Fatal complications of otitis media rarely occur owing to the widespread use of antibiotics to treat otitis media.1 Prior to the availability of antibiotics, complications of suppurative otitis media were more frequent and included meningitis, abscess, petrous apicitis, and death. This article presents the case of a man with diplopia and neck and facial pain who was found to have bilateral mastoiditis and petrous apicitis manifesting as Gradenigo’s syndrome. The clinical presentation, evaluation, and treatment of this rare complication of otitis media are reviewed.

CASE PRESENTATION

Patient Presentation and History

A 76-year-old man with no prior significant past medical history except for a 30 pack-year smoking history presented to the internal medicine clinic for medical evaluation. He had been referred from the otolaryngology clinic with new onset of diplopia of 1 day’s duration.

He was in his usual state of health until approximately 6 months prior to the onset of diplopia, when he had right-sided otitis media that was treated by his primary care physician with a 2-week course of oral amoxicillin-clavulanate followed by trimethoprim/sulfamethoxazole. He continued to have purulent drainage and ear infection on the right side after antibiotic therapy.

Computed tomography (CT) of the mastoids performed 2 months after the symptoms had first occurred revealed changes signifying chronic infection within the right mastoid. The patient underwent mastoidectomy with canaloplasty and placement of a tympanostomy tube on the right side. Cultures taken at surgery grew Pseudomonas aeruginosa sensitive to ciprofloxacin, and the patient was treated with an oral course of ciprofloxacin for 2 weeks.

Approximately 6 months after the original onset of right-sided otitis media, the patient developed tinnitus and otalgia on the left side. He returned to his local physician and was prescribed ciprofloxacin eardrops for the left side. He subsequently underwent tympanostomy tube placement on the left for recurrent otitis media. His infection continued despite surgical drainage, and he was treated with another course of oral ciprofloxacin. Over the 10 days prior to presentation at the internal medicine clinic, he developed dysphagia, neck and facial pain, and hoarseness. On the day prior to presentation, he noticed the new onset of double vision that was more pronounced upon looking to the left.

Diagnostic Evaluation

On physical examination, the patient appeared uncomfortable and was wearing a neck brace due to neck pain. His voice was hoarse. Vital signs were as follows: temperature, 36.0°C; pulse, 106 bpm; respirations, 18 breaths/min; and blood pressure, 157/94 mm Hg. Visual acuity was 20/20 and 20/25 in his right and left eye, respectively. His left eye was unable to abduct (Figure 1). Both tympanic membranes had tympanostomy tubes in place and were draining purulence. The postauricular area was without redness, swelling, or tenderness to palpation bilaterally. The neck had no lymphadenopathy.

The patient was subsequently seen by the ophthalmology service. Further ocular examination revealed that intraocular pressure was within normal limits at 14 and 19 mm Hg in the right and left eye, respectively. Visual field testing was full to confrontation bilaterally. The postauricular area was without redness, swelling, or tenderness to palpation bilaterally. The neck had no lymphadenopathy.

Laboratory studies revealed an elevated leukocyte count. Dr. Quisling is a resident in internal medicine at the University of Iowa Hospitals and Clinics, Iowa City, IA. Dr. Johnson is a professor of medicine, Division of General Internal Medicine, Brody School of Medicine at East Carolina University, Greenville, NC.
count \((13.3 \times 10^3/mm^3)\) with differential of 8525/mm\(^3\) neutrophils, 2793/mm\(^3\) lymphocytes, 1011/mm\(^3\) monocytes, 692/mm\(^3\) eosinophils, and 93/mm\(^3\) basophils. Platelet count and hematocrit were within normal limits. Erythrocyte sedimentation rate was 38 mm/h. Electrolyte levels were within normal limits.

The otolaryngology service was informed of the patient’s new onset of diplopia and the patient was admitted to their service. The possibility of nasopharyngeal carcinoma was raised due to the bilateral otitis media in an older patient with no prior history of ear disease and the patient’s poor response to antibiotic therapy. The patient denied any history of poor compliance, alcohol abuse, or diabetes, which could have lead to the poor response to antibiotics.

At this point, magnetic resonance imaging (MRI) of the orbit and brain was ordered and revealed bilateral fluid in the mastoid air cells and an inflammatory process invading the skull base (Figure 2 and Figure 3). There was no evidence of sinus thrombosis, and the appearance of both orbits on MRI was within normal limits. To further define the extent of the lesion, the patient underwent a gallium citrate Ga 67 nuclear study, which revealed osteomyelitis of the sphenoid bone and the medial aspect of the left petrous temporal bone (Figure 4).

Fluid from the middle ear was aspirated and sent for Gram stain and culture. Rare colonies of *P. aeruginosa* were isolated and were susceptible to cefepime, ciprofloxacin, gentamicin, levofloxacin, and piperacillin. Fungal cultures were obtained and were negative.

**Management**

The patient was taken to the operating room for simple mastoidectomy on the left side to obtain mastoid tissue for pathologic examination and fluid for culture. Both bacterial and fungal cultures from the
mastoid bone were negative and the final pathology report noted necrosis and no tumor. Infectious disease consultation was obtained, and it was recommended that the patient be started on intravenous (IV) cefepime and IV levofloxacin for double coverage of *P. aeruginosa* and IV metronidazole to cover anaerobes as there was no growth of cultures taken at time of left mastoidectomy.

