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Gradenigo's syndrome: successful conservative treatment in adult and paediatric patients

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Abstract
A triad of retro-ocular pain, discharging ear and abducens nerve palsy, as described by Gradenigo, has been recognized for 150 years. It has traditionally been treated with surgery, but recent advances in imaging, allied with improved antibiotic treatment, allow conservative management of these cases. We present two cases of Gradenigo's syndrome: a 6-year-old child and a 70-year-old man, both without cholesteatoma, who were managed without mastoidectomy. They both had full recovery of abducens nerve function, although this took 6 and 12 weeks, respectively. In order to manage patients with Gradenigo's syndrome safely, accurate diagnostic radiology is essential, and our findings are presented and discussed. With changing medical technology, a review of the diagnostic and treatment options for this rare but serious condition, is timely.

Key words: Mastoiditis; Abducens Nerve Diseases; Petrous Bone

Introduction

Prior to the introduction of widely available antibiotics, apical petrositis was a frequently fatal complication of otitis media.[1-3] Since the increased use of antibiotics in the community for the management of otitis media, the prevalence of both acute and chronic forms of the disease has decreased markedly. Despite this, unrecognized and under-treated petrositis can lead to clinically important complications including meningitis, extradural and intracranial abscesses, cranial nerve palsies, venous sinus thrombosis, subdural empyema, labyrinthitis, and death.[4] The signs and symptoms of the disease process are often indistinct and presentations vary enormously, and therefore a high index of suspicion is required to make the diagnosis.

In 1907, Gradenigo described a triad of symptoms related to petrous apicitis, including acute suppurative otitis media, deep facial pain resulting from trigeminal involvement and abducens nerve palsy.[5] Despite this, only 42 per cent of his series of 57 patients demonstrated the full quota of symptoms. Lindsay, in 1938, found that only three of his series of six patients with petrous apicitis had the classic triad as described by Gradenigo.[6] Chole and Donald analysed eight cases of apical petrositis and found that two of them presented with abducens nerve paralysis and only one had the full triad of symptoms.[1] They concluded that abducens nerve palsy must not be relied on in the diagnosis of petrous apicitis, as the majority of cases present without it. They found that the most reliable feature was the presence of deep facial pain. In contrast, Price and Fayad reported a case of petrous apicitis where the only presenting feature was an abducens nerve palsy, further highlighting the varied nature of the clinical scenario.[7]

The close proximity of the abducens nerve and the trigeminal ganglion to the petrous apex render them susceptible to the resultant extradural inflammation seen in petrous apicitis, and account for the triad of symptoms seen in Gradenigo's syndrome.[8-10] The uncommon presentation of abducens nerve palsy may relate to the variability of extradural involvement in the inflammatory process.

The advent of the antibiotic era has facilitated the conservative management of a select cohort of patients with apical petrositis, a disease process that historically has been managed with surgical intervention. We present two cases with Gradenigo's triad of symptoms, of differing aetiologies, in paediatric and adult patients, that resolved without the need for surgical decompression of the mastoid.

Case reports

Case 1

A previously well 6-year-old boy without any significant otological history, presented whilst on holiday in France, with 2 weeks of worsening otalgia, headache and vomiting, refractory to oral antibiotic therapy. At the local hospital he was subjected to bilateral myringotomies under local anaesthesia, which resulted in resolution of his symptoms.

Two weeks later, having returned to the UK, he re-attended his local hospital with severe frontal headaches, bilateral otalgia and vomiting. His CNS examination on admission was normal, although he was pyrexial, with left-sided mastoid tenderness, sero-sanguineous aural discharge and a 40 dB left-sided conductive hearing loss. With a raised C-reactive protein and leucocytosis he was commenced on i.v. co-amoxiclav, but 48 hours later he developed diplopia on left gaze, due to left lateral rectus palsy. A CT scan showed only an adenoidal mass and some soft tissue density material in the left middle-ear cleft.

