Gradenigo's Syndrome: A report of two cases with review of literature
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Citation

Abstract
The syndrome of constant otorrhea, headache, and diplopia, which is attributed to inflammation of the petrous apex, is known as Gradenigo's syndrome. It is often the result of chronic otitis media with long-standing purulent otorrhea. We report two cases of Gradenigo's syndrome, the first case was a 17-year-old boy who presented to the emergency department with 7 days history of right-sided headache, ear discharge, facial pain, and diplopia. Examination demonstrated a right eye lateral gaze palsy and diplopia, and otoscopy revealed a pinpoint perforation with a congested tympanic membrane. A magnetic resonance imaging study confirmed a moderate amount of fluid in the right petrous apex consistent with Gradenigo's syndrome. Imaging with computed tomography and magnetic resonance is an important tool in the evaluation of petrous apex lesions. The second case was a 20 year old female who presented in our department with headache, diplopia and a profuse discharge from her left ear. Her examination revealed a left lateral gaze palsy, a central perforation with congestion of tympanic membrane remnant. A contrast enhanced CT scan of the patient revealed clouding of the middle ear cleft region with collection of fluid in the petrous apex. Gradenigo's syndrome is a rare condition that does not always present with the classical triad of otorrhea, headache, and diplopia. But in both our cases the triad was present. Appropriate management requires antibiotic treatment and possible surgical intervention.

INTRODUCTION
The syndrome, first described by Gradenigo in 1907, consists of the clinical triad of acute otitis media, unilateral pain in regions innervated by the first and second branch of the trigeminal nerve, and ipsilateral abducens nerve paralysis. These cranial nerve dysfunctions are caused by osteitis of the petrous apex (petrous apicitis) and are very rare complications of otitis media, especially since the widespread use of antibiotics [1,2]. However, in recent years, a rise in the incidence of intratemporal and intracranial complications of purulent middle ear infections have been mentioned in the literature, mainly in younger children [1,3]. The trigeminal nerve ganglion and the abducens nerve are separated from the petrous apex only by dura mater and are therefore vulnerable to any inflammatory process occurring in this region [4,5].

CASE REPORT 1
A 17-year old boy presented with history of right-sided otorrhoea for 3 weeks. It was accompanied with headache, vomiting and diplopia. On examination, this afebrile patient was noted to have ipsilateral sixth nerve palsy (Fig 2) and a pinpoint perforation in the tympanic membrane of the right ear. The right mastoid was tender. On examination the patient had papilloedema and neck stiffness. The leucocyte count was 9700/ mm3 [polymorphs 68%, lymphocytes 21% and monocytes 5%] while the ESR was 67 mm at the end of 1 hour.

The computed tomography showed obliteration of the right mastoid air cells with sclerosis of the mastoid antrum and petrous bone(Fig 3). The external and middle ear structures also showed obliteration of normal definition. There were features of mild destruction of the ipsilateral petrous apex. The mastoid antrum, the middle and inner ear structures and the brain parenchyma on the contralateral side were normal. On magnetic resonance imaging, the T1 (Fig 1) showed isointense petrous and mastoid parts of the right temporal bones. The middle ear structures and the external auditory canal were also isointense. The clinical, laboratory and radiological findings helped to establish the diagnosis of Gradenigo’s syndrome. No organisms were grown in the exudates from the middle ear and histopathological examination of the mastoid antrum revealed non-specific inflammatory tissue. The patient was managed and put on intravenous antibiotics [crystalline penicillin,
chloramphenicol, and metronidazole], but the patient subsequently developed signs of raised intracranial tension and was shifted to neurosurgery department for further management. The patient was further managed with prolonged course of combination antibiotics of third generation cephalosporins and metronidazole with some improvement in symptoms. The patient was later shifted back to ENT department where tympanomastoidectomy was done after 2 months of presentation. The lateral rectus palsy persisted with recovery of other features.

**Figure 1**
Fig 1: T1 weighted MRI image with isointense lesion in the right petrous apex (black arrow)

CASE REPORT 2
A 20 year old female presented in our department with headache, diplopia and a profuse discharge from her left ear of 3 days duration. The patient did not give any history of sinus congestion, sore throat, and cough, but had history of fever and chills. Her examination revealed a left lateral gaze palsy, a central perforation with congestion of tympanic membrane remnant. The right mastoid was tender. On examination the patient had no papilloedema, but her neck
stiffness was due to muscle spasm as any signs of meningeal irritation were absent. The LP subsequently done was negative for meningitis. The leucocyte count was 10300/mm³ [polymorphs 74%, lymphocytes 19% and monocytes 3%] while the ESR was 45 mm at the end of 1 hour.

