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Case Report

Diffuse large B-cell non-hodgkin lymphoma of the ear with intracranial invasion

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ABSTRACT

We report a 62-year-old woman with primary diffuse large B-cell lymphoma (DLBCL) of the ear. The patient presented with facial palsy, left ear hearing loss and a mass in the left external auditory canal. CT and MRI showed an occupied external auditory canal, middle ear and temporal bone with extensive intracranial invasion, R-CHOP therapy was started, but she died after one course. Primary lymphoma of the ear is extremely rare and to the best of our knowledge this is the first case reported in a Mexican medical center, and also the first overall with such an extensive invasion.

Keywords: Primary lymphoma, Temporal bone, Ear, External auditory canal, Diffuse large B-cell lymphoma, Intracranial invasion

INTRODUCTION

Lymphomas account for the third most frequent malignant tumor of the head and neck, following squamous cell carcinoma and thyroid carcinoma, but these neoplasms are rarely present in the temporal bone, in such cases usually associated to an immunocompromised patient.[1] Approximately 23% percent of non-Hodgkin (NHL) and 4% of Hodgkin lymphomas (HL) of the head and neck are extranodal, and mainly involve the following sites: Waldeyer's ring, paranasal sinuses, nasal and oral cavities and the salivary glands. Cases of isolated temporal bone lymphomas come from either metastatic foci, distant primaries or invasion from contiguous locations.[1-3]

Diffuse large B-cell lymphoma (DLBCL) is the most common type of malignant lymphoma, representing 30-40% of cases in adults. Lymphoma of the ear are rarely reported. We report a case of primary B-cell lymphoma involving the external auditory canal, middle ear and temporal bone, a site rarely reported and a review of the literature.[4,5]

CASE REPORT

A 62-year-old woman with past medical history of type 2 diabetes, systemic arterial hypertension and vitiligo presented for evaluation of a four-month history of left facial palsy, left ear progressive hearing loss, tinnitus, aural fullness and severe otalgia. She denied B symptoms (weight loss, fever, night sweats). In the preceding three months she was treated by family practitioner for acute

otitis media with clarithromycin and local ciprofloxacin. Despite treatment, her symptoms deteriorated and referral to our otolaryngology department was made.

Figure 1: (A) Incomplete palpebral closure (Bell's phenomenon); (B) VI C.N. paralysis left eye.

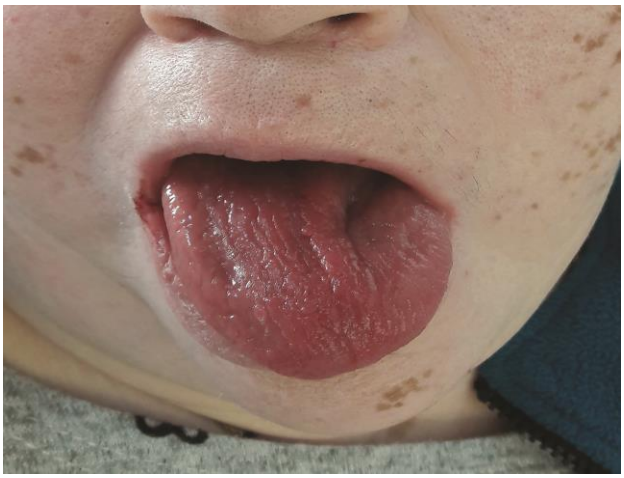

Figure 2: Hypoglossal nerve paralysis.

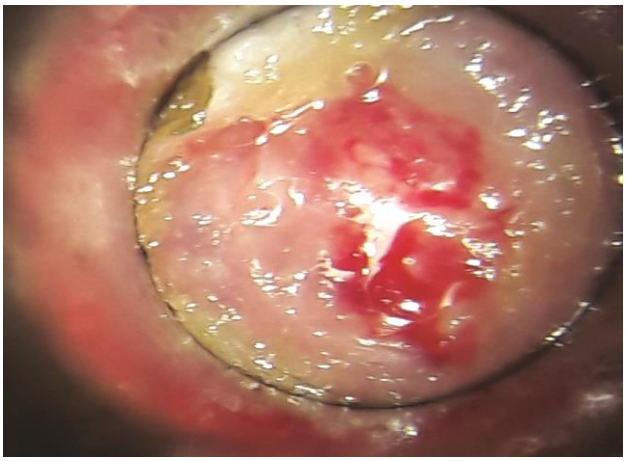

Figure 3: Left otoscopy showing a mass filling the external auditory canal.

