Delayed diagnosis of central skull-base osteomyelitis with abscess: case report and learning points

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ABSTRACT

Central skull-base osteomyelitis (CSBO) is a rare life-threatening infection, usually resulting from medial spread of necrotising otitis externa. Here, we describe a case with no identifiable source of infection, causing a delay in diagnosis. An 80-year-old man with Crohn's disease treated with mesalazine presented with collapse and tonic-clonic seizure. Computed tomography and magnetic resonance imaging showed a nasopharyngeal mass that was initially thought to be a neoplasm. Awaiting formal biopsy, he represented with collapse and repeat imaging showed features of abscess formation. Review of previous scans revealed skull-base erosion and the diagnosis was revised to skull-base osteomyelitis. This is the first reported case of CSBO associated with mesalazine use, an aminosalicylate used in Crohn's disease. It is only the second reported case with abscess formation. We discuss the learning points in making a timely diagnosis and examine the potential association of factors such as mesalazine use and abscess formation in this case.

KEYWORDS

Osteomyelitis – Skull base – Crohn's disease – Abscess – Mesalazine

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Introduction

Skull-base osteomyelitis is a rare condition which usually develops from severe otitis externa with bony involvement; so-called necrotising otitis externa. The infection escapes the ear canal via the vertical fissures of Santorini in the anterior canal cartilage. Several patterns of spread have been described, including anterior, posterior and inferior. A fourth direction of spread – medial – results in the still rarer complication of central skull-base osteomyelitis (CSBO).

Here, we report a case of CSBO with no clear infective source. This led to diagnostic confusion and delay. To our knowledge, this is also the first case associated with long-term use of mesalazine, an aminosalicylate used in Crohn's disease. It is only the second reported case with abscess formation. In our report, we discuss the diagnostic and management challenges involved as well as learning points. We also consider what role mesalazine might have played.

Case history

An 80-year-old man with Crohn's disease on long-term mesalazine presented with collapse and tonic-clonic seizure. There was a preceding 3-month history of headache, weight loss, nausea and vomiting, and he had been investigated for flare-up of Crohn's disease. General medical,

neurological and otolaryngological examination (including postnasal space) failed to yield a diagnosis and inflammatory markers were not significantly raised.

A computed tomography (CT) head scan reported no gross abnormalities. Magnetic resonance imaging (MRI) of the head, however, demonstrated a submucosal nasopharyngeal soft-tissue mass and a neoplasm was suspected. He was discharged from hospital awaiting a planned urgent biopsy of the lesion. Unfortunately, he represented with recurrent collapse and bilateral hearing loss.

A repeat head MRI to assess progression of this putative neoplasm showed infiltrative soft tissue extending bilaterally to each foramen lacerum, both jugular foramina and abutting both internal carotids. This time, contrast was given and revealed a rim-enhancing collection within the mass, as well as abnormal enhancement throughout the clivus, suggestive of an infective process. On review of the original CT images, clival bony erosion was now apparent. Based on these appearances, the diagnosis was revised to central skull-base osteomyelitis, despite the absence of any otological or other infective source. He underwent urgent CT-guided biopsy. Histology was in keeping with an abscess and microbiology grew *Pseudomonas aeruginosa*.

The patient received 6 weeks of intravenous ceftazidime followed by 6 weeks of oral ciprofloxacin. His symptoms improved and post-treatment head CT showed a marked

Figure 1A Axial computed tomography showing subtle clival erosion on the right side (arrow) which was not appreciated at the time of the examination

Figure 2A Sagittal T1 magnetic resonance imaging showing loss of the normal T1 fat signal in the clivus (arrow); the preclival mass is again noted (arrowhead)

Figure 1B Axial T2 magnetic resonance imaging showing the inferior slices of the study and demonstrating a T2 hyperintense retropharyngeal/preclival mass (asterisk); bilateral middle ear and mastoid effusions are also present

Figure 2B Fat-saturated axial T1 post IV gadolinium scan demonstrating a rim-enhancing mass in the preclival region consistent with an abscess (arrowheads); diffuse inflammatory change and enhancement is seen in the clivus and surrounding soft tissues, in keeping with central skull base osteomyelitis; note the abnormal retroclival dural enhancement (arrows)

reduction in size and extent of the mass. A further 8 weeks of ceftazidime was given on microbiological advice after his headaches resurfaced on completion of the first course of antibiotics. He remains under long-term follow-up to detect late recurrence of infection.

