Case report

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Endolymphatic sac tumour (ELST). Case report of a rare tumour of the temporal bone, presenting as a mass in a cerebello-pontine angle

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Abstract

Endolymphatic sac tumour (ELST) is a primary low-grade, locally invasive adenocarcinoma of the endolymphatic sac, characterized by the proliferation of cuboidal cells forming a papillotubular pattern and colloid-filled cysts. Rare in the general population, it coincides significantly with the presence of von Hippel-Lindau disease. The natural history, mechanisms underlying the early symptoms, anatomical origin of ELST and optimal timing of their treatment are unknown. In this study, we report a Polish male patient with sporadic ELST (without a family history of VHL disease) along with a review of literature. The light microscopic and immunohistochemical features as well as clinical presentation were typical of ELST.

Key words: *endolymphatic sac tumour, ELST, temporal bone, von Hippel-Lindau disease.*

Introduction

Endolymphatic sac tumour (ELST) is a rare, locally invasive neuroectodermal neoplasm occurring in the posteromedial petrous portion of the temporal bone. It is presumed to originate from pars rugosa of the endolymphatic sac. Symptoms betokening ELST usually include hearing loss, tinnitus, vertigo, aural fullness, and facial nerve dysfunction. Histologically, ELST is characterized by the proliferation of cuboidal cells forming a papillotubular pattern and occasional colloid-filled cysts, reminiscent of thyroid papillary carcinoma. The presence of ELST coincides with von Hippel-Lindau disease (VHL). It remains to be verified what the natural history and optimal timing of treatment are.

Case description

An 70-year-old Caucasian male presented with a 2-year history of progressive left-sided hearing loss and six-month history of ipsilateral facial paresis. On examination he was deaf in the left ear and had a complete left facial nerve paralysis. Other symptoms included: disequilibrium, tinnitus and hypoesthesia of the left half of the face. Eight weeks before medical examination he reported experiencing swallowing problems.

Magnetic resonance imaging showed a solid, heterogeneous enhancing mass in the petrous portion of the left temporal bone with severe erosion and damage to the anterior petrous pyramid. The 5th, 7th and

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8th cranial nerves were involved but cerebellar incisure of dura remained intact.

The patient underwent resection of the tumour by a retrosigmoid approach. The seventh and eighth cranial nerves and all adjacent dura and bone were removed. A small portion of the tumour was firmly adherent to the petrous bone and could not be removed completely. The patient recovered uneventfully.

Six months later, the patient complained of facial symptoms similar to those reported before surgery along with swallowing difficulties. Computed tomography revealed recurrence, but due to poor general condition he was disqualified for surgery and referred to the radiation therapy unit at the neurological hospital.

Two years after the operation, he died because of heart attack.

The patient did not show any evidence of VHL and his family histories were negative as well.

Histopathology

Microscopically, the tumour consisted of complex papillary glandular structures present in the fibrous stroma. The papillae were covered by a single or double layer of cuboidal cells, partially flattened. The papillary stroma was richly vascularized. There was a slight nuclear polymorphism of the tumour cells, and only two mitotic figures were counted in the microscopic slides. The growth pattern was invasive, with destruction of the bone.

Formalin-fixed, paraffin-embedded tissues from the ELST were routinely processed and stained with hematoxylin and eosin. For immunohistochemical studies, 4 µm-thick sections were cut from paraffin blocks, mounted on slides coated with 3-aminopropyltriethoxy-silane (Sigma, St. Louis, USA), deparaffinized in xylene, and rehydrated in descending grades (100-70%) of ethanol. Sections were then subjected to heat-induced epitope retrieval in a 0.01 mol/l concentration of citrate buffer (pH 6.0) in the microwave oven for 40 min. Endogenous peroxidase was blocked by a 5 min. treatment with 3% hydrogen peroxidase in absolute methanol.