On examination she had left-sided facial nerve palsy (Grade IV House-Brackmann classification) and absent left eye movements (Figure 1 A, B). Hypoglossal nerve palsy was also found (Figure 2). Otoscopy of the left ear showed a round, pale, sessile, mobile, friable, non-pulsatile mass filling two thirds of the external auditory canal (Figure 3). Tuning fork and audiometry test confirmed an anacusic left ear.

Laboratory studies on admission showed a white blood cell count of $4.57x10^3/\mu L$, hemoglobin of 8.0 g/dl, hematocrit of 27.8%, and platelet count of $180x10^3/\mu L$, with progressive descent showing pancytopenia four days later with a white blood cell count of $1.21x10^3/\mu L$, hemoglobin of 7.1 g/dl, hematocrit of 25.2%, and platelet count of $91x10^3/\mu L$. C-reactive protein (CRP) was 40.28 mg/L (normal value less than 10 mg/L) and erythrocyte sedimentation rate of 19 mm/hr (normal value less than 30 mm/hr). Anti-hepatitis C virus antibody, hepatitis B surface antigen and anti-human immunodeficiency virus antibodies were negative.

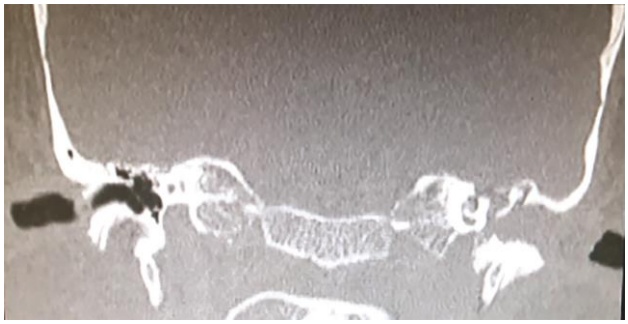

Figure 4: Coronal CT scan showing a soft tissue density opacification of the external auditory canal and middle ear, with erosion of the tegmen tympani is also noted.

Computed tomography (CT) of the left ear showed homogenous opacification of the mastoid cells, tympanic cavity and external auditory canal, erosion of the tegmen tympani, tegmen mastoideum (Figure 4), petrous apex, carotid canal, lesser sphenoidal wing and petroclival articulation was also noted.

Multiple biopsies were taken under local anesthesia, which were reported as cholesteatoma and lymphoid cell groups in a diffuse pattern with necrotic areas, but histological examination was inconclusive (Figure 5) Immunohistochemical studies revealed a positive CD20, BCL2 (100%), Ki67 (70%) and negative Cytokeratin AE1/AE3, monoclonal anti-episialin antibody and ALK, suggesting a non-Hodgkin's lymphoma classified as diffuse large B-cell lymphoma.

A bone marrow aspiration and biopsy showed primarily hematopoietic cells with less than 5% blasts and lymphocytes, with no increase in plasma cells. B-cells accounted for 2-3% of cellularity and showed

heterogeneous Kappa expression. A normal 46, XX karyotype was reported. Magnetic resonance imaging (MRI) of the head revealed a large irregular, heterogeneous mass with low signal intensity on T1-weighted, destroying the left temporal bone, occupying the middle ear and external auditory canal, and involving the cavernous sinus, temporal lobe, mesencefalus and pons, an important contrast uptake was noted. The lesion showed intermediate signal intensity on T2-weighted images, while mastoid air cells showed high signal intensity corresponding to effusion (Figure 6).