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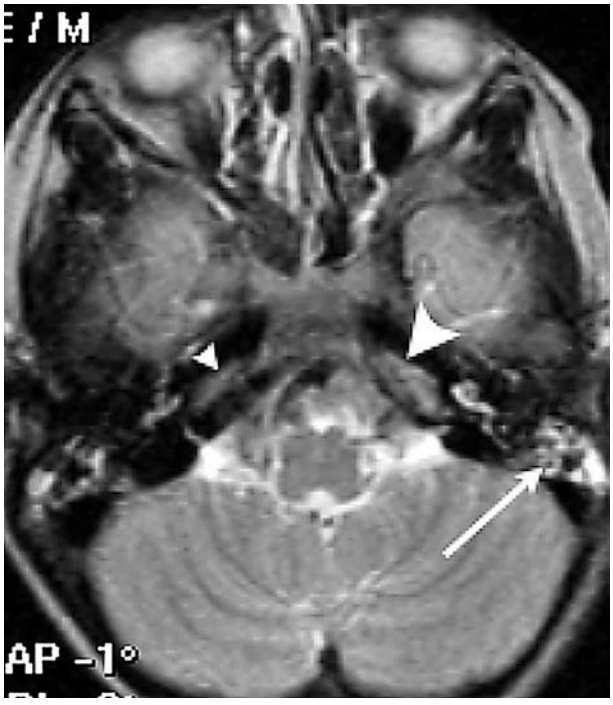

FIG. 1(a)

Axial T2-weighted magnetic resonance image through the petrous bones showing fluid in the left mastoid air-cells (arrow). The left petrous apex (large arrowhead) returns slightly higher signal than the right (small arrowhead).

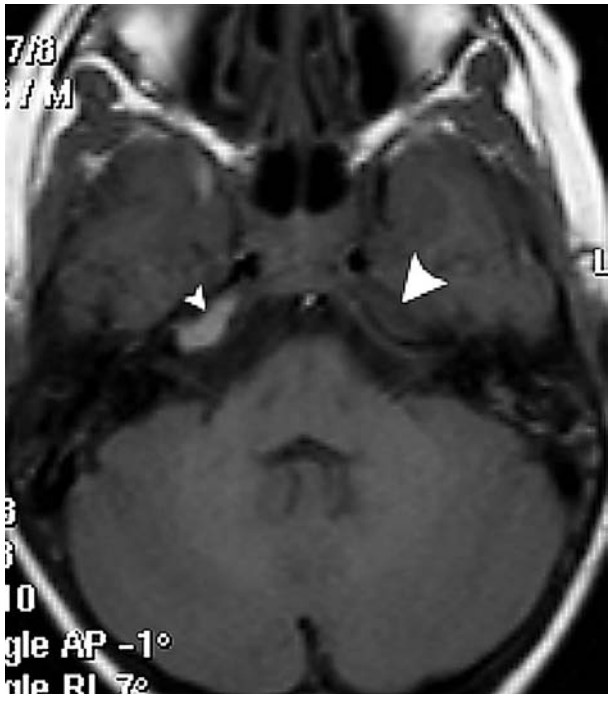

FIG. 1(b)

Axial T1-weighted magnetic resonance image. The right petrous apex returns high signal in keeping with normal marrow-fat (small arrowhead) while the left petrous apex returns intermediate signal suggesting an inflammatory process (large arrowhead).

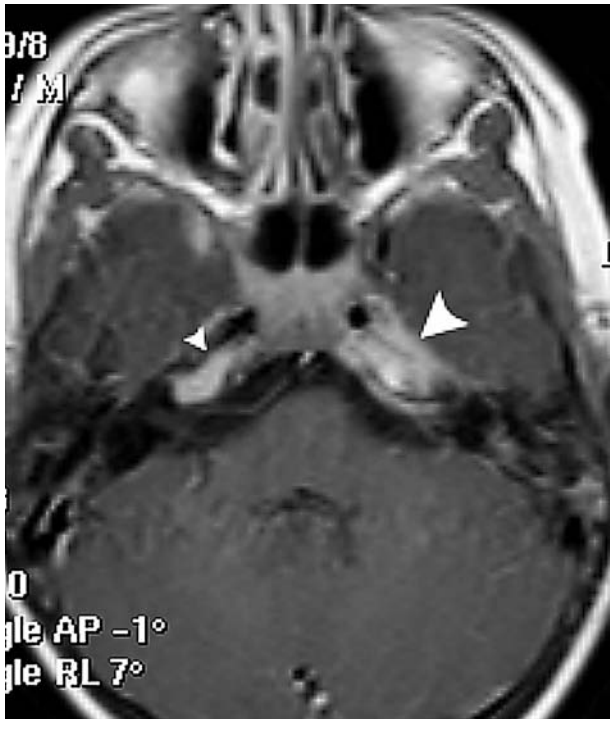

FIG. 1(c)