The slides were incubated for 60 min. at room temperature with the primary antibodies: S-100 protein (Dako, cat. no Z0311, at dilution 1 : 300), EMA (Dako, cat. no M0613, at dilution 1 : 100), CK (Dako, cat. no M0821, at dilution 1 : 100), NSE (Dako, cat. no M0873, at dilution 1 : 200) GFAP (Dako, cat. no Z0334, at dilution 1 : 600), CK7 (Dako, cat. no M7018, at dilution 1 : 50), CK20 (Dako, cat. no M7019, at dilution 1 : 50), transthyretin (Dako, cat. no A0002, at dilution 1 : 200), Kir 7.1 (Abcam, cat. no ab81117, at dilution 1 : 300), and Ki-67 (DAKO, cat. no M7240, at dilution 1 : 100). The bound antibodies were visualized with techniques according to manufacturers' schemes. The slides were counterstained with Mayer's hematoxylin.

Immunohistochemical studies displayed an expression of S-100 protein, EMA, CK and NSE in the tumour cells (see Fig. 1). Only some epithelial cells express CK7. The cells did not express CK20, transthyretin, GFAP or Kir 7.1. Proliferation index (Ki-67) was at the range of 5%.

Discussion

Endolymphatic sac tumour as a distinct entity was described in the 1980s [14,15]. Since that time a total of less than 100 cases have been reported. They usually present in the third and fourth decades of life; some studies report a female predominance [13,22]. The occurrence of ELST in paediatric patients has also been described [2,9,11].

Very rarely ELST might occur sporadically as well as hereditary connected to von Hippel-Lindau disease [30]. This connection was observed in 1992 for the first time and then confirmed by molecular genetic analyses of the VHL gene (3p25) which acts as tumour suppressor [20,21,28]. The association with VHL disease is estimated for 11-16% [8,24]. 30% of patients with VHL syndrome and endolymphatic sac tumours have bilateral disease [24]. When ELSTs occur bilaterally, von Hippel-Lindau syndrome is always present [31], and in most reports, ELST may be a manifestation of VHL syndrome [24,29,30,34].

The ectodermal endolymphatic sac is a part of the membranous labyrinth and plays an important role in regulating inner ear endolymph [1]. ELSTs are thought to arise from the pars rugosa of the endolymphatic sac (adjacent to the endolymphatic duct, partially intraosseous), and therefore invade petrous temporal bone as well as dura-mater of the posterior fossa [15,23,25]. Also, they are reported to arise from the distal smooth portion of the endolymphatic sac and extend predominantly from the inner ear to the region of the jugular foramen, sparing the petrous pyramid. The facial nerve is often involved and invaded by the tumour. Tumour may also be found adherent to the ascending vertical portion of the petrous carotid artery [10].

The slow pattern of growth correlates with the insidious onset of hearing loss, vertigo, and facial nerve pare-

