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Case report

ANTERIOR AND POSTERIOR PARALYSIS ASSOCIATED WITH RAPIDLY EVOLVING MALIGNANT OTITIS EXTERNA AND CO-INFECTION OF SARS-COV2

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ABSTRACT

Malignant otitis externa (MOE) also known as skull base osteomyelitis or necrotizing otitis externa, is a rare inflammatory and infectious condition mainly caused by Pseudomonas Aeruginosa, mainly affects elderly, diabetic and immunocompromised patients. Due to the rapidity of development, it is associated with a high rate of motility/morbidity. In this case report, we describe a rare neurological presentation in a 58-year-old male patient, diabetic, who presented with onset of right otitis externa associated with otalgia, otorrhea, and ipsilateral headache. The auricular swab was positive for Pseudomonas Aeruginosa, the necrotizing inflammation evolved rapidly with progressive clinical involvement of right cranial nerves VII, V, X (Right recurrent laryngeal nerve), III, IV, VI. The role of imaging was to confirm the initial oto-mastoid involvement and to specify the extent of the lesion. CT-scan assessed bone involvement and the MRI delineated the extent of the inflammatory pathology. During the first months of his recovery, the patient contracted SARS-COV-2 infection, which induced a clinical and radiological worsening of the initial pattern in relation to the hypoxemic states achieved in the course of interstitial pneumonia. Finally the patient was treated with Meropenem 1 g ev per day. At the end of treatment, the patient presents almost complete resolution of pathology on both clinical and radiological bases. The aim of this manuscript is to report the management and treatment of a rare case of MOE co-infected with SARS-COV-2.

1. Introduction

Malignant otitis externa (MOE) is a potentially life-threatening infection of the external ear canal, skull base, and nearby soft tissues. Osteomyelitis of the temporal bone associated with necrotizing otitis externa has been described in the literature as early as 1838 (1).
The term "malignant" was first used in 1968 by Chandler to reflect the ominous outcome of the condition (2), some prefer to use the terms "necrotizing," to make the point that MOE is not a neoplastic condition (3).
The pathology usually occurs with otalgia that comes and goes radiating to the frontotemporal and parietal regions, associated with purulent and foul-smelling otorrhea (4).
The extension to the skull base of the inflammatory pathology leads to suffering of the cranial nerves and structures therein, this places the pathology in a particular area of severity, as it places the patient at serious risk of life. The facial nerve is the most involved cranial nerve (5).
The most common etiologic agent is Pseudomonas Aeruginosa, identified in 1959 (6). This bacterium is able to initiate an infectious process through small traumatic lesions on tissues (4). MOE is usually unilateral, but bilateral cases have also been reported in the literature (7).
The aim of this manuscript is to report the management and treatment of a rare case of MOE co-infected with SARS-COV-2.

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2. Case report

We report the case of a 58-year-old male patient, hypertensive, decompensated untreated diabetic, who reports onset of right otalgia, associated with otorrhea and persistent headache for several days. On clinical examination: the patient presented with a red, edematous severely painful outer ear with pus discharge.

Clinical history reported any drug allergies, an ear swab is performed, and in the meantime, therapy with Amoxicillin-Clavulanic acid (1 tablet every 12 hours for 6 days) is initiated, associated with topical therapy (Ciprofloxacin-Desamethasone 3 times daily). The dietary/behavioral lifestyle profile is regularized and insulin therapy is started, as directed by specialists to optimize the glycemic profile.

With persistence of symptomatology and bacteriological sample that allowed isolation of Pseudomonas Aeruginosa (aerobic gram-negative bacterium) treatment with Ceftazidime (C3G) and fluoroquinolones is initiated for 6 weeks, in combination with topical preparations and local care. The histology examination was unspecific, resulting in a diagnosis of "inflammatory polyp."

During treatment, the patient was admitted to Unit of Infectious Diseases for SARS-COV-2 pneumonia, during hospitalization he manifested a severe urticarial reaction to antibiotic treatment, so therapy with (Piperacillin-Tazobactam 4.5 g every 6 hours in 1-hour infusion) was initiated.

Severe respiratory failure induced by SARS-COV-2, forcing the patient to non-invasive mechanical ventilation (NIV) support in order to improve gas exchange and reduce respiratory work. Hypoxemic states associated with the aggressive inflammatory showed clinical and radiological worsening of the picture, with appearance of peripheral paralysis of the right cranial VII nerve.