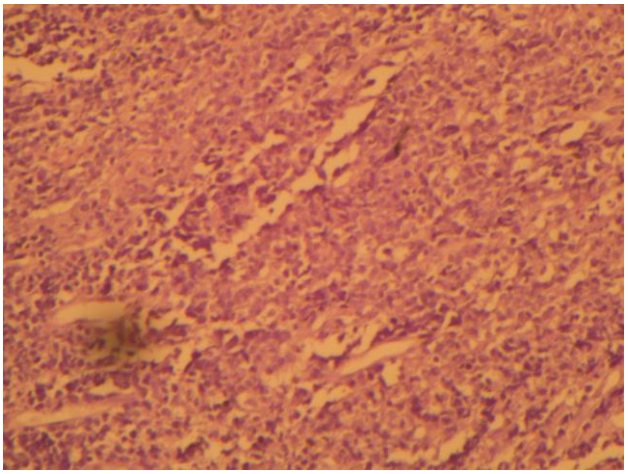

Figure 5: Lymphoid cell groups in a diffuse pattern with necrotic areas.

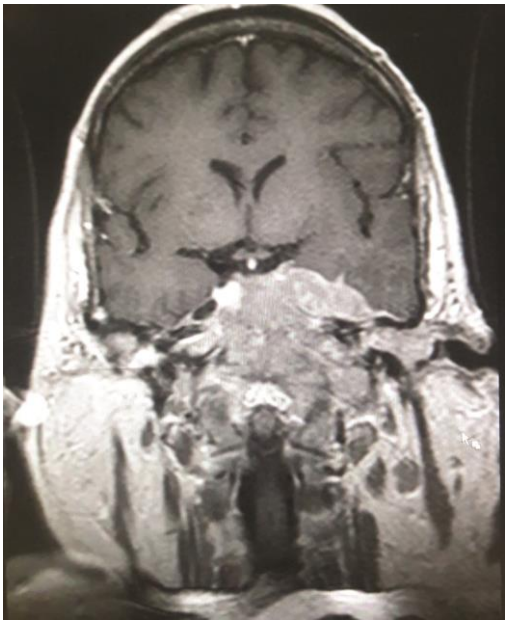

Figure 6: T1-weighted Coronal MRI illustrating extensive enhancing mass filling the right external auditory canal, middle-ear cleft and mastoid, with intracranial extension.

The patient was referred to an Oncologic Center where a F18-FDG PET scan was taken showing an irregular high signal lesion in the middle ear and external auditory canal, left temporal lobe and cerebellum, involving the ipsilateral masticator and pharyngeal mucosal space (Figure 7). Further investigation revealed involvement of lymph nodes in both sides of the diaphragm, and extranodal sites (lungs, liver, psoas, peritoneum) were also noted.

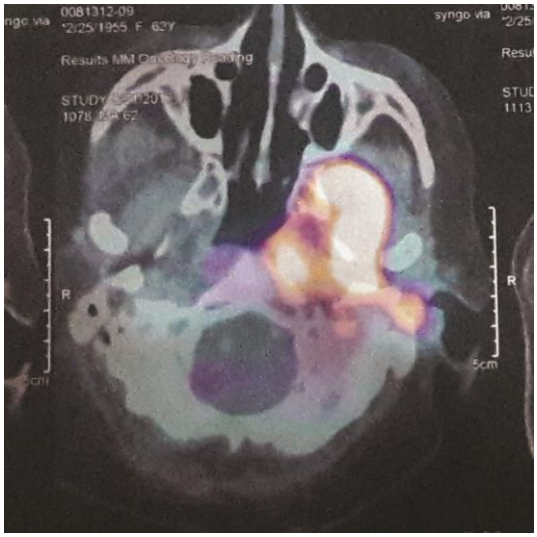

Figure 7: High signal lesion in the middle ear and external auditory canal, left temporal lobe and cerebellum.

The patient was admitted at the Oncologic Center where she was classified according to the Ann Arbor classification as a stage IV_E. She started chemotherapy with R-CHOP scheme (Cyclophosphamide, adriablastin, vincristine, rituximab, and methylprednisolone). She died 3 weeks after being admitted, after receiving 1 cycle of cyclophosphamide.