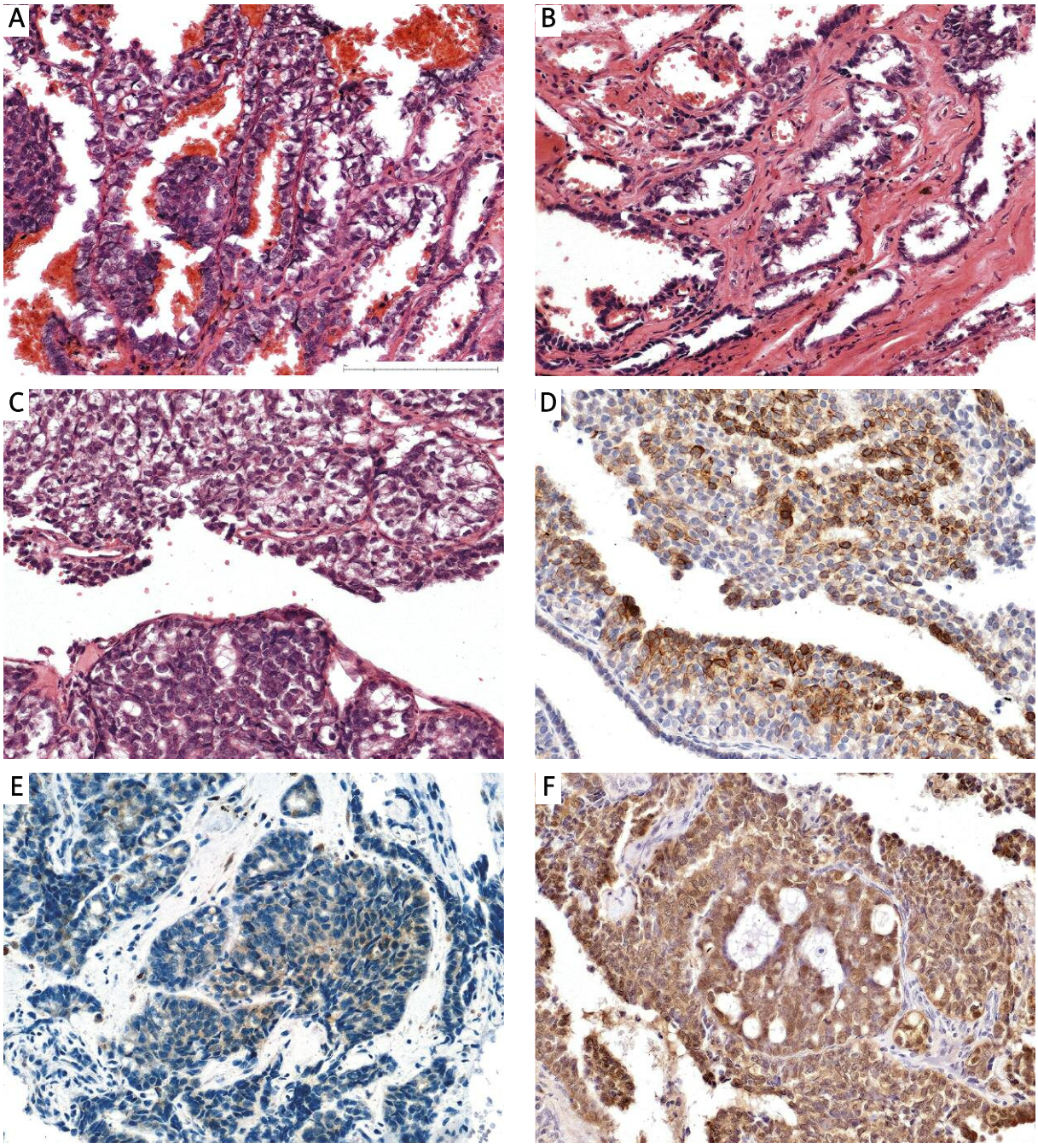

Fig. 1. Endolymphatic sac tumour microscopic patterns: **(A)** papillary **(B)** cystic and **(C)** solid with clear cells (haematoxylin-eosin). The tumour cells showed positivity with cytokeratin **(D)**, NSE **(E)** and S-100 **(F)**. All photographs taken under objective with magnification 20×.

sis, although onset of sudden unilateral deafness has been described secondary to ELST [12]. The average duration of symptoms varies from 9.3 to 10.6 years [17].

Radiologically (in CT and MR) a heterogeneous mass located and eroding the structures of the temporal bone is seen, centred in the sigmoid sinus, and growing towards the cerebello-pontine angle [4]. They appear hyper-intense on both T1- and T2-weighted MR images and show heterogeneous contrast enhancement [11]. Calcifications are seen in the tumour (spiculae),

there may be also a thin rim of calcification in the posterior border of the tumour. Angiography reveals a blood supply from branches of the external carotid artery (ECA), usually the ascending pharyngeal and occipital arteries [11].

