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Malignant otitis externa with subsequent internal jugular vein thrombosis and hypoglossal palsy: a report and review of literature

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ABSTRACT

Inflammation of a part or whole of the temporal bone and surrounding soft tissue is termed as malignant otitis externa, which typically spreads to skull base to involve cranial nerves VII. Rarely can it also effect one or more of cranial nerves IX, X, XI, and XII. We present a case of malignant otitis externa which presented with symptomatic palsy of IX and XII nerves sparing the VII cranial nerve. The patient though later on had internal jugular vein thrombosis, which we presume is due to the involvement of the parapharyngeal space that prompted us to reconsider the diagnosis, and later on, to aggravate the therapy. With proper blood sugar control and appropriate long term antibiotics, not only that the patient is disease free at one year follow up, but the cranial nerve deficits also recovered. Apart from sharing the clinical and management details of this patient, we have reviewed the relevant literature in the discussion, which has shed some light onto some of the interesting facts about this condition and its prognosis.

1. Introduction

Malignant otitis externa (MOE) also known as otogenic skull base osteomyelitis (SBO) is an inflammatory condition of the external ear and adjacent temporal bone that is commonly seen in diabetic patients, and is attributed to Pseudomonas infection (Karaman et al., 2012; Blyth et al., 2011; Chen et al., 2010; Carfrae and Kesser, 2008; Ali et al., 2010; Das et al., 2019; Loh and Loh, 2013; Stern Shavit et al., 2016; Lee et al., 2008; Spielmann et al., 2013). Despite aggressive antibiotic therapy, many of the affected patients have an extension of the disease to surrounding soft tissue and bones of the skull base (Chen et al., 2010; Carfrae and Kesser, 2008). The VII nerve is the most common cranial nerve to be involved in MOE, followed by the lower cranial nerves like IX, X, XI and XII that could result in morbid outcomes (Chen et al., 2010; Ali et al., 2010; Das et al., 2019; Lee et al., 2008; Mani et al., 2007; Huang and Lu, 2006). We had a patient of MOE who received treatment initially but presented later with an unusual cranial nerve involvement along with internal jugular vein (IJV) thrombosis. The purpose of this report is to share our experience in managing this atypical case and discuss some peculiar implications.

2. Case details

A 61-year-male patient with type-II diabetes mellitus initially presented with left-sided ear pain for three weeks. The pain was associated with blood-stained mucoid discharge and reduced hearing on the same ear. He had no history of giddiness or tinnitus, nor did he complain of facial asymmetry or headache. Examination revealed tragal tenderness and edematous external auditory canal with granulation tissue arising from posterior canal wall of the deep meatus, and the tympanic membrane showed grade II retraction. Culture from ear swab grew *Pseudomonas aeruginosa* that showed good sensitivity to ciprofloxacin, amikacin and ceftazidime. His erythrocyte sedimentation rate (ESR) was 56 and the glycosylated hemoglobin was 9.7%. With the clinical diagnosis of uncomplicated MOE and a poorly controlled diabetes mellitus, he was started on injectable ceftazidime and oral ciprofloxacin, along with topical diluted acetic acid ear drops. His blood sugar levels were strictly maintained under permissible limits with the help of Insulin therapy. After taking IV antibiotic and round the clock analgesics for a week, the patient had no signs and symptoms, and hence was discharged with a six weeks course of oral ciprofloxacin

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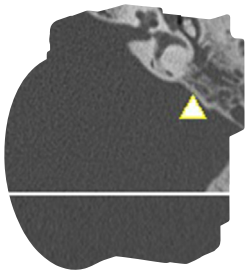

Fig. 1. Plain computed tomography of the temporal bone, axial (A) and coronal (B) images, showing fluid in the left mastoid without any bone erosion(triangle) and normal jugular foremen region(yellow arrow), respectively.

and an Insulin regimen for strict glycemic control.

