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Case Report

Multicranial neuropathy secondary to endolymphatic sac tumor

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ABSTRACT

Endolymphatic sac tumors (ELST) are rare neuroectodermal neoplasms arising from the epithelium of the endolymphatic sac or duct. Despite their benign histopathological features, ELSTs frequently demonstrate a locally destructive growth pattern with involvement of the skull base and cranial nerves. While ELSTs may arise sporadically, the majority of cases occur in association with Von Hippel-Lindau (VHL) syndrome. ELSTs are commonly diagnosed late due to their slow growing nature and non-specific symptomatology. Surgical resection is the treatment of choice. However, due to the location of these tumors in the lateral skull base surgical intervention carries a high risk of injury to critical neurovascular structures in close proximity. We presented the case of a 51 years old gentleman with a three-months history of hearing loss and otalgia. He subsequently developed multiple cranial neuropathies and was diagnosed with a sporadic ELST. He underwent a complete surgical resection and received adjuvant radiotherapy.

Keywords: Endolymphatic sac tumor, Von Hippel-Lindau disease, Head and neck oncology, Lateral skull base surgery

INTRODUCTION

Endolymphatic sac tumors (ELST) are a rare neuroectodermal tumour only described in case reports or case series within the literature. They arise from the epithelial lining of the endolymphatic duct or sac. ELSTs have a benign histopathological appearance with multiple papillomatous projections, which closely resemble a low-grade adenocarcinoma.

This is in contrast to the clinically aggressive natural progression of ELSTs, which have the potential to erode bone and critical neurovascular structures at the base of the skull. ELSTs are typically associated with Von Hippel-Lindau (VHL) syndrome, with an incidence of approximately 10% in these patients.[3] ELSTs associated with VHL present earlier with more aggressive disease in comparison to sporadic ELSTs.

ELSTs tend to remain clinically silent until they penetrate nearby structures which accounts for the prolonged latency phase.[1] Early ELST's may present with non-specific otological symptoms, such as otalgia, vertigo, tinnitus or most commonly progressive sensorineural hearing loss (SNHL).[2] As the tumour progresses, it's symptomatology and morbidity is dependent on the structures affected by tumour extension.

Classically described affected structures are cranial nerves VII, VIII, IX and X which are in close proximity to the origin of ELSTs. Invasion of these structures by ELSTs will lead to patients developing lower motor neuron cranial nerve palsies. Infiltration beyond the skull base to involve the dura may occur and this is associated with a poor prognosis. Prompt diagnosis and surgical resection is critical to successful treatment and minimizing morbidity in these patients. Surgical resection of advanced disease is often challenging and necessitates sacrifice of local

neurovascular structures to achieve total tumour extraction. Considering the atypical presentation of ELSTs, and the rarity of encountering these tumours in clinical practice, there are many diagnostic and therapeutic dilemmas that require further investigation. Herein, we presented the case of a 51 years old man who presented to our institution with a three-month history of hearing loss and otalgia, and subsequently progressed to develop multiple cranial neuropathies secondary to an ELST.

CASE REPORT

During the peak of the coronavirus disease 2019 (COVID-19) pandemic, a previously healthy 51 years old gentleman was referred from the primary care physician with a three-month history of left-sided otalgia and hearing loss. Approximately one-month before his presentation, he began to note a hoarse quality to his voice and left-sided facial weakness. His past medical history was unremarkable.

The patient had no history of tobacco use or excessive alcohol consumption. A thorough head and neck examination was conducted. On otomicroscopy, an aural polyp with surrounding granulation tissue was noted overlying the posterosuperior quadrant of his left tympanic membrane. Examination of his cranial nerves revealed a left-sided facial nerve palsy (House-Brackmann grade 2). Flexible nasendoscopy demonstrated restricted mobility of the left vocal cord with incomplete glottic closure. Audiometric examination showed a left-sided mixed hearing loss between 50-60 decibels at frequencies 0.25. 0.5, 1, 2, 4 and 8 kHz. Laboratory studies revealed a white cell count of 12.5×10^9/l and C-reactive protein of 58 mg/l. Computed tomography (CT) scan of temporal bone revealed extensive osteolysis of the left temporal bone and lateral skull base with the direct involvement of the left internal auditory meatus, internal jugular foramen, and foramen lacerum (Figure 1).