At surgery, ELSTs are seen as reddish, firm lesions with a nodular or polypoid surface. They are highly vascularized and haemorrhagic [11,17,27]. The tumours also may be dense and fibrous, and can adhere to vascular structures and cranial nerves. Erosion of adjacent temporal bone and dura mater is common. In advanced cases, cerebellar tissue and/or cranial nerves could be infiltrated. Location of tumour origin determines tumour extension: if the neoplasm arises in the pars rugosa, it extends into the petrous bone; if the tumour arises in the intradural part of the endolymphatic sac, it extends into the cerebellopontine angle and the jugular foramen. Large tumours show a combined extension [31].

Histologically, ELST is adenocarcinoma of variable cellularity that can invade and erode bone and soft tissues. It is characterized by highly vascularized, poorly circumscribed proliferation of cuboidal epithelial cells forming a papillotubular pattern and occasional colloid-filled cysts. These formations are lined by a single row of cuboidal to low columnar or more flattened epithelial cells with eosinophilic or vacuolated cytoplasm [16,20]. The proportions of clear cells, follicle-like structures and of tumour stroma is variable [15,18,31]. Siderophages, siderosis of tumour cells and cholesterol clefts are frequently found [6,15,32]. A capillary network immediately subjacent to the epithelium corresponds to findings in normal endolymphatic sac [15]. PAS-positivity of tumour cells is typical and cytokeratin- and EMA-immunoreactivity are regularly found [15,18,31]. Vimentin-positivity of the basal portions of cytoplasm has previously been reported [13]. Immunohistochemical detection of GFAP, NSE, synaptophysin and S-100 protein may show focal positivity [4,15,18,31-33]. Mitotic figures are rarely present, necrosis is absent, and pleomorphism is minimal. From the point of view of diagnostic pathology, ELST located in the cerebellopontine angle may be misleading towards diagnosis of a metastatic adenocarcinoma. It is especially the case, when the part of extensive destruction of petrous bone is unknown for the pathologist (i.e. it is not reported).

In differential diagnosis of ELST the most attention should be given to the folliculopapillary metastatic adenocarcinomas with similar morphologic features, especially from thyroid, prostate, kidney and lung, but this is unlikely in the absence of clinical knowledge of the primary disease. Moreover, considering the male gender of the patient and the profile of cytokeratins (CK7+/CK20-) theoretically only metastatic lung carcinoma could be taken into account. However it must emphasized that the tumour did not show any traces of necroses in any form of inflammatory-reactive process, which is typical of metastasis. Moreover, from the morphological point of view, the local neoplastic processes (like paraganglioma and choroid plexus papilloma) could be considered, but the first one does not express cytokeratins and the second is quite unlikely to be found inside the temporal bone.

Complete surgical resection of the endolymphatic-sac tumours is curative and reported as the best treatment for this neoplasm [2,35]. Morbidity is thought to be related to the tumour size, however, 5-year survival rates are not yet available. At early stages it can be performed with the preservation of hearing and the alleviation of vestibular symptoms. Deaf patients with evidence of a tumour on imaging should undergo resection if other neurologic symptoms are present [19].

The importance of adjunctive radiation remains unclear [26], but inoperable tumours have been radiated [5]. Radiological follow-up with yearly MRI is indicated because of the aggressiveness and the proclivity for bony invasion of these neoplasms [19]. The stereo-tactically focussed radiotherapy (gamma-knife radiation) was also used to treat residual and recurrent ELST [3,7,11].

Conclusions

We have described a rare case of endolymphatic sac tumour which presented most of typical clinical, radiological and morphological features, with a history longer than 6 years. The patient did not show any evidence of VHL syndrome and his family histories were negative. The course of the disease confirms a relatively low aggressiveness of ELST. Until now, there has been no wide agreement concerning diagnosis and therapy. The tumour natural history and the role of various therapies will hopefully become available as the number of reports of ELST increases.

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