Within two months of initial episode, the patient presented with a one-week history of slurring of speech and swallowing difficulty along with recurrence of left ear pain. He had no signs of acute inflammation in external ear nor any granulation tissue this time, but the tympanic membrane retraction persisted along with moderate conductive hearing loss. Further examination revealed IX and XII cranial nerve palsies on the left side with the intact VII, X and other cranial nerves on both sides. Radiological evaluation in the form of computed tomography (CT) showed soft tissue density in mastoid air cells suggestive of fluid without any bone erosion, as shown in Fig-1. However, significant inflammatory changes were noted below the region of the temporal bone on magnetic resonance imaging (MRI). The inflammation was seen involving the ipsilateral skull base and the adjacent parapharyngeal space as shown in Fig-2, with thrombosis of the left IJV. His repeat ESR was 74 and the glycosylated hemoglobin was 10.4% reflecting the active disease and the poorly controlled blood sugars, respectively. The patient was re-started on injectable ceftazidime at 2gm 12hourly, oral ciprofloxacin at a twice-daily dose of 500 mg, and was given oral Itraconazole at 200 mg twice a day dose. He was started on subcutaneous injections of low molecular weight heparin and oral warfarin at 2 mg with monitoring of international normalized ratio (INR). Insulin dose was also regularly adjusted for optimal blood sugar control. Given the persistence of ear pain after five days of intravenous antibiotics, and for obtaining the sample for histopathological and microbiological analysis to rule out any other unexpected pathology, he was taken up for cortical mastoidectomy. Intraoperatively, mastoid cells were filled with glue-like material without any significant granulations or bone erosion. The glue was also drained from mesotympanum after myringotomy, and a grommet was inserted. The surgery, though was intended as diagnostic tool in this case, since it drained the fluid from middle ear cleft, it could have got some therapeutic value also. Nevertheless, the pathological as well as culture reports from the middle ear mucosa and the drained fluid were negative for neoplasm and fungal elements, and were consistent with pseudomonas infection sensitive to both of the antibiotics given, similar to the earlier culture report from ear canal.

The intravenous ceftazidime was continued for four weeks, and oral ciprofloxacin for five months, however, the oral antifungal was discontinued after two weeks of initiation. During this period, the patient was monitored clinically for pain relief, for local signs of inflammation and the status of cranial nerve deficits. Repeated measures of ESR was also used for surveillance, however the values were fluctuating between 50 and 80 even after three months of treatment despite patient having no signs and symptoms, and hence was not considered further. The ultrasonography was repeated three monthly for assessing the status of IJV thrombosis and inflammation in the neck. Blood sugar levels were maintained strictly under normal limits by continuous home-based monitoring and Insulin dose adjustment. The warfarin was continued for around four and half months with regular monitoring of INR and was discontinued when the serial Doppler scans showed normal blood flow in the affected IJV. Oral ciprofloxacin was given for two more weeks after that and was stopped based on the clinical and ultrasonographic absence of any disease. At 15 months of completing the treatment, patient is asymptomatic and has no signs of infection in ear canal or in skull base. The palatal movements are normal, and the hypoglossal palsy has recovered. He is on regular follow up with adequately controlled blood sugar levels.

3. Discussion

MOE was the phrase coined by Chandler in 1968 to denote a severe infection that arises from the external auditory meatus and rapidly extends to the temporal bone and adjacent soft tissue (Chandler, 1968). Like in the index case, it is seen commonly in elderly male diabetics in their VI and VII decade of life (Blyth et al., 2011; Das et al., 2019; Lee et al, 2008, 2017). *Pseudomonas aeruginosa* is the commonly isolated organism, representing more than 50% in most of the series, followed by methicillin-resistant *Staphylococcus aureus* and Klebsiella pneumonia (Chen et al., 2010; Ali et al., 2010; Loh and Loh, 2013; Stern Shavit et al., 2016; Lee et al, 2008, 2017; Hobson et al., 2014; Le Clerc et al., 2014). Though the causative organism was identified to be Pseudomonas in our case, the culture reports may not always yield positive results (Ali et al., 2010; Loh and Loh, 2013; Lee et al, 2008, 2017; Spielmann et al., 2013; Le Clerc et al., 2014; Sokołowski et al., 2019). Irrespective of the culture reports, the empirical treatment with ceftazidime and fluoroquinolone combination has been shown to be equally efficacious as culture-directed antibiotic therapy in MOE (Loh and Loh, 2013; Sokołowski et al., 2019). However, since many authors have isolated bacterial strains that are resistant to one or more anti-pseudomonal antibiotics in MOE, it is advisable to get the culture and antibiotic sensitivity test done in all cases (Loh and Loh, 2013; Spielmann et al., 2013; Le Clerc et al., 2014). Apart from the drug-resistant organism, the non-responsiveness to empirical antibiotics could also be due to the fungal infection, which is also not uncommon in MOE (Blyth et al., 2011; Chen et al., 2010; Lee et al, 2008, 2017; Le Clerc et al., 2014). Fungal MOE cases would have an atypical presentation and carry higher morbidity and mortality rates (Blyth et al., 2011; Lee et al, 2008, 2017; Le Clerc et al., 2014). Because of the initial non-responsiveness to culture directed combination anti-bacterial therapy, we presumed fungal etiology and started on anti-fungal treatment in our case. Nevertheless, we did not find substantial microbiological evidence or clinical benefit to continue it for more than two weeks.

