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Seminars in
ROENTGENOLOGY

Imaging Necrotizing Otitis Externa

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Introduction

Necrotizing otitis externa (NOE), also known as malignant otitis externa, is an invasive infection of the external auditory canal (EAC) with extension beyond the confines of the EAC, into the adjacent soft tissues and typically into the skull base. Imaging plays a vital role in in the diagnosis and management of patients with this potentially lethal disease. Computed tomography (CT), magnetic resonance imaging (MRI), and nuclear medicine evaluation can all play an important role. Each modality has its own strengths and weaknesses. Some are more useful during the initial diagnosis of the disease, some have greater utility monitoring response to treatment, and some are more effective at establishing a new imaging baseline after successful therapy.

Imaging findings; however, must be correlated with clinical findings. During diagnostic evaluation this is important since there is overlap of some of the imaging findings with other etiologies. The potentially extensive and destructive nature of this process can be confused with underlying malignancy. Other processes, including inflammatory pseudotumor, can share similar imaging features. During the course of treatment, imaging findings may persist well beyond the resolution of active infection and lag behind improvement in signs and symptoms. Certain imaging features resolve earlier than others. After resolution of the disease process, particularly if the patient is at risk for recurrent infection, a new baseline study can be obtained to compare with potential future studies.

This paper will review the imaging evaluation of NOE. After a synopsis of the clinical features, CT, MRI, and nuclear medicine studies will be examined regarding their utility during the different stages of patient management. Finally, a description of some of the imaging features of other pathologic processes in the imaging differential diagnosis will be considered.

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Clinical Features

NOE most commonly occurs in elderly diabetics although individuals with other immune compromised conditions are also at risk. This includes those with HIV infection/acquired immune deficiency syndrome (AIDS), undergoing chemotherapy, or on immunosuppressive therapy for prior transplant. Children are rarely affected but tend to have generally a more favorable prognosis, although facial paralysis recovery may be poorer.[1] It is unclear why NOE is much more common in elderly diabetics. A combination of immune dysfunction and microangiopathy in the ear canal in this population likely makes them vulnerable to more invasive infection. An increased pH of cerumen in diabetics may also be a contributing factor. NOE may be precipitated by aural water exposure, such as with irrigation, and recent surgery or trauma/irritation, including cleaning.

Pseudomonas aeruginosa is the infectious agent more than 95% of the time. This is a gram-negative bacterium that is not a component of normal ear flora. It has a propensity for vascular invasion, vasculitis, and vessel wall necrosis. Other organisms reported include *Staphylococcus aureus, Staphylococcus epidermidis, Proteus mirabilis, Klebsiella oxytoca, Pseudomonas cepacia, Aspergillus fumigatus*, and *Candida parapsilosis*. Fungal infection is more common in immunocompromised patients who are not diabetic.

Patients typically present with severe to profound otalgia, refractory to typical outpatient analgesics, and otorrhea. The pain is usually more severe than in simple external otitis, is often worse at night, and can extend to the preauricular region overlying the temporomandibular joint. Erythrocyte sedimentation rate and C-reactive protein levels are typically elevated. On physical examination there are varying degrees of mucosal edema of the EAC. There is often granulation tissue along the inferior wall, at the bony-cartilaginous junction, although there often is a relative lack of granulation tissue formation in patients with AIDS.[2]

There are diverse patterns of spread of the infection. The infection may penetrate inferiorly into the subtemporal soft tissues through the fissures of Santorini along the cartilaginous EAC. The infection can invade the osseous structures medially as it spreads from the bony-cartilaginous junction into the temporal bone and toward the petrous apex,

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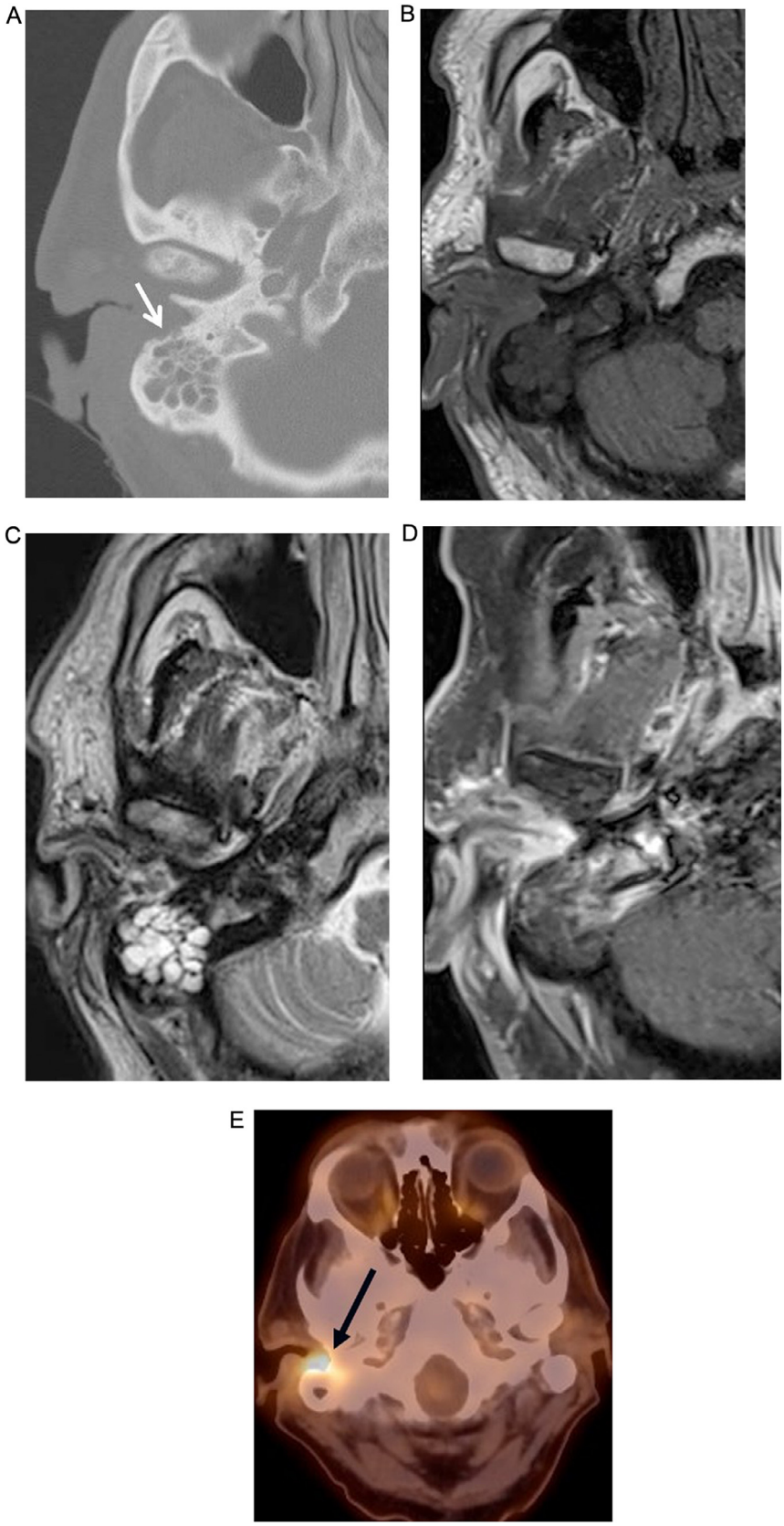

Figure 1 63 m h/o diabetes with pseudomonas infection. Axial CT image (A) shows soft tissue within the EAC with osseous erosion of the posterior wall of the EAC (arrow) not evident on axial T1W (B), T2W (C), or postcontrast T1W with fat saturation (D) images. FDG-PET/CT fused image (E) shows increased uptake (arrow).

