An Apparent Sporadic Endolymphatic Sac Tumor in a 14-Year-Old Boy

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Abstract

Endolymphatic sac tumors (ELSTs) are rare, low-grade, histologically benign tumors arising from the epithelial lining of the endolymphatic duct or sac. They are slow growing but locally invasive and can be associated with von Hippel-Lindau disease. While there are cases in the medical literature documenting this type of tumor in adults, reports of ELSTs in the pediatric population are limited.

The authors report the fifth reported case of a pediatric ELST in the English literature. A 14-year-old Jehovah’s Witness presented with a progressive two-year history of right-sided hearing loss, balance problems, gait difficulty, and bleeding behind the right tympanic membrane. Computed topography (CT) and magnetic resonance imaging (MRI) of the brain and temporal bone revealed a large lesion eroding into the petrous and mastoid bones with extension abutting the brain stem and invading the right transverse sinus. Due to the size and hypervascularity of the tumor, as well as the refusal of the patient and family to receive possible intra-operative blood transfusion, the patient was first taken to the interventional suite for pre-operative diagnostic angiogram and embolization of the tumor. Selective right internal carotid cerebral angiogram revealed mild tumor blush from the pars rugosa of the endolymphatic sac or duct in the posterior part of the petrous temporal bone [1,2]. Often presenting with symptoms including tinnitus, vertigo, hearing loss, or various cranial nerve deficits, ELSTs can also be associated with von Hippel-Lindau disease [3].

Hassard et al. first described a papillary adenomatous tumor that adheres to the endothelium of the endolymphatic sac in 1984 [4]. Jeffner proposed the endolymphatic origin of this tumor type through a review of the histological and immunohistochemical features of 20 temporal bone tumors in 1989 [5]. Subsequently in 1993, Li coined the term "endolymphatic sac tumors" [6].

With an average age of presentation in the 5th decade of life, few pediatric cases of ELSTs have been reported in the literature [7-13]. This is the only reported case of pediatric ELST in a Jehovah’s Witness and details a multidisciplinary approach for resection of a pediatric ELST, including the use of pre-operative embolization as well as operative staging.

Case Report

History, examination, and diagnostic studies

A 14-year-old male Jehovah’s Witness presented with a 2-year history of progressive right-sided hearing loss and difficulty with balance and gait. On physical examination, he was morbidly obese with complete hearing loss in the right ear, ataxia, and old blood behind the right tympanic membrane. The results of routine balance and hearing tests, including pure tone audiometry, tympanometry, auditive brainstem response (ABR), and video-nystagmography (VNG) were not available. Preoperative complete blood count and coagulation panel were within normal limits. Examination of his facial nerves and all other cranial nerves were normal. There was no family history of ELST or von Hippel-Lindau disease. Computed topography (CT) of the brain and temporal bone demonstrated an enhancing, partially calcified mass in the region of the right temporal bone. The lesion involved the petrous ridge and right sigmoid sinus with mass effect upon the right brachium pontis. Erosion of the posterior margin of the wall of the right internal carotid artery as well as the right jugular foramen could also be appreciated (Figure 1). Magnetic resonance imaging (MRI) of the brain revealed a 6.3x4.7x3.6 centimetre expansile mass centered in the right posterior petrous temporal bone with extension to the right cerebellopontine angle with multiple fluid-levels; it had, central areas of T2 hypointensity and enhancement, and scattered areas of T2 hyperintensity consistent with chronic hemorrhage (Figure 2). CT scan of the chest, abdomen, and pelvis did not reveal other lesions consistent with von Hippel-Lindau disease.