Discussion

CSBO is a rare entity; it is even more rare in the absence of a necrotising otitis externa – a recent review found only 42 such cases in the world literature.¹ This is an important

Figure 3 An axial computed tomography guided biopsy was performed using a paramaxillary and subzygomatic approach

Figure 4 Fat-saturation axial T1 post IV gadolinium post-treatment scan showing a marked reduction in size of the preclival abscess with a residual rim-enhancing cleft seen on the right side (arrow); the clivus signal has now returned to normal and the dural enhancement has also resolved

factor leading to misdiagnosis – clinicians had a low index of suspicion. Had there been an associated otogenic infection, the correct diagnosis may have been considered sooner. Other sources of infection, including spread from the post-nasal space, can also occur. The differential diagnosis of a

nasopharyngeal mass should include both infection and neoplasm until a histological diagnosis is made.

An opportunity to diagnose CSBO was missed on imaging; on the initial CT, the reporting radiologist missed subtle skull-base erosion in the inferior scan slices. This erosion became apparent when images were re-reviewed after the MRI scan revealed a ring-enhancing lesion (an abscess) in the postnasal space soft tissues. Findings can be missed on clinical and radiological examination; this highlights the importance of reviewing the data when the clinical picture does not fit with the putative diagnosis. It also underlines the importance of clear communication between clinical and radiological colleagues as to the differential diagnosis and what the imaging being requested is intended to prove or disprove.

Our patient was taking long-term mesalazine, an anti-inflammatory drug, for Crohn's disease. Known adverse effects of mesalazine include blood dyscrasias such as agranulocytosis, aplastic anaemia, leucopenia and neutropenia.² These blood states may lead to immunocompromise and, subsequently, uncommon infections such as CSBO. Although our patient's blood count did not reveal any overt abnormalities, we proffer that long-term mesalazine may have altered the immune system, rendering it vulnerable to spontaneous and unusual infection such as CSBO. We emphasise, however, that this is a single observation in one patient and does not currently represent an association or causation.

This is only the second case of CSBO with abscess formation. The first, reported by Parmar,⁵ was in an 80-year-old man with diabetes mellitus. He presented with mild fever and palsy of cranial nerves VII, IX, X and XI, again with no history of ear infection. The diagnosis was made on CT and MRI, which demonstrated a 9 mm ring-enhancing lesion in the preclival space. The patient responded to broad-spectrum antibiotics. By comparison, our patient had no cranial nerve palsies. Whereas our patient's diagnosis was based on radiology and tissue sampling, Parmar's case relied solely on imaging. Our patient's abscess was significantly larger (20mm vs 9mm) but, in both cases, the patients responded to antibiotic treatment without aspiration.

The factors predisposing to CSBO abscess formation remain unclear. It is nevertheless a rare occurrence. This may be because there are no naturally occurring potential spaces at the skull base for pus to collect. Infection would need to be severe, prolonged or facilitated by other factors (for example by immunocompromise) to progress to an abscess. In our case, the main potential factors for immunocompromise were Crohn's disease and mesalazine, whereas in Parmar's case it was diabetes mellitus.

Although cranial nerve involvement is a commonly reported symptom in skull-base osteomyelitis, our patient did not suffer from this despite his extensive disease. Rapid onset of bilateral deafness at his second presentation raised concerns of eighth nerve involvement; however, an audiogram showed conductive loss with flat tympanometry, indicating bilateral middle-ear effusions as the cause. This was confirmed on MRI, which showed the mass to be occluding both Eustachian tube orifices, causing middle-ear effusions.

The optimal length of therapy for any form of osteomyelitis, long bone or skull base, is not known.^{4,5} Based on a review of the literature, Courson advocates at least 6 weeks of systemic antibiotics following which antibiotic duration is guided by clinical, radiological and inflammatory marker response. Our patient required two courses of antibiotic to achieve satisfactory treatment, totalling 20 weeks. He remains under regular outpatient review as recurrence rates have been estimated up to 20%.⁵

Our case demonstrates the difficulty in reaching a correct diagnosis quickly. The lesion was initially misdiagnosed as a neoplasm. Retrospective review of the original CT showed clival bony erosion, which was not appreciated at the time. A nasopharyngeal mass should prompt a differential diagnosis of both infection and neoplasm and a high index of suspicion should be maintained until tissue diagnosis. Furthermore, close communication between clinical and radiology

colleagues in addition to microbiology input will help to ensure the most appropriate imaging and a more relevant radiological report.

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