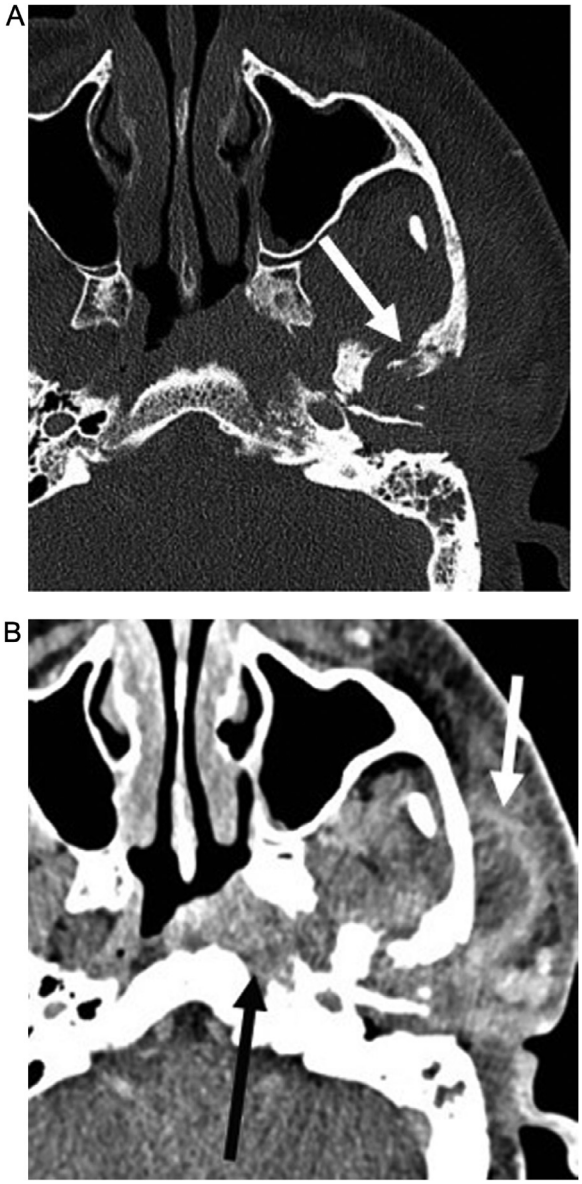

Figure 2 51 m h/o diabetes with pseudomonas infection. Axial CT (A) shows extension of NOE anteriorly with erosion of the TMJ including the mandibular condyle (arrow). Axial postcontrast CT (B) shows a masticator space abscess in the masseter muscle (white arrow) and also extension of infection to the nasopharynx (black arrow).

anteriorly into the temporomandibular joint (TMJ), and posteriorly into the mastoid. The infection can spread even further anteriorly into the nasopharynx and clivus as well as intracranially. There can also be one or more cranial nerve palsies. The facial nerve is most commonly involved due to the proximity of the stylomastoid foramen, and the lower cranial nerves can be affected with more medial extension. If the infection advances intracranially it can potentially lead to the development of a subdural empyema, meningitis, cerebritis, and intraparenchymal abscess formation. There can also be involvement of the vasculature leading to infarcts. These may be secondary to any combination of vasospasm, arteritis, or thrombophlebitis. Skull base osteomyelitis,

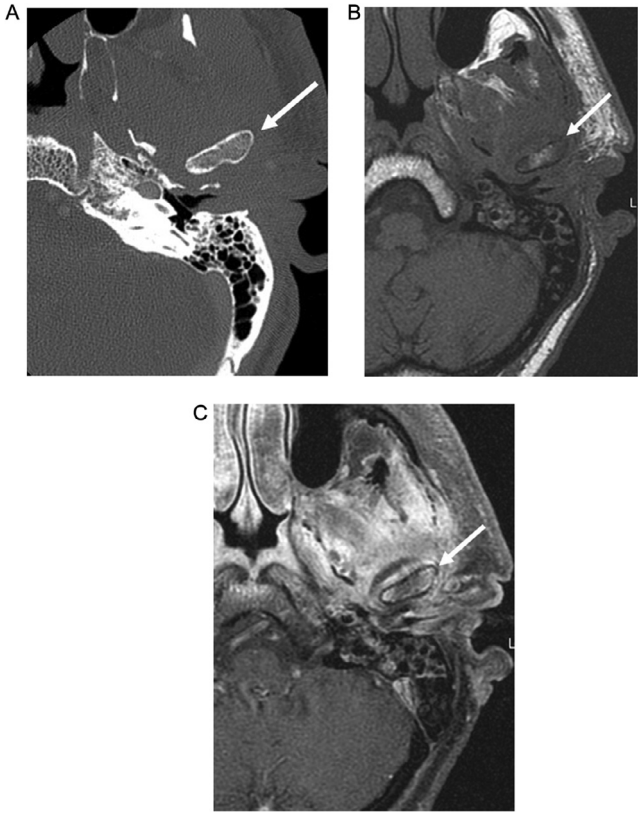

Figure 3 75 m h/o diabetes with fungal infection extending from the EAC into the TMJ. Axial CT (A) shows no evidence of erosion of the mandibular condyle (arrow). Axial T1W image (B) shows decreased signal replacing normal hyperintense fatty marrow (arrow). Axial postcontrast T1W image with fat saturation (C) shows corresponding marrow enhancement (arrow).

intracranial extension, and involvement of multiple cranial nerves are correlated with increased mortality.[3]

Treatment of NOE includes both systemic and topical antimicrobial therapy and glucose control. High dose oral ciprofloxacin is usually the initial drug of choice, combined with a topical ciprofloxacin-steroid drop. Once the ear canal skin has returned to normal appearance, the drops can be stopped, though systemic therapy will typically need to continue for much longer. Surgery is reserved for local debridement, abscess drainage, and biopsy, particularly if underlying neoplasm is questioned. Treatment response can be followed clinically with improvement of pain, drainage, and EAC skin inflammation, and normalization of white blood cell count, erythrocyte sedimentation rate, and C-reactive protein levels. Before the development of systemic agents, the mortality of NOE was approximately 50%.[4] Currently, the mortality is reported less than 15%.[5]

Imaging Evaluation

The imaging evaluation of NOE is complex since there is a potential role for each of the different modalities. The effectiveness of CT, MRI, and nuclear medicine studies is dependent on the stage of patient care. Each type of study has its