Axial T1-weighted, gadolinium enhanced magnetic resonance image. There is gadolinium uptake in the left petrous apex (large arrowhead) confirming petrous apicitis. Note how similar the appearance of the enhancing left petrous apex is to that of the normal, marrow-filled right petrous apex (small arrowhead).

Bilateral myringotomies were performed with ventilation tube insertion. There was mucopus in the aspirate from the left myringotomy. His antibiotics were changed to ceftriaxone to cover intracranial sepsis, and topical gentisone drops were started. Magnetic resonance imaging (MRI) (Figure 1) demonstrated a non-pneumatized true petrous apex containing bone marrow, and abnormal contrast enhancement in the left petrous apex consistent with petrous apicitis. There was no evidence of cerebritis or abscess formation in the adjacent brain. Over 48 hours, there was improvement in his headache, pyrexia, vomiting and otalgia, and his inflammatory markers return to normal. Repeated blood cultures throughout his admission and swabs performed at the time of grommet insertion were all negative on culture.

A week later his symptoms relapsed, with a repeat MRI confirming left petrositis with adjacent focal meningitis, but once again there was no intracerebral abscess. He was recommenced on i.v co-amoxiclav in addition to metronidazole, with rapid subsequent improvement in his headache and vomiting. His ocular movement returned to normal some 6 weeks after initial commencement of the intravenous antibiotic therapy, and at this point he was converted to oral co-amoxiclav and metronidazole for a further 6 weeks.

He made a full recovery, and other than requiring replacement of a failed left-sided grommet, he has remained well over the ensuing 12 months.

Case 2

A 71-year-old man was admitted with a 4-day history of diplopia, vomiting, frontal headache and left discharging ear. He had a previous history of bilateral chronic suppurative otitis media, and a left pars tensa perforation,

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but had no previous otological surgery. He had no other relevant medical conditions. His ears had been dry for 2 months prior to presentation. His Glasgow coma score was 15, and his cranial nerves were intact, except for an isolated left lateral rectus palsy. His left ear was discharging mucopus, and microbiological swabs were taken. There was no post-auricular pain or swelling.

His C-reactive protein was elevated at 88, with normal white cell count on presentation. A CT scan was performed showing opacification of the mastoid, middle ear and petrous apex on the left. There was evidence of bone destruction involving the intercellar septae and anterior cortex of the left petrous apex in keeping with petrous apicitis (Figure 2a). He was commenced on ceftriaxone, metronidazole and ciprofloxacin, as well as gentisone HC topical ear drops.

An MRI scan showed abnormal enhancement of the left petrous apex extending into Meckel's cave and along the dura of the middle cranial fossa floor (Figures 2b-d).

His clinical condition improved over a week. Culture of the initial ear swab grew *Streptococcus milleri*. He was treated with 4 weeks of i.v. metronidazole, 6 weeks of i.v. ceftriaxone, and oral ciprofloxacin, followed by a further 6 weeks of ciprofloxacin and clindamycin. Over a 3-month period, there was a resolution of his left VIth nerve palsy and he had no further ear discharge.

Discussion

These two cases of apical petrositis arose in two very different patients, one a child of 6 with acute otitis media, and the second, a 70-year-old with a history of chronic suppurative otitis media. The pathology of the two processes also differs. In acute apicitis the inflammatory changes seen within the bone and mucosal surfaces are diffuse, and parallel those found within the middle-ear cavity. In chronic disease the thickened mucosa tends to be more localized and may enclose air-filled cystic spaces, acting as a sump to trap mucopurulent material.[11] Despite this, they both presented with the full triad of symptoms, as described by Gradenigo, highlighting the serious sequelae that can arise from seemingly innocuous or 'safe' middle-ear disease.