Operation

Due to the hypervascularity of ELSTs, coupled with diagnostic imaging concerning for vascular compromise and refusal of the patient and family to receive possible intra-operative blood transfusion, the patient was first taken to the interventional suite for pre-operative diagnostic angiogram and embolization of the tumor. Selective right internal carotid cerebral angiogram revealed mild tumor blush from

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the cavernous branches of the internal carotid artery. Selective right external carotid artery angiogram revealed a large tumor blush in the right petrous temporal bone region and posterior fossa (Figure 3A). Additionally, there was evidence of arteriovenous shunting in the tumor with early venous filling to the paracervical venous plexus. Multiple feeders to the tumor were also revealed. The five most prominent feeders to the tumor, including one feeder from the occipital artery, two feeders from the middle meningeal artery, and two feeders from the posterior auricular artery, were successfully embolized using polyvinyl alcohol particles measuring between 45 to 150 microns in size. Post-embolization angiography demonstrated a modest reduction in the amount of tumor blush (Figure 3B).

The patient was taken to the operating room one day following tumor embolization, for surgical excision of the tumor. A combined petrosal and middle temporal fossa skull-base approach was used for tumor resection with assistance from an otologist. The tumor infiltrated a large portion of the sigmoid sinus and also encased the facial nerve from the horizontal segment at the geniculate to the stylomastoid foramen. Because of the local invasiveness of the tumor, coupled with the high rate of recurrence from partial resection of ELSTs, we proceeded with complete removal of the tumor from the middle ear up to and including obligatory removal of the facial nerve from the level of the geniculate to the stylomastoid foramen while preserving the inner ear. Once the patient’s blood loss had reached 800 milliliters, we elected to stop the operation and return for completion resection at a later date so as to eliminate the need for immediate blood transfusion. The patient did receive CellSaver (Haemonetics, Braintree, MA) but based upon a pre-operative contract with the patient and family we were allowed to proceed with surgery including the use of CellSaver up until the point of one liter blood loss as long as the surgery could be stopped safely at that point. From an oncological perspective, it was unclear pre-operatively if the tumor was benign and amenable to staged resection, but to assist in at least obtaining histological confirmation of the diagnosis we agreed to this contract with the patient and family. However, for future cases, autologous blood transfusion or hemofiltration blood salvage, if acceptable by the patient and family would provide the best surgical option from an oncological perspective by allowing the surgery to be performed in a single stage.

Five weeks later, the patient was taken back to the operating room for the second stage of tumor resection. The previous incision was reopened and extended both to the pre-auricular and retrosigmoid skull base. A right-sided infratemporal/postauricular/transjugular approach was used to access the middle cranial fossa, including the internal auditory meatus, petrous apex, tentorium, and infratemporal fossa. The tumor was infiltrating into the dura at multiple sites. The affected dura was carefully resected, repaired with a dural patch graft, and dead space was filled with abdominal fat graft. Blood loss during the second operation was 300 milliliters.
Pathological findings

Hematoxylin and eosin staining demonstrated papillary arrangements of bland cuboidal to columnar cells forming monolayers and containing round to oval nuclei with no discernible mitotic activity and clear cytoplasm (Figure 4A). Methylene blue-staining again demonstrated papillary growth of tumor cells with minimally osmophilic subnuclear vacuoles associated with glycogen-like staining material (Figure 4B). All histopathological findings were consistent with endolymphatic sac papillary tumor. Electron microscopy imaging revealed polarized epithelial cells containing predominantly electron-lucent granules consisting of mucin and confirming the diagnosis of ELST (Figure 4C).

Post-operative course

At four month and twenty-one month follow-up, the patient’s physical examination was unchanged relative to his immediate post-operative examination including a persistent House-Brackmann grade 4 right facial nerve paralyses and complete hearing loss of the right ear. Four month, eight month, and 12 month post-operative imaging did not show any evidence of tumor recurrence (Figure 5). The patient and family were not compliant with post-one year follow-up recommendations and subsequent routine imaging twenty-one months post-intervention did reveal recurrence with a 3.6 x 3.3 centimetre lesion seen within the right cerebropontine angle containing internal solid enhancing components as well as spiculated calcification (Figure 6). Options for surgical resection versus Gamma Knife therapy were discussed with the patient and family. Given this recurrence, the family is currently considering re-operation versus Gamma Knife therapy. The possible use of radiosurgery for recurrence was, in part, based upon recent reports in the literature demonstrating the efficacy of delivering up to 15 Grays of radiation to recurrent ELST tumors with no further recurrence through up to 3 years of follow-up [14].

