Case Report / Olgu Sunumu

# Histopathological Findings and Differential Diagnosis of Endolymphatic Sac Tumor: A Rare Case

## Endolenfatik Kese Tümörünün Histopatolojik Bulguları ve Ayırıcı Tanısı: Nadir Bir Olgu

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**Abstract:** An Endolymphatic Sac Tumor is a locally aggressive tumour that grows slowly, is associated with Von-Hippel-Lindau disease and originates from the endolymphatic canal. A 64-year-old male patient presented with pain behind the ear and numbness in the cheek. The cranial magnetic resonance examination revealed a slow-growing, locally aggressive tumour originating from the endolymphatic canal, extending to the pontocerebellar angle and eroding the mastoid and temporal bones. The tumour consisted of glandular and papillary structures composed of a single layer of cuboidal cells. In addition to morphological findings, an endolymphatic sac tumour diagnosis was confirmed by positive staining for immunohistochemical markers such as Vimentin, NSE, EMA, PAX8, and Cytokeratin 7. Endolymphatic sac tumour is rare, even in Von Hippel-Lindau disease. Due to its location, slow growth, and locally aggressive nature, this diagnosis may be considered. However, due to its formation of tubular and papillary structures, the differential diagnosis should include thyroid papillary carcinoma, adenoma of the middle ear, papillary renal cell carcinoma, and papillary meningioma. Along with morphological findings, immunohistochemical stains for the diagnoses considered in the differential diagnosis will be instructive.
**Keywords:** Endolymphatic sac tumour, metastasis, PAX8, VHL, Immunohistochemistry

**Özet:** Endolenfatik kese tümörü, özellikle von Hippel-Lindau hastalığı ile ilişkili, endolenfatik kanaldan orjin alan, yavaş büyüyen lokal agresif bir tümördür. 64 yaşında erkek hasta, kulak arkasında ağrı ve yanakta his kaybı ile başvurdu. Kranial manyetik rezonans incelemesinde; sol akustik kanal ve orta kulakta yerleşen, mastoid ve temporal kemikleri erode eden pontoserebellar köşeye uzanan tümör mevcuttu. Tümör, glandüler ve papiller yapılar oluşturan, tek sıra kuboidal hücrelerden oluşmaktaydı. Morfolojik bulgular yanısıra, Vimentin, NSE, EMA, PAX8, Sitokeratin 7 gibi immünohistokimyasal belirteçlerin pozitif boyanması ile endolenfatik kese tümörü tanısı verildi. Endolenfatik kese tümörü Von Hippel-Lindau hastalığında bile oldukça nadirdir. Tümörün yerleşim yeri, yavaş büyümesi ve lokal agresif özelliği nedeniyle bu tanı akla gelebilir. Fakat, tubuler ve papiller yapılar oluşturması nedeniyle ayırıcı tanıya, tiroid papiller karsinom, orta kulağın adenomu, papiller renal hücreli karsinom ve papiller meningiom alınmalıdır. Morfolojik bulgular ile birlikte, ayırıcı tanıda düşünülen tanılar için yapılacak immünohistokimyasal boyamalar yol gösterici olacaktır.
**Anahtar Kelimeler:** Endolenfatik kese tümörü, metastaz, PAX8, VHL Sendromu, immünohistokimya

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## 1. Introduction

An endolymphatic sac tumour (ELST) is a neuroectodermal tumour originating from the epithelium responsible for the production and resorption of endolymph in the cochlea and semicircular duct. It is rare and sporadic, while it occurs in 6-15% of the patients with von Hippel-Lindau Disease (VHL) (1). Patients with ELST most commonly presented with tinnitus, facial nerve palsy and sensorineural hearing loss (2). The tumour has a slow-growing pattern but is locally aggressive, can erode the temporal bone and extend into the pontocerebellar angle (3).

## 2. Case Report

A 64-year-old male patient with a diagnosis of VHL was admitted to the neurosurgery clinic with a complaint of pain behind the left ear and loss of sensation in the left cheek. The patient had left facial paralysis, while the rest of the neurological examination was unremarkable. Magnetic resonance imaging of the brain with contrast showed a 6,5 cm lesion in the left pontocerebellar angle, which extends into the left acoustic canal, left jugular bulb, middle ear cavity and the mastoid bone with compression to the pons and cerebellar hemisphere. The lesion destructed the petrous part of the temporal bone and surrounded the V4 segment of the left vertebral artery. The lesion also showed intracranial extension by destructing the tegmen tympani. There were also lesions in the right cerebellar hemisphere 5 mm and 3 mm in size with contrast enhancement (Figure 1,2).

