Surgical Treatment of Endolymphatic Sac Tumor With Adjunctive Stereotactic Radiation Therapy

—Case Report—

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Abstract

A 44-year-old man presented with an endolymphatic sac tumor (ELST) associated with von Hippel-Lindau disease, which required four surgical procedures within 10 years. The earlier two surgeries resulted in only partial removal of the tumor because of vigorous intraoperative bleeding. Stereotactic radiation therapy was performed twice. The intraoperative bleeding was easy to control in the third operation, and ultimately the tumor was totally extirpated in the fourth operation. Histological examination of the tumor specimen harvested in the final surgery showed that the tumor cells had clearly decreased in number, and the interstitial tissue had become fibrous with organization of the tumor vessels, compared with the tumor specimen from the first surgery. Preoperative radiotherapy may be effective to reduce the devastating intraoperative bleeding of ELST.

Key words: endolymphatic sac tumor, von Hippel-Lindau disease, surgery, radiation therapy, middle ear tumor

Introduction

Endolymphatic sac tumor (ELST) is a rare tumor originating from the endolymphatic sac of the petrous part of the temporal bone.1,14,15,17,22) ELST was called ceruminous gland tumor,4) choroidplexus papilloma,18) adenocarcinoma,7) or aggressive papillary middle ear tumor,5,6) before the tumor origin was confirmed.5,9) The incidence of ELST has not been clarified, but 13 patients with ELST were treated over the same period of 27 years as 2,300 acoustic neuromas.4)

ELST grows slowly, destroying the petrous bone and involving the cranial nerves, and is supplied by rich feeding vessels. Most of these tumors follow a benign clinical course, but some behave aggressively and extend intracranially.21) Half of the patients with unresectable ELST die of the disease.5,6,17) The involved cranial nerves and vigorous intraoperative bleeding make surgical excision of the tumor very difficult. The indications for radiation therapy as adjuvant treatment for ELST remain obscure.4,6,7,17,18,20,21)

We present a patient with a large ELST associated with von Hippel-Lindau disease (VHL) which required multiple surgical procedures and radiation therapy during the long clinical course, and discuss the significance of the early discovery of newly formed contralateral ELST in patients with VHL.

Case Report

A 44-year-old man had a past history of otic bleeding on the right of unknown origin when attending high school. He underwent surgical treatment for a cerebellar hemangioblastoma associated with VHL as a university student. The cause of the otic bleeding was suggested to be a tumor occupying the petrous part of the temporal bone. He was initially admitted to our hospital aged 33 years on October 15, 1991.

Neurological examination showed disturbance of the trochlear, trigeminal, and abducens nerves, deafness, facial paresis of the peripheral type, limb ataxia on the right, swallowing and speech disturbances, and ataxic gait. Magnetic resonance
Fig. 1 T1-weighted magnetic resonance (MR) images with gadolinium enhancement. (A) On initial admission in 1991, the large tumor had occupied and destroyed the petrous part of the right temporal bone. The cystic component of a hemangioblastoma is visible immediately medial to the tumor (arrow), and another hemangioblastoma is in the left cerebellar hemisphere (arrowhead). (B) The tumor of the petrous bone had developed intradurally before the second surgery in 1995. (C) The tumor had compressed the brainstem (arrow) before the third surgery in 1999. (D) The tumor had grown anteromedially and compressed the base of the temporal lobe (arrow) before the fourth surgery in 2001.

(MR) imaging showed a large tumor occupying and destroying the petrous part of the right temporal bone. The tumor appeared isointense on the T1-weighted image, hyperintense on the T2-weighted image, and was heterogeneously enhanced after gadolinium injection (Fig. 1A). Other abnormal lesions associated with VHL were simultaneously revealed, including multiple hemangioblastomas of the cerebellum (Fig. 1A) and cervical spinal cord, retinal angiomas, and a renal cyst.

