CASE REPORT

A diagnostic dilemma of central skull base osteomyelitis mimicking neoplasia in a diabetic patient

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SUMMARY

We present a case which illustrates the diagnostic difficulty in distinguishing between osteomyelitis of the central skull base and base of skull tumours. A woman in her early forties presented with seizures and multiple cranial nerve palsies. She also had a background of chronic otalgia and poorly controlled diabetes mellitus. The clinical diagnosis of skull base osteomyelitis (SBO) was made, but both MRI and bone scans were unable to distinguish this from a skull base malignancy on imaging criteria. Eventually biopsies were required to exclude the diagnosis of malignancy and the patient was treated for central SBO.

BACKGROUND

Osteomyelitis of the skull base, also known as malignant otitis externa (MOE) or necrotising otitis externa is a rare complication of acute otitis externa. It usually occurs in the diabetic, immunocompromised and elderly patient population.^{1–4} Patients may present with cranial neuropathies, most commonly a unilateral lower motor neuron VII nerve palsy, intractable headache and otorrhoea. In the majority of cases with the typical presentation, the diagnosis is unambiguous. However, in this case the condition occurred bilaterally and within the apex of the petrous temporal bone with little external auditory canal signs. This, therefore, posed a diagnostic dilemma with malignancy of the skull base as both conditions may present with similar signs and symptoms and have similar findings on imaging.

CASE PRESENTATION

A woman in her early 40s presented to a primary healthcare centre with severe generalised headache on a background of a 3-month history of left-sided otalgia. During her admission for assessment, she was noted to have an episode of loss of consciousness and had a witnessed seizure. A contrast CT scan of the head performed at the time showed features suggestive of bilateral skull base osteomyelitis (SBO) and the patient was transferred to a tertiary centre for further assessment and treatment.

In the preceding months prior to admission, she had seen various general practitioners for non-specific otalgia which was treated with several short courses of oral antibiotics, topical ciprofloxacin ear drops and a ventilation tube for presumed chronic suppurative otitis media. She was noted to also have tenderness around the temporomandibular joint and was diagnosed with an element of temporomandibular joint dysfunction.

Her medical history includes diabetes (which was poorly controlled with insulin), hypertension and hypercholesterolaemia. She was a non-smoker and consumed no alcohol.

When the admitting ear, nose and throat team eventually reviewed the patient, the patient felt her tongue was abnormal and she also reported some dysphagia. On examination, her otoscopy was surprisingly unremarkable with little evidence of otitis externa. However, a cranial nerve examination revealed a left-sided lower motor neuron IX, X, XI and XII nerve palsies. Fiberoptic nasendoscopy examination of the larynx revealed left vocal cord palsy.

Given the history of ear pain, poorly controlled diabetes and the presence of multiple cranial neuropathies a clinical diagnosis of MOE was made. The patient was then given intravenous tazocin and ciprofloxacin while a high-resolution CT and MRI scan of the temporal bones were obtained together with a bone scan.

Although her cranial neuropathies improved over the subsequent days symptoms of headache associated with severe nausea and vomiting continued to complicate her stay in the hospital.

INVESTIGATIONS

On presentation, the patient had raised inflammatory markers, with a raised erythrocyte sediment rate (ESR) and C reactive protein. The white blood cell count (WBC) however, was normal.

The initial imaging with high-resolution CT scanning of the temporal bones showed bilateral middle ear and mastoid opacification, but showed no evidence of bony destruction or ossicular erosion. This was further investigated with an MRI scan of the temporal region which showed abnormal signal intensity within the central skull base extending from the occipital condyles bilaterally to involve the clivus (figure 1). There was also thickening of the nasopharyngeal soft tissue. Postgadolinium contrast MRI studies, interestingly showed a soft tissue lesion centred on the nasopharynx, which continued superiorly to involve the foramen lacerum bilaterally. A Gallium+SPECT bone scan also revealed intense uptake within the soft tissues of the skull base without matching increased uptake in the osseous skull base structures (figure 2). The MRI scan and gallium bone scan findings therefore contradicted the initial clinical suspicion and CT temporal bone scans, and suggested that a skull base malignancy would be a more likely diagnosis.