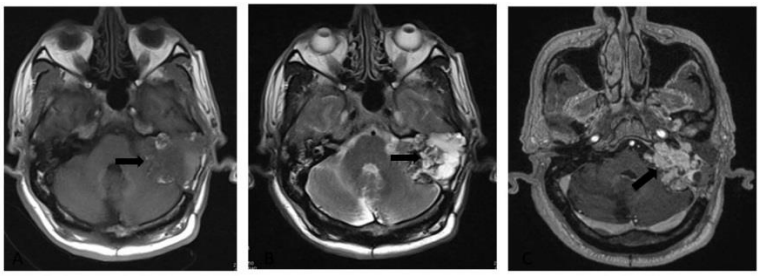

**Figure 1.** In the Axial T1A (A), T2A (B), and postcontrast fat-suppressed T1A (C) series,

T1A hypointense that extended into the local acoustic channel and left jugular bulb in the left pontocerebellar angle, T2A hyperintense, a postcontrast diffuse heterogeneous densely contrasted lobulated lesion that had a contour are observed, respectively. The lesion extends into the left middle ear cavity and mastoid cells. Cystic necrosis in the mass lesion site draws attention. The tumour puts pressure on the pons and cerebellum from the lateral side.

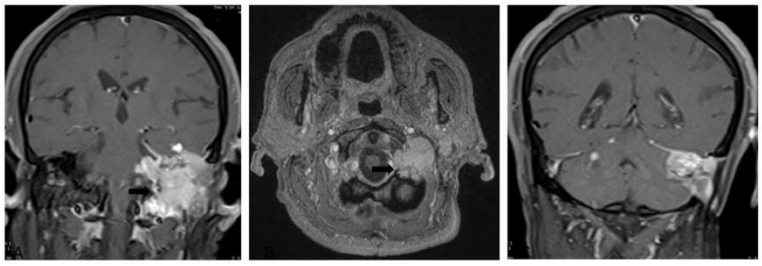

**Figure 2.** Coronary fat-suppressed postcontrast T1A image shows a lesion that extends intracranially by destroying the tegmen tympani. Dural involvement, thickening, and opacification are observed in the left temporal region of the lesion. In the left posterior temporal segment, the nodular enhancement in the subcortical region is continued (A). Axial fat-suppressed postcontrast T1A shows a lesion in the medial anteroinferior section extending to the cranial base (mass measured approximately 6,5x6 cm) (B). Coronal fat-suppressed post-contrast T1A image reveals a nodular contrast-enhanced lesion about 5 mm in diameter at the right superior cerebellar vermis level, enhancing contrast with a diameter of 3 mm. It is known that the patient was operated for hemangioblastoma in this localisation (C).

The patient's past medical history revealed hemangioblastoma in the cerebellar region 18 years ago, multifocal renal cell carcinoma 14 years ago, and choroidal plexus papilloma seven years ago. The patient's systemic physical examination was normal. The patient underwent surgical resection of the tumour located in the cerebellopontine angle. However, complete resection could not be performed since the tumour was quite infiltrative and surrounded the vessels. A postoperative MRI of the brain showed a residual tumour. Then, the patient underwent Gamma Knife radiosurgery for the residual lesion.

Histopathological examination of the lesion showed a large area of fibro-hyalinised tissue with simple cubic-columnar, coarse, complex papillary structures with follicular epithelium and follicular tumour. The nucleoli were prominent and had clear and eosinophilic cytoplasm. The colloid-like compact eosinophilic material in which the follicle lumens were observed to have an eosinophilic appearance, and some parts with alterations were remarkable (Figure 3).

