Metastasis in von Hippel–Lindau Disease

To the Editor: Not long ago in the Journal of Neurosurgery, Jarrell et al. (Jarrell SA, Vortmeyer AO, Linehan WM, et al: Metastasis to hemangioblastomas in von Hippel–Lindau disease. J Neurosurg 105:256–263, August 2006) thoroughly reviewed all cases of von Hippel–Lindau disease at the National Institute of Neurological Disorders and Stroke that had been treated with resection or found at autopsy to have metastases to a hemangioblastoma.

Object. Patients with hereditary cancer syndromes may be at increased risk for the development of tumor-to-tumor metastases. To gain insight into the biological nature of these lesions in the central nervous system (CNS), to determine their prevalence in a familial neoplasic syndrome, and to better define their management, the authors retrospectively examined a series of cases in which metastatic lesions developed within hemangioblastomas in patients with von Hippel–Lindau (VHL) disease.

Methods. The study included all cases of VHL disease in which patients underwent resection of a CNS hemangioblastoma that contained a metastasis or were found at autopsy to have a metastasis to a hemangioblastoma between January 2002 and December 2005 at the National Institute of Neurological Disorders and Stroke (NINDS). Clinical, histopathological, imaging, and surgical and/or autopsy findings were analyzed.

Metastasis to a CNS hemangioblastoma was found in six resected tumors (8% of all hemangioblastomas resected from patients with VHL disease at the NINDS during the study period) from six patients (five women, one man; mean age at surgery 42.5 years). The primary site of metastatic disease was the kidney in five patients (renal cell carcinoma) and the pancreas in one (a pancreatic neuroendocrine tumor). Only one patient had systemic metastases at the time of resection of the hemangioblastoma containing the metastasis. Neurologically, all patients had remained at baseline or were improved at last clinical follow-up examination (mean follow-up duration 16.5 months, range 3–40 months). In all cases, postoperative imaging revealed that the hemangioblastoma resection was complete, and there was no evidence of recurrence in any of the patients at the last follow up. Two patients (including one who was also in the surgical group) were found at autopsy to have CNS metastases exclusively to spinal hemangioblastomas.

Conclusions. Hemangioblastomas are an early and preferred site for metastasis in VHL disease. Emerging histopathological techniques may lead to recognition of an increasing number of cases of tumor-to-hemangioblastoma metastasis. Management of cases involving tumor-to-hemangioblastoma metastases in VHL disease should be based on the histological characteristics of the primary tumor, extent of the primary disease, and completeness of the resection.

Whereas 5 of 6 cases involved renal cell carcinoma metastatic to the hemangioblastoma, 1 case involved a pancreatic neuroendocrine tumor (PNET) that spread to a hemangioblastoma. This latter case was the first reported example of the so-called tumor-to-tumor metastasis involving a PNET metastatic to a hemangioblastoma. I recently cared for this same patient during a follow-up. Von Hippel–Lindau disease had been diagnosed when the patient was 19 years of age following surgeries for a retinal malformation (age 5 years) and an endolymphatic sac tumor (age 17 years). The metastatic neuroendocrine tumor involving her liver had been diagnosed in 2002. In 2006 a review of the histological studies at the National Institutes of Health revealed that a resected hemangioblastoma was seeded with the neuroendocrine tumor, prompting the report by Jarrell et al. In 2008 the patient has had 2 additional cerebellar hemangioblastomas removed, each with tumor-to-tumor involvement of a “far more abundant” component of PNET.

Because renal cell carcinoma and PNETs are common visceral tumors associated with VHL and because newer agents and improved surgical techniques are prolonging the survival of patients with these diseases, more cases of tumor-to-tumor metastases will likely be described for this and other syndromes involving multiple primary tumors. As Jarrell and colleagues discussed, hemangioblastomas may provide an ideal environment for tumor-to-tumor metastases given their vascularity. These lesions might also be referred to as “piebald” tumors, that is, neoplasms composed of varied components. Antiangiogenic therapy has already shown activity in hemangioblastomas and other VHL-associated tumors including neuroendocrine tumors.1–4 More reports are needed to determine whether VHL-associated visceral tumors metastatic to the highly vascular hemangioblastomas are even more promising targets for these agents.

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References

Response: We appreciate Dr. Sorscher’s interest in our report and the follow-up of our patient (Case 4) with a PNET metastatic to a hemangioblastoma. As noted in his letter, this patient with VHL underwent the resection of 3 additional PNET metastases to hemangioblastomas after the publication of our report. The removal of these additional PNET metastases to hemangioblastomas underscores the finding that hemangioblastomas appear to be a preferred site of metastasis for primary visceral malignancies (that is, renal cell carcinoma, pheochromocytoma, and PNET) in patients with VHL.

Because serial surveillance and judicious treatment of
VHL-associated tumors is reducing the morbidity and mortality rates in these patients, it is likely that more cases of tumor-to-tumor metastases will be found in patients with VHL who frequently have multiple, contemporaneous, systemic malignancies and CNS hemangioblastomas. Moreover, the findings in the patient in Case 4 further emphasize the importance of the serial surveillance of visceral and CNS neoplasms as well as a thorough histopathological examination of resected hemangioblastomas for tumor-to-tumor metastases in VHL. Ultimately, a deeper understanding of the biology underlying this phenomenon—preferential metastasis to hemangioblastomas in VHL—should provide critical insight into optimal treatment strategies for these neoplasms. (DOI: 10.3171/JNS/2008/109/9/0568)

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Endolymphatic Sac Tumors


Abstract

Object. Although endolymphatic sac tumors (ELSTs) frequently destroy the posterior petrous bone and cause hearing loss, the anatomical origin of these neoplasms is unknown. To determine the precise topographic origin of ELSTs, the authors analyzed the imaging, operative, and pathological findings in patients with von Hippel-Lindau disease (VHL) and ELSTs.

Methods. Consecutive VHL patients with small (≤ 1.5 cm) ELSTs who underwent resection at the National Institutes of Health were included. Clinical, imaging, operative, and pathological findings were analyzed.

Results. Ten consecutive VHL patients (6 male and 4 female) with 10 small ELSTs (≤ 1.5 cm; 9 left, 1 right) were included. Serial imaging captured the development of 6 ELSTs and revealed that they originated within the intraosseous (vestibular aqueduct) portion of the endolymphatic duct/sac system. Imaging just before surgery demonstrated that the epicenters of 9 ELSTs (1 ELST was not visible on preoperative imaging) were in the vestibular aqueduct. Inspection during surgery established that all 10 ELSTs were limited to the intraosseous endolymphatic duct/sac and the immediately surrounding region. Histological analysis confirmed tumor within the intraosseous portion (vestibular aqueduct) of the endolymphatic duct/sac in all 10 patients.

Conclusions. ELSTs originate from endolymphatic epithelium within the vestibular aqueduct. High-resolution imaging through the region of the vestibular aqueduct is essential for diagnosis. Surgical exploration of the endolymphatic duct and sac is required for complete resection.

The authors report the intraosseous part of the endolymphatic duct/sac system (vestibular aqueduct) as the origin of ELSTs and recommend the complete surgical removal of these lesions, including the intraosseous portion of the endolymphatic duct/sac system. The tumor was successfully extirpated by performing a retro labyrinthine posterior petrosectomy (RLPP) in that and a previous series. However, I wonder about accessibility to the anterior portion of the endolymphatic duct/sac system, that is, the region just posterior to the junction between the endolymphatic duct and the saccular and utricular ducts. This part of the endolymphatic system is located just medial to the posterior semicircular canal whose plane is almost parallel to the posterior plane of the temporal bone (Fig. 1). Therefore, preservation of the posterior semicircular canal may be difficult when attempting to expose the entire anterior part of the endolymphatic system by performing an RLPP. Access to this region may be gained more easily via an intradural approach through a retrosigmoidal lateral subtotal craniotomy. This surgical maneuver is a modification of the technique used for removing the posterior meatal wall to address a vestibular schwannoma. As shown in Fig. 3 of the authors’ article, drilling the posterior surface of the temporal bone between the external aperture of the vestibular aqueduct and the region posterior to the posterior meatal lip can expose the intraosseous part of the endolymphatic system, including the most anterior portion. The approximate location of the vestibular aqueduct is 5–11 mm (average 7.5 mm) from the posterior meatal lip and 0.6–3 mm (average 1.5 mm) from the posterior surface of the temporal bone.

Have the authors encountered difficulties exposing the most anterior part of the endolymphatic system behind the posterior semicircular canal during an RLPP? I would like assurance that my concern regarding accessibility to the structure to be totally removed is unwarranted.

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References

3. Shimizu S, Tanaka R, Oka H, Fuji K: Risk of damage to the
RESPONSE: We appreciate Dr. Shimizu’s interest in our recent report. Although there are several operative approaches for the removal of ELSTs, the choice of a surgical approach is often dictated by tumor size and hearing status. To successfully remove the smaller ELSTs (< 1.5 cm) analyzed in our report and to preserve hearing, we used the RLPP, which has been described in detail. With this procedure, the endolymphatic sac and duct can be clearly and easily delineated medial to and behind the posterior semicircular canal once the bone over the sigmoid sinus and posterior fossa dura mater has been removed and these structures are retracted posteriorly. Endolymphatic sac tumors within or extending out of the vestibular aqueduct can then be safely removed while tracing the endolymphatic sac/duct proximally into the vestibular aqueduct and visualizing the limits of the inner ear structures, including the posterior semicircular canal. The RLPP also provides excellent exposure to the petrous apex and jugular bulb via the retrofacial air cells. Because ELSTs commonly extend to the petrous apex and jugular bulb as they grow, the RLPP can be used to provide excellent access to these anatomical regions when removing tumors near these structures.

Megerian and colleagues have reported using a retrosigmoid approach for ELST resection. In our experience, the retrosigmoid approach alone can be suboptimal because it can be difficult to safely delineate the entire posterior semicircular canal and endolymphatic duct from the posterior fossa side, it is associated with a higher risk of cerebrospinal fluid leak via exposed mastoid air cells, it requires cerebellar retraction, and it may necessitate dissection through the postoperative scar tissue that is frequently found in patients with VHL who have undergone multiple posterior fossa operations. However, we and others have combined the retrosigmoid approach with the RLPP for the removal of large ELSTs that extend to the internal auditory canal, into the cerebellopontine angle and/or the petrous apex medial to the internal auditory canal in patients with serviceable hearing. For those without serviceable hearing and large ELSTs extending into the cerebellopontine angle, we have used a combined retrosigmoid–translabyrinthine or transotic approach for tumor resection. (DOI: 10.3171/JNS/2008/109/9/0569)

References


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Erratum

To The Editor: Thank you for publishing our paper entitled “A novel endovascular clip system for the treatment of intracranial aneurysms: technology, concept, and initial experimental results. Lab investigation” (J Neurosurg 108: 1230–1240, June 2008). Unfortunately, we incorrectly listed the stain for Figs. 8, 9, and 10 as H & E when, in fact, Verhoeff elastic trichrome was used. (DOI: 10.3171/JNS/2008/109/9/0571)

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