The patient underwent a cookie swallow evaluation, revealing left vocal fold paralysis and poor elevation of the palate, suggestive of cranial nerve involvement. Because of his dysphagia, he was started on enteral feedings. He was discharged home on IV metronidazole and IV cefipime for a total of 7 weeks and IV levofloxacin for a total of 8 weeks. His diplopia was relieved initially by fitting his glasses with prisms. After 8 weeks of IV antibiotic therapy, the patient’s hoarseness, dysphagia, and diplopia resolved completely, except for diplopia with extremes of gaze and with fatigue. The result of an indium-111 leukocyte scan was negative, which was interpreted as no active infection following completion of antibiotics. He continued to be followed by the infectious disease, otolaryngology, and ophthalmology services until the resolution of his infection.

**DISCUSSION**

**Clinical Presentation of Petrous Apicitis**

Petrous apex inflammation has long been known to cause a variety of symptoms, including deep headache or facial pain, diplopia or other signs of abducens nerve (cranial nerve VI) involvement, otorrhea, and facial paralysis from involvement of cranial nerve VII. Dysphagia and hoarseness may also be present owing to involvement of cranial nerves IX and X. The triad of otorrhea, headache, and abducens nerve palsy was first described by Gradenigo in 1907. When present, this triad should alert the physician to consider the diagnosis of petrous apicitis. However, most patients with petrous apicitis do not have all three components of Gradenigo’s syndrome; it has been observed that only 42% of the patients described in Gradenigo’s paper had the classical symptom triad. The most common presentation of petrous apicitis is deep facial pain in the presence of purulent otitis media; cranial nerve signs are variable. The abducens nerve palsy in Gradenigo’s syndrome is caused by inflammation of the petroclinoid ligaments, which affect the abducens nerve as it passes through Dorello’s canal. The facial pain is caused by the direct extension of the infection from the petrous apex to the gasserian ganglion of the trigeminal nerve.

Petrous apicitis manifesting itself as Gradenigo’s syndrome is not frequently seen in today’s hospital practice. Diagnosis is difficult owing to lack of familiarity with the disease and the nonspecific symptoms in the absence of fever. Because there is significant variation in presentation of the disease, the argument over which symptom is more reliable in diagnosis has continued since Gradenigo first described the classical manifestations.

Osteomyelitis of the petrous temporal bone occurs because the petrous apex contains mucosa-lined air cells that can be obstructed by middle ear infection, rendering them particularly susceptible to infection. Petrous apicitis can be acute or chronic. The acute form develops rapidly and is caused by obstruction of the pneumatized petrous apex air cells. The chronic form develops from chronic mastoid inflammation.

**Evaluation and Treatment Monitoring**

Because the mortality rate for intracranial complications of mastoiditis continues to be around 20%, patients with signs of petrous apicitis require urgent evaluation...
with CT or MRI imaging and medical and surgical management. All patients with chronic paresis of the sixth cranial nerve should undergo neuroradiologic investigations to rule out a petrous apex-cavernous sinus mass lesion. CT scan can show destruction of the bones of the petrous apex and skull base, delineating the complications of aggressive otitis media. MRI with gadolinium can suggest the diagnosis by enhancing the signal intensity of infected tissue. MRI may show an ill-defined, irregular increase in signal intensity. MRI has been found to be of little use in determining the extent of the lesion in this setting, however, as bony detail is poor, and thus gallium citrate Ga 67 nuclear imaging is recommended. Ga 67 binds to lactoferrin in inflammatory processes such as infections.

Imaging is an important component of treatment monitoring. Technetium bone scanning is not effective for treatment monitoring because uptake will continue to be abnormal long after the infection has resolved. MRI also may show abnormalities months after the infection has resolved. Gallium scanning is helpful in monitoring the infection and decreased uptake correlates with therapeutic response. Negative uptake on gallium scanning correlates with sterility of the bone. Indium-111–tagged leukocyte scanning is more specific to an inflammatory process such as infection, but further study is needed to determine whether indium or gallium are best for treatment monitoring. In the present case, an indium-111–tagged leukocyte scan was used to confirm resolution of infection.

Treatment

Some authors have suggested that conservative medical treatment without surgery may be considered in some patients. Treatment with oral ciprofloxacin has been successful for malignant otitis externa when the organism is P. aeruginosa. When osteomyelitis of the skull base is present, however, long-term intravenous antibiotics are necessary to eradicate infection. In one case report, oral ciprofloxacin after intravenous antibiotics were initially given could not prevent recurrence of disease. Antibiotic therapy should be guided by tissue culture and sensitivities. Duration should be 6 weeks or greater, and termination of therapy should be guided by negative gallium or indium scanning.

CONCLUSION

There is little recent medical literature regarding the now uncommon condition of petrous apicitis. Few internists or family doctors are even aware of the symptoms of Gradenigo’s syndrome or of osteomyelitis of the skull base as complications of otitis media. Because of the rarity of these complications, it is important to be aware of the potential of otitis media to progress to osteomyelitis. Ophthalmology, otolaryngology, and infectious disease consultations are important in the evaluation and management of these conditions. If the infection spreads into the skull base and osteomyelitis is present, neurosurgical evaluation may also be warranted, especially if epidural abscess occurs. The presence of multiple cranial nerve abnormalities in the setting of otitis media may indicate the presence of osteomyelitis of the petrous temporal bone and possibly of the skull base. Treatment with intravenous antibiotics and close follow up are important to decrease morbidity from these potential fatal complications of otitis media.

REFERENCES