DISCUSSION

Lymphomas are very common malignancies of the head and neck, most commonly present as asymptomatic lymphadenopathies, 60-80% occurring in the cervical and supraclavicular nodes, or presenting B symptoms: fever, unexplained weight loss and night sweats, in up to 50% of patients with advanced disease. However, in our case, as mentioned before, the patient did not present any of these symptoms.[1,6]

Lymphomas in the ear and temporal bone are usually due metastatic foci or invasion from contiguous locations as was commented, but primary lymphomas of the ear are exceedingly rare, therefore histological and clinical features have not been extensively characterized.

The nature of the lesion can be characterized by contrast enhanced TC and MRI, but a definite diagnosis must be histopathological.[7]

Staging for HL and NHL is based on the Ann Arbor classification. Stage I consists in involvement or a single

lymph node or extranodal site in the absence of any lymph node involvement. Stage II involves two or more lymph node regions on the same side of the diaphragm or involvement of a single extralymphatic organ or site in association with regional lymph node involvement. Stage III involves lymph node regions on both sides of the diaphragm, extralymphatic extension accompanied by lymph node involvement or involvement of the spleen. Stage IV is characterized by diffuse or disseminated involvement of one or more extralymphatic organs, with or without lymph node involvement.[8]

Table 1: List of primary lymphoma of the ear case reports.

Case	Year	Author	Age	Sex	Localization	Immunophenotype	Therapy	Outcome
1	1976	Malik et al.[13]	6	M	ME	Lymphocytic	S	Relapse, lost
2	1980	Harner et al.[14]	66	M	ME	Lymphocytic	CT	Dead
3	1980	Gapany-Gapanavicius et al.[15]	32	F	ME, TB	Nodular, histiocytic	S, CT, RT	Dead
4	1981	Oyetunji & Ladapo[16]	7	M	TB	Burkitt, B-cell	CT	Dead
5	1987	Conley et al.[8]	-	-	TB	NHL	Unknown	Unknown
6	1987	Welling & McCabe[17]	6	M	ME	Burkitt, B-cell	S, CT	Alive
7	1988	Toriumi et al.[18]	76	M	ME	DLBCL	Unknown	Unknown
8	1991	Maiche et al.[19]	71	M	EAC (bil)	Diffuse centrocytic	CT	Alive
9	1992	Tucci et al.[20]	66	M	TB	DLBCL	S, CT, RT	Dead
10	1992	Tucci et al.[20]	5	M	TB	DLBCL	CT	Alive
11	1993	Ide et al.[21]	55	M	ME	Pleomorphic, T-cell	CT, RT	Dead
12	1993	Noguchi et al.[22]	40	M	TB	DSBCL	CT, RT	Alive
13	1995	Bockmuhl et al.[23]	2	M	TB	Blastic, B-cell, EBV+	S, CT	Alive
14	1997	Saigusa et al.[24]	66	F	TB	DLBCL, immunoblastic	RT	Dead
15	1997	Danino et al.[25]	16	M	TB	Large T-cell, immunoblastic	CT, RT	Dead
16	1998	Angeli et al.[26]	56	F	IAC	Large B-cell	S, CT, RT	Alive
17	2000	Merkus et al.[10]	83	F	EAC	Anaplastic large cell	RT	Alive
18	2000	Merkus et al.[10]	75	M	TB, ME, EAC	DLBCL	CT, RT	Alive
19	2002	Fish et al.[12]	53	F	EAC	DLBCL	S, CT	Alive
20	2002	Shuto et al.[27]	49	M	EAC (bil)	B-cell small lymphocytic	S, CT	Alive
21	2003	Lang et al.[28]	5	M	ME, TB	Lymphoblastic, B-cell	CT	Alive
22	2003	Koral et al.[29]	15	M	TB	Diffuse histiocytic large cell	CT	Alive
23	2004	Chang et al.[30]	81	F	TB	DLBCL	CT, RT	Unknown
24	2006	Ogawa et al.[4]	74	F	TB, EAC	DLBCL	CT, RT	Alive
25	2006	Hersh et al.[2]	83	F	EAC	DLBCL	RT	Alive
26	2008	González et al.[31]	53	F	EAC	Anaplastic T-cell	CT	Alive
27	2009	Liu et al.[32]	7	F	ME, TB, EAC, IE	Lymphoblastic, B-cell	S, CT	Alive
28	2013	Bruschini et al.[5]	46	M	EAC	DLBCL	CT	Alive
29	2015	Ryou et al.[33]	35	M	IAC, TB	DLBCL	CT	Dead
30	2016	Li et al.[34]	11	M	ME	Lymphoblastic, T-cell	CT	Alive
31	2017	Maithrea et al.[3]	53	M	ME, TB, EAC	Nodular sclerosis HL	CT	Alive

