1,119 patients screened in 12 tertiary medical centers, 766 patients were not included (322 had otitis externa, 326 had a different ENT (Ear Nose and Throat) diagnosis). From the 353 remaining, 197 were excluded (92 were lost to follow up/missing data, 105 were treated as necrotizing otitis externa but didn't meet our criteria) (Fig 1)

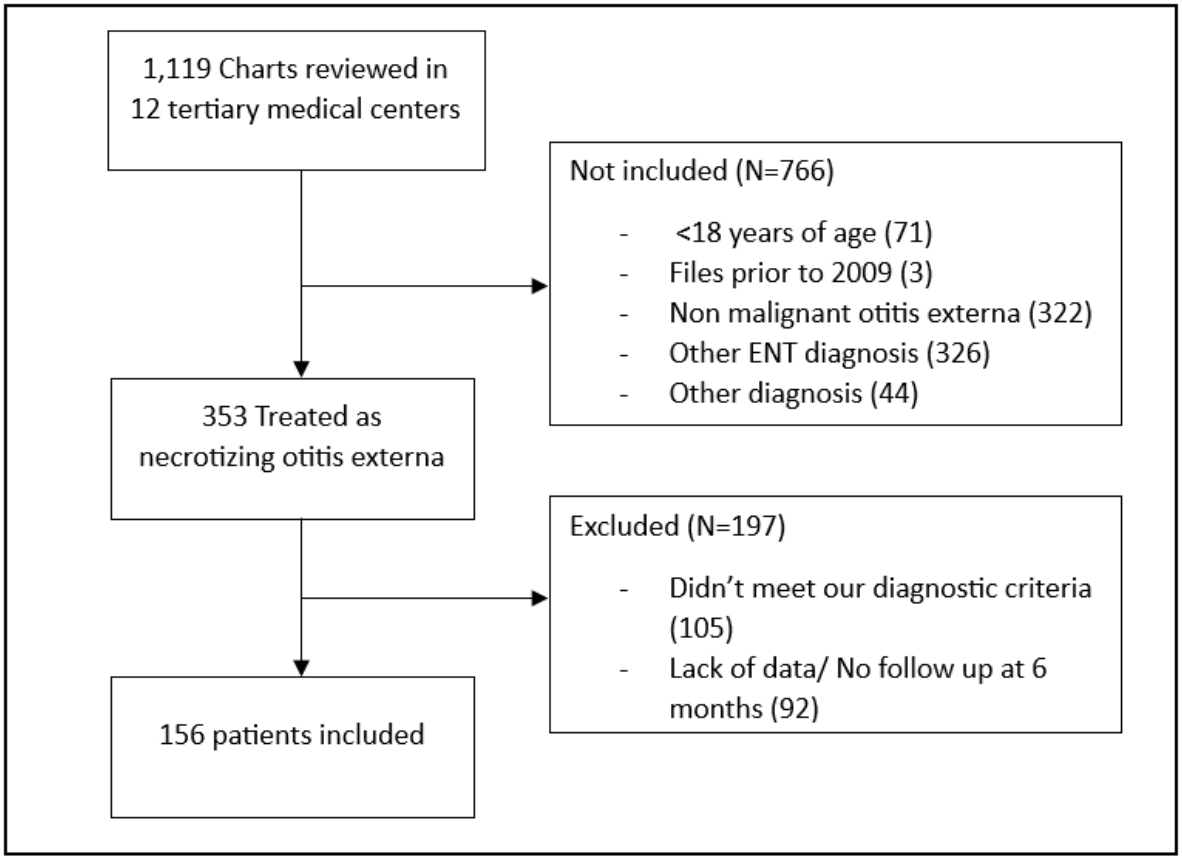

Figure 1. Flow chart

Demographics : median age was 78 years (IQR 70-85). One hundred and sixteen of 156 (73.9%) were male, 108/156 (68.8%) diabetic, 41/156 (26.1%) had a Body Mass Index (BMI) over 30, 17 (10.8%) were immunosuppressed, 5 (3.2%) had undergone previous ENT radiotherapy. The median Charlson score was 3.5 (IQR 1-5).

