Clinical Study

Cranial nerve root entry zone primary cerebellopontine angle gliomas: a rare and poorly recognized subset of extraparenchymal tumors

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Summary

With the exception of patients with neurofibromatosis type II, pediatric extraparenchymal cerebellopontine angle (CPA) tumors of any sort are extremely rare. Most gliomas encountered in the CPA in either children or adults involve the CPA as exophytic extensions of primary brain stem and/or cerebellar tumors. We encountered an unusual case of a giant CPA pilocytic astrocytoma arising from the proximal trigeminal nerve, completely separate from the brain stem. A nine-year-old girl with no evidence for any neurocutaneous syndrome, presented with headaches, mild obstructive hydrocephalus, trigeminal hypesthesia and a subtle peripheral facial paresis. Pre-operative neuroimaging suggested a petroclival meningioma. The tumor was completely resected via a right pre-sigmoid, retro-labyrinthine, subtemporal, transtentorial ('petrosal') approach, using intraoperative neurophysiological monitoring, with minimal morbidity. This appears to be the first reported case of a pediatric primary CPA glioma and the seventh reported case of primary CPA glioma, overall. It represents the second reported case of a primary CPA pilocytic astrocytoma. Given the findings in this case and the six other cases of primary CPA gliomas reported in the literature, as well as the results of histological studies of normal cranial nerves, we hypothesize that the point of origin of these rare and unusual tumors is the root entry zone of the involved cranial nerves. The differential diagnosis of primary CPA tumors should be expanded to include cranial nerve root entry zone primary CPA gliomas.

Introduction

Extra-axial cerebellopontine angle (CPA) tumors account for approximately 10% of all intracranial tumors in adults, but only 0.2–3% of posterior fossa tumors in children. A large portion of these are found in children with neurofibromatosis type II (NF2) with bilateral vestibular schwannomas. In children without NF2, CPA tumors are even more rare. The differential diagnosis of CPA tumors includes cranial nerve schwannomas (vestibular most common), meningiomas, neurofibromas, metastatic tumors, epidermoid, dermoid and arachnoid cysts, ependymomas, choroid plexus papillomas, lipomas, medulloblastomas, ependymoblastomas, glomus jugulare tumors, cholesteatomas, and exophytic brain stem gliomas [4,5,7,9–17,19,23,24,26,31,34,36].

Exophytic brain stem gliomas are rare. Most cases reported in the literature have been either fibrillary or gemistocytic astrocytomas [5,14,16,19,31]. While pilocytic astrocytomas are common in children, especially in the posterior fossa, they are almost always intraparenchymal in origin and are rarely exophytic in nature. The literature suggests that all but six gliomas, of any sort, encountered in the CPA have been exophytic extensions of a brain stem glioma. Beutler and colleagues reported a single case of a pilocytic astrocytoma arising from the eighth cranial nerve, completely separate from the brain stem. Five additional extra-axial non-pilocytic CPA gliomas have been reported arising from the eighth nerve. All six occurred in adults [4,8,17,27,31].

We recently encountered a giant pilocytic astrocytoma in the CPA of a child arising from the proximal trigeminal nerve, completely separate from the brain stem. Pre-operatively, neuroimaging had strongly suggested a petro-clival meningioma. Since cranial nerve eight and five have the first and second longest root

entry zones, respectively, of any cranial nerve (optic and olfactory nerves excluded), it is likely that both our case, and six previously reported cases, arose from the root entry zone of the cranial nerve.

Case

Presenting symptoms and neurological findings

A nine-year-old, right-handed, African American girl presented to our Emergency Room with a two month history of intermittent headaches, significantly increasing in intensity over the past two weeks. They were accompanied by nausea and vomiting 2–3 times per day for the last four days. The patient's mother also reported one 'blackout' episode that has occurred on the morning of presentation. Her past medical, surgical and family histories were all noncontributory.

On general physical examination she had no oculocutaneous stigmata of any neurocutaneous syndrome. There was no papilledema. Neurological examination revealed right-gaze horizontal nystagmus, but full extra-ocular movements without diplopia. The right corneal reflex was significantly decreased. Light touch sensation in her right V 1–3 distribution was decreased; pinprick sensation in the same area was preserved. She had House-Brackmann grade 2 facial function on the right [14]. Hearing tested by audiogram was normal and symmetric. Gag, voice, and swallowing function were normal. Tests for dysmetria and dysdiadokinesis revealed relative impairment on the right. Gait was moderately ataxic. The rest of her neurological examination was normal.

