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Case Report

Bilateral diffuse temporal bone osteoradionecrosis: a diagnostic and therapeutic challenge

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ABSTRACT

Temporal bone osteoradionecrosis (TBORN) is a rare complication of head and neck radiotherapy. It usually presents as a unilateral disorder with a long latency between the exposition to radiation and the symptoms onset, which might overlap with other clinical entities, making it difficult to establish the diagnosis. It can be classified as localized, when confined to the tympanic bone; or diffuse, when extended to other portions of the temporal bone, with the inherent implication in treatment selection and prognosis. The authors present a case of a 53 years old patient with multiple comorbidities, including an immunosuppressive state, who presented an infected massive diffuse TBORN bilaterally. The diagnosis was challenging and the patient was initially treated for a malignant otitis externa, but after established diagnosis of TBORN, the patient was treated resorting to surgery, topical treatment and hyperbaric oxygenotherapy, with consequent symptoms resolution. This case illustrates the difficulty in establishing the diagnosing and treatment of TBORN and highlights the importance of a low suspicion threshold for this rare complication of radiotherapy, for which there is still no consensus regarding the best treatment.

Keywords: Temporal bone, Osteoradionecrosis, Necrosis, Radiotherapy, Mastoidectomy

INTRODUCTION

Exposure of the temporal bone to radiation might lead to several complications such as sensorineural hearing loss, chronic otitis media and osteoradionecrosis.[1] TBORN is a rare complication of patients undergoing radiotherapy in head and neck, usually presenting several years after the exposition to the radiation and usually as a unilateral disease, being extremely rare a bilateral presentation.[2]

The presenting symptoms are not pathognomonic and include otorrhea, hearing loss, otalgia, tinnitus and facial nerve palsy, being transversal to other otologic pathologies, which makes the diagnosis challenging, even more considering the latency of their presentation after the exposition to radiation.[2] TBORN can be classified as localized, when confined to the tympanic bone; or diffuse, when extended to other portions of the temporal bone. The distinction has inherent implications in treatment selection and prognosis.[3] Unfortunately, due to the rarity of the disease, there is a lack of evidence to support optimal treatment guidelines and the current treatment recommendations are suggested by a few case reports and case series.

The objective of this article is to present and discuss a rare and challenging case of extensive bilateral diffuse TBORN, contributing to a reinforcement of the scarce bibliography regarding this pathology in the literature.

CASE REPORT

A 53 years old male, with a past habit of drug abuse (heroin and cocaine) but no active consumption for about

12 years presents a medical history positive for a human immunodeficiency virus (HIV) infection and an acquired immune deficiency syndrome (AIDS), as well as previous treated hepatitis C virus (HCV) infection, cerebral toxoplasmosis and pulmonary tuberculosis. He was diagnosed in 2010 with a primary cerebral non-Hodgkin's lymphoma, reason why he underwent holocranial radiotherapy and surgery, with a spastic left hemiparesis as a sequel. This patient was also diagnosed with a chronic myeloid leukemia (CML) in 2015 and in 2018 he had neurosurgery for a head trauma, with a resultant chronic subdural hematoma. He is currently under treatment for the HIV infection, presenting a good viral load control, and for CML with good disease control.

The patient was referred to the emergency department of otorhinolaryngology (ORL) with complaints of longstanding bilateral otalgia, otorrhea and hearing loss. He had been previously treated with courses of topical and systemic antibiotics for recurrent otorrhea, for more than two years. At presentation, the patient was febrile with intense pain and on the otologic examination a profuse otorrhea was evident, with edema of the skin, some granulation tissue and areas of bony exposure with some sequestered bony fragments on the ear canal bilaterally, as well as some debris. Tympanic membrane seemed intact on both years and on the right ear, it was slightly bulged and a retro auricular fistula with purulent discharge was present. Blood tests were performed, of notice: 4100 leucocytes/ul, 2900 neutrophils/ul, sedimentation rate 3 mm/h (which increased to 98 mm/h one week later), a negative C-reactive protein (1.49 mg/dL). The patient underwent imaging evaluation with computerized tomography (Figure 1) where it was evident a non-specific soft tissue opacification of the middle ear and external canal, with a massive temporal bone destruction in both ears. This bone destruction involved the ear canal, the temporomandibular joint, the ossicular chain and the mastoid where, an extensive coalescence and a dehiscence of the fallopian canal on both tympanic and mastoid portions was evident, as well as a right lateral semicircular canal erosion.