Clinical diagnosis : Median time from beginning of symptoms to diagnosis was 43 days (IQR 23-77). The most frequent clinical signs were otalgia (151/156 patients, 96.2%), hearing impairment (68/156 patients, 43.3%) otorrhea (136/156 patients, 86.6%), granuloma in external ear canal (90/156 patients, 57.3%) and external ear canal stenosis (98/156 patients, 62.4%). The most common neurological complication was cranial nerve palsy : among 45/156 patients (28.8%) that presented with cranial nerve palsy, 39 had simple facial palsy and 9 patients had multiple cranial nerve involvement.

Table 1. Patients characteristics		**n**	**%/IQR**
Epidemiology	**Age (years)**	**78**	**[70-85]**
	Male gender	116	(74.4%)
	Charlson score	3	[1-5]
	Diabetes	108	(69.2%)
	Obesity	41	(26.3%)
	Immunosuppression	17	(10.9%)
	Previous ENT radiotherapy	5	(3.2%)
Symptoms	Time to diagnosis (days)	43	[23-77]
	Otalgia	151	(96.8%)
	Otorrhea	136	(87.2%)
	Hypoaccousia	68	(43.6%)
	Fever	9	(5.8%)
	Granuloma in EAC	90	(57.7%)
	EAC stenosis	98	(62.8%)
	Cranial nerve palsy	45	(28.8%)
	Facial palsy	39	(25%)
	Multiple cranial nerve involvement	9	(5.8%)
	CRP C-Reactive Protein(mg/l)	34	[11-70]
	Neutrophils (g/l)	7	[4.6-9.1]

Microbiology: Microbiological identification was made in 121/156 patients (77.1%) (111 on EAC swab, 10 on surgical sample). The pathogens mostly involved were *Pseudomonas aeruginosa* in 95 patients (60.4%) (87 identified via ear swab, 14 via surgical biopsy), enterobacteria in 11 patients (7.0%) (10 on ear swab, 3 on surgical biopsy), *Staphylococcus* spp in 9 patients (5.7%) (7 on ear swab, 2 on surgical biopsy). Fungi were found in 23 patients (14.6%) (18 on ear swab, 9 on surgical biopsy), (Table 2).

Treatment: Among patients treated with antibiotics exclusively, median duration was 44.8 days and 107 patients out of 138 received a bitherapy for a median duration of 21 days. Duration of antimicrobial treatment was 143 days when antifungals were added. Side effects were noted in 19 patients (12.1%), mostly acute kidney injury (6 patients), confusion (2 patients), digestive intolerance (2 patients), tendinitis (2 patients), and DRESS syndrome in 1 patient. Surgery was performed in 37 patients (23.6%). The most common objectives of surgical management were biopsy in 26 patients, mastoidectomy in 11 patients, debridement in 3 patients, facial nerve decompression in 1 patient, drainage of intracerebral abscess in 1 patient, (Table 3).

Table 2. Microbiology and imaging characteristics			n=156	%
Microbiology	Positive microbiological identification		121	(77.1%)
	EAC swab		142	(90.4%)
	Surgical sample		32	(20.4%)
	EAC swab and surgical sample		16	(10.2%)
	No microbiological sample		29	(18.5%)
	Pseudomonas aeruginosa	Total	95	(60.5%)
		EAC swab	87	(55.8%)
		Surgical sample	14	(9%)
		EAC swab and surgical sample	6	(3.8%)
	Enterobacteriae		11	(7.0%)
	Staphylococcus		9	(5.7%)
	Streptococcus		3	(1.9%)
	Fungi	Total	23	(14.6%)
		EAC swab	18	(11.5%)
		Surgical sample	9	(5.8%)
		EAC swab and surgical sample	4	(2.6%)
	Polymicrobial		18	(11.5%)
Imaging	Scanner		148	(94.3%)
	MRI (Magnetic Resonance Imaging)		63	(40.1%)
	PETscan (Positon Emission Positrons)		19	(12.1%)
	Scintigraphy		18	(11.5%)
	Soft tissue involvement		120	(76.9%)
	Bone lesion		128	(82.1%)