Discussion

Endolymphatic sac tumors (ELSTs) are rare, low-grade, hyper vascular, invasive tumors arising from the epithelium of the endolymphatic sac or duct and found in approximately 11-30% of patients with von Hippel Lindau (VHL) disease. They most commonly present with an insidious onset of hearing loss, facial nerve palsy, or other cranial nerve deficits in patients most commonly in their fifth decade of life or older. Tumors less than 3 cm in diameter are usually fed by ECA branches, whereas tumors greater than 3 cm usually have additional feeders from the ICA and posterior circulation [15]. The dural branches of the ascending pharyngeal and stylomastoid artery usually supply these tumors. Treatment of choice for ELST is complete excision with wide-margins given the long disease-free survival of patients in previous series following gross total resection, as well as the relative radio-resistance of these tumors [16].

ELSTs have been shown to be associated with VHL disease in some cases, and extensive research has been devoted in studying the VHL gene in relation to ELSTs [16-23]. VHL-associated ELSTs were shown to have a earlier age of onset compared to the sporadic form of the disease in a study with 149 patients by Bambakidis et al. (31.3 years old for VHL patients and 52.5 year old for non-VHL patients) [14]. Bilateral ELSTs are also more common in patient with VHL disease [14,24]. Patients with VHL often have concomitant conditions, such as retinal hemangiomas, intracranial hemangiomas, renal cell carcinomas, pancreatic cysts and pheochromocytomas [9]. Metastasis of ELSTs is exceedingly rare, with only 2 cases of drop metastases to spine having ever been reported [25,26].

On CT imaging, ELSTs usually present as a retrolabyrinthine mass with an epicenter in the retrolabyrinthine/presigmoid area, growth in all directions, and destruction of adjacent structures. On MRI, a hyperintense foci on T1 and T2 sequences is appreciated [14]. Bilateral ELSTs are also more common in patient with VHL disease [14,24]. Patients with VHL often have concomitant conditions, such as retinal hemangiomas, intracranial hemangiomas, renal cell carcinomas, pancreatic cysts and pheochromocytomas [9]. Metastasis of ELSTs is exceedingly rare, with only 2 cases of drop metastases to spine having ever been reported [25,26].

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chondrosarcoma, or plasmacytoma due to similarities on CT and MRI imaging [26].

Histologically, ELSTs may have an appearance similar to metastatic thyroid cancer, renal cell cancer, or paraganglioma. ELSTs, however, classically have the appearance of colloid filled cysts lined by a single layer of cuboidal to columnar cells with basally displaced nuclei and glycogen vacuolations [28,29]. ELSTs have positive immunohistochemical reactivity for anti-cytokeratin (CAM 5.2), epithelial-marker antigen (EMA), and glial fibrillary acidic protein (GFAP) [1]. ELSTs also have immunoreactivity for cytokeratin and S100, the latter of which is a family of low molecular weight protein found in vertebrates [28].

Treatment of choice for ELSTs is complete excision with wide-margins. A retrolabyrinthine approach may be used if hearing is preserved. If the tumor has invaded the labyrinth, a translabyrinthine or transcochlear approach can be used. Heffner reported a 90% cure rate with total resection, whereas 71% of patients with partial tumor resection followed by radiotherapy developed recurrence/regrowth of ELSTs over an average follow-up period of 5.7 years [5]. Twelve of fourteen (85.7%) patients with complete resection remained disease-free over an average n follow-up period of 59.4 months in another study by Hansen and Luxford further supporting complete resection as the treatment of choice [9]. Additionally, two studies have shown ELSTs to be relatively radio-resistant [5,30]. However, a case report by Balasubramaniam et al. demonstrated the efficacy of delivering 15 Grays of radiation to a recurrent ELST tumor, though the follow-up period in this report was only 3 years [31]. Long-term survival data in patients with ELST have not been widely reported through the literature, though patients with drop metastases to the spine appear to have poor long-term survival [25,26,32].