The mastoid air cells and middle ear cleft were completely opacified. Considering both the clinical and radiological features, we discussed the case with the local microbiology department and commenced intravenous antimicrobial therapy for necrotizing otitis externa. The patient underwent examination under anesthesia and biopsy of the left external auditory canal granulation tissue and polyp.

The biopsy specimen was sent to the laboratory for microbiological culture and sensitivities (MC+S) and histopathological analysis. Histopathological examination of the biopsy demonstrated a preponderance of fibroblasts and keratinocytes, without evidence of dysplasia, consistent with granulation tissue. MC+S were positive for Pseudomonas Stutzeri alone. A PET-CT was performed which revealed significant uptake throughout the petrous temporal bone. Given the complexity of the current case, we transferred the patient to the national tertiary referral skull base unit for further investigation. Under the care of a specialized lateral skull base surgeon, further, more invasive biopsies were obtained for evaluation. Subsequent histopathological analysis of these additional biopsies demonstrated papillary structures, with pale-clear cytoplasm and distinct boundaries, indicative of an ELST. Following discussion at the skull base multidisciplinary team meeting, our patient underwent successful tumour resection via a left-sided combined approach tympanomastoidectomy. The malleus and incus were removed, and the tympanic membrane was reconstructed with cartilage and fascia grafts. Post-operatively, his facial nerve was intact and histological examination demonstrated a negative surgical margin. On day 2 post-operatively, he was discharged home.

At his 6 months follow-up appointment, his cranial nerve function had fully recovered with complete resolution of his hoarseness and facial weakness, and fully mobile vocal folds bilaterally, supporting the fact that neuropathies were due pressure effect of tumor. Unfortunately, audiometry displayed a maximal conductive hearing loss of 60 decibels across all frequencies. The patient is attending community audiology services for amplification.

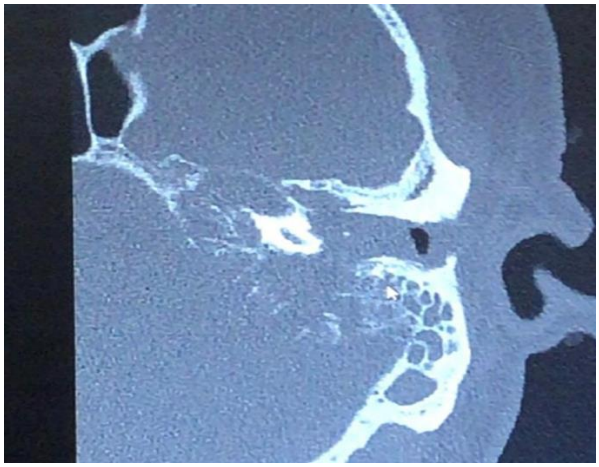

Figure 1: CT scan film of temporal bone.

DISCUSSION

ELSTs are benign neuroectodermal neoplasms arising from the endolymphatic sac or duct. Despite their slow progression, they may cause severe morbidity by invading vital neurological structures at the base of the skull as demonstrated in our patient. Prompt diagnosis and surgical resection minimizes post-operative complications and provides patients with the best opportunity for an optimal outcome.