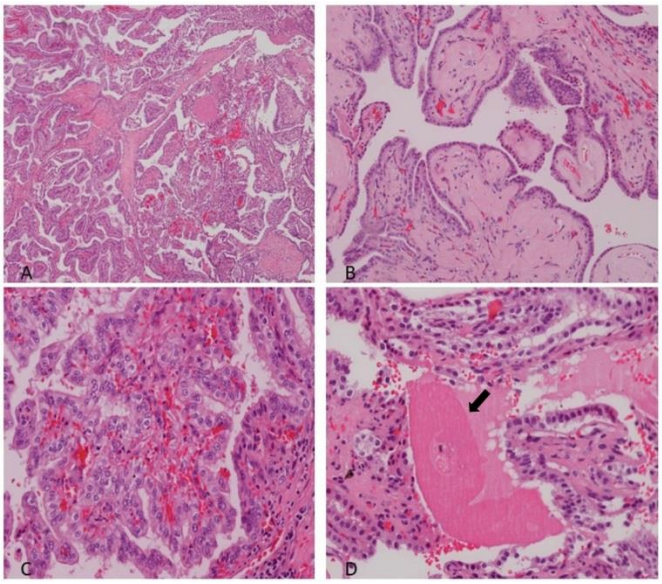


**Figure 3.** Tumoral tissue forming coarse short papillary structures in histological examination (A, HEx200), Rough papillary structures paved with a simple cuboidal epithelium (B, HEx100), Tumoral cells with prominent nuclei, centrally located nuclei and eosinophilic cytoplasm(C, HEx100), Colloid-like material between papillary structures in compact eosinophilic appearance (D, HEx200).

Significant pleomorphism and atypical mitosis were not detected in the tumour cells. Inflammatory cell infiltration, vascular proliferation and hemosiderin pigment were observed around the tumour. In addition, cartilage structure, keratinised epithelium and durable fibro-hyalinized tissue were present in the surrounding tissue. ELST, adenoma of the middle ear, thyroid papillary carcinoma metastasis, renal cell carcinoma metastasis, papillary meningioma, paraganglioma and choroid plexus tumours were included in the differential diagnosis. In immunohistochemical examination, positive staining was obtained in tumoral tissue by using Vimentin, Cytokeratin 7, NSE, Cytokeratin 5/6, EMA, PAX8 (Figure 4), and negative staining was seen by using TTF-1, Tyroglobulin, S100, Chromogranin, Synaptophysin, AMACR, RCC, CD10. Although PAX 8 was positive, renal cell carcinoma metastasis was excluded with RCC, AMACR and CD10 negativity and thyroid papillary carcinoma with thyroglobulin and TTF-1 negativity.

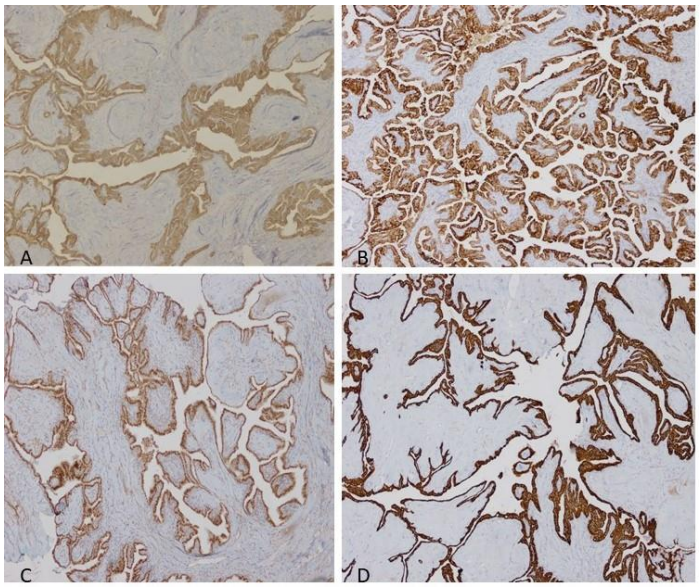


**Figure 4.** The tumour cells were diffusely and firmly positive for NSE (A,x100), Epithelial membrane antigen immunostaining (B, x200), and Pax-8 immunostaining (C, x100). Cytokeratin 7 immunostaining (D, x100).

The predominance of papillary structures, the absence of the pattern of Zellballen, the presence of colloid-like material, Chromogranin, Synaptophysin and S100 negativity were excluded from the paraganglioma.