The patient in this case was only 14 years old, much younger than the most ELST patients who usually presenting during their fourth or sixth decades of life. Additionally, this patient represents the only Jehovah’s Witness pediatric case of ELST in the literature. While most patients present with an insidious onset of symptoms over many years, this patient developed symptoms over a relatively short course of only two years, much more acutely than the 4 year course of symptoms demonstrated in the case report of an 11-year old with ELST by Ferreira et al. [8]. Similar to the case reports by Ferreira et al. and Kupferman et al., our patient presented with hearing loss, though our patient did not present with facial nerve paralysis, as did the Ferreira and Kupferman patients [8,10]. The cases by Ferreira et al. and Kupferman et al. unfortunately did not report upon the size or extension of tumors, but patients in both these series as well as our own reported patient had tumor involvement of the facial nerve requiring its sacrifice. It is unclear why our patient did not present with facial paralysis, aside from this child, Megerian and Semaan [11] and Bae et al. [33] have reported the only other patients described in the literature thus far to have presented with vertigo.

Although the use of pre-operative embolization and staged procedures for removal of ELSTs in children has been reported before by both Ferreira et al. and Bae et al. [8,33], this report represents the first to specify technical aspects of the actual embolization technique utilized. While the reports by Ferreira et al. and Bae et al. both described embolization of occipital feeders into ELSTs [8,33], this

Figure 5: Post-op MRI including (A) T1 without contrast, (B) T1 with contrast, (C) T2, and (D) FLAIR sequences one-year following completion resection demonstrating no evidence of tumor recurrence.

Figure 6: Post-op MRI including (A) T1 without contrast, (B) FLAIR, (C) T1 with contrast, and (D) T2 sequences twenty-one months following completion resection demonstrating evidence of tumor recurrence, inclusive of a right cerebropontine angle lesion with enhancing components and spiculated calcification.
report additionally notes the first embolization of arterial feeders from the middle meningeal artery and posterior auricular artery. Additionally, this case represents the first description of an initial combined petrosal/middle temporal fossa skull-base approach followed by an infratemporal/postauricular/transjugular approach to resect an ELST. All previous reports within the pediatric literature have exclusively utilized a translabyrinthine approach, with the exception of the case reported by Diaz et al. in which a 17-year-old underwent a petrosal/transjugular approach followed by proton beam therapy for treatment of ELST (Table 1) [7].

Care of our patient was also complicated by the patient’s religious beliefs, precluding use of blood transfusions. Though previous reports have not specified their operative blood loss, the standardized use of pre-operative embolization in patients, particularly children, seeking to minimize operative blood loss during resection of these hypervascular lesions may serve as a helpful adjuvant tool to the operating room in the future.

The presentation of this case is limited in several respects. First, the follow-up time period for this patient following his second, completion resection is only 21 months, as opposed to the 4.5 year follow-up of the Ferreira et al. Case [8]. However, our follow-up is greater than the 18 month follow-up of the Kupferman et al. Case [10]. Nevertheless, our relatively short follow-up period does limit our ability to comment on pertinent long-term follow-up issues, including the need for potential future radiosurgery or reoperation. Additionally, our screening for von Hippel Lindau disease included primarily an imaging survey for additional lesions via CT scanning. A more robust work-up may have included genetic testing.

**Conclusion**

ELSTs are rare tumors, with pediatric cases being exceedingly rare. The hypervascularity of these tumors pose potential challenges in surgical resection due to higher risks of bleeding. However, with pre-operative embolization of feeder arteries, utilization of Cell Saver intraoperatively, and with carefully planned operative staging, complete resection of these tumors is possible. Even in patients in whom a gross total resection is achieved, routine post-operative imaging should be pursued to evaluate for possible recurrence.

**References**