The tumor of the temporal bone was resected via a lateral suboccipital craniectomy with partial mastoidectomy on January 30, 1992, after preoperative intravascular embolization of the feeding arteries of the tumor. The reddish, soft, fragile tumor contained many small vascular channels, and the enlarged bony cells of the petrous part showed sheet-like growth. Considerable hemorrhage caused 6,700 ml of blood loss during extirpation of the tumor, so only partial removal could be achieved. The histological diagnosis was ELST (Fig. 2A, B).

The tumor gradually enlarged after the first surgery (Fig. 1B), and required a second tumor resection on March 7, 1995, after preoperative intravascular embolization of the feeding arteries. Uncontrollable intraoperative hemorrhage, totaling 2,800 ml of blood loss, resulted in partial removal of the tumor located close to the cerebellum. Linac stereotactic radiotherapy was performed for the residual tumor on April 7, 1995 with a central dose of 30.0 Gy and a marginal dose of 24.0 Gy.

The tumor gradually increased in size after the radiotherapy and compressed the brainstem. The patient rejected a third tumor resection, so stereotactic radiosurgery (gamma knife) was carried out in April 1999 in 3 fractions over 3 days to prevent damage to the brainstem using a central dose of 86.7 Gy and a marginal dose of 26.0 Gy. The tumor continued to grow close to the brainstem after the gamma-knife surgery (Fig. 1C), resulting in worsening of the lower cranial nerve dysfunctions, cerebellar ataxia, and hemiparesis on the left. A third operation was performed on October 5, 1999 but only the intracranial part of the tumor compressing the brainstem was removed. The intraoperative bleeding was easy to control, totaling only 300 ml, which was a marked improvement from the previous losses.

A fourth operation was performed on December 11, 2001, 32 months after the gamma-knife surgery, because the tumor had grown anteromedially into the middle cranial fossa (Fig. 1D). The tumor mainly consisted of fibrously organized tissue, partly containing bony fragments, and most tumor vessels were thrombosed and organized, so the intraoperative bleeding was easy to control. The internal carotid artery and lower cranial nerves were preserved, but the facial and vestibulocochlear nerves were sacrificed with the tumor because the nerve functions were already lost. The internal jugular vein and lateral sinus on the right, which were involved by the tumor, were also sacrificed. The tumor was totally removed, corresponding to subtotal petrosectomy, and the space after tumor removal was filled with a vascularized muscle graft transposed from the trapezius muscle. The total blood loss during the surgery was 980 ml.

Gadolinium enhancement on MR imaging after the radiotherapy slightly decreased but only in the center of the tumor, but cerebral angiography
Fig. 2 Photomicrographs of the tumor specimens obtained from the first surgery showing (A) papillary-cystic structures lined by low columnar epithelium, reminiscent of the endolymphatic sac (HE stain, ×100), and (B) a crowded proliferation of glandular tumor cells with rich tumor vessels (HE stain, ×200). (C) Fibrosis and vestigial islands of the tumor cells are present in the specimen from the fourth surgery after irradiation (HE stain, ×200).

Fig. 3 Cerebral angiograms showing the tumor fed by small branches of the right external carotid artery. The main tumor stain occupying the petrous bone (A) became fainter after radiation therapy (B, 2 years after radiotherapy; C, 4 years after radiotherapy; D, 2 years after gamma-knife radiosurgery).

showed obvious reduction in the intensity of the main tumor stain occupying the petrous part (Fig. 3). Histological findings of the tumor specimens changed in parallel with the angiographic findings. The tumor specimen before radiotherapy showed crowded proliferation of glandular tumor cells with rich tumor vessels (Fig. 2B), whereas the specimen obtained from the final surgery revealed tumor cell depletion and fibrosis with hyalinized and thickened vessel walls (Fig. 2C). The MIB-1 index was 37.8% in the highest-density area of the newly formed part of the tumor obtained from the final surgery, and 0% in the irradiated part.