Ear discharge was collected for microbiologic culture, which came negative and a biopsy of the right ear canal was performed. The patient underwent a magnetic resonance imaging (MRI) to exclude infectious intracranial complications. Besides chronic subdural hematoma and encephalic changes of the patient, the MRI revealed an increased signal of the inner ear and the facial and vestibulocochlear nerves in the inner auditory canal, after gadolinium injection, suggesting labirintitis and neuritis (Figure 2). Lumbar puncture and hemocultures were negatives.

Audiometric evaluation was performed, despite important limitations in its execution due to the clinical condition of the patient, revealing a cofotic right ear and a severe mixed hearing loss on the left (Figure 3), according to the WHO classification.[4]

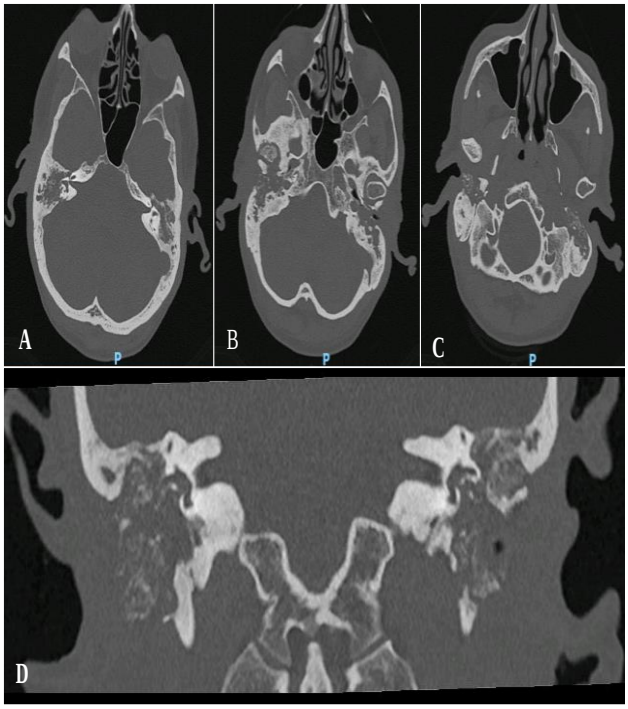

Figure 1 (A-D): CT scan showing a bilateral soft tissue opacification of the middle ear and ear canal and a diffuse temporal bone destruction with bone sequestrum. This bone destruction includes the anterior wall of the ear canal, with an involvement of the temporomandibular joint, the posterior wall of the ear canal in contiguity to the mastoid which is also highly destroyed, the inferior and superior walls of the ear canal and the ossicular chain with no identifiable ossicles. Of notice, also a complete dehiscence and exposure of the facial nerve in both the tympanic and mastoid portions bilaterally, as well as an erosion of the lateral semicircular canal on the right.

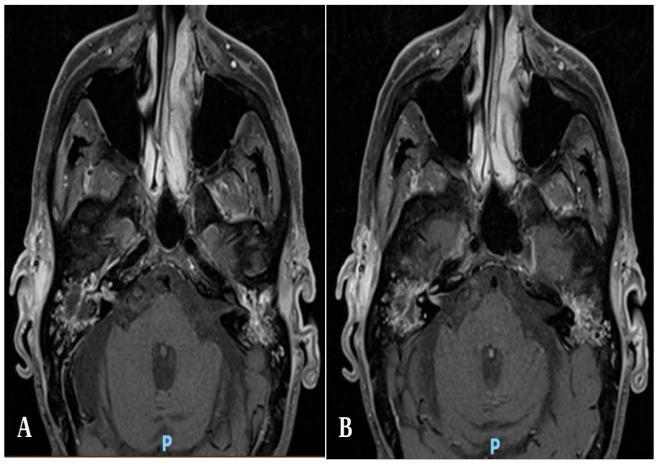

Figure 2 (A and B): MRI after gadolinium injection, where an increased sign of the right inner ear and the facial and vestibulocochlear nerves at the inner auditory canal is evident, suggesting labyrinthitis and neuritis.

