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CORRESPONDENCE

High Resolution MRI of Vestibulocochlear Nerve Involvement by a Posterior Fossa Ganglioglioma: Case Report and Review of Literature

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Introduction

White matter tracts from brainstem cranial nerve (CN) nuclei are organized within the brainstem in axonal bundles before emerging from the brainstem as individual CN. The CN transitional zone (TZ) is the segment of the CN where transition from the myelinated axons of oligodendrocytes to the more robust fascicular organization of the peripheral nervous system myelinated by Schwann cells occurs [1, 2]. In rare cases, brainstem glial tumors have been observed to involve the TZ manifesting as asymmetric thickening and enhancement on magnetic resonance imaging (MRI). We present a case of brainstem ganglioglioma with involvement of the proximal cisternal segment of the vestibulocochlear nerve. To the best of our knowledge, this is the first reported case of a posterior fossa ganglioglioma with CN involvement. The unique combination of MRI findings and clinical data provide insights into the pathophysiologic mechanism of CN involvement by glioma.

Case Report

A 27-year-old male patient presented with a longstanding history of generalized headache and frequent intermittent vertigo attacks averaging 5 times per day and lasting 2–10 min in duration. The nature of the vertigo was rotational with the feeling of objects tipping to one side. Subjectively, the patient also experienced unsteadiness especially with sideways lateral head movements. The patient had left-sided neurosensorial hearing loss without reported tinnitus. Neurological examination revealed hypermetric saccades to the left and saccadic pursuit. There was spontaneous nystagmus to the right and gaze-evoked nystagmus to the right on right lateral gaze. Cerebellar testing demonstrated an intention tremor and past pointing with the left hand and positive oscillopsia test. Vestibulo-ocular reflex cancellation was abnormal to the right. The gait was broad based. Post-headshake nystagmus was positive to the right. On Hallpike testing, he had multidirectional nystagmus. There was a torsional element to the right side. On the left side, there was geotropic torsional nystagmus, which then converted into a left beating lateral nystagmus. No evidence of palatal myoclonus. Brain MRI performed on a 3T scanner (MAGNETOM Skyra, Siemens, Erlangen, Germany) (Fig. 1) showed a heterogeneous intra-axial mass located on the left side of the lower brainstem (medulla and pons) and left cerebellum with involvement of the inferior, middle and superior cerebellar peduncles. Post-gadolinium-enhanced T1-weighted (T1-W) sequence showed "paint brush" pattern of contrast enhancement. There was subtle left cerebellar atrophy present likely secondary to Wallerian degeneration. Susceptibility weighted imaging (SWI) demonstrated areas of coarse intra-lesional calcifications, which were also confirmed on a prior plain head computed tomography (CT) scan. Axial fluid attenuation inversion recovery (FLAIR) demonstrated asymmetrical thickening of the left vestibulocochlear nerve over a distance of 10 mm and post-gadolinium enhanced T1-W sequence showed asymmetric thickening and enhancement of the involved left vestibulocochlear nerve. The patient underwent biopsy via a left suboccipital approach. Histopathologic examination of the sample revealed abnormal neurons arranged in proliferation of benign astrocytic cell with numerous Rosenthal fibers,a sclerotic vasculature with perivascular inflammation consistent with a World Health Organization (WHO) grade I ganglioglioma. The patient was managed conservatively and clinical radiologic surveillance over a period of 10 years showed no appreciable change in the appearance of the posterior fossa ganglioglioma or the involved left vestibulocochlear nerve.

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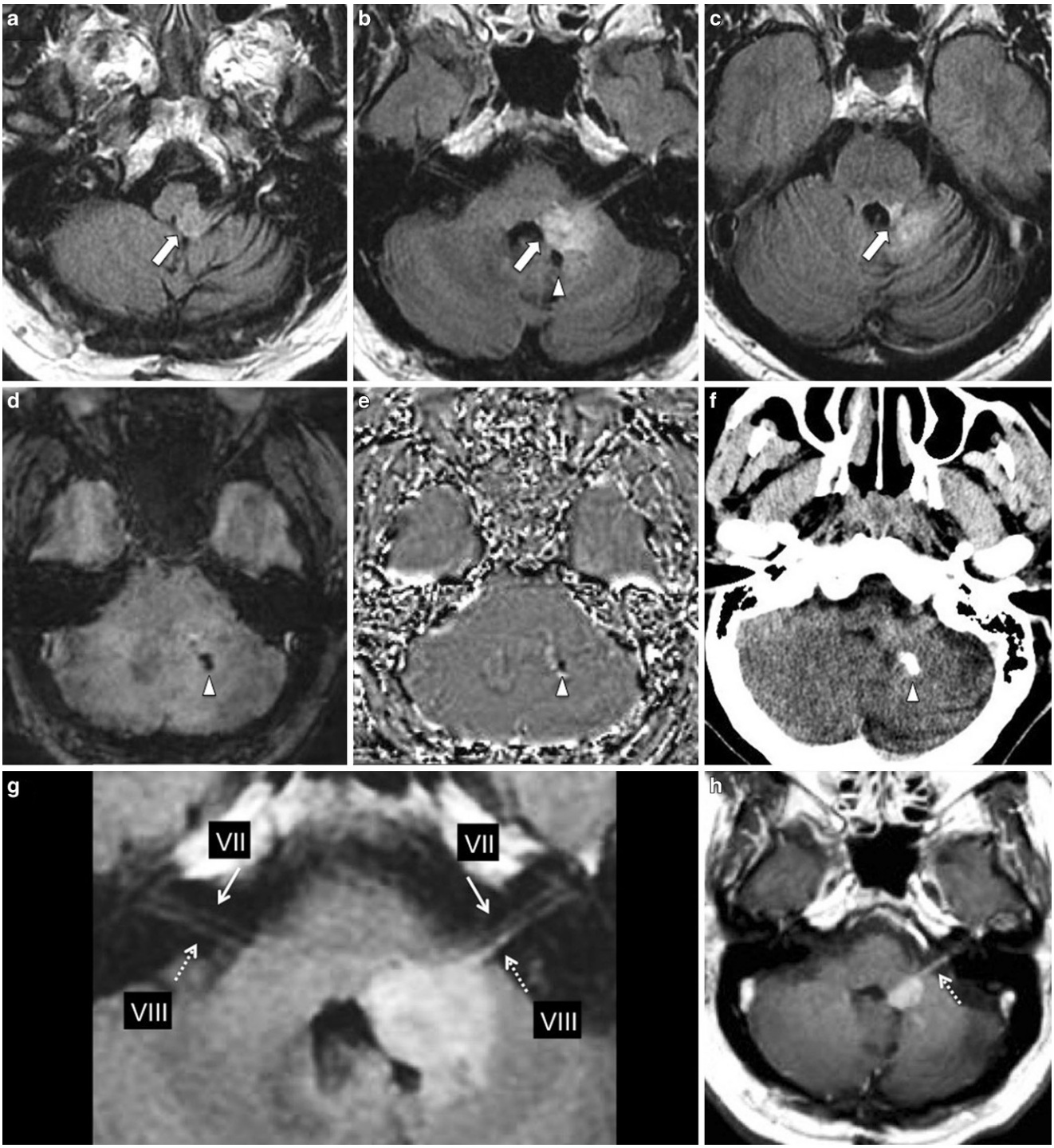

Fig. 1 MRI brain axial FLAIR images (**a**–**c**) showing an expansile intra-axial lesion involving the left side of the brainstem, paramedian left cerebellar hemisphere and the left inferior, middle and superior cerebellar peduncle (*arrows*). An intralesional hypointense focus is evident (*arrowhead*) on the FLAIR image (**b**) which appears hypointense on both SWI and SWI phase images (**d**, **e**). Plain head CT (**f**) confirms presence of coarse intralesional calcification. Magnified FLAIR image (**g**) showed the left middle cerebellar peduncle mass at the level of the cerebellopontine angle with contiguous involvement of the cisternal segment of the left vestibulocochlear nerve over a distance of 10 mm (*dotted arrow*). Post-gadolinium-enhanced T1W image (**h**) demonstrates the enhancing left middle cerebellar peduncle mass and asymmetric thickening and enhancement of the left vestibulocochlear nerve (*dotted arrow*)

Discussion

Direct CN involvement by glioma is an exceedingly rare phenomenon with only 19 reported cases in the literature. The characteristic MRI features include a brainstem lesion with either contiguous nodular or linear extension into the cisternal segment of the involved CN over a variable length (average distance of 9.4 mm) and asymmetric thickening and enhancement of the CN (average abnormal thickness of 5.9 mm) [3–10]. The vestibulocochlear (47.4%) and trigeminal (42.1%) nerves are most commonly involved followed by facial (5.3%) and oculomotor nerves (5.3%) [3–10]. The varying frequency of the extent of CN involvement may be partially attributed to the inherent histopathologic difference in the length of the TZ. The vestibulocochlear nerve has the longest TZ (11.5 mm), followed by facial (2.86 mm) and trigeminal nerves (2.47 mm lateral aspect of the nerve and 1.13 mm medial aspect of the nerve) [1, 2, 11, 12]. The two hypotheses for glial tumor involvement of the TZ include direct tumor extension into the TZ from the brainstem and de novo tumor arising from nests of glial and neuronal cells within the TZ. The latter hypothesis is more plausible given the majority of the previously reported cases manifested on MRI as direct tumor extension along the intra-axial pathway into the TZ of the CN. Very rarely, CN involvement by glial tumor manifests as a discrete CN mass. Microanatomically, neoplastic astrocytic cells are known to utilize both oligodendrocyte membrane-associated ligands as well as extracellular matrix (ECM) proteins of the basement membranes for disease dissemination [13]. Enzymatic modification of the extracellular space or deposition of ECM by the tumor cells may also create a more permissive environment [13]. The CN intra-axial pathway consist of axonal fibers arranged in parallel configuration lacking the fascicular organization of the peripheral nervous system which may serve as a conduit for glial infiltration similar to the mechanism of white matter tract infiltration of the brain. We hypothesized that beyond the TZ the more resilient fascicular organization of the peripheral CN may act as a physical barrier for glial tumor infiltration. This hypothesis is supported by our review of the literature with involved CN by glial tumors showing an average peripheral extension of less than 10 mm likely within the TZ for most CN [3–10]. We also must emphasize that the pathological basis of CN involvement by glial tumors differs from the more commonly encountered perineural disease from head and neck carcinoma or melanoma where the neurotropic tumor cells infiltrate the perineurium and the nerve fascicles and can travel in both an antegrade and retrograde fashion reaching notable distances from the site of primary disease [14].

Reported cases of CN involvement by glial neoplasms include a combination of low and high-grade lesion consisting of WHO grade I–II fibrillary astrocytoma (44.44%) and pilocytic astrocytoma (44.44%), followed by WHO grade IV glioblastoma (11.11%) [3–10, 15, 16]. It is worthy to mention that our case was the first reported case of CN involvement by a ganglioglioma. Posterior fossa gangliogliomas are less common than their supratentorial counterpart and display more variable imaging features including infiltrative patterns and striking heterogeneous enhancement patterns with a linear distribution, so-called paintbrush type enhancement [17, 18]. Morphologically, the posterior fossa gangliogliomas can exhibit three morphologic appearances: exophytic (majority of the tumor volume outside the brainstem and a larger part of the trunk exhibits normal morphology and signal), intrinsic (tumors within the brainstem without brainstem surface compromise) and endo-exophytic (tumors within the brainstem with brainstem surface penetration, extending into peri-brainstem areas) [17, 18]. In our case example the ganglioglioma was intrinsic but we are unsure of this significance in relation to the CN involvement. The biologic behavior of posterior fossa gangliogliomas differs to the supratentorial counterpart with a worse progression-free survival and a higher mortality rate [16, 17, 19]. The majority of gangliogliomas are designated as WHO grade I; however, rare cases of anaplastic gangliogliomas have been reported [17]. Criteria for WHO grade II are not yet established. The histopathologic hallmark criteria for the diagnosis of gangliogliomas is a combination of the presence of neoplastic glial and ganglionic cells, which can be mixed or geographically separated. A subgroup of posterior fossa ganglioglioma with a BRAF V600E mutation are associated with shorter progression-free survival but exhibit no unique imaging features, and carry promising treatment implications by BRAF inhibitors [17, 19]. The ganglioglioma presented in our case was WHO grade I but at the time of diagnosis the BRAF V600E mutation status was not tested.

Clinical manifestations of CN involvement by glial tumor differ from head and neck perineural disease. The clinical symptoms of conventional perineural disease from head and neck malignancies are diverse and including pain, paresthesia, numbness, burning sensation, visual changes and weakness, following the distribution of the respective nerve and eventual denervation atrophy and paralysis in advanced cases [20]. The diagnosis can be subtle and slowly progressive hence there is often a delay in the diagnosis. In contrast, CN involvement by glial tumor presents with central CN neuropathy or palsy from the onset due to direct involvement of both the cranial nerve nuclei and intra-axial pathways. Specifically, posterior fossa gangliogliomas usually present with ataxia, progressive CN deficits and even sudden death induced by impairment of respiratory centers in the brainstem [16]. In our patient the vestibulocochlear nuclei and nerve involvement produced clinical symptoms

of debilitating vertigo, nystagmus, unsteadiness and sensorineural hearing loss at the time of initial diagnosis even though there was no evidence of radiologic progression over a decade.

Conclusion

A CN involvement by a glial tumor is an extremely rare entity and we described the first reported case of vestibulocochlear nerve involvement by a ganglioglioma. We discussed in-depth the clinical radiologic findings and pathophysiologic mechanism of this rare entity as one of the contributing cause of debilitating cranial neuropathy.

Conflict of interest B. Trapp, C. Chia-Tsong Hsu, J. Panwar and T. Krings declare that they have no competing interests.

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