Typically, the MOE spreads to contagious sites in a predictable manner. Due to the proximity of stylomastoid foramen to the nidus of inflammation, VII nerve palsy is the commonest as well as the earliest neurological deficit to be seen in MOE (Karaman et al.,

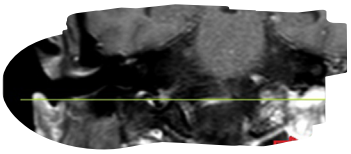

Fig. 2. T1 weighted magnetic resonance imaging pictures, axial (A) and coronal (B) cuts showing the hyperintense lesion in the left parapharyngeal space(brown arrow). Green line represents the level of the jugular foramen, located much above the epicenter of inflammation in parapharyngeal space.

2012; Chen et al., 2010; Carfrae and Kesser, 2008; Spielmann et al., 2013). If the predisposing factors are not controlled or if the infective organism is highly virulent or is resistant to the antibiotic given, the inflammation may progress further inferio-medially to involve lower cranial nerves of the jugular foramen namely, IX, X, and XI, and at times could result in IJV thrombosis or even internal carotid artery thrombosis (Ali et al., 2010; Das et al., 2019; Lee et al., 2008; Spielmann et al., 2013; Mani et al., 2007; Huang and Lu, 2006; Conde-Diaz et al., 2017; Low and Lhu, 2018). If conditions prevail, the skull base inflammation can rapidly extend further medially to involve cranial nerves V and VI at the petrous apex, anteriorly to include temporomandibular joint, zygomatic bone, and posteriorly or superiorly, can enter the intracranial compartment causing meningitis, cerebral infarction or sigmoid sinus thrombosis (Das et al., 2019; Spielmann et al., 2013; Mani et al., 2007; Sikka et al., 2015). Extensive spread of the disease and consequent cranial nerve palsies is the primary reason for morbidity and mortality in MOE.

The absence of classical clinical signs like granulation tissue in the ear canal during the subsequent presentation, with the atypical involvement of the ipsilateral IX and XII cranial nerves, and the sparing the VII nerve could actually lead to the argument of diagnosis not being MOE. However, considering the various circumstantial reasons explained below, the treating team considered the MOE has the most probable diagnosis in the index case and treated it accordingly, obtaining a favorable outcome. Since the first episode of inflammation in the index case started in the left external ear as MOE with the classical signs of canal wall inflammation and granulation tissue in a relatively poorly controlled diabetes mellitus patient, it is improbable to overlook the diagnosis of MOE during the subsequent episode. The symptoms in the same ear within the short span of diagnosing MOE (which is known to have chronic course) prompted us to consider the subsequent episode as sequel of MOE itself. The investigations like culture sensitivity and ESR which supported the initial diagnosis of MOE also showed the same results on the subsequent presentation. The radiological images in the form of CT showed circumferential soft tissue density in the left ear canal as in Fig-1, suggesting on ongoing ear canal inflammation despite the absence of visible granulations clinically. This also is supported by the MRI which shows some hyperintensity of the ear canal on the same side, and the epicenter of inflammation in skull base being in continuity with the floor of ear canal as in Fig-2B. Though the radio-isotope scans repeated during this episode and while on follow up would have been conclusive in this regard, unfortunately we couldn't do it in our case. The other possibility to consider in our case is acute otitis media or acute mastoiditis complicating as thrombosis of sigmoid sinus and IJV thrombosis (Davidoss et al., 2015; Turan et al., 2014). However, when the mastoid was explored, the middle ear inflammation was not significant and there was no involvement of the sinus plate. The partial thrombosis of sigmoid sinuses seen on MRI is probably due to the retrograde progression of thrombus from IJV to sigmoid sinus, as a result of sluggish or hampered blood flow. The MOE is also known to cause jugular foramen syndrome with IJV thrombosis (Low and Lhu, 2018; Kornilenko et al., 2017). However, jugular foremen was also an unlikely site of involvement in our case since the cranial nerves X and XI were normal clinically, and the jugular foremen was not involved radiologically. As shown in Fig-2, the MRI itself revealing the parapharyngeal space as the epicenter of inflammation rather than the sigmoid sinus or the mastoid antrum makes the otitis media an unlikely diagnosis. The overall available clinicoradiological findings put forth the incompletely treated MOE as the probable etiological factor for subsequent parapharyngeal space inflammation and the associated complications in the form of IJV thrombosis and atypical cranial nerve deficits.