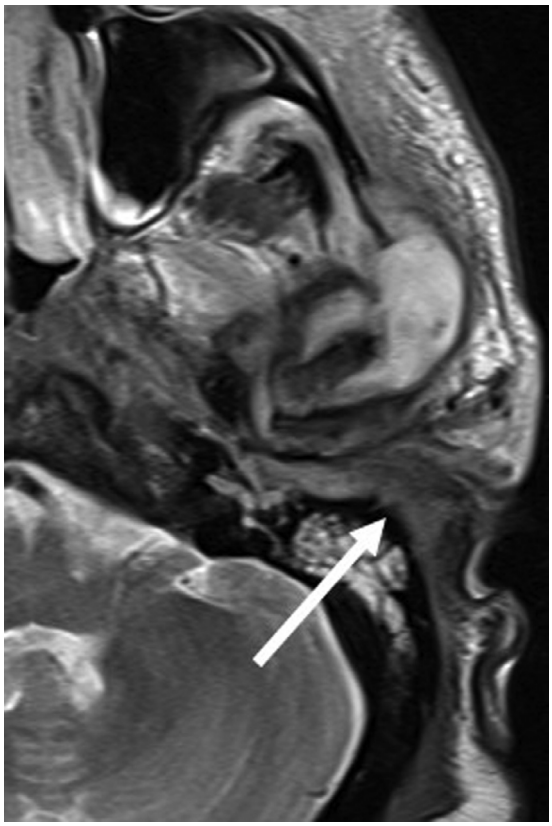

Figure 4 Same patient as Fig. 2. Axial T2W image shows the soft tissue lesion within the EAC is predominantly low in signal intensity (arrow).

own strengths and weaknesses for establishing the diagnosis and extent of disease, monitoring therapy, or establishing a new baseline after successful treatment. Imaging practice patterns have not only changed in time, due to the development and advances of new modalities, but are also variable among different clinicians.[6] Not only is there variability in the types of studies that clinicians prefer to depend on, but there is also variability in how extensively imaging is utilized. For example, during the monitoring phase, some practitioners rely more on the clinical findings to assess treatment response while others more consistently obtain imaging. After the completion of treatment, some practitioners utilize imaging only if they are clinically suspicious for possible persistent infection while others use it to ensure the imaging findings are consistent with the clinical findings. After treatment, some may or may not obtain a new baseline study that could be compared to future studies should there be a question of recurrent infection. Regardless there is a practical way to approach the utility of each imaging modality during the care of patients with NOE.

Computed Tomography

Prompt diagnosis of NOE is critical as early initiation of antimicrobial therapy is necessary to prevent complications that increase mortality. From an imaging perspective, demonstration

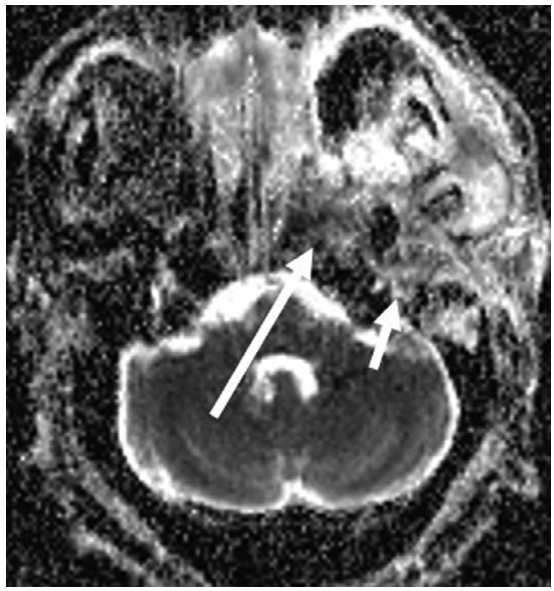

Figure 5 Same patient as Fig. 2. Axial ADC map shows mildly hypointense signal within the lesions of the EAC (short arrow) and nasopharynx (long arrow).

of extension of infection beyond the EAC into the subtemporal soft tissues and/or involvement of the adjacent osseous structures of the skull base is consistent with the diagnosis in the appropriate clinical setting. Retrocondylar fat infiltration is also an early finding. CT is preferred as the initial method to evaluate for NOE due to its ability to detect early osseous erosion. Areas of subtle cortical erosion within the EAC and adjacent areas of the skull base can be identified on CT imaging that may not be detected on MR imaging (Fig. 1).[7,8] CT is also very useful for evaluating the adjacent soft tissues to detect extension of infection beyond the EAC into the adjacent soft tissues since effacement of the readily visualized adjacent fat planes is well seen. Increased density with stranding in the soft tissues along the fat and fascial planes with thickening of the overlying skin and adjacent musculature can be identified representing cellulitis/phlegmon and myositis respectively. This may demonstrate enhancement on postcontrast imaging. Abscesses are identified when well-defined fluid collections, typically with an enhancing wall, are visualized (Fig. 2). Fluid and mucosal thickening within the middle ear and mastoid air cells, if present, can also be easily identified.

CT can be used to monitor treatment response during therapy. If there is a positive response to therapy, soft tissue within the EAC is often the first imaging feature to resolve.[8] During the course of successful treatment, soft tissue changes may persist but should appear improved from the initial study. Advancing soft tissue inflammation and/or the development of new or enlargement of pre-existing abscesses suggests poor response to treatment. After the completion of successful therapy, although there may be granulation tissue and fibrosis resulting in residual soft tissue thickening, the edema from active inflammation should at least substantially improve. However, when patients are imaged after an appropriate course of treatment, even if there is no longer persistent infection, the CT findings of osseous erosion will usually remain.[9]