Table 3. Treatment modalities	n	%/IQR
Exclusive antibiotherapy	139	(89.1%)
Antibiotherapy duration (median, IQR) (days)	42	[38-46]
Bitherapy	108	(77.7%)
Bitherapy duration (median, IQR), (days)	21	[14-42]
Antibiotic		
Tazocilline	26	(18.7%)
Ceftazidime	100	(71.9%)
Fluoroquinolones	114	(82%)
Others	35	(25.2%)
Combination of antibiotics and antifungals	13	(8.3%)
Exclusive antifungal therapy	4	(2.6%)
Antifungal therapy duration (median, IQR, days)	143	[54-311]
Surgery	37	(23.7%)

Outcome: Rate of failure at 6 months follow up was 29.9%: 38 patients had a relapse (24.2%) and 10 patients died before 6 months (6.4%). Neurological sequelae were noted in 31 patients (19.7%), remaining facial palsy was detected in 21 patients out of 39 (53.8%). 15 patients (9.6%) had died at 12 months, with 4 deaths reported as related to necrotizing otitis externa, (Table 4).

Table 4. Outcomes	n	%
Failure at 6 months	47	**(30.1%)**
Relapse	38	(24.4%)
Death	10	(6.4%)
Related death	4	(2.6%)
Neurological sequelae at 6 months	31	(19.9%)
Mortality rate at 12 months	15	(9.6%)
Related	4	(2.6%)
Unrelated	11	(7%)

Primary outcome analysis: First we observed that facial palsy had been found in 22 patients (20.2%) who didn't present with treatment failure versus 17 (36.2%) who presented with treatment failure ($p<0.05$). Weight loss affected 17.4% of patients in the non-failure group vs 34.8% in the failure group ($p <0.05$). Among the 4 patients who had previously undergone ENT radiotherapy, 1 didn't have treatment failure and the other 3 did ($p<0.05$).

Some other factors however did not show any significant difference : Diabetes (69.4% of patients in the non treatment failure group vs 70.2% of patients in the treatment failure group), male gender (73.4% vs 76.6%), Chronic Kidney Disease (CKD) (25.7% vs 25.5%), underlying immunosuppression (10.1% vs 12.8%), Charlson score (3 vs 3), age (78 years vs 80). The absence of microbiological identification represented 22.9 % in the non-failure group vs 36.2% in the failure group ($p=0.09$), Pseudomonas aeruginosa had been identified in 72 patients (66.1%) in the non-failure group vs 24 patients (51.1%) in the failure group ($p= 0.077$) and fungi were found in 15 patients in the non-failure group vs 8 patients in the failure group ($p= 0.79$) (Table 5).

Table 5. Comparison between patients with or without failure at 6 months follow-up

	No failure at 6 months N= 109	Failure at 6 months N=47	p-value
Age (median, years)	78	80	0.205
Male gender	80 (73,4%)	36 (76,6%)	0.674
Charlson score (median)	3	3	0.743
Diabetes	75 (69,4%)	33 (70,2%)	0.924
Obesity	30 (30,3%)	11 (23,4%)	0.386
Chronic kidney disease	28 (25,7%)	12 (25,5%)	0.983
Immunodepression	11 (10,1%)	6 (12, 8%)	0.623
ENT radiotherapy	1 (0,93%)	4 (8,5%)	0.030
Time from symptoms to diagnosis (days)	37	52.5	0.225
Weight loss	19 (17,4%)	16 (34,8%)	0.018*
Facial palsy	22 (20,2%)	17 (36,2%)	0.034*
Multiple cranial nerve involvement	3 (2,75%)	3 (6,38%)	0.367
CRP (mg/L)	31	36	0.332
PNN (G/L)	6.4	7.9	0.339
Albumine (g/L)	34	32	0.690
No microbiological identification	25 (22,9%)	17 (36,2%)	0.087
Pseudomonas aeruginosa	72 (66,1%)	24 (51,1%)	0.077
Fungi	15 (13,7%)	8 (17,0%)	0.779
Duration of antibiotherapy (median, days)	42	42	0.391
Presence of bitherapy	79 (81,4%)	28 (68,3%)	0.091
duration of bitherapy (median, days)	21	21	0.910
Exclusive use of antifungal therapy	3 (2.8%)	1 (2.1%)	1
Surgery	23 (21,1%)	14 (29,8%)	0.334

DISCUSSION

To our knowledge, this article presents the widest retrospective study describing 156 patients that presented with NOE across 12 tertiary centers in Western France. Failure at 6 months follow up was 29.9%, a number that was already reported in previous studies : Danjou *et al.,* described of relapse rate of 25% with a median time to relapse of 11 weeks (9). We found that facial palsy, weight loss on diagnosis and previous ENT radiotherapy were risk factors associated with treatment failure.