The IJV thrombosis in MOE by itself has been reported sparsely and very rarely has this been attributed to parapharyngeal space involvement (Kornilenko et al., 2017; Low and Lhu, 2018; Kornilenko et al., 2017; Davidoss et al., 2015; Turan et al., 2014). On the other hand, though many authors have reported a non-predictable spread of the MOE to involve non-contagious sites belonging to separate compartments causing VI, VII, IX, X, XI, XII nerve palsies in various combinations very rarely these deficits have been thought to be due to parapharyngeal space involvement.(Sokołowski et al., 2019; Conde-Diaz et al., 2017; Kornilenko et al., 2017; Saha et al., 2013; Kulkarni et al., 2005). Interestingly, only once before the index case, there has been a mention of MOE induced isolated XII nerve palsy with sparing of VII nerve (Kasfiki et al., 2013). Moreover, similar to our case, the authors of the previous report also have reported improvement in XII nerve deficit.

Review of the literature revealed that most of these cranial nerves deficits in MOE recover with long term antibiotics, except for the paralyzed VII nerve which shows very low propensity to recover even after decompressive surgery (Mani et al., 2007; Conde-Diaz et al., 2017; Saha et al., 2013; Kulkarni et al., 2005; Kasfiki et al., 2013). However, there is some controversy surrounding the prognostic value of cranial nerve deficits in MOE, wherein some of the authors report it to be predictive of unfavorable outcomes and few others downplay its predictive ability (Loh and Loh, 2013; Stern Shavit et al., 2016; Lee et al, 2008, 2017; Mani et al., 2007; Hatch et al., 2018; Soudry et al., 2007). Nevertheless, the involvement of multiple cranial nerves, especially those affecting the swallowing like the IX and the X is likely to have a harmful effect. Persistent aspiration not only hampers the general wellbeing but could also worsen the underlying medical morbidity predisposing to poorer outcomes. We believe the sparing of X

cranial nerve in the index case had a crucial rule in surmounting the disease and in achieving the favorable prognosis. The other factors that are shown to be associated with poor survival in the literature are older age, male gender, poorly controlled diabetes mellitus, uncontrolled immunosuppression, extension of disease to multiple sites especially to jugular foramen, petrous apex or clivus and fungal infection or mixed infection (Blyth et al., 2011; Loh and Loh, 2013; Stern Shavit et al., 2016; Lee et al, 2008, 2017; Hatch et al., 2018). The overall mortality rates in MOE have been reported to be around 2.5%–15% in recent times (Blyth et al., 2011; Das et al., 2019; Spielmann et al., 2013; Hatch et al., 2018). More than the surgical treatment and the time of initiation of therapy, the long duration of antibiotic treatment and the adequate control of underlying diabetes seem to be the best predictors of the favorable outcome in MOE (Lee et al., 2017; Hatch et al., 2018; Khan et al., 2018). The reported duration of prolonged antibiotic therapy to completely eradicate the infection in MOE varies from three months to 11 months (Conde-Diaz et al., 2017). During the course of prolonged antibiotic therapy the activity of disease can be monitored by the biochemical assay of acute phase reactants like ESR or C-reactive protein as well as by the radiological studies like gallium scan or single-photon emission -CT (Lee et al., 2017; Conde-Diaz et al., 2017). However, follow up with repeated assay of ESR was not correlating with clinical improvement in our case and hence was not considered for treatment planning. We sparsely used the radiological imaging in our case due to some of the technical issues, and relayed our decision mainly on clinical and sonographic findings. Along with the favorable clinical parameters like sustained improvement in pain and consistently normal blood sugar levels, we utilized Doppler evidence of IJV recanalization as one of the predictors signifying the resolution of inflammation, as well as for discontinuing the anticoagulants, and subsequently, the antibiotics.

4. Conclusion

MOE is a rapidly progressive disease of the temporal bone and surrounding skull base, commonly seen in elderly diabetic patients having poor glycaemic control. We think the MOE is the most probable cause for parapharyngeal space inflammation and IJV thrombosis along with IX and XII nerve palsies seen in our case. Though VII nerve is most commonly involved, the infection can at times spread to non-contagious sites like middle ear cleft, jugular foramen and parapharyngeal space causing deficits of one or the other lower cranial nerves or thrombosis of the IJV. Literature review supports that the long term antibiotics and adequate control of underlying medical morbidity are critical in achieving favorable outcomes, which can even reverse the cranial nerve deficits except that of VII nerve.

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Declaration of competing interest

None.

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Appendix A. Supplementary data

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