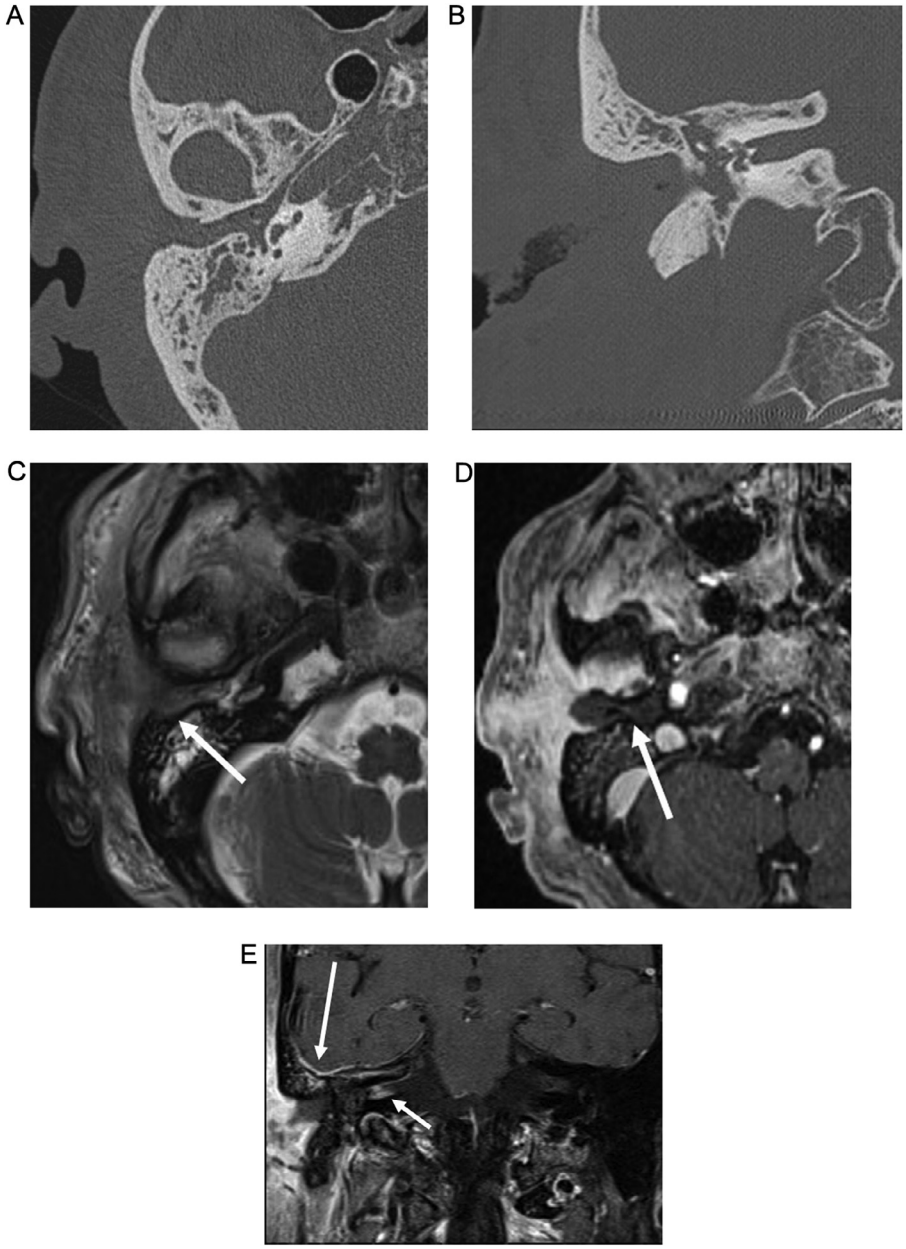

Figure 6 65 m h/o AML and acute onset facial weakness with fungal infection. Axial (A) and coronal (B) CT images show soft tissue within the EAC without osseous erosion. Axial T2W image (C) shows hypointense soft tissue within the EAC (arrow) and extending into the surrounding soft tissues with adjacent areas of hyperintense edema. Axial postcontrast T1W image with fat saturation (D) shows enhancement and extension of the infection anteriorly into the TMJ and masticator space. Much of the soft tissue in the EAC shows lack of enhancement consistent with debris and necrotic mucosa (arrow). Coronal postcontrast T1W image with fat saturation (E) shows enhancement of cranial nerves and dura within the internal auditory canal (short arrow) and mild dural thickening in the middle cranial fossa (long arrow).

Even though CT may demonstrate persistent osseous erosion after the eradication of the infection, it can still be successfully utilized to establish a new imaging baseline. Even though this new imaging appearance may not revert to a normal scan, it is still useful for future comparison. On future studies, new inflammatory changes or new osseous erosion would accurately predict recurrent infection if suspected clinically.

Magnetic Resonance Imaging

Other than for detecting osseous cortical erosion, MR imaging is the most useful imaging technique to determine the full extent of infection as it demonstrates the soft tissue, bone marrow, and intracranial involvement to best advantage. Although it is not as sensitive as CT for determining osseous cortical erosion, it is much better than CT at evaluating bone marrow involvement (Fig. 3). Marrow involvement results in

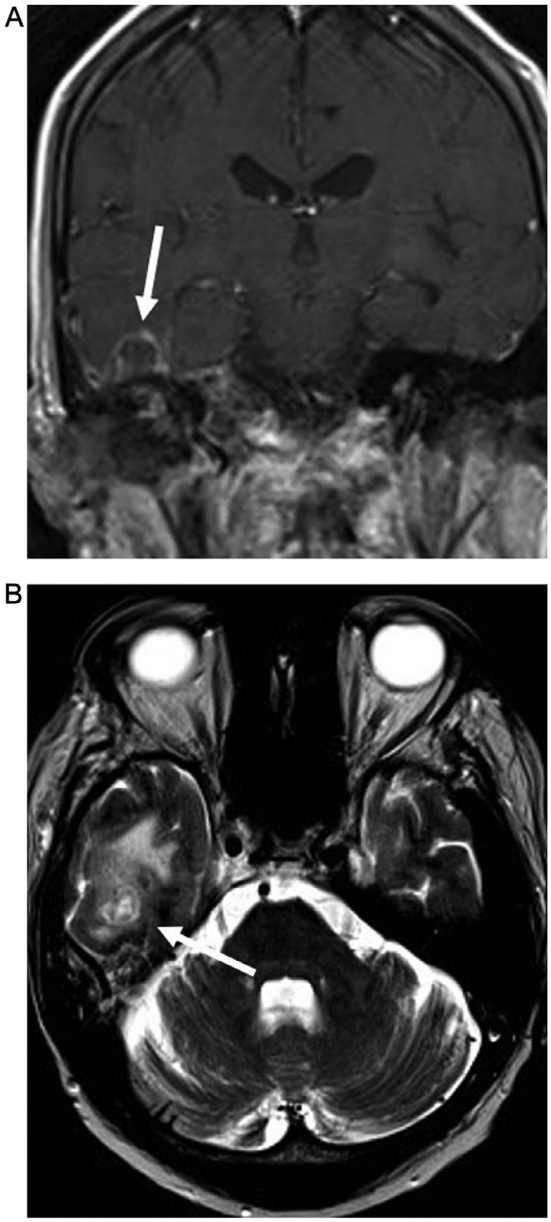

Figure 7 Same patient as Fig 6. Coronal postcontrast T1W image (A) shows progression of the infection resulting in intraparenchymal abscess formation (arrow). Axial T2W image shows the right temporal lobe abscess with surrounding hyperintense edema (arrow).

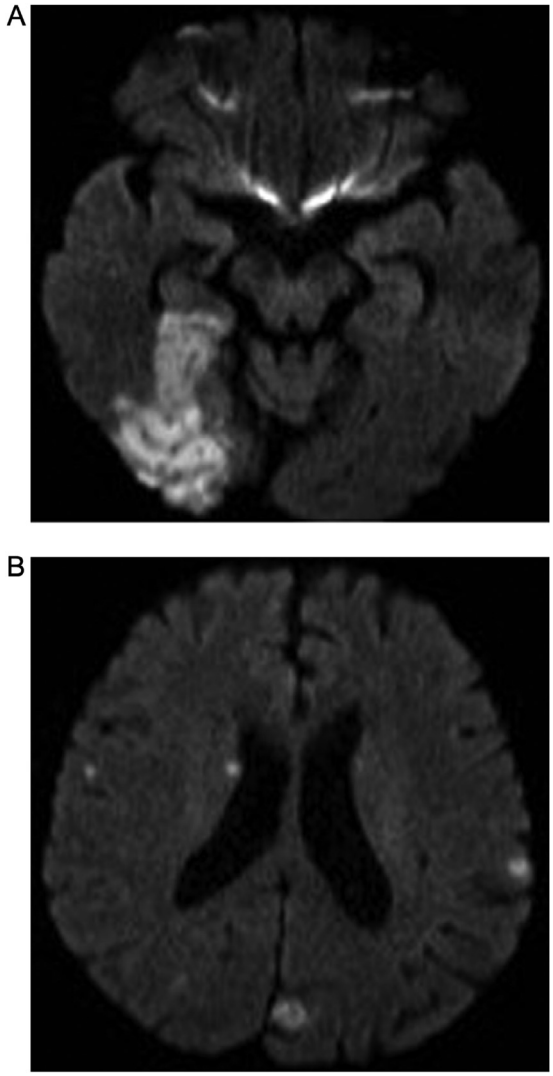

Figure 8 Same patient as Fig 6. Axial DWI shows multiple areas of restricted diffusion including a right occipital posterior cerebral artery territory infarct with possible associated cerebritis (A) and multiple small infarcts within the bilateral cerebral hemispheres (B).

the loss of normal fatty marrow signal and appears as decreased signal on T1-weighted images, increased signal on T2-weighted images, and can demonstrate enhancement after contrast. CT can occasionally demonstrate lytic changes with decreased marrow density; however, this is not a common finding. Marrow signal is abundant in the skull base but is lacking in the smaller osseous structures of the external auditory canal, and as a result CT remains a more appropriate imaging study for initial diagnosis. Although the extracranial soft tissues are effectively evaluated with CT, subtle areas of edema are more easily appreciated on MRI.