As the technology of diagnostic radiology gathers pace, more and more petrous apex lesions are being identified. Current imaging not only offers accurate localization of the lesion, but in the majority of cases is also able to give important diagnostic information about the nature of the abnormality. CT scanning remains the first-line investigation for any possible lesions of the petrous apex, because it is more widely available than MRI, and is sensitive enough in detecting bone erosion and demonstrating the extent of temporal bone pneumatization. CT scanning can also detect intracranial abscess formation but is generally less sensitive than MRI in detecting early intracranial complications. MRI scanning is utilized to establish the extent of meningeal and cerebral involvement and help discern between the differing pathologies that feature in the petrous apex, namely osteomyelitis, petrous apicitis, cholesteatoma, cholesterol granuloma, and neoplastic lesions.[12]

The interpretation of imaging studies of the petrous apex is complicated by normal anatomical variation in the degree of pneumatization in this region. Pneumatized petrous apices, as seen in Case 2, are present in only approximately 33 per cent of individuals. In 60 per cent of people the petrous apices are filled with bone marrow, as seen in Case 1, and in the remaining seven per cent it is made up of dense sclerotic bone.[13] Pneumatization is asymmetrical in only four to seven per cent of individuals. In non-pneumatized petrous apices, as demonstrated in Case 1, the abnormality can be difficult to appreciate on T2- (Figure 1a) and contrast enhanced T1-weighted (Figure 1c) magnetic resonance images, due to similarities in signal characteristics with fat on these sequences. In our case, confusion was avoided by performing an unenhanced T1-weighted sequence (Figure 1b). Using a fat suppression technique for the post-gadolinium T1-weighted sequence would similarly allow easy distinction between the normal, marrow-fat containing side and the abnormal, enhancing side.

In only one of these cases did we determine the causative organism involved in the disease process. This is frequently the case with this condition, and may be due to prior administration of antibacterial agents, or perhaps the use of inappropriate transport culture media. Therefore when faced with the need to initiate empirical antibiotic therapy, one must appreciate the likely organisms responsible. In acute otitis media, the most frequently isolated organisms are *Streptococcus pneumoniae*, beta haemolytic streptococci, *Staphylococcus* species, *Haemophilus influenzae*, *Pseudomonas* species, *Moraxella catarrhalis*, and various anaerobes.[14] In chronic suppurative disease, where granulation tissue is a frequent finding, anaerobes and Gram-negative organisms tend to predominate.[2] Of the eight cases studied by Chole and Donald in 1983 they were able to isolate a causative organism in six (five *Pseudomonas* species and one *Streptococcus pneumoniae*).[1] It remains impossible to recommend an all-encompassing strategy for antibiotic usage in the management of petrous apicitis; as not only is the arsenal of available antibiotics changing constantly, but also the infecting pattern of the organism and its antibiotic resistance profile are continually being modified.

There remain very few published case reports of apical petrositis associated with abducens nerve palsy, yet of those, differing authors have reported variable times for resolution of the lateral rectus paralysis. Hilding and Price reported improvement in the VIth nerve palsy of a 9-month-old with mastoiditis, some 11 days after mastoidectomy and intravenous antibiotics.[15] Gillanders described a case of a 40-year-old with Gradenigo's syndrome who proceeded to posterior petrosectomy and treatment with high-dose antibiotics,[10] following which the lateral rectus palsy subsided within 6 weeks of the surgical intervention. Price and Fayad treated a 7-year-old, noted to have an abducens nerve palsy and ring enhancing mass in the petrous apex, with attico-antrostomy and commencement of antibiotic therapy, and observed resolution of the VIth nerve palsy after only 9 days.[7] Woody *et al*. managed a 4-year-old who developed chronic petrositis complicated by a VIth nerve palsy, with mastoidectomy and described resolution of the lateral rectus palsy within 3 weeks.[16] Minotti and Kauntakis explored the outcomes of two patients presenting with petrositis and abducens nerve palsy, one arising from acute disease, the other developing it bilaterally against the background of chronic bilateral otitis media.[4] They found the acute picture responded well to conservative management, employing myringotomy, tube tympanotomy and antibiotics, with complete resolution of the abducens nerve paralysis within 4 days of antibiotic therapy. The chronic scenario failed to respond to conservative management and proceeded bilaterally to surgical decompression of the petrous apex, with prompt resolution within 5 days of the abducens nerve palsy. They recommended that patients who failed to respond to conservative therapy or who had evidence of chronic disease should proceed to prompt surgical decompression. We present here examples of acute and chronic forms of petrous apicitis, from both extremes of age, which have