The presence of facial palsy among these factors may be explained by the fact that it could be a clinical sign of extensive disease. Previous data on this subject were rather controversial, most

likely because of insufficient power in previous studies. Our insight could lead physicians to monitor closely these patients presenting with facial nerve palsy, (10–13).

Weight loss at presentation was also associated with treatment failure. We couldn't find similar analysis consistent with this finding in the literature. Malnutrition is usually associated with a lesser efficacy of antimicrobial therapy due to an increase of volume distribution (due to an increase of the unbound fraction of drugs) (14). Interestingly, we couldn't validate this theory in our study as albumin levels didn't seem different in the 2 groups of patients. However, while non statistically significant, we note that the median CRP in patients presenting with initial weight loss was 41 vs 26 in patients without reported initial weight loss. This could support the hypothesis that weight loss in this specific pathology could be considered as an indirect sign of extensive disease via swallowing impairment (through cranial nerve palsy that was not properly addressed) or the reflection of a longer inflammatory process.

Necrotizing otitis externa occurring in patients with history of ENT localized radiotherapy also seems to be associated with treatment failure. Interestingly, the same prognostic factor has been described in a setting of periprosthetic joint infection(15). This very special and scarce population could potentially be more at risk due to the fibrotic post radic composition of the bone and surrounding tissues that could prevent good diffusion of antimicrobial therapy (16).

Early sensitive imaging would be indicated in patients as soon as clinical suspicion for NOE is raised (even more so in the ones with the three previously described characteristics). Ideal imaging for both diagnosis and follow up have been a source of debate in the literature up until now.

CT scan, being the most affordable and routinely available imaging technic, is the most represented in this study. Although it has proven to be useful in describing bone lesions, it will not help making a very early diagnosis as bone erosion can be seen only after a demineralization >30% of initially healthy bone structures. Moreover, previous studies have failed to correlate clinical complications (especially facial palsy) with radiological signs on CT scans (17). MRI, as a complementary technique, has been proven to show soft tissue changes more accurately (18,19) and therefore should be recommended in the setting of high clinical suspicion especially when CT scans have failed to confirm diagnosis.

As 99mTechnetium methylene diphosphonate (99mTc-MDP) hybrid single-photon emission computed tomography (SPECT-CT) was found to provide high sensitivity for NOE diagnosis

and to accurately describe anatomical structures involved, it would seem to be a good alternate to the combination of CT scan and MRI but it isn't routinely offered in most tertiary medical centers in western France at the present timing(20,21). More recent evaluations have highlighted the advantages of hybrid imaging techniques such as PET-CT and even more importantly PET MRI (although the lastest are not available in our centers on routine) for both early diagnosis and follow up as they combine functional and anatomical imaging (22,23). Therefore, in the actual setting, we would highly recommend integrating more systematically PET-CT (or PET-MRI when available) as the imaging of reference for diagnosis of NOE.

Overall, our population characteristics matched with the literature : in 2020, Hopkins *et al*., described a prevalence of diabetic patients of 65 %, 85% being over the age of 65, and 25% suffering from cranial nerve palsy on diagnosis (24,25). Microbiological agents were also consistent with previous findings described in the literature : in 2016, Stern Shavit *et al.,* in their observatory study including 88 patients, *Pseudomonas aeruginosa* was also detected in 50% of cases, followed by enterobacteriae (23%) and fungi (15%). Interestingly, the rate of absence of microbiological identification was also similar (22,7%) (12,26).