Although classic infection appears as decreased signal on T1-weighted images and increased signal on T2-weighted images, due to the edema and hyperemia, the soft tissue lesion seen with NOE, centered in the EAC, more commonly has relatively decreased signal on both T1 and T2-weighted images (Fig. 4).[7] This may be due to the relative lack of edema, denser matrix, and associated fibrosis that can be seen with the lesion in these patients.[10,11] The underlying microangiopathy in diabetics, further comprise of the vasculature by invasion from the infectious agent, and blunted inflammatory response likely contribute to the decreased edema.[7] More typical increased signal on T2-weighted images, representing more advanced edema, may be more prominent in the soft tissues adjacent to the main lesion where the inflammatory response may be less compromised. The abnormal tissue typically enhances to some degree except in areas of necrosis or fluid/abscess collection (Fig. 1).

Diffusion-weighted imaging (DWI) has been used to characterize the composition of different tissues. The diffusion characteristics of a tissue depend on certain features including its cellularity, the nucleus/cytoplasm ratio of the cells,

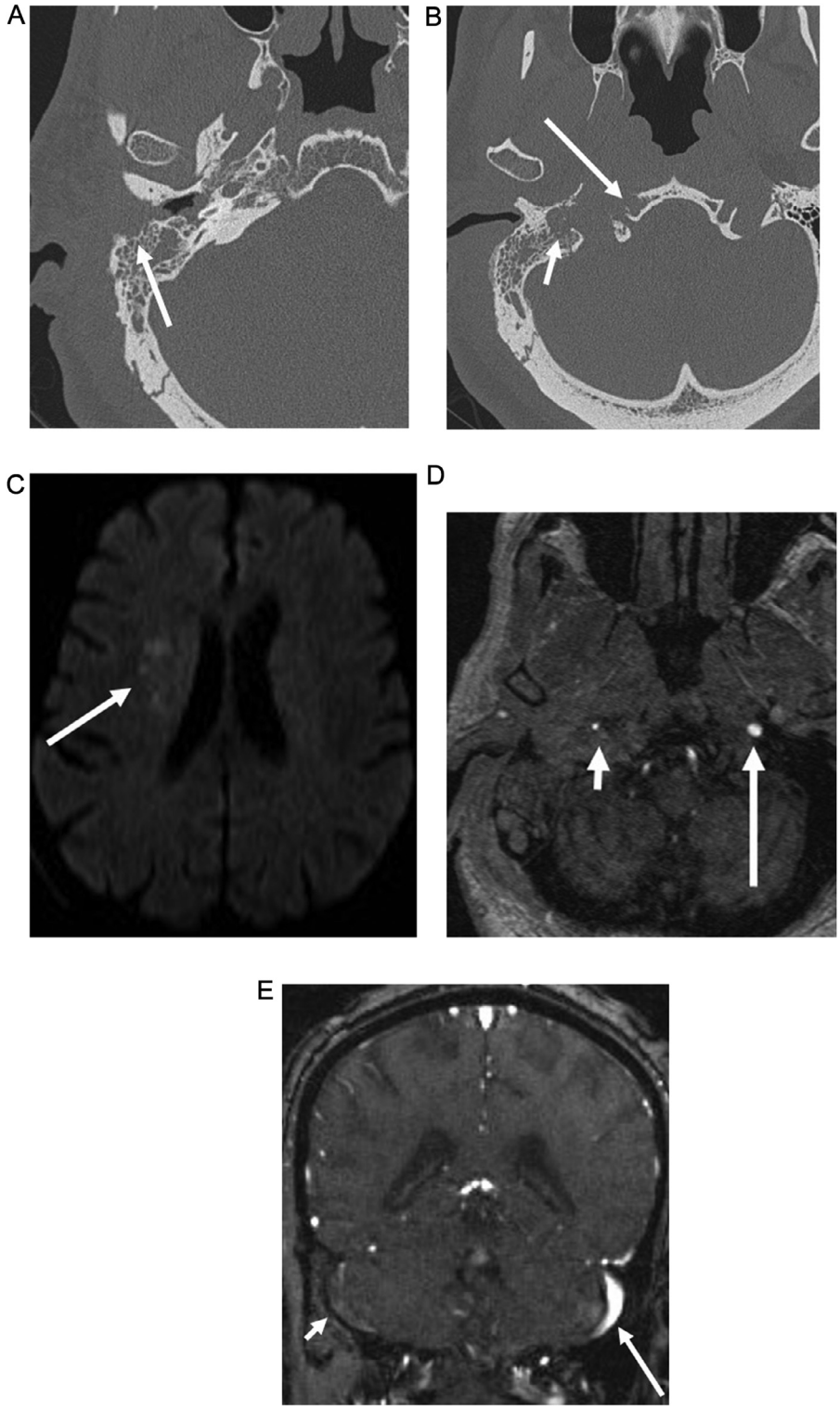

Figure 9 70 m h/o diabetes with staphylococcus infection with NOE, mastoiditis, and facial weakness. Axial CT images show soft tissue within the EAC with erosion of the roof and posterior wall/mastoid air cells (arrow A) and erosion of the skull base more inferiorly (short arrow B) including the clivus (long arrow B). DWI (C) shows infarcts within the deep white matter of the right hemisphere (arrow) which may be in the carotid watershed. Source image from MRA (D) shows marked narrowing of the right internal carotid artery (ICA) adjacent to the infection (short arrow) compared to the normal left ICA (long arrow). Source image from MRV shows lack of flow signal consistent with slow flow vs occlusion of the right sigmoid sinus (short arrow) compared to the normal left sigmoid sinus (long arrow).