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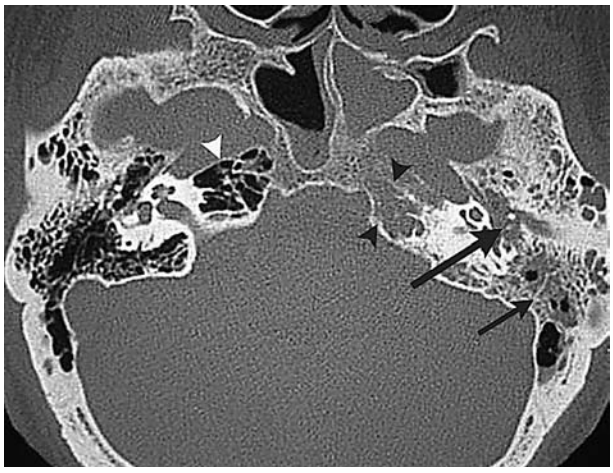

FIG. 2(a)

Axial CT through the petrous bones imaged on bone window settings. There is opacification of the left mastoid air-cells (small arrow), middle-ear cleft (large arrow) and petrous apex (black arrowheads). There is lysis of the bony septae between the individual air-cells of the left petrous apex as well as erosion of the anterior cortex of the petrous apex. Note the normal intercellar septae and surrounding cortical bone of the well-pneumatized right petrous apex (white arrowhead).

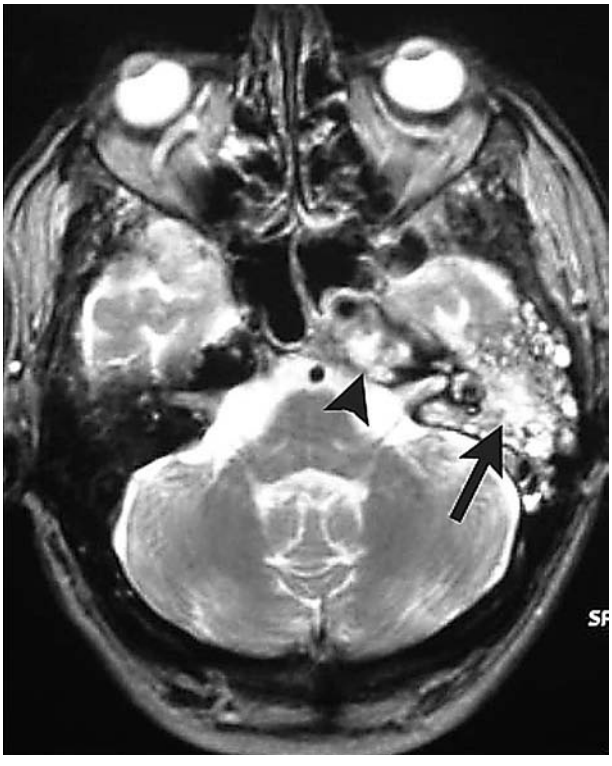

FIG. 2(b)

Axial T2-weighted magnetic resonance image. There is extensive high signal in the left mastoid air-cells (arrow) and petrous apex (arrowhead) indicating mucoperiosteal disease. This is in stark contrast to the black (signal void) appearance of the air-filled mastoid and petrous apex on the right. Note the slightly disconjugate gaze.