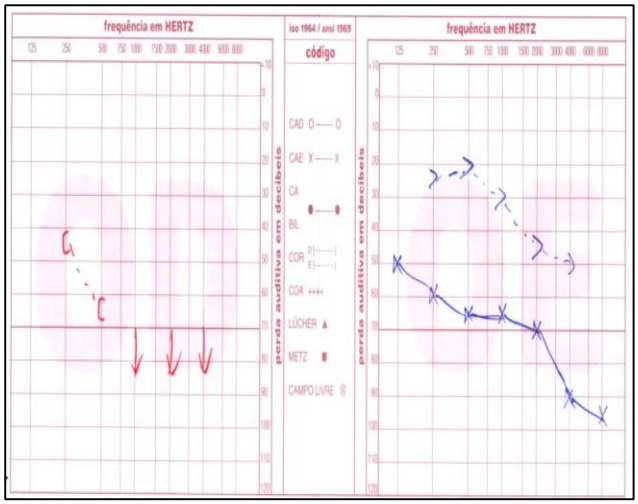

Figure 3: Audiometric examination at presentation.

Several pathologies were considered in the initial differential diagnosis, including necrotizing otitis externa (NOE), malignancy, cholesteatoma and a complicated otitis media. A biopsy of the right ear canal was negative for malignancy, but suggestive of cholesteatoma. It was not possible to exclude both a NOE with middle ear involvement or a complicated otitis media extended to the external ear, but considering the immunosuppressive status of the patient and the clinical and laboratory findings, a presumptive diagnosis of NOE was made and the patient was admitted to the hospital for clinical surveillance and intravenous antibiotic treatment. No microbiological agent was identified and the patient was treated empirically with ceftazidime for 8 weeks and voriconazole, as well as regular aural toilet and topical antibiotic treatment. Unfortunately, due to a patient's SARS-COV2 infection during the hospital stay and COVID-19 restrictions, it was not possible to perform nuclear medicine imaging to confirm the diagnosis of NOE ad initium. Considering the extension of the disease and diagnostic uncertainty, the patient was also eligible for surgical intervention, aiming an exploratory procedure with tissue debridement, as well as a representative tissue harvest for cultural and pathologic examination. Unfortunately, once again, due to the patient's COVID-19 infection, the surgery was deferred until clinically fit for the anesthetic process.

Six weeks after beginning the antibiotic treatment, the symptoms persisted, despite some clinical improvement and the patient underwent surgery. A wall down tympanomastoidectomy was performed on the right ear, where an extensive bone necrosis and sequestrum was found, with distortion of the external and middle ear anatomy. No cholesteatoma was found. Tissue debridement was performed and a widespread facial nerve dehiscence and exposure was found on the tympanic and mastoid portions. Although the neurophysiological monitoring of the facial nerve and surgical care, a right facial palsy grade V of House-Brackman (HB) classification resulted after he surgery, possibly due to a conjugation of traumatic manipulation and inflammation, and eye protection measures and steroid therapy were implemented. Tissue samples were sent to microbiological culture and histologic evaluation, once again with no identified agent and negative for malignancy, but with keratin debris suggestive of cholesteatoma.

Considering the clinical presentation, surgical findings with diffuse bone necrosis, the history of previous exposure to radiotherapy, as well as the results of a gallium scintigraphy performed at 8 weeks of treatment, with no evidence of osteomyelitis, the diagnosis of diffuse TBORN was assumed.

Four weeks after the first surgery, an extended wall down mastoidectomy was performed on the left ear and, besides an extensive bone necrosis, a large retraction pocket with cholesteatomatous matrix was found at the mastoid, which seemed to be secondary to the bony destruction of the posterior wall of the external ear canal. A microbiological sample was collected during the surgery and a multiresistant *Corynebacterium* was cultured. According to the antibiogram, the patient was treated with doxicyclin for 7 weeks and topical vancomycin on the right ear, as well as bilateral acidification of the cavity and regular aural toilet. Hyperbaric oxygen therapy (HOT) was offered to the patient as an adjuvant treatment, and the patient completed forty sessions.