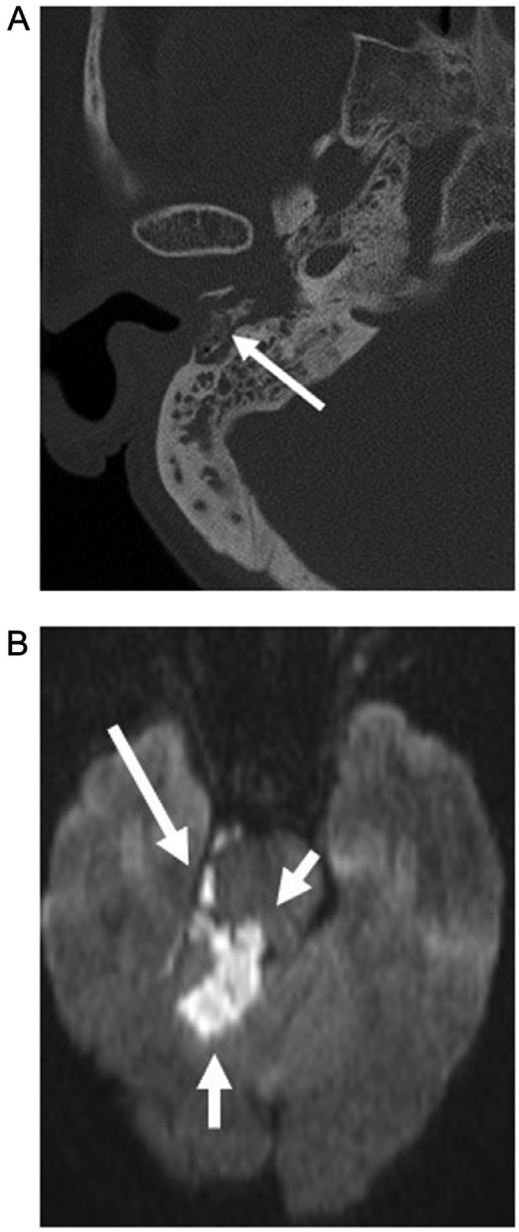

Figure 10 48f with NOE. Axial CT image (A) shows soft tissue in the EAC with erosion of the anterior and posterior walls and osseous fragments (arrow) in the EAC. DWI (B) shows increased signal within the perimesencephalic cistern consistent with extension of infection into the subarachnoid space representing meningitis (long arrow) and increased signal within the cerebellum and brainstem (short arrows) likely representing infarcts, presumably from vasculitis, and possibly areas of cerebritis.

and the nature of the extracellular matrix.[12] In general, tissues with increased cellularity, a higher nucleus to cytoplasm ratio, and decreased extracellular water have relative restricted diffusion and lower values on apparent diffusion coefficient (ADC) maps. The tissue in NOE typically demonstrates mild relative restricted diffusion with mildly hyperintense signal on DWI and mildly lower signal on ADC maps than normal tissue likely due to the denser matrix and associated fibrosis.[12] However, the appearance is often

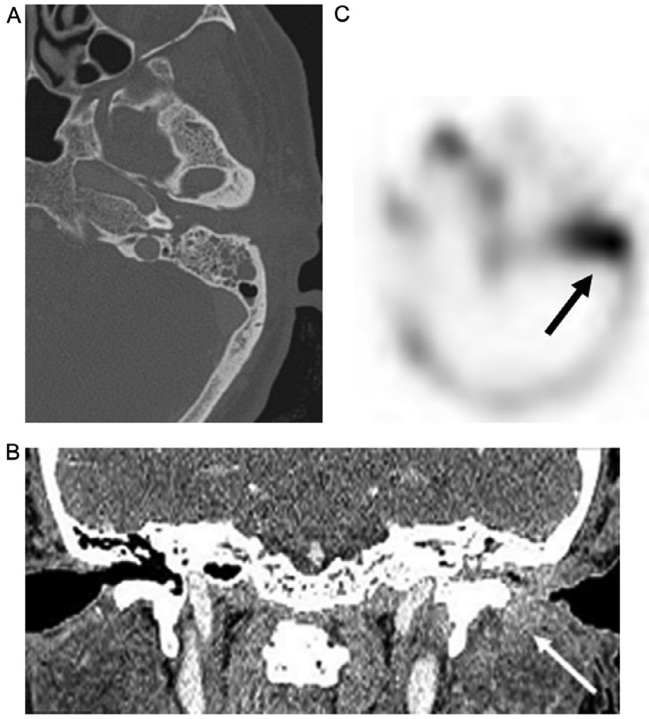

Figure 11 71f h/o AML with pseudomonas infection. Axial CT image (A) shows soft tissue in the EAC without osseous erosion. Coronal postcontrast image (B) shows extension of infection through the floor of the EAC (arrow). Tc-99 m MDP bone scan with SPECT (C) shows increased osseous uptake on delayed imaging (arrow).

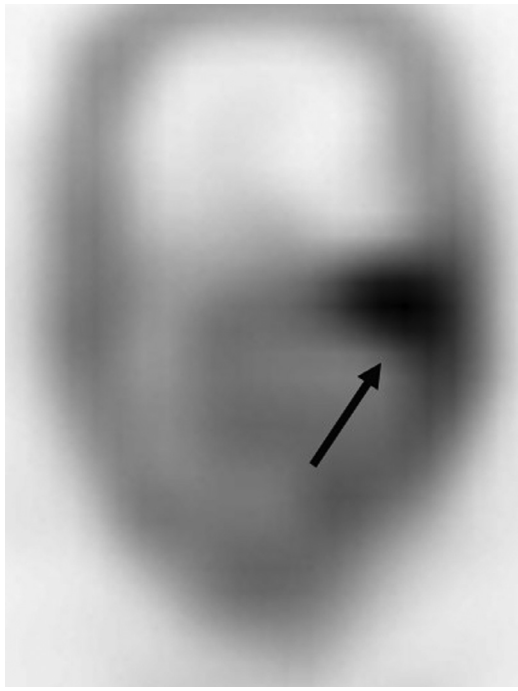

Figure 12 Same patient as Fig. 3. Gallium scan shows increased uptake in the left temporal bone and TMJ (arrow).

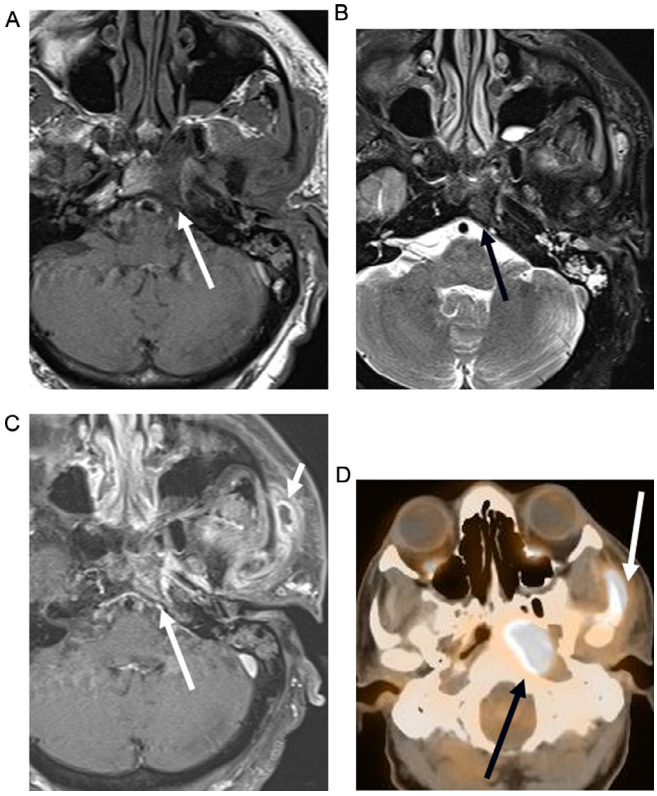

Figure 13 Same patient as Fig. 2. 10 weeks later, follow-up axial T1W (A), T2W (B), and postcontrast T1W with fat saturation (C) images demonstrate skull base marrow signal abnormality and enhancement (long arrows) that is nonspecific after treatment; however, residual masticator space abscess (short arrow C) is concerning. FDG-PET/CT fused image (D) shows residual infection at the skull base (black arrow) and masticator space (white arrow).

heterogeneous perhaps due to some areas of edema resulting in increased extracellular water (Fig. 5).