Given this dilemma, the patient then proceeded to an examination under anaesthesia of the paranasal sinuses and postnasal space. Bilateral

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Figure 1 MRI scan showing bilateral and central skull base enhancement. Note that the appearances are difficult to distinguish from central skull base neoplasia, especially in the setting of cranial nerve palsies.

sphenoidotomies were performed, and biopsies for histology and microbiological swabs were taken of the post-nasal space with the aim to differentiate infection from malignancy. The histological specimens, however, showed only inflammatory changes with no sign of malignancy. Microbiological specimens taken from the same region cultured a multiresistant *Staphylococcus aureus* (MRSA) and *Corynebacterium jeikeium*. *Candida albicans* was also cultured from the sphenoid ostium specimens.

DIFFERENTIAL DIAGNOSIS

Skull base malignancy such as nasopharyngeal carcinoma, lymphoma, melanoma or neuroendocrine tumours.

Figure 2 CT axial scan showing increased soft tissue in the post nasal space and central skull base region.

TREATMENT

Given the possibility of MOE the patient was started on intravenous tazocin and ciprofloxacin on admission. Ciprofloxacin was ceased as it thought to cause side effects of nausea and vomiting in the patient. Tazocin was continued as an antipseudomonal agent. Tazocin was later discontinued because the patient developed tazocin-induced neutropaenia, and instead meropenem was substituted with eventual resolution of the neutropaenia. She was later started on vancomycin after confirmed MRSA was cultured and oral fluconazole was started prior to discharge.

The patient was reviewed by the inpatient neurosurgical services who excluded raised intracranial pressure secondary to malignancy, since she had persistent nausea, vomiting and headache.

OUTCOME AND FOLLOW-UP

The patient's stay in the hospital was complicated by persistent headaches and vomiting which were due to adverse reactions from administered intravenous antibiotics. She was eventually discharged back to a rural healthcare centre, with a domiciliary nurse program to continue intravenous vancomycin, meropenem and oral fluconazole for 6 weeks. A follow-up MRI scan was due after this course of treatment to assess response. Upon discharge, her cranial nerve palsies improved significantly which was in keeping with an infectious aetiology (figure 3).

DISCUSSION

We have described this case to highlight the diagnostic dilemma between central osteomyelitis of the skull base and skull base malignancy. SBO typically is a rare complication of acute otitis externa and occurs when infection within the external auditory canal spreads to the skull base via the fissures of Santorini and usually affects the temporal bone and the structures contained within it.⁵ Usually it presents in the elderly, diabetic or

Figure 3 Interval MRI scan post-treatment with intravenous antibiotics showing an improvement in the central and bilateral skull base enhancement. This correlated with the patient's improvement in symptoms.

immunocompromised patients and therefore a high index of suspicion is required in these patients.

Often the diagnosis is made several months after the onset of symptoms due to the non-specific nature of the symptoms. Patients often present with headache, otalgia and rarely, cranial neuropathies which maybe single or multiple. In the more typical cases, granulation tissue is seen on the floor of the external auditory canal. The most common pathologic organism cultured is *Pseudomonas aeruginosa*.⁶ When the first case of MOE was described by Melzer and Keleman in 1959, it often carried a fatal course and 50 years later, MOE still remains a very serious condition with a death rate of up to 15%.⁷ Cases of MOE often lack the normal responses to infection such as fever, raised WBC and positive blood cultures.⁸ The ESR is almost always raised in patients with MOE.⁹

In contrast with the typical features described above, several atypical cases have been reported. In atypical cases of MOE, often a source of infection is not found. Paranasal sinuses and haematological spread from distant sites of infection are considered possible sources. However, patients usually have a history of episodic otitis externa in the months prior to presentation. The infection in atypical cases is not only limited to the temporal bone, but may involve the sphenoid, occipital and clival bones. Atypical MOE may be caused by organisms other than *P aeruginosa* such as *S aureus*, coagulase-negative species and fungal organisms. At times no pathogenic organism is cultured resulting in culture negative MOE, although this may be the result of suboptimal treatment of presumed uncomplicated otitis externa with antibiotics.¹⁰

One marker of disease severity is cranial nerve neuropathy. Involvement of the petrous apex, as in this case, often leads to cranial nerve palsies. The most common cranial nerve to be involved is the VII nerve, and most commonly this is due to the involvement of the stylomastoid foramen by infection. The involvement of the jugular foramen leads to palsies of IX, X and XI nerves due to their anatomical relationship.¹¹ Cranial nerve involvement is one of the main reasons why MOE is difficult to distinguish from malignancy because tumours such as nasopharyngeal carcinoma and lymphoma remain the most common cause of cranial nerve palsies in this area. Keane¹² studied 21 cases of VI and XII cranial nerve palsies and found that 17 had malignancy as the underlying cause and only one case was due to MOE. Cranial neuropathies in MOE however may resolve, as opposed to malignancy, which would represent regression or resolution of the disease.