The patient symptoms subsided after surgery and concurrent treatments, with the exception of the hearing loss and the right facial palsy. However, an audiometric improvement was achieved bilaterally (Figure 4) and the facial palsy improved to a HB grade IV. At the last follow up visit, seven months after the presentation, a complete epithelization was achieved on the left ear, whereas on the right a small area of exposed bone with some granulation tissue is still evident on the mastoid cavity, for which a conservative care has been taken on follow-up. Informed consent for publication was provided.

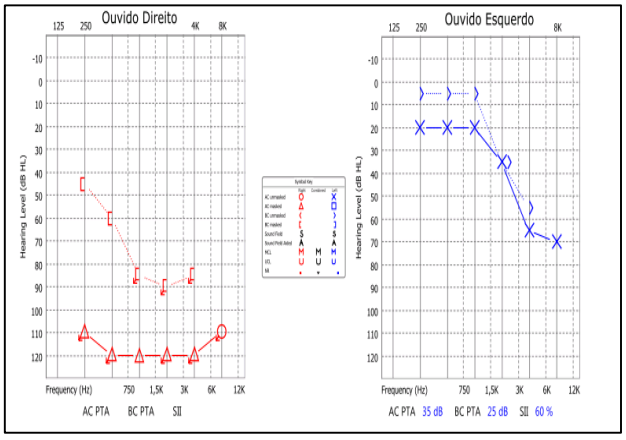

Figure 4: Audiometric examination after treatment.

DISCUSSION

Bone necrosis induced by radiation therapy was firstly described in 1926 by Ewing as a "radiation osteitis" but the involvement of the temporal bone as a complication of radiotherapy was only documented for the first time in 1952.[5,6] TBORN is a rare complication, occurring in up to 8.5% of all head and neck radiation patients, most commonly nasopharyngeal carcinoma (36,6%), parotid tumors (20,1%) and external ear canal pathology (16,3%).[2,7] The basic histologic explanation is an avascular necrosis through an obliterative endarteritis induced by radiation. Temporal bone, particularly the tympanic ring, is specially at risk due to its superficial location, the thin layer covering, delicate blood supply and its exposure to the flora of the upper airway.[8]

According to a systematic review by Yuhan, the mean age at the time of diagnosis is 52 years old, but it can occur at any age, ranging from 3.5 to 96 years.[2] TBORN presents mainly as a unilateral disease (97% of the cases), being extremely rare the bilateral involvement and, usually, a long latency exists between radiotherapy and symptoms onset (mean time of 7.9 years, ranging from 0 to 48 years), which makes it difficult to establish the diagnosis. Besides that, the most common presenting symptoms are otorrhea (40%), hearing loss (29.1%), otalgia (17%), tinnitus (8%) and facial nerve palsy (2.9%), overlapping the presentation of other usual otologic diseases and making the diagnosis even more challenging. Our patient is an example of this description and for whom the diagnosis was also delayed and difficult to establish. In this case, considering the patient's immunosuppressive status and the persistent otorrhea and intense otalgia, as long as the bone destruction and an increased sedimentation rate, the first diagnosis considered was a NOE, which is more common than TBORN. Unfortunately, it was not possible to perform a nuclear medicine scan to confirm the diagnosis ad initium and it was only undertaken 8 weeks after the beginning of empiric antibiotic treatment, which result was negative for active bone infection at that time. Nevertheless, one diagnosis is not exclusive of the other, considering that bone exposure and necrosis by TBORN predisposes to ear infection. On the other hand, the role of the infection in the pathogenesis of TBORN is not established. It is still unknown if bacteria are a cause for TBORN but invariably complicate and prolong its course, leading to difficult to treat infections by a biofilm formation, along with a compromised vascularization of necrotic bone, which limits systemic drugs to reach the target.[9] Other diagnosis to be considered in cases with this presentation is malignancy and a biopsy should be undertaken to rule it out. A cholesteatoma must also be included in the differential diagnosis, considering that it can lead to bone destruction and each of the symptoms of TBORN. Curiously, in this patient, a cholesteatoma was found at the mastoid of the left ear but the extension of bone destruction in both ears and the location of the cholesteatoma led the authors to consider that the cholesteatoma was not the primary disease responsible for the clinical presentation but instead a consequence of that bone destruction towards the mastoid caused by TBORN. In this case, a complicated otitis media should also be included in the differential diagnosis but due to the massive involvement of the middle and external ears, it could not be completed ruled out. However, considering the extensive bilateral involvement around the external ear canal, the lack of acute inflammatory markers on blood tests, the immunosuppressive status of the patient, the imaging and the previous diagnosis of otitis externa with several courses of antibiotics made the diagnosis of NOE more likely at that time.