MRI is much more sensitive than CT in evaluating the intracranial compartment. Meningeal, parenchymal, and cranial nerve involvement are optimally visualized (Fig. 6). Dural thickening appears as linear enhancement beneath the calvarium, around the brain parenchyma. Leptomeningeal involvement, which is more specific for meningitis, appears as linear enhancement that extends into the sulci. Purulent material in the subdural space, representing subdural empyema, and within the subarachnoid space, signifying meningitis, is typically hyperintense on fluid attenuated inversion recovery and DWI images. Cerebritis is reflected by edema in the parenchyma in the face of infection which can progress to a ring enhancing, walled off abscess collection (Fig. 7). It is important to keep in mind that infarcts and seizure activity can also have imaging features similar to cerebritis.

The infection can involve the vascular structures of the arterial and venous system, and although these can be studied with CT angiography and CT venography, vascular imaging techniques, including MR angiography and MR venography, can be performed at the time of intracranial MRI evaluation. This is particularly important due to the proximity of the internal carotid artery, vertebral artery, basilar artery, transverse sinus, sigmoid sinus, and the internal jugular vein to the site of infection. Narrowing or occlusion of the arteries can be due to mass effect, vasospasm from inflammatory irritation of the vessel walls, or due to direct invasion of the pathogen resulting in vasculitis, a feature that can be seen with *Pseudomonas aeruginosa* and invasive fungal species. Arterial infarcts can take the form of small infarcts due to compromise of small penetrating vessels, larger territorial infarcts, and watershed infarcts (Figs. 8,9,10). Venous involvement typically takes the form of thrombosis/thrombophlebitis and may result in venous infarcts that manifest variable signal intensities on DWI, sometimes accompanied by hemorrhage (Fig. 9).

MRI can be helpful to monitor treatment. With successful therapy, inflammatory changes should improve in a similar fashion to CT although the soft tissue changes seem to be more obvious on MRI.[7] In addition, if there is intracranial involvement, these findings are more effectively evaluated. Finally, the improvement in marrow changes, only identified on MRI, can also be assessed, although these changes may persist in some form beyond resolution of the infection.

The establishment of a new baseline post-treatment imaging appearance can be performed with MRI. There are advantages over CT in this regard since recurrent soft tissue changes may be more apparent with recurrent infection, and new marrow signal or intracranial abnormalities can be more effectively detected. However, as in initial diagnosis, new cortical erosion is seen to best advantage with CT.

Nuclear Medicine

The role of nuclear medicine in the evaluation of NOE has changed over time. Technetium-99 m methylene diphosphonate (Tc-99 m MDP) bone scans are sensitive to detecting NOE.[13] Infection can be detected even when the CT does not suggest osseous erosion (Fig. 11).[14] Since Tc-99 m MDP concentrates wherever there is osteoblastic activity, it is not specific for infection, but would also show increased uptake in trauma and with underlying neoplasm. Gallium-67 citrate concentrates where there is active inflammation, in the bone and soft tissues, by attaching to lactoferrin, which is abundant in leucocytes, and binding to transferrin and bacteria directly (Fig. 12).[15]

The advances in CT and MRI reflect the change in practice patterns regarding the use of nuclear medicine studies, both in the initial diagnosis and follow-up of NOE.[6] However, nuclear medicine remains the most accurate imaging modality to determine the persistence or resolution of infection during the treatment phase. Ga-67 scanning (gallium scan) can be utilized to determine clearance of infection since the findings on CT, MRI, and TC-99 m MDP scans may persist after resolution of active infection.[16,17] Gallium scans therefore, are the imaging study of choice at many centers for evaluating treatment response.

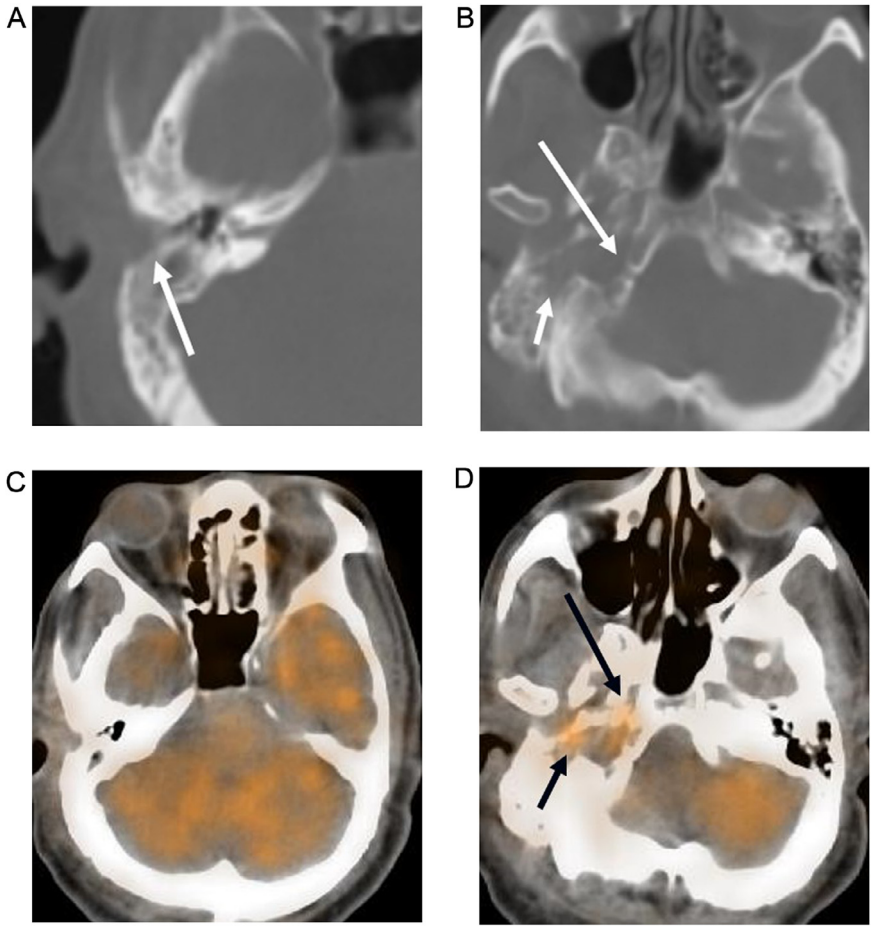

Figure 14 Same patient as Fig. 9. 6 weeks later, follow-up FDG-PET/CT shows residual erosion of the EAC (arrow A) and skull base (arrows B) on the CT images as described in Fig. 9. On the FDG-PET/CT fused images there is no evidence of residual infection at the EAC (C), but there is mild residual uptake at the sites of more inferior skull base erosion (arrows D).

Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT), which can detect increased utilization of glucose and metabolism of tissues before morphologic changes, is also a useful modality for the diagnosis and follow-up of patients with NOE (Figs. 1,13,14).[18] This test combines the spatial resolution of CT with the metabolic information of F-18 FDG-PET and is reliable for diagnosis and in decision making regarding treatment in patients with NOE. Overall, metabolic assessment with nuclear medicine evaluation is particularly helpful when clearance or persistence of infection is difficult to otherwise confirm. There is no role for establishing a new baseline nuclear medicine imaging appearance.

Differential Diagnosis

It is important to recognize that other pathologic processes in this region can be difficult to distinguish from NOE. Squamous cell carcinoma (SCC) of the EAC can have similar imaging findings (Fig. 15). Nasopharyngeal carcinoma, with invasion of the skull base, eustachian tube obstruction resulting in middle ear and mastoid effusions, and potentially superimposed infection can also have some similar imaging features. Inflammatory pseudotumor can be confused with infection or neoplasm due to its infiltrative appearance. It is typically iso- to hypointense on T2-weighted imaging and can erode bone. EAC cholesteatomas can scallop or erode the osseous walls and can also contain internal bone fragments. Clinical findings may be more suggestive of one pathologic process over another, but ultimately biopsy may be necessary. Biopsy should also be considered when inflammation persists after appropriate therapy to exclude an underlying malignancy.

Certain imaging features may be helpful to distinguish between NOE and malignancy. Features that may suggest NOE with skull base osteomyelitis as opposed to nasopharyngeal carcinoma are more prominent lateral extension of the process, more prominent increased signal on T2-weighted images in the adjacent tissues, lack of architectural distortion, and enhancement greater than or equal to the mucosa.[19] With regard to diffusion-weighted imaging, nasopharyngeal carcinoma and lymphoma tend to have lower ADC values (0.74 ± 0.18 and 0.59 ± 0.11 respectively) compared to the mildly decreased ADC values typically seen with skull base osteomyelitis (1.26 ± 0.19) (Fig. 5).[12] Biopsy may be necessary if the diagnosis remains uncertain.

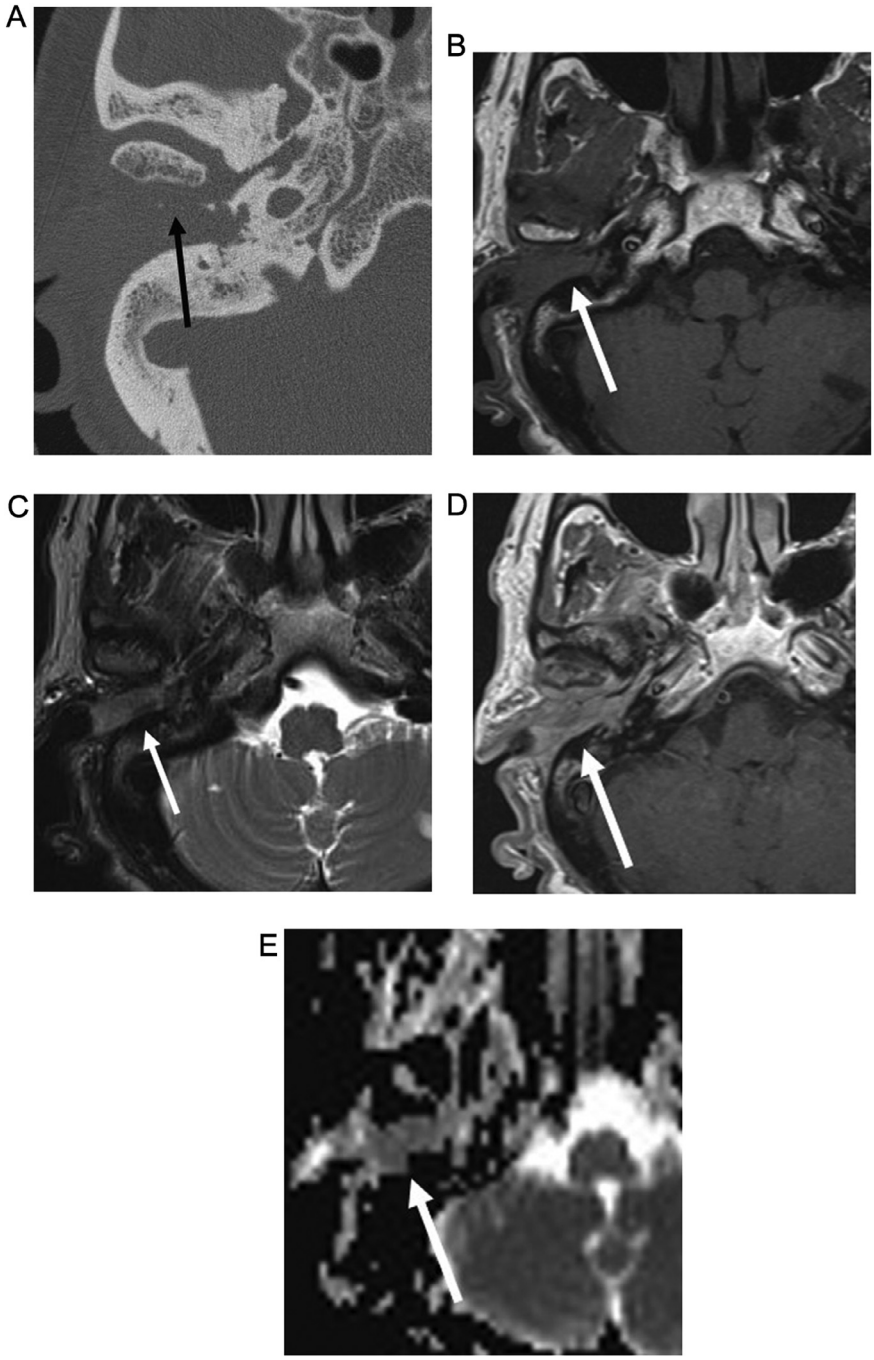

Figure 15 81f with EAC SCC. Axial CT image (A) shows erosion of the anterior wall of the EAC (arrow). Axial T1W image (B) shows the lesion to be hypointense (arrow) without surrounding streaking/inflammation in the surrounding soft tissues. Axial T2W image (C) shows the lesion to be hypointense (arrow) without cellulitis in the adjacent soft tissues. Axial postcontrast T1W image (D) shows enhancement of the lesion (arrow). ADC map image (E) shows homogeneous low signal within the lesion (arrow).

Conclusion

Prompt diagnosis of NOE is critical so that appropriate therapy can be initiated to limit morbidity and mortality. Imaging plays an important role in the care of these patients. For diagnosis on initial presentation, CT is helpful in identifying extension into the soft tissues beyond the EAC and early osseous involvement. MR imaging is most useful for determining the full extent of infection and is essential if there is concern for intracranial extension of disease, which increases mortality. Vascular imaging should also be considered. Some clinicians rely on clinical features to determine the length of therapy since resolution of CT and MR features typically lags behind clearance of active infection. However, nuclear medicine studies, such as gallium scanning and F-18 FDG-PET/CT scanning, provide more specific diagnostic information with regard to the presence or absence of persistent infection. In addition, particularly if the patient is at risk for recurrent

infection, CT or MR imaging can be obtained after the clearance of infection to establish a new baseline study to compare with potential future imaging studies. Finally, it is critical to recognize that other pathologic processes, including underlying malignancy, can present with similar imaging and clinical features, and biopsy may be necessary.

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