Although not statistically significant, our study showed that the absence of microbiological identification might be associated with a poor outcome. It is not surprising, as such patients were treated empirically (usually with anti pseudomonal therapy) (30–32). This would highlight the need for repeated samples, probably surgically guided rather than peripheral although our analysis didn't suggest that getting surgical samples could be a prognosis factor. These results are probably due to the fact that few were listed and such samples were obtained only when patients were particularly altered.

Analysis of patients with fungal infection was limited by the small number of cases. However, the trend would suggest that they might be linked to a higher rate of treatment failure (representing 13.7% in the non-failure group vs 17% in the failure group) and interestingly despite the fact that the duration of antifungals alone was longer than antibiotics course (median of 143 days vs 42 days). These matters will need to be properly addressed in the future in separate studies. Based on these two previous findings, we would still advise getting surgical samples early in the process if peripheral cultures (both bacterial and fungal) came back negative.

Notably, median time to diagnosis was 43 days, a long period that reflected a failure in early detection, as was already described in previous studies (33). This could partially be explained

by the fact that all these patients are being primarily treated for simple otitis externa prior to being suspected of such a specific pathology. Conversely to previous articles, we couldn't show an association between a longer period of time from beginning of symptoms to diagnosis and the advent of treatment failure (34). Still, this number supports the need for both awareness in physicians in the community and easy access to more precociously sensitive imaging methods as we previously discussed.

Mean duration of antibiotic course was 44.8 days, a number that, despite the absence of clear recommendations correlate to usual duration of treatment for bacterial osteomyelitis in general. This duration hasn't proved to increase risk of relapse (2,26–29). In our study, longer duration wasn't associated with a better outcome. We noted however that only 68,3% of patients who had had failure had undergone bitherapy (vs 81,4% in the non failure group p=0,09), a non significant difference but it tends in the same direction as Pulcini *et al.,* in 2012 (30).

Various challenges were met building this study: in addition to the usual bias inherent to retrospective studies, the lack of scientifically validated criteria for necrotizing otitis externa is a major limit to our article. We voluntarily chose to narrow our analysis down to strict clinical criteria for otitis externa associated with radiological signs of progressive disease, criteria that have been often used in previous studies (1,8,9) and that have been more recently proposed to be next validated in the Delphi study (35).

However we are aware that this design exposes us to a selection bias especially with the imaging criteria (being located in very specific areas in which interpretation requires a well-trained head and neck radiologist and having no clear recommendations of which imaging might have the best early detection/availability/cost ratio). Under these conditions, our study would have benefited from a blinded review of the images with a standardized questionnaire filled by 2 of these specialists in order to confirm both the diagnosis and the 3D extension of the disease.

We also faced difficulties in obtaining a standardized list of targeted patients from different tertiary medicals centers, as our method relied more commonly on coding, an element that is often overlooked. Using the same software in all participating medical centers for data extraction from medical reports would have allowed to harmonize this list, minimizing the risk of missing patients and gaining in efficacy to fill up our database.

In this study, we observe that from the 353 patients for whom a diagnosis of necrotizing otitis externa was made, we excluded 92 for missing data and/or absence of follow up. This fact could

lead to uncertainty concerning the quantification of the rate of treatment failure (either to an overestimation as patients who evolve positively tend to stop going to follow-up clinic or a falsely low rate due to a lack of follow up in the most elderly population who lives in nursing homes).

The wide variety of management across Western regions of France from diagnostic tools, to microbiological evidence and antimicrobial modalities reflected patients management in real life but limited our ability to reduce confusion bias. This probably explains why we could not reveal a clear trend based on antibiotherapy duration or the use of multiple drugs. This highlights the need for a national cohort in order to proceed with more targeted analysis (with subsequent subgroups) and an even more pressing need for validation of diagnostic criteria that will strengthen these future studies.

CONCLUSION :

In conclusion, this study is the largest retrospective study describing necrotizing otitis externa. It showed that facial palsy and weight loss on diagnosis and history of ENT radiotherapy are associated with a higher rate of treatment failure in patients managed for necrotizing otitis externa. It will hopefully contribute to raise awareness in physicians' mind for early detection and will open a new interest to conduct a national prospective study to validate diagnostic criteria and optimize antimicrobial therapy.