The computed tomography showed obliteration of the left mastoid air cells with clouding of the mastoid antrum and fluid filled petrous apex. The patient was advised a contrast enhanced MRI but was refused on financial grounds. The patient left the hospital against medical advice and was lost to follow-up.

**Figure 4**

Fig 4: File photo of the patient with left lateral gaze palsy.

**Figure 5**

Fig 5: Shows profuse otorrhoea from her left ear.

**Figure 6**

Fig 6: A contrast enhanced axial CT scan of the patient showing clouding of the left middle ear cleft with enhancement of the left petrous apex.
DISCUSSION

Gradenigo’s syndrome, characterised by persistent otorrhoea, pain in the region innervated by the first and second divisions of the trigeminal nerve and ipsilateral abducens nerve palsy, is one of the complications of middle ear infection. CT and MRI scans provide evidence of this complication. However, there are only a few reports[1],[2],[3],[4],[5],[6] in the literature describing these findings. Gradenigo’s syndrome consist of abducens nerve paralysis, retroorbital pain and middle ear infection. Although classically attributed to petrositis, the syndrome has also been described in association with extradural abscess, pachymeningitis overlying the petrous apex and lateral sinus phlebitis.[6] It is thought that the manifestations of the syndrome result from the extension of the inflammatory process, that begins in the middle ear, to the top of the petrous part of the temporal bone.[7] The raised intracranial pressure itself is, probably due to, a combination of lateral sinus thrombosis and superior sagittal sinus obstruction. The former impedes the cranial venous outflow while the latter impedes the CSF absorption by pacchionian bodies.[8] The main isolated agents are Streptococcus pneumoniae and Pseudomonas aeruginosa. There is also Proteus mirabilis and Staphylococcus aureus, as well as mycobacteria. In immunodepressed patients, cases of otitis media can perpetuate and lead to the development of apical petrositis due to difficulty treated atypical agents. Even when the agent is not isolated the use of a broad spectrum of antibiotics can treat most of the infections. The isolation can be difficult, including by culture methods difficult to cultivate (anaerobic).

The CT scans demonstrate fluid-filled mastoid air cells and sclerosis of the bones and one can assess the degree of periosteal reaction and status of the middle ear structures based on CT scan findings. [2] The MRI scans are best for assessing the soft tissue lesions. These lesions appear hypointense on T1-weighted images and hyperintense on T2 weighted images and enhance following contrast.[7]

The main differential diagnosis includes cholesteatoma and mastoiditis. Other diseases include chondroma, clival chordoma, epidural abscess, cholesterol cyst and rarely metastases. When considers of cranial nerve VI palsy, remember the possibility of a localizing false signal by intracranial hypertension. This can also happen in vascular complications such as venous sinus thrombosis adjacent to the petrous apex. The nonrecognition of Gradenigo’s syndrome can lead to life threatening intracranial complications such as epidural empyema of the posterior fossa, cerebral abscess and cavernous sinus thrombophlebitis.

Management consists of administration of appropriate antimicrobial agents and surgical intervention. However, improvement without the administration of anti-microbial agents has also been described. McHugh et al reported a case of Gradenigo syndrome, where CT scan showed a small mass in the left IAC and MRI showed evidence of petrositis. These lesions showed marked improvement without treatment.[6] The report also underlined the utility of gadolinium enhanced MRI in identifying soft tissue inflammation and intra-osseous disease in the absence of bone destruction.[7] Complications like brain abscess have been described.[5] Homer et al. [8] reported three cases with middle ear infection and sixth nerve palsy without petrositis and raised intracranial pressure. Erosion of the malleus and incus, a loculus of gas in the sinodural angle, opacification of the left mastoid antrum and clouding of the mastoid antrum were the lesions demonstrated in these patients on the CT scan. As otitic hydrocephalus, another complication of the middle ear infection is also associated with abducens nerve palsy, neuroimaging should be employed to differentiate between these two conditions. Surgical treatment is restricted to refractory cases, with intense mastoiditis, intracranial complications and osteomyelitis (9). Patients that have been inadequately treated with non culture-directed antibiotics for otitis media can lead to partially treated infections and to the development of resistant organisms. Thus they could be considering to
surgery. The approach, if considered, should remove as much of temporal bone infected as possible with preservation of hearing and facial nerve functions. This includes mastoidectomy and exposition of petrous apex by media fossa. Circumferential petrosectomy is another option with low risk of morbity (8,9).

CONCLUSION

Gradenigo syndrome is a very rare but serious complication of acute otitis media and should be suspected in the presence of unilateral headache and abducens nerve palsy. The management varies from radical surgery to conservative therapy depending on the clinical presentation.

References

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