The diagnosis of MOE can sometimes be difficult. This is because it can be difficult to recognise the initial onset of symptoms which may be non-specific especially if atypical features are present. Once MOE is suspected, it is important to obtain imaging with CT, MRI with gadolinium enhancement and nuclear medicine scans (particularly Technetium-99 and gallium) which have been shown to be useful in making the diagnosis. Positron emission tomography (PET) and indium-111 WBC scan have limited use in the investigation of MOE.

The CT scan findings, which support the diagnosis of MOE, are bony erosion and decreased skull base density. These findings may not be evident in the early stages of the disease. Studies by Seabol *et al* and Sudhoff showed that 13 of 35 and 7 of 23 cases, respectively, of MOE showed no bony erosion in the initial stages of the disease.^{3 4} In order for bony erosion to be evident on CT, approximately 30% of the bone has to be demineralised and therefore in the early stages this may not be radiologically detectable.¹³ Moreover, the CT findings may not be specific to MOE. Sudhoff *et al*³ concluded that CT is more

useful in determining the anatomical extent and progression of the disease. Interestingly, CT scanning may not be useful in follow-up because the radiological abnormalities rarely normalise, and when they do, often only after considerable delay.^{3 11}

The advantage of MRI scanning is its ability to view the soft tissue changes surrounding the affected bone and in determining the exact anatomical location and extent of the disease. This includes critical areas such as the basal foramina and cranial nerves.¹⁴ The typical MRI findings in MOE include clival enhancement with hypointensity in the marrow space on T1-weighted images, hyperintensity on T2-weighted images, the presence of dural enhancement, effacement of the parapharyngeal fat planes as well as the soft tissue masses at the skull base.¹⁵ The hypointensity of the marrow space on T1-weighted images is thought to be secondary to the infective processes replacing the fatty marrow. As with CT scanning, the MRI findings are considered highly sensitive of MOE, but not specific because clival enhancement can also be seen with malignant processes.¹⁶

A retrospective study by Ozgen *et al*⁷ examined the use of diffusion-weighted MRI to better distinguish MOE from malignancy. This was based on the previously noted finding that diffusion-weighted sequences can help distinguish benign from malignant lymph nodes. In principle, malignant neoplasms have low apparent diffusion coefficients (ADC) and benign masses have higher ADC. This study showed that ADC values of lymphomas and nasopharyngeal carcinomas were significantly lower than that of the group with SBO; however the ADC values of the patients with metastatic disease overlapped with the SBO group. The sample in each group was small and consisted of only nine patients. The authors concluded that further studies with larger patient groups are needed for more definitive outcome.⁷

Gallium and technetium-99 bone scans have also been shown to be useful in aiding the diagnosis of MOE as these scans become diagnostic much earlier than CT scans. Technetium-99 scans are positive in almost all cases of MOE, but may also be positive for malignant disease. Some studies have shown that technetium-99 scintigraphy performed at 4 and 24 h postinjection may be a more sensitive method of diagnosing MOE.¹⁶ Gallium scans show areas of active inflammation and can give useful information about the involvement of soft tissue and bony structures. However, once again, these changes are often non-specific.¹⁷

The indium-111 WBC scan involves radiolabelling the patient's own neutrophils and reinjecting them to localise to areas of acute inflammation. Okpala *et al*¹⁸ in a case series examined the utility of this scan in diagnosing MOE. Indium-111 WBC scans were only used after 6 weeks of intravenous antibiotics. In some situations, this scan was found to be negative in the presence of infection and therefore a negative scan cannot exclude MOE. One explanation given for the poor sensitivity of the test is the difficulty in counting slow turnover radio-labelled leucocytes.

PET is a commonly used technique for detecting metastatic disease. This is based on the principle that many tumours preferentially take up fluorodeoxyglucose. PET may have a role in diagnostic dilemmas such as in this presented case because the presence of disseminated metastases would make the diagnosis of malignancy more likely. However, increased uptake at the local site in the skull base can occur in the presence of infection as well as malignancy.