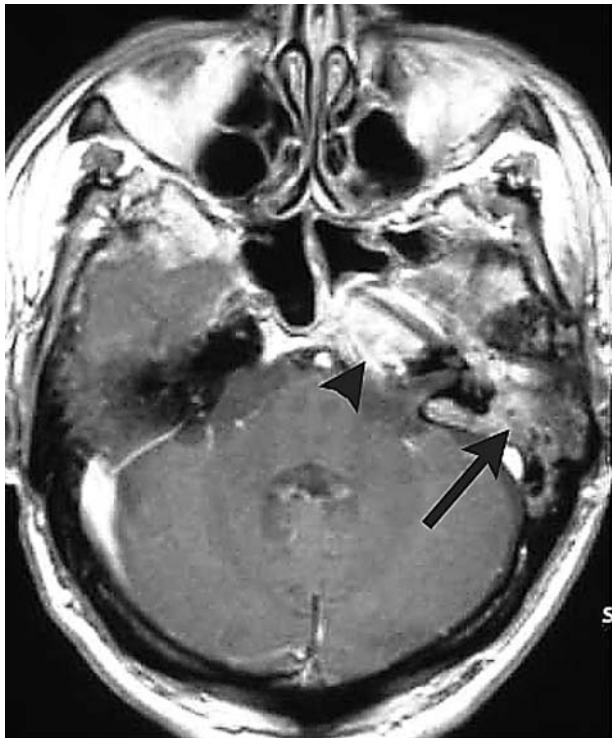

FIG. 2(c)

Axial T1-weighted, gadolinium enhanced magnetic resonance image. There is intense enhancement of the left petrous apex (arrowhead) indicating petrous apicitis. Less dramatic enhancement is also evident in the left mastoid (arrow).

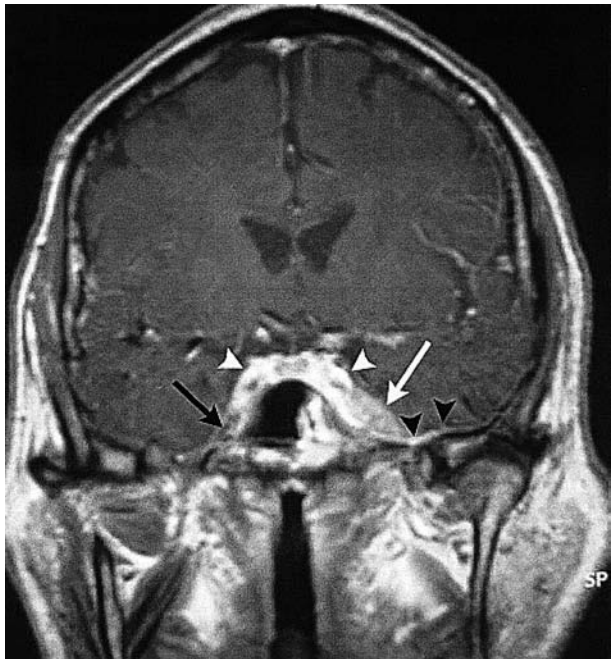

FIG. 2(d)

Coronal T1-weighted, gadolinium enhanced magnetic resonance image. In addition to the normal enhancement of the cavernous sinuses (white arrowheads), there is enhancement in Meckel's cave on the left (white arrow) compared to the normal CSF signal within Meckel's cave on the right (black arrow). There is also dural enhancement along the floor of the left middle cranial fossa (black arrowheads).

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demonstrated resolution of their lateral rectus palsies without the need for surgical intervention.

Although Gradenigo's triad of symptoms remains a rare presentation, clinicians must be aware of the more subtle and varied ways in which petrous apicitis may present, and hence initiate the most appropriate investigative modality. As complications from middle-ear disease are rarely in isolation it remains imperative to initiate treatment whilst investigations are ongoing, as delay may prove fatal from any intracranial extension. We have demonstrated here that patients developing petrous apicitis and abducens nerve palsy, whether from acute or chronic otitis, will respond to high-dose antibiotic therapy and simple aeration of the middle-ear cleft. Despite this, for those patients who do not respond to conservative measures or who present with established intracranial complications, surgical intervention remains mandatory.

- **This paper describes two cases of Gradenigo's syndrome and discusses the radiological investigations and findings**
- **A review of the diagnostic and treatment options is also presented**

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