BIBLIOGRAPHY

1. Cohen D, Friedman P. The diagnostic criteria of malignant external otitis. J Laryngol Otol. mars 1987;101(3):216-21.

2. Franco-Vidal V, Blanchet H, Bebear C, Dutronc H, Darrouzet V. Necrotizing external otitis: a report of 46 cases. Otol Neurotol Off Publ Am Otol Soc Am Neurotol Soc Eur Acad Otol Neurotol. sept 2007;28(6):771-3.

3. Sokołowski J, Lachowska M, Karchier E, Bartoszewicz R, Niemczyk K. Skull base osteomyelitis: factors implicating clinical outcome. Acta Neurol Belg. sept 2019;119(3):431-7.

4. Kamalden TMIT, Misron K. A 10-year review of malignant otitis externa: a new insight. Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol - Head Neck Surg. 5 juill 2021;

5. Lee JE, Song JJ, Oh SH, Chang SO, Kim CH, Lee JH. Prognostic value of extension patterns on follow-up magnetic resonance imaging in patients with necrotizing otitis externa. Arch Otolaryngol Head Neck Surg. juill 2011;137(7):688-93.

6. J RG, Bf B, Vl Y. The changing face of malignant (necrotising) external otitis: clinical, radiological, and anatomic correlations. Lancet Infect Dis [Internet]. janv 2004 [cité 16 nov 2021];4(1). Disponible sur: https://pubmed.ncbi.nlm.nih.gov/14720566/

7. Byun YJ, Patel J, Nguyen SA, Lambert PR. Necrotizing Otitis Externa: A Systematic Review and Analysis of Changing Trends. Otol Neurotol Off Publ Am Otol Soc Am Neurotol Soc Eur Acad Otol Neurotol. sept 2020;41(8):1004-11.

8. Stevens SM, Lambert PR, Baker AB, Meyer TA. Malignant Otitis Externa: A Novel Stratification Protocol for Predicting Treatment Outcomes. Otol Neurotol Off Publ Am Otol Soc Am Neurotol Soc Eur Acad Otol Neurotol. sept 2015;36(9):1492-8.

9. Danjou W, Chabert P, Perpoint T, Pradat P, Miailhes P, Boibieux A, et al. Necrotizing external otitis: analysis of relapse risk factors in 66 patients managed during a 12 year period. J Antimicrob Chemother. 25 août 2022;77(9):2532-5.

10. Soudry E, Joshua BZ, Sulkes J, Nageris BI. Characteristics and prognosis of malignant external otitis with facial paralysis. Arch Otolaryngol Head Neck Surg. oct 2007;133(10):1002-4.

11. Mani N, Sudhoff H, Rajagopal S, Moffat D, Axon PR. Cranial nerve involvement in malignant external otitis: implications for clinical outcome. The Laryngoscope. mai 2007;117(5):907-10.

12. Stern Shavit S, Soudry E, Hamzany Y, Nageris B. Malignant external otitis: Factors predicting patient outcomes. Am J Otolaryngol. 2016;37(5):425-30.

13. Chen CN, Chen YS, Yeh TH, Hsu CJ, Tseng FY. Outcomes of malignant external otitis: survival vs mortality. Acta Otolaryngol (Stockh). 2010;130(1):89-94.

14. Ulldemolins M, Roberts JA, Rello J, Paterson DL, Lipman J. The effects of hypoalbuminaemia on optimizing antibacterial dosing in critically ill patients. Clin Pharmacokinet. févr 2011;50(2):99-110.

15. Fujiwara T, Ebihara T, Kitade K, Setsu N, Endo M, Iida K, et al. Risk Factors of Periprosthetic Infection in Patients with Tumor Prostheses Following Resection for Musculoskeletal Tumor of the Lower Limb. J Clin Med. 28 sept 2020;9(10):3133.

16. Stone HB, Coleman CN, Anscher MS, McBride WH. Effects of radiation on normal tissue: consequences and mechanisms. Lancet Oncol. sept 2003;4(9):529-36.

17. Sudhoff H, Rajagopal S, Mani N, Moumoulidis I, Axon PR, Moffat D. Usefulness of CT scans in malignant external otitis: effective tool for the diagnosis, but of limited value in predicting outcome. Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol - Head Neck Surg. janv 2008;265(1):53-6.