The rapid development of the inflammation led within about 20 days to a clinical catastrophy, due to involvement of the: X (Right Recurrent Laryngeal Nerve) with marked dysphonia, Involvement of the III, IV, V, and VI ipsilateral cranial nerves with marked diplopia, strabismus (corrected in the early stages with eye wraps and prism), and marked neuralgia.

CT-scan with contrast agent, made it possible to evaluate the osteo-disruption and vascularization of the affected anatomical districts, identifying the apex of the petrous temporal bone as the origin of the infectious-inflammatory-necrotic process. (Figure 1a-b).

The nasopharyngeal swelling was biopsied for further diagnosis, with a histological finding of "Submucosal lymphoid hypertrophy".

Radiological evaluation of the affected anatomical district by contrast-enhanced MRI method better delineated the limits of the pathological process (Figure 1c-d-e).

Vocal recovery with nomal vocal cord motility, good regression of diplopia and strabismus.

At approximately 2 months after starting Meropenem treatment, MRI radiological evaluation with contrast agent is performed, which shows good pathological regression (Figure 3b-c).

Antibiotic treatment was continued until complete resolution of the inflammatory process, (evidenced by PET/CT-scan study with glucose tracer) with initial epicenter in the right oto-mastoid site, always taking care in performing constant hematologic/functional monitoring.

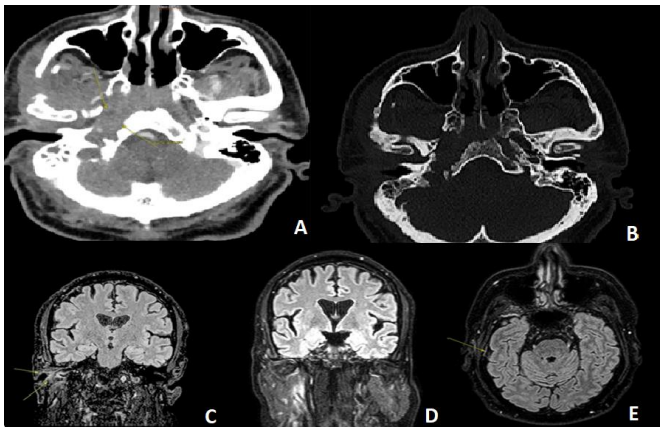

Figure 1. A. CT-scan with contrast agent)- Transverse plane: Pathologic tissue with epicenter at the level of the apex of the right petrous bone, with swelling of the vault of the nasopharynx. Posteriorly medial extension of the right prevertebral and carotid spaces with abscessing of the ICA. Posteriorly extending to the ipsilateral jugular foramen and hypoglossal canal. Infiltration of the right jugular vein appearing filiform; B. CT-scan Tranverse plane: Osteodisgregation of the petrous apex, clivus, and right occipital condyle. Also right tissue component in the right masticatory space. Bony remnant of the right zygomatic arch; C. MRI with contrast agent- Coronal plane. Concentric thickening of the mucosal-submucosal planes along the walls of the external ear canal, with stenosis of its lumen, T2 sequence; D. MRI with contrast agent- Coronal plane. Hypersignal extending: Postero- inferiorly to the insertion of the sternocleidomastoid muscle, anteriorly to the mandibular condyle, laterally and cranially to the temporalis muscle. Caudally, the tissue reaches to affect the deep portion of the ipsilateral parotid gland as far back as the lateral wall of the oropharynx.; E. MRI with contrast agent, Tranverse plane: dural thickening is denoted in the right temporal region

In view of the clinical/radiological situation, the diagnosis of necrotizing otitis externa was maintained.

MRI is the most preferred modality for the study of soft tissue and is crucial in advanced forms. However, these modalities do not allow differential diagnosis, therefore there is a lack of specificity with tumor processes (8)(9). It is then decided to perform a PET/CT study (with glucose metabolic tracer) (10), (Figure 2) and start IV treatment with Meropenem (1G TID/die).

In the view of SARS-COV-2 negativization and pulmonary functional restoration (SpO2 98% in ambient area), there was evidence after about 30 days of Meropenem therapy, a clear improvement of symptomatology with complete regression of right otalgia, otoscopic objectivity (Fig.3a), evidence of total regression of auricular inflammation.