Despite the issues related to the different imaging modalities, in most cases of MOE, the history, clinical findings and imaging are sufficient to make a diagnosis. However, in atypical cases where the clinical findings are ambiguous on imaging it is often

necessary to conduct a biopsy to confirm the diagnosis, excluding malignancy and culture the pathogenic organisms. The importance of early referral to an ear nose and throat service, the role of biopsy and empirical treatment has been echoed by previous authors.

Learning points

- Some cases of malignant otitis externa (MOE) pose a diagnostic difficulty because the clinical and radiological features can mimic malignancy.
- Lower cranial nerve neuropathies can occur in both MOE and malignancy.
- Cranial nerve neuropathies usually recover in MOE after a period of antibiotic treatment.
- CT, MRI and radionuclear studies can be non-specific and may not be able to exclude infection from malignancy.
- Biopsy of the postnasal space and sphenoid should be considered to confirm diagnosis of osteomyelitis and exclude malignancy in the cases where the diagnosis is in doubt.

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REFERENCES

- 1 Grandia JR, Branstetter BF, Yu VL. The changing face of malignant (necrotising) external otitis: clinical, radiological and anatomic correlations. *Lancet Infect Dis* 2004;4:24–39.
- 2 Vourexakis Z, Kos MI, Guyot JP. Atypical presentations of malignant otitis externa. *J Laryngol Otol* 2010;124:1205–8.
- 3 Sudhoff H, Rajagopal S, Mani N, et al. Usefulness of CT scans in malignant external otitis: effective tool for the diagnosis, but of limited value in predicting outcome. *Eur Arch Otorhinolaryngol* 2008;265:53–6.
- 4 Clarke MP, Pretorius PM, Ivor B, et al. Central or atypical skull base osteomyelitis: diagnosis and treatment. *Skull Base* 2009;19:247–54.
- 5 Carfrae M, Kesser BW. Malignant otitis externa. *Otolaryngol Clin North Am* 2008;41:537–49.
- 6 Malone D, Paul L, Dewey K, et al. Osteomyelitis of the skull base. *Neurosurgery* 1992;30:4.
- 7 Ozgen B, Oguz KK, Cila A. Diffusion MR imaging features of skull base osteomyelitis compared with skull base malignancy. *AJNR Am J Neuroradiol* 2011;32:179–84.
- 8 Chang PC, Fischbein NJ, Holliday RA. Central skull base osteomyelitis in patients without otitis externa: imaging findings. *AJNR Am J Neuroradiol* 2003;24:1310–16.
- 9 Chandler JR, Quencer R, Grobman L, et al. Osteomyelitis of the base of the skull. *Laryngoscope* 1986;96:245–51.
- 10 Rowlands RG, Lekakis GK, Hinton AF. Masked pseudomonas skull base osteomyelitis presenting with a bilateral Xth cranial nerve palsy. *J Laryngol Otol* 2002;116:556–8.
- 11 Amorosa L, Modugno GC, Pirodda A. Malignant external otitis: review and personal experience. *Acta Otolaryngol* 1996;521:3–16.
- 12 Keane JR. Combined Vth and XII cranial nerve palsies: a clival syndrome. *Neurology* 2000;54:1540–1.
- 13 Hariga I, Mardassi Ali, Younes FB, et al. Necrotizing otitis externa: 19 cases' report. *Eur Arch Otorhinolaryngol* 2010;267:1193–8.
- 14 Cavel O, Fliss DM, Segev Y, et al. The role of the otorhinolaryngologist in the management of central skull base osteomyelitis. *Am J Rhinol* 2007;21:281–5.
- 15 Subburaman N, Chaurasia MK. Skull base osteomyelitis interpreted as malignancy. *J Laryngol Otol* 1999;113:775–8.
- 16 Sreepada GS, Kwartler JA. Skull base osteomyelitis secondary to malignant otitis externa. *Curr Opin Otolaryngol Head Neck Surg* 2003;11:316–23.
- 17 Giuseppe M, Varacalli S, Ciofalo A. Osteomyelitis of the skull base with atypical onset and evolution. *Ann Otol Rhinol Laryngol* 2000;109:326–30.
- 18 Okpala NCE, Nilssen E. Radiological and radionuclide investigation of malignant otitis externa. *J Laryngol Otol* 2005;119:71–5.

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