The first documented case of ELST was by Gaffey et al in 1988, who described the neoplasm as an adenocarcinoma of the middle ear.[4] However, Heffner in 1989 was the first to accurately describe the histologic features and source of ELSTs with his description of these tumours now widely endorsed.[5] ELST's may arise sporadically, or more commonly in association with VHL syndrome. VHL syndrome is an autosomal dominant disease caused by

inactivation of the VHL tumour suppression gene located on the third chromosome. It is associated with the development of ELST, cerebellar hemangioblastoma, renal cell carcinoma and phaeochromocytoma. A study comparing sporadic ELST with VHL associated ELST found VHL associated tumours to occur approximately 2 decades younger than sporadic tumours (31 vs 52 years).[6]

However, the radiological surveillance of VHL patients for ELST may be accounting the earlier detection in these patients. In addition, sporadic ELST appears to occur in women more frequently (F:M, 2:1), compared to VHL-related disease, which has no gender predilection.[7] ELST's initially presents with non-specific symptoms including hearing loss, vertigo, tinnitus, and rarely otorrhea.[4,6] Later symptoms are caused by further tumour invasion leading to recurrent otalgia or headaches in the temporal or occipital region, and cranial nerve palsies with the vestibulocochlear and facial nerves most commonly affected.[6] Otorrhea is an uncommon symptom in ELST patients.[7] In our patient, otorrhea resulted from eustachian tube dysfunction and subsequent tumour invasion of the middle ear and mastoid leading to chronic inflammation, infection and purulent discharge.

Cross-sectional imaging, with computed tomography (CT) or magnetic resonance imaging (MRI) plays a key role in the diagnosis of ELSTs. Multi-dimensional CT imaging of the temporal bone is frequently the first-line investigation. Common features on CT include a retrolabyrinthine mass with 'moth-eaten' erosion of the petrous bone. Additionally, the mass shows intense enhancement with intravenous contrast and spicules of central calcification.[8] On MRI, ELSTs are classically described as a hyperintense mass on T1 weighted images and they demonstrate heterogenous signaling on T2 weighted imaging.[8,9] While the diagnosis of ELSTs is often suspected radiologically, larger more invasive tumours present a diagnostic challenge as they abut many neurovascular structures making their likely site of origin unclear. Furthermore, their location within the vestibular aqueduct in the posterior petrous bone makes tissue sampling challenging. Possible differential diagnoses for ELST on cross-sectional imaging includes glomus jugulare tumour, choroid plexus papilloma, enlarged vestibular aqueduct, petrous apicitis, cholesterol granuloma, meningioma, or metastatic malignancy.[2] Confirmation of an ELST diagnosis requires histopathological examination of the surgically resected specimen. The microscopic appearance of ELST displays an encapsulated tumor with areas of focal calcifications, papillary projections and large cystic spaces within the tumour capsule.[10] The tumour stroma is well-vascularized, and the cystic fluid often contains extravasated red blood cells.[11] Immunohistochemical testing is a useful tool in diagnosing ELST, with tumours staining positively for keratin, vascular endothelial growth factor, vimentin and synaptophysin.[4]

Surgical resection is the first-line treatment for ELST. R0 surgical resection is associated with a low recurrence rate, and a favorable prognosis. However, due to the location of these tumours in the lateral skull base, negative margins are often difficult to achieve and as a result recurrence of disease may occur.[12] In addition, extensive tumours involving the lower cranial nerves are likely to be associated with post-operative morbidity, such as multiple cranial neuropathies. The surgical approach is dependent on the anatomical location and the extent of the tumor.

The common surgical approaches include transpetrosal, translabyrinthine, and transmastoid approaches with the approach used in each case determined by the size and anatomical location of the lesion.[6] In our case a transmastoid approach was utilised with acceptable postoperative morbidity. Other treatment approaches include radiosurgery such as gamma knife surgery or a combination of resection and adjuvant radiotherapy.[13,14] The effectiveness of radiation therapy and gamma knife as a primary therapy is equivocal and further research is needed.[13] Given the small number of cases, no guidelines for following up these tumours exist. However, at present, most cases are surveilled with an annual MRI following treatment.[2]

CONCLUSION

Endolymphatic sac tumors are a rare disease. Limited data exists to guide our management strategies. Early diagnosis and treatment is critical to good patient outcomes. Complete surgical resection of disease remains the mainstay of treatment, with the transmastoid approach being a favourable surgical technique for its acceptable postoperative morbidity. However, further research is needed to better understand ELST and develop clear treatment algorithms and follow-up for this locally destructive disease.

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