The diagnosis of TBORN is established when a persistent necrotic bone exposure is present within the external ear canal in a patient previously treated with radiotherapy to the head or neck.[8] According to Ramsden, it can be classified as localized, when confined to the external ear canal and tympanic bone or diffuse disease, when extended to other portions of the temporal bone, including labyrinth, facial nerve, temporomandibular joint or intra-cranially.[3] Usually, the localized form is associated to a less intense symptomatology, while the diffuse disease is associated with a severe otalgia and profuse otorrhea, along with a loss of the architecture of the temporal bone.

Regarding the treatment of TBORN it is primarily directed to symptom control rather than complete resolution or removal of necrotic bone and the therapeutic options include both conservative or surgical measures. However, due to the rarity of the disease, there is a lack of evidence to support optimal treatment guidelines and the current treatment recommendations are suggested by some case reports and case series. It seems to be consensual that for localized disease conservative measures are appropriate, which might include regular aural toilet, topical oxygen peroxide, acidification, topical or systemic anti-microbiologic drugs and local debridement of necrotic tissue. However, in cases of diffuse TBORN, as well as in cases with major symptoms or refractory to conservative measures, uncontrolled infection, progressive disease with cranial neuropathies or when a cholesteatoma is present surgery might be indicated and it includes mastoidectomy, subtotal petrosectomy or lateral temporal bone resections, with or without flap obliteration.[8,10] Regarding the treatment outcomes, according to the systematic review by Yuhan, 89% of the cases treated with conservative measures were considered successful with adequate symptom control, whereas in the surgically treated patients, the success was dependent on the surgical technique: 93.8% in the subtotal petrosectomy, 90.9% in lateral temporal bone resections and 59.76% in mastoidectomy.[2] According to a recent study by Lovin, representing one of the largest single-institution experience, a conservative management for localized disease was successful in 75% of the cases and produced disease resolution (defined as skin coverage over all previously exposed bone) in 27%,

whereas for diffuse disease, conservative treatment was successful in only 19% but surgery was successful in 87% (89% for lateral temporal bone resection with mastoid obliteration and 100% for mastoidectomy without mastoid obliteration) and produced disease resolution in 91% of the cases.[11] In our patient, the surgical treatment was considered successful with adequate symptoms control bilaterally (100%) and produced disease resolution on the left side with complete skin coverage over all previously exposed bone, at last follow-up (even considering the right facial palsy sequel).

Other therapeutic option to be considered in the treatment of TBORN involve HOT, a standard treatment for ORN of the mandible and that has been recommended for TBORN by some authors, aiming the promotion of angiogenesis and wound healing. However, the efficacy of this treatment in temporal bone is variable across studies and it is difficult to access, considering the lack of standardization and its use in association with other surgical treatments.[2] Though the lack of unequivocally efficacy for recommendation in TBORN, it was offered to our patient as an adjuvant therapy to surgery, aiming an improvement of wound healing and also to eradicate chronic infections, considering its bactericidal effect.[8] Another treatment suggested in the literature includes a protocol with a combination of pentoxifylline-tocopherol-clodronate and antimicrobials, which has shown promising results in the treatment of ORN of mandible, but with only one successful temporal bone case reported.[12] Despite all treatment modalities, probably the best measure regarding TBORN is prevention. In patients who are candidates for head and neck radiotherapy, it is advised to avoid self-inflicted injuries to the skin of the ear canal, especially if within the field of irradiation, to avoid radiation in patients with exposed bone when feasible, and regular ointment application to the skin of the ear canal.[8] Considering the possible impact on hearing caused by TBORN, one should also consider hearing rehabilitation in these patients, in order to improve the quality of life.

CONCLUSION

TBORN is a rare complication of head and neck radiotherapy, usually presenting several years after the exposure to radiation and its symptoms might overlap other otologic entities, which makes the diagnosis challenging. We present the case of an immunosuppressed patient with bilateral diffuse TBORN but whose initial established diagnosis was a necrotizing otitis externa, highlighting the importance of a low threshold for considering TBORN in patients with previous exposure to radiation.

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