The histomorphological findings and immunohistochemical markers of the tumour were evaluated, and the endolymphatic sac papillary tumour was diagnosed. The patient's medical history of VHL also supported this diagnosis.

## 3. Discussion

VHL is an autosomal dominant syndrome that can affect many organs, such as the central nervous system, kidneys, pancreas, adrenals, and genitourinary system. One in 36000 live births is involved (4). In VHL disease, hemangioblastoma (60-80%) is the most common in the central nervous system, while the incidence of ELST is 6-15% (5). ELST is a slow-growing tumour with low malignancy features, whereas this is a locally aggressive tumour (6). It was first described by Hassand et al. in 1984 (7). Sporadic cases are rare. It is usually unilateral, and there is no gender difference. VHL-associated ELSTs are bilateral, and the risk for women is twice as high (8).

ELST often gives clinical signs in the 5th decade. The most common symptoms are sensorineural hearing loss, tinnitus, and dizziness. Other symptoms may occur related to involved cranial nerves as the tumour can reach large dimensions and move up to the base of the head and pontocerebellar corner (6,8). In our case, the tumour extended into the external auditory canal, and there was pain in the back of the ear and sensory loss in the face.

Histopathologically, the tumour consists of tubular and papillary structures. Papillary structures are coarse and thick. Cells are usually cuboidal and columnar, with a hyperchromatic nucleus and clear-slightly eosinophilic granular cytoplasm. Tubul lumens contain eosinophilic colloid-like material in a compact appearance. In the surrounding tissue, lymphoplasmacytic inflammatory cells, histiocytes with foamy cytoplasm, cholesterol clefts, bleeding, and congestion are usually observed. A small biopsy specimen from this region may not represent the lesion. ELST may be considered due to its location, especially in a patient with a known history of VHL. Still, similarities in morphological appearance and exclusion of lesions in differential diagnosis are essential for the treatment (1,2,9).

The differential diagnosis included primarily papillary and follicular carcinoma of the thyroid. Although there are morphological similarities, immunohistochemical evaluation is valuable in the discrimination of TTF-1 and thyroglobulin negativity in ELST. The PAX 8 marker, which may exert positive staining in thyroid tumours, also shows positive staining in 85% of the

patients with ELST, according to Thompson et al. Similarly, in our case, diffuse nuclear-positive staining was detected with PAX 8 (1).

Another vital tumour in the differential diagnosis is RCC. RCC has been recently identified in many subtypes; the absence of colloid-like material, positive staining with AMACR, CD10 and RCC as immunohistochemically, and negative reaction with neuronal markers such as NSE are essential in the differential diagnosis. The risk of metastasis should be kept in mind, as RCC is common, especially in patients with VHL. PAX-8 and carbonic anhydrase staining in RCC and ELST have no role in differentiation (1). In our case, multifocal renal cell carcinoma was diagnosed years ago. Metastasis was excluded as no staining was observed with CD10, AMACR, and RCC used for differentiation. The middle ear adenoma, which should be considered in differential diagnosis, is of neuroectodermal origin and has morphological similarities with ELST. Distinction by immunohistochemical staining is not possible. However, middle ear adenoma is not aggressive and is usually found to be self-limited (10). There is no colloid-like material in papillary meningioma nor positive staining with NSE, PAX8. Choroid plexus papillom and paraganglioma are also included in the differential diagnosis (1,9).

Complete resection is vital for the treatment of ELST. However, complete resection is usually impossible, given that the tumour is primarily invasive. Also, recurrence was reported in 50% of the patients who underwent radiotherapy after incomplete resection and in 20% of those who underwent complete resection in one year (11). Therefore, the role of postoperative radiotherapy is still unclear (11). Gamma knife radiosurgery has been suggested to help reduce recurrence rates in the postoperative period (12).

In conclusion, ELST is quite rare. Although the tumour location, presence of VHL history, and histomorphological findings suggested ELST, this had a wide range of histopathological differential diagnoses. The diagnosis of ELST should be kept in mind in such cases, and necessary immunohistochemical stainings should be performed.

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**Ethics**

**Informed Consent:** The authors declared that informed consent form was signed by the patient.
**Copyright Transfer Form:** Copyright Transfer Form was signed by the authors.
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