18. Grandis JR, Curtin HD, Yu VL. Necrotizing (malignant) external otitis: prospective comparison of CT and MR imaging in diagnosis and follow-up. Radiology. août 1995;196(2):499-504.

19. Peled C, Kraus M, Kaplan D. Diagnosis and treatment of necrotising otitis externa and diabetic foot osteomyelitis - similarities and differences. J Laryngol Otol. sept 2018;132(9):775-9.

20. Younis JA. Additive value of 99mTechnetium methylene diphosphonate hybrid single-photon emission computed tomography/computed tomography in the diagnosis of skull base osteomyelitis in otitis externa patients compared to planar bone scintigraphy. World J Nucl Med. 2018;17(4):286-92.

21. Courson AM, Vikram HR, Barrs DM. What are the criteria for terminating treatment for necrotizing (malignant) otitis externa? The Laryngoscope. févr 2014;124(2):361-2.

22. van Kroonenburgh AMJL, van der Meer WL, Bothof RJP, van Tilburg M, van Tongeren J, Postma AA. Advanced Imaging Techniques in Skull Base Osteomyelitis Due to Malignant Otitis Externa. Curr Radiol Rep. 2018;6(1):3.

23. Stern Shavit S, Bernstine H, Sopov V, Nageris B, Hilly O. FDG-PET/CT for diagnosis and follow-up of necrotizing (malignant) external otitis. The Laryngoscope. avr 2019;129(4):961-6.

24. Hopkins ME, Bennett A, Henderson N, MacSween KF, Baring D, Sutherland R. A retrospective review and multi-specialty, evidence-based guideline for the management of necrotising otitis externa. J Laryngol Otol. juin 2020;134(6):487-92.

25. Yang TH, Xirasagar S, Cheng YF, Wu CS, Kao YW, Shia BC, et al. Malignant Otitis Externa is Associated with Diabetes: A Population-Based Case-Control Study. Ann Otol Rhinol Laryngol. juin 2020;129(6):585-90.

26. Lazzarini L, Lipsky BA, Mader JT. Antibiotic treatment of osteomyelitis: what have we learned from 30 years of clinical trials? Int J Infect Dis IJID Off Publ Int Soc Infect Dis. mai 2005;9(3):127-38.

27. Lew DP, Waldvogel FA. Osteomyelitis. Lancet Lond Engl. 24 juill 2004;364(9431):369-79.

28. Systemic antibiotic therapy for chronic osteomyelitis in adults - PubMed [Internet]. [cité 17 oct 2023]. Disponible sur: https://pubmed.ncbi.nlm.nih.gov/22157324/

29. PubMed [Internet]. 2012 [cité 17 oct 2023]. Antibiotics for treating chronic osteomyelitis in adults. Disponible sur: https://pubmed.ncbi.nlm.nih.gov/?term=antibiotics+for+treating+chronic+osteomyelitis+in+adults

30. Pulcini C, Mahdyoun P, Cua E, Gahide I, Castillo L, Guevara N. Antibiotic therapy in necrotising external otitis: case series of 32 patients and review of the literature. Eur J Clin Microbiol Infect Dis. déc 2012;31(12):3287-94.

31. Chawdhary G, Pankhania M, Douglas S, Bottrill I. Current management of necrotising otitis externa in the UK: survey of 221 UK otolaryngologists. Acta Otolaryngol (Stockh). 3 août 2017;137(8):818-22.

32. Pankhania M, Bashyam A, Judd O, Jassar P. Antibiotic prescribing trends in necrotising otitis externa: a survey of 85 trusts in the United Kingdom: Our Experience. Clin Otolaryngol Off J ENT-UK Off J Neth Soc Oto-Rhino-Laryngol Cervico-Facial Surg. juin 2016;41(3):293-6.

33. Mahdyoun P, Pulcini C, Gahide I, Raffaelli C, Savoldelli C, Castillo L, et al. Necrotizing otitis externa: a systematic review. Otol Neurotol Off Publ Am Otol Soc Am Neurotol Soc Eur Acad Otol Neurotol. juin 2013;34(4):620-9.