ME: Middle ear, TB: Temporal bone, EAC: External auditory canal, IAC: Internal auditory canal, IE: Inner ear.

The differential diagnosis of an external auditory canal masses is commonly benign, including cholesteatoma, adenoma, exostoses and osteoma, malignant tumors are uncommon, typically limited to squamous cell carcinoma, but basal cell carcinoma, melanoma and adenocarcinoma can also arise. Middle ear neoplasms include glomus tympanicum, glomus yugulare, adenoma, rhabdomyosarcoma, osteosarcoma, lymphoma, adenocarcinoma, melanoma, and metastatic lesions, while inner ear, petrous apex and cerebellopontine angle

presents benign tumors like vestibular schwannomas, nonvestibular cranial nerve schwannomas, meningiomas and lipomas, malignant tumors are rare, the most common is chondrosarcoma of the skull base.[9]

According to Schuknecht, the mucosa of the mastoid antrum, tympanum, or the tympanic orifice of the eustachian tube have a layer of lymphoid tissue deep to the epithelium and can a site for lymphoma.[10]

Extranodal lymphoma is extremely rare, retrospective studies report an incidence of 1.9 to 11.4 cases per year. It has a peak incidence in the 6th and 7th decades, with a median age of 68, although it can affect all ages and more often in males. The head and neck is the second most common site of presentation of extra nodal lymphomas behind the abdomen.[1,11,12]

We found only 31 reported cases of primary lymphoma of the ear in the international literature, detailed in Table 1. Men (64%) being more affected than women (36%). The age at diagnosis ranged from 2 to 83 years with a tendency for pediatric and elderly populations. Otologic symptoms such as otalgia, otorrhea, hearing loss, and ear fullness were the more common. Facial nerve palsy was present at diagnosis in 8 of 32 patients, including our case, however there were no cases reported of associated cranial nerve paralysis other than the facial and vestibulocochlear nerves, meanwhile our patient had paralysis of the III, IV, IV and XII cranial nerves. On otoscopic examination, 11 patients, had a mass in the external auditory canal, in only 4 of them, including our patient, the tumor extended beyond the external auditory canal. The most frequent immunophenotype was B-cell type in 19 of 32 patients (59%).

Treatment of diffuse large B-cell lymphoma is primarily multiagent chemoradiation. In this patient an R-CHOP scheme was initiated but the patient died after 1 cycle of cyclophosphamide.

We report a rare case of primary lymphoma involving the external auditory canal, middle and inner ear with intracranial invasion, which to our knowledge and revision of the literature hasn't been described before, also this is the first case described in a Mexican patient.

Our case and a review of the literature show the natural history of an untreated malignant lymphoma and this should be taken into consideration as a differential diagnosis in cases of therapy-resistant ear disease.

CONCLUSION

Primary lymphoma of the ear is extremely rare and to the best of our knowledge this is the first case reported in a Mexican medical center, and also the first overall with such an extensive invasion at diagnosis. In cases of therapy-resistant ear disease or peripheral facial paralysis a benign or malignant tumor should be excluded by computed tomography. These patients have a progressive and deteriorating course that goes from weeks to months, and biopsy should be taken for diagnosis. Uniform therapy this disease not been established. Radical tumor resection is discouraged, as it sacrifices vital structures and typically doesn't increase survival rates. Recent therapy attempts are focusing on multiagent chemoradiation as the primary modality.

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