In addition to the above operations, several surgical treatments for cerebellar and spinal cord hemangioblastomas have been performed in our hospital since 1991. The patient is now living at home and using a wheelchair with a Karnofsky scale of 50.

Discussion

Complete excision of the ELST is desirable, but the vigorous tumor bleeding and encasement of the cranial nerves make successful resection very difficult. In the present case, the profuse bleeding from the intraosseous tumor was impossible to manage during the early surgical procedures.
Preoperative embolization of the tumor vessels did not effectively manage the bleeding as expected.\textsuperscript{20} The effectiveness of radiotherapy for the treatment of ELST remains controversial.\textsuperscript{1,4,6,7,17,18,20,21} Preoperative and postoperative radiotherapy have not received any positively recommendation as adjunctive therapy.\textsuperscript{2,9,20} However, no evidence of tumor activity or disease progression was observed during 1 to 8 years after postoperative radiotherapy of 50–65 Gy, or stereotactic radiosurgery of 14 Gy.\textsuperscript{16} Choroid plexus papilloma in the petrous bone, which is currently considered to be ELST, definitely regressed after radiotherapy of 49.5 Gy.\textsuperscript{6}

In the present case, postoperative radiotherapy was performed in the expectation of achieving tumor stabilization. Histological examination of the tumor specimens revealed that the tumor vessels had definitely decreased in number, and the tumor cells became organized with fibrosis of the interstitial tissue with an MIB-1 index of 0%. Cerebral angiography also showed that the main tumor stain became faint. Easy control of the intraoperative bleeding and the successful extirpation of the tumor in the final surgery were certainly the result of the effectiveness of radiotherapy. The clinical course of this case suggests that preoperative radiotherapy can be important in the treatment of ELST. The influence of radiation on the surrounding structures of the tumor should be minimized, but any cranial nerves involved by the tumor will be difficult to preserve. Therefore, preoperative radiotherapy is indicated if vigorous intraoperative bleeding is predicted, or if partial cranial nerve disturbances are acceptable. Treatment of more patients with ELST will determine the suitable dose of preoperative radiotherapy, and the suitable observation period for the radiation effect, because another dose of radiation was unintentionally employed before the final surgery in the present case.

VHL is a multisystem neoplasic disorder with an autosomal dominant inheritance pattern, and a predisposition to develop multiple tumors including retinal angiomas, cerebellar and spinal cord heman-gioblastomas, renal cell carcinomas, pheochromocy-tomas, ependymal cysts, and pancreatic cysts.\textsuperscript{3,15} ELST is sometimes associated with VHL, and the allelic deletion and mutation of the VHL tumor suppressor gene probably contributes to the oncogenesis of the ELST as well as the other tumors in VHL.\textsuperscript{10,11,13,16,22,23} Review of previous cases of aggressive papillary tumor of the middle ear, which is currently called ELST, found that seven of 46 documented cases of ELST arose in patients with VHL.\textsuperscript{5} Screening MR imaging revealed evidence of 15 ELSTs in 13 of 121 patients with VHL, but in none of 253 patients without VHL.\textsuperscript{15} These two studies revealed a frequent association between VHL and ELST.

Audiologic screening for patients with VHL found that 43 of 66 patients with VHL had pure tone threshold abnormalities, although MR imaging detected no evidence of ELST.\textsuperscript{15} Furthermore, the audiologic abnormalities occurred bilaterally in 23 of the 43 affected patients. Considering that all patients with ELST had a history of sensorineural hearing loss several years before tumor discovery,\textsuperscript{15,10} possibly most or all patients with VHL have ELST which is too small to detect by MR imaging. Furthermore, half of the affected patients had bilateral ELSTs. All reported patients with bilateral ELSTs also had VHL.\textsuperscript{12,15,16,19} Therefore, patients with unilateral ELST should be periodically followed by audiologic examination and MR imaging to detect the development of newly formed nontotal lesions. Early identification of ELST will enable monitoring of its growth and excision of the lesion with preservation of hearing.\textsuperscript{15,19}

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References


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