34. Hodgson SH, Sinclair VJ, Arwyn-Jones J, Oh K, Nucken K, Perenyei M, et al. Characteristics, management and outcome of a large necrotising otitis externa case series: need for standardised case definition. J Laryngol Otol. juill 2022;136(7):604-10.

35. Hodgson SH, Khan MM, Patrick-Smith M, Martinez-Devesa P, Stapleton E, Williams OM, et al. UK consensus definitions for necrotising otitis externa: a Delphi study. BMJ Open. 20 févr 2023;13(2):e061349.

APPENDIX

Codes PMSI :

H602: Otite externe maligne

H609: Otite externe

H603: Autres otites externes infectieuses

H622: Otite externe au cours de mycoses

B448: Autres formes d'aspergillose {Otite externe à aspergillus}

H620 : Otite externe au cours de maladies bactériennes classées ailleurs.

Lists of tertiary medical centers involved :

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MICKAEL THY	CHU Bichat

Vu, le Directeur de Thèse

Faire signer obligatoirement le Directeur de Thèse, avant l'impression

Vu, le Doyen
De la Faculté de Médecine de Tours
Tours, le

Descours Charlotte
38 pages-7 figures

Résumé

Contexte : L'otite externe nécrosante est une pathologie rare et mal codifiée, de pronostic sévère (rechute jusqu'à 50% des patients) retrouvée principalement chez les patients âgés diabétiques ou immunodéprimés. A ce jour, il n'existe pas de consensus sur sa prise en charge globale et plus précisément les modalités de traitement anti infectieux. L'objectif principal de cette étude est de décrire les facteurs de risque associés aux échecs à 6 mois de prise en charge de cette pathologie.

Matériel et Méthodes: Il s'agit d'une étude rétrospective descriptive multicentrique (hôpitaux du Grand Ouest en France) recueillant les données de patients majeurs présentant un diagnostic d'otite externe nécrosante entre janvier 2009 et janvier 2023. Les données démographiques, clinico-biologiques et radiologiques ont été assemblées. L'échec était défini comme réapparition des signes cliniques et/ou radiologiques, reprise d'un traitement antiinfectieux, décès dans les 6 premiers mois post traitement.

Résultats : Parmi 1119 patients screenés sur 12 centres hospitaliers, 156 patients avec un diagnostic d'otite externe nécrosante ont été inclus. Parmi ceux-là, 116 (74,4%) sont des hommes, avec un âge médian de 78 ans, et un score de Charlson médian de 3. Les patients diabétiques étaient au nombre de 108 (69,2%) et 17 (10,9%) étaient des patients immunodéprimés. Les symptômes cliniques les plus fréquemment retrouvés étaient : une otalgie pour 151 patients (96,8%), une otorrhée pour 136 patients (87,2%), un granulome du conduit auditif externe pour 90 patients (57,7%), une sténose du canal auditif externe pour 98 patients (62,8%), une atteinte des paires crâniennes pour 45 patients (28,8%), avec un délai médian diagnostic à 43 jours. La documentation microbiologique était retrouvée pour 121 patients (77,1%) dont 95 (60,5%) à *Pseudomonas aeruginosa*, 23 (14,6%) fongiques et 18 (11,5%) polymicrobiens. La durée médiane d'administration des antibiotiques est de 42 jours avec une bithérapie dans 108 cas (77,7%). Le taux d'échec à 6 mois est de 33% (48 patients). Les variables semblant augmenter le risque d'échec sont la présence d'une paralysie faciale (20,2% vs 36,2%) ainsi qu'une perte de poids (17,4% vs 34,8%) au diagnostic et d'un antécédent de radiothérapie locale.

Conclusion : L'otite externe nécrosante est une pathologie sévère à l'origine d'ostéite de la base du crâne dont le taux d'échec de prise en charge est encore majeur. La présence d'une paralysie faciale ainsi qu'une perte de poids semblent être des variables associées avec un pronostic défavorable à 6 mois. Une étude prospective de grande échelle afin de valider des critères diagnostiques nous semblerait cruciale pour la conduite de futures études visant à définir les modalités optimales d'antibiothérapie.

Mots clés : Otites externes nécrosantes, otites malignes externes, ostéite de la base du crâne

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