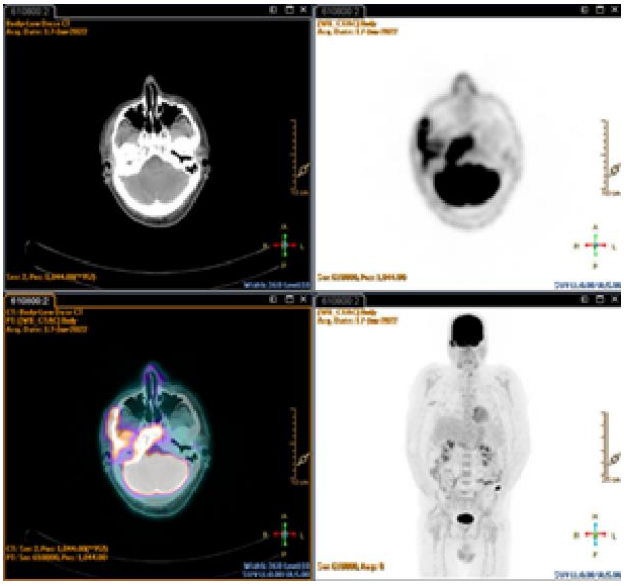

Figure 2. PET/CT-scan with 18F-FDG: High tracer uptake at the right foramen lacerum involving the apex of the ipsilateral petrous temporal bone, clivus and the vault of the nasopharynx, extending to the ipsilateral jugular hole. Uptake area at right temporomandibular joint with extension to ipsilateral zygomatic arch and preauricular region.

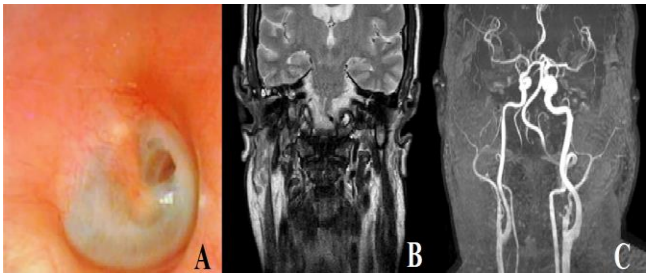

Figure 3. A. Right otoscopy, sequel perforation; B. MRI with contrast agent IV. Coronal plane: Reduction in volume and extent of pathologic tissue at intense enhancement, with right oto-mastoid epicentre; C. Magnetic Resonance Angiography. Transversal plane: Partial restoration of the vessel diameter of the intracranial tract of the right internal carotid artery.

4. Discussion

MOE is an aggressive, soft tissue infection of the external ear, which can involve the periosteum and skull base bone. It needs an initial diagnosis of suspicion and long-term therapy that requires regular monitoring. Kwon et al., described four patterns of infiltration of the pathology:

- medial spread,
- anterior,
- cross
- intracranial.

The main complication of MOE is cranial nerve involvement, especially the facial nerve (11). This infection is frequently seen in elderly patients, diabetics and patients with hematological disorders (12).

Diabetes mellitus predisposes to MOE as it induces microangiopathy in the ear canal, impedes leukocyte and antibiotic chemotaxis, resulting in greater susceptibility to infection and slower healing time. (13-15)

One study found that patients older than 70 years had a 5-year survival of 44%, while patients younger than 70 years had a 5-year survival of 75%. (16) MOE is rare in children, where a higher incidence has been reported in children with diabetes (17), IgG deficiency (18), IgA deficiency (19), leukemia (20), neutropenia (21), and after bone marrow transplantation. (22)

Other risk factors include immune deficits,such as human immunodeficiency virus (HIV) patients, transplant patients, patients with advanced stages of cancer, and radiation treatments. (23-24) The pathogen most involved is Pseudomonas aeruginosa, in 50-90 % of MOE cases. It is a gram-negative obligate aerobic bactereum. (25)

Other pathogens such as Proteus mirabilis, Aspergillus fumigatus, Proteus spp., Klebsiella spp. and Staphylococci have been described in the literature (26). The most common symptoms are otalgia, otorrhea, muffling and hearing loss. Many of the symptoms of otitis externa are common to MOE, which can make diagnosis difficult and may lead to a delay in treatment (27).

The complications most described in the literature are: osteo-mielitis, paralysis of cranial nerves, especially VII, meningitis, and brain abscess (28).

The diagnosis of MOE is established by a series of clinical, laboratory, and radiographic findings. When a patient with diabetes reports persistent otalgia, otorrhea, hyperemia, edema of the CUE, presence of granulation, the possibility of MOE should be considered (29).

The criteria for making a diagnosis of MEO are based on at least three of five of these signs and symptoms:

1. Persistent inflammation of the CUE;
2. Granulation tissue in the external auditory canal;
3. Radiographic confirmation of osteomyelitis of the external auditory canal, mastoid cells and/or skull base;
4. Basicranial involvement;
5. Isolation of P. aeruginosa (30-31).

Useful is the evaluation of inflammatory markers: erythrocyte sedimentation rate (ESR), white blood cell count, PCR (C-reactive protein), which may be significantly increased in patients with MOE (32).

CT scan of the temporal bone is the investigation of choice for initial evaluation and to define the affected bone boundaries. Magnetic resonance imaging is the complement to CT scan, allowing analysis of soft tissue involvement and possible intracranial complications.

PET-CT studies, are used to evaluate osteomyelitis and response to treatment (33). Courson et al. (34) performed a meta-analysis to determine the most accurate method, they deduced that FDG PET-CT is an accurate method in the evaluation of osteomyelitis, at the same level with bone scintigraphy with 99mTc and Ga67. The combination of radiological and radionuclide studies plays a crucial role in the diagnosis and follow-up of this disease. (35) The diagnosis of malignant external otitis requires a multidisciplinary approach. In addition to the radiologist, the figure of the infectiologist is crucial, so as to set up appropriate antimicrobial therapy in order to prevent bone destruction and further spread of MOE to intracranial structures. (36-37)

The use of oral and topical fluoroquinolones in the treatment of MOE, has greatly reduced the necessity of hospitalization [38]. These antibiotics, have excellent bone distribution, making them a first-line therapy. (39-40)

Oral ciprofloxacin is the most widely used, with a 6- to 8-week schedule at a dosage of 750 mg twice daily. (41) If resistance to quinolones is present, good alternatives are: piperacillin-tazobactam, ceftazidime, cefepime, and meropenem. (42-43) The combined use of semisynthetic penicillin and aminoglycosides is recommended only if multiresistance is shown in the antibiogram (44). The increasing prevalence of therapy-resistant organisms makes the collection of culture and tissue samples, essential. Culture results should be evaluated before the initiation of antibiotic therapy. Because MOE can reoccur up to a year after completion of treatment, it is essential to follow these patients for at least a year after treatment (45).

Hyperbaric oxygen therapy may be an effective treatment option in unresponsive or advanced cases. However, its efficiency remains unproven due to the lack of strong scientific evidence. Its therapeutic value should not be underestimated considering the good results and few adverse events reported (46). Nuclear imaging is recommended to assess response to treatment. Inflammatory markers, such as erythrocyte sedimentation rate, leukocyte count, and C-reactive protein, combined with periodic radiological examinations, can also be used to assess disease progression (47). Gallium scanning is the imaging of choice for follow-up, as it returns to normal once inflammation is reduced (48). FDG-PET/CT can be a good alternative; it has been seen in the literature to have excellent sensitivity and specificity for both diagnosis and follow-up (49).

Surgery should be considered in cases of advanced symptoms, central involvement, severe facial nerve palsy, refractory MOE, defined as no clinical improvement after six weeks of conventional treatment (50). Surgery in the severe forms, allows reduction of local infectious, also removes necrotic tissue and allows growth of healthy tissue, which increases local vascularization and allows systemic anti-biotics to reach the required area (51). The treatment must be individualized on a case-by-case basis, with multidisciplinary cooperation between the specialties in order to set the most appropriate therapy.

5. Conclusions

MOE is a rare but life-threatening condition that can evolve with severe neurological complications. Facial nerve palsy is certainly the most frequent clinical finding, but other times the clinical evolution can be nonspecific, making early diagnosis more difficult. It is important to setup specific therapy as soon as possible due to the variability in response of the trigger agent, and most importantly, it is critical that the patient be fully confident with the diagnosis and medical therapy set. It is important to inform the patient about the disease, the importance of food/behavioral routines for regular control of glycemic parameters, its evolution, and the long treatment that is essential for its eradication. Imaging allows to confirm the diagnosis and to make an increasingly specific assessment of the pathological extent, as well as to allow close follow-up of patients, due to the very high sensitivity/specificity of the procedures and the possibility of combining conventional radiological examinations with more specific radionuclear examinations. In the past surgical eradication was the treatment of choice, but currently due to the wide medication choices available to us, it is reserved for tissue sampling and occasionally for debridement

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