Gradenigo's syndrome – A Diagnostic Challenge

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ABSTRACT

We report a case of a 5-year-old healthy child that presented to the emergency department with a 4-day history of prostration, headache, cervical pain, and fever. She had a history of acute otitis media 8 weeks before. She presented a hyperaemic and bulged left tympanic membrane as well as limitation of left eye abduction. Blood tests showed increased inflammatory markers. She performed a cerebral, cervical and ear region computed tomography showing the left mastoid region, left ear, and left petrous apex filled with secretions in relation with mastoiditis and petrositis. A lumbar puncture was performed and treatment with ceftriaxone 100mg/kg/day was initiated. After exclusion on meningitis, the antibiotic was changed cefuroxime 150mg/Kg/day.

She was submitted to a left myringotomy with tympanostomy tube placement and, after, she presented a rapid improvement of cervical pain and headache with no more documented fever. During hospitalization, she performed a magnetic resonance imaging that show signs of mastoiditis and petrosis. There was no evidence of cerebral extension of inflammatory process and all the venous sinus presented preserved flow. At discharge, she was clinically asymptomatic with normalization of inflammatory parameters. At physical examination she still presented limitation of left eye abduction. She completed a total of 6 weeks of antibiotic treatment. Due to persistent VI cranial nerve palsy one month after discharge, an injection of botulinum toxin was performed, with complete resolution.

Keywords
Gradenigo's syndrome, Mastoiditis, Petrositis.

Case Report

A 5-year-old female healthy child presented to the emergency department (ED) with a 4-day history of prostration, headache, posterior cervical pain, and fever (maximum tympanic temperature of 39°C). She was diagnosed with acute otitis media (AOM) 8 weeks before admission. She had a complete Portuguese immunization schedule and there was no relevant family history.

At physical examination she presented cutaneous pallor, a hyperaemic oropharynx without other pathologic signs, and the left eardrum was hyperaemic with no visible bulging. She was apyretic, had no petechia or cutaneous eruptions and meningeal signs (neck stiffness, Kernig and Brudzinski signs) were negative. The remaining physical examination was unremarkable. Blood tests showed normochromic and normocytic anaemia (haemoglobin 10.2 g/dL, MGV 78.4 fL, MCHC 32.3 g/dL), leucocytosis (14900/uL) with neutrophilia (12220/uL) and lymphopenia (1730/uL), thrombocytosis (559000/uL) and elevation of C-reactive protein (CRP) (11.35 mg/dL). Glucose, kidney function, hepatic function, electrolytes, and creatine-kinase were considered normal for age. Blood bacterial cultures were obtained at the same time. The antigen test for group A Streptococcus in the oropharynx and SARS-CoV-2 polymerase chain reaction test were both negative. During her stay in the ED, cervical pain and headache persisted despite adequate analgesia, so she was admitted to the paediatrics department.

On the first day of hospital stay she presented persistent fever and worsening of symptoms, especially posterior cervical pain with...
painful cervical flexion. At revaluation (still during the first day of hospitalization), a hyperaemic and bulged left tympanic membrane was noticed as well as a limitation of left eye abduction. She was observed by a paediatric ophthalmologist that diagnosed paralysis of VI cranial nerve (Figure 1). Considering these physical signs, she performed a cerebral, cervical and ear region computed tomography (CT) showing thickening of the left maxillary sinus, ethmoidal cells and left sphenoidal sinus. The left mastoid region, left ear and left petrous apex were filled with secretions in probable relation with mastoiditis and petrositis (Figure 2). The left sigmoid venous sinus was intact. She repeated blood tests with increasing CRP value (12.4 mg/dL).

A lumbar puncture was performed and treatment with ceftriaxone 100mg/kg/day was initiated.

The cerebrospinal fluid (CSF) cytochemical study had no pleocytosis or other pathologic findings. The Streptococcus pneumoniae antigen in CSF was negative. A CSF bacterial culture was obtained. At this point, after excluding the diagnosis of meningitis, the antibiotic regimen was changed, according to our known local resistances, to intravenous cefuroxime 150mg/Kg/day to cover Staphylococcus aureus, since it is a known cause of mastoiditis.

She was submitted to a left myringotomy with tympanostomy tube placement and to a diagnostic nasal endoscopy. Surgical samples were obtained for bacteriological studies. After this procedure, she presented a rapid improvement of cervical pain and headache with no more documented fever. Furthermore, during hospitalization, she performed a magnetic resonance imaging (MRI) that showed complete left mastoid and left ear filling with inflammatory content. The left petrous apex showed high signal in T2-weighted images due to the extension of the inflammatory process (Figure 3). There was no evidence of cerebral extension of inflammatory process and all the venous sinus presented preserved flow. At discharge, after 13 days of hospital stay, she was clinically asymptomatic with normalization of haemoglobin and leucocytes levels and decrease of inflammatory markers (CRP value of 2.64 mg/dL). The blood cultures of admission, the CSF bacteriological culture and the bacterial studies of the pus drained during ear surgery were negative. At physical examination she had a normal otoscopic exam but still presented limitation of left eye abduction. She completed a total of 13 days of intravenous cefuroxime and 6 weeks of total treatment. She was further referred to paediatric infectiology, ENT and ophthalmology medical appointments. Due to persistent VI cranial nerve palsy one month after discharge, an injection of botulinum toxin was performed, with complete resolution.

Discussion

Gradenigo syndrome is extremely rare in the modern antibiotic era, affecting about 2 in every 100,000 children with AOM [1-4]. It is characterized by the triad of acute otitis media with petrositis, VI cranial nerve paralysis and headache (usually referred to the distribution of the V cranial nerve) [1-3]. The most common clinical presentation in paediatric age is AOM, unspecific headache, fever, and de novo strabismus (ipsilateral to AOM) [3]. The clinical findings are unspecific, difficult to identify particularly in paediatric age and may not be present simultaneously, requiring a high level of clinical suspicion for diagnosis [3]. PETOSIS happens by direct extension of the ear’s inflammatory process or due to spread via venous channels causing obstruction of the petrous apex [1,4]. The period between the occurrence of AOM until the development of petrositis can vary between one to twelve weeks [3,4], what is in agreement with the present clinical report. The neurological manifestations occur due to the involvement of cranial nerves passing next to the petrous apex, so different nerves can be affected besides the VI cranial nerve [2-4]. Gradenigo syndrome can cause life-threatening complications such as meningitis, cerebral venous sinus thrombosis, cerebral abscesses, or empyema and internal carotid stenosis [1-5]. The clinical suspicion of Gradenigo syndrome should lead to exclude the presence of
meningitis and to perform a cerebral CT, due to its sensitivity and low false positive rate [3]. It is an exam with good bone definition that easily identifies mastoiditis and petrositis and excludes other non-infectious diagnosis [3,4]. A cerebral MRI should be further performed to support the diagnosis and completely rule out cerebral venous thrombosis [3]. The treatment should always include at least 3 to 6 weeks of antibiotic treatment, with the antibiotic choice depending on local protocols and bacterial resistances [3-5]. The surgical approaches are not consensual and should be individualized for each patient [1-4], and include myringotomy with tympanostomy tube placement or even mastoidectomy in patients who failed to respond to previous treatments [1-4]. The most consensual treatment is the combination of antibiotic therapy and myringotomy with tympanostomy tube placement with complete resolution in most patients [1,3,4]. Usually, as in this clinical report, the VI cranial nerve paralysis is the last clinical sign to disappear and if it does not happen spontaneously, a non-surgical approach with botulinum toxin can be considered [3,6].

References