Neuroimaging

Computerized tomography (CT) scan revealed a diffusely-enhancing, hypodense, right extra-axial, petro-clival CPA mass with an apparent broad linear base along the posterior surface of the petrous bone (Figure 1). Magnetic resonance imaging (MRI) revealed a diffusely enhancing giant extra-axial CPA tumor (3.5 cm × 4 cm × 4.5 cm) with significant brain stem, fourth ventricular, and cerebellar compression (Figure 2). The tumor was hypointense on short TR, and strongly hyperintense on long TR sequences (Figures 1 and 2). Magnetic resonance angiography (MRA) demonstrated relative right-sided dominance of

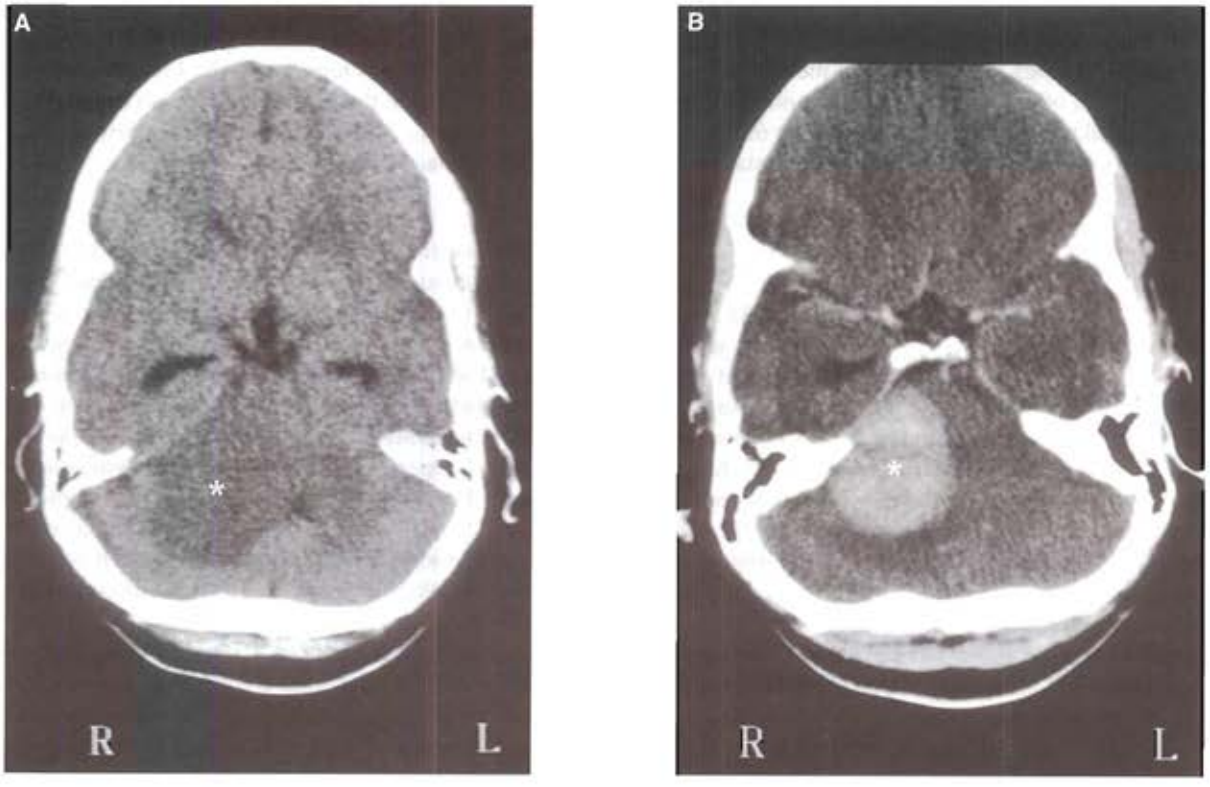


Figure 1. A: Unenhanced axial cerebral CT scan of demonstrating a giant right hypodense petro-clival CPA tumor (*). B: Postcontrast axial cerebral CT scan demonstrating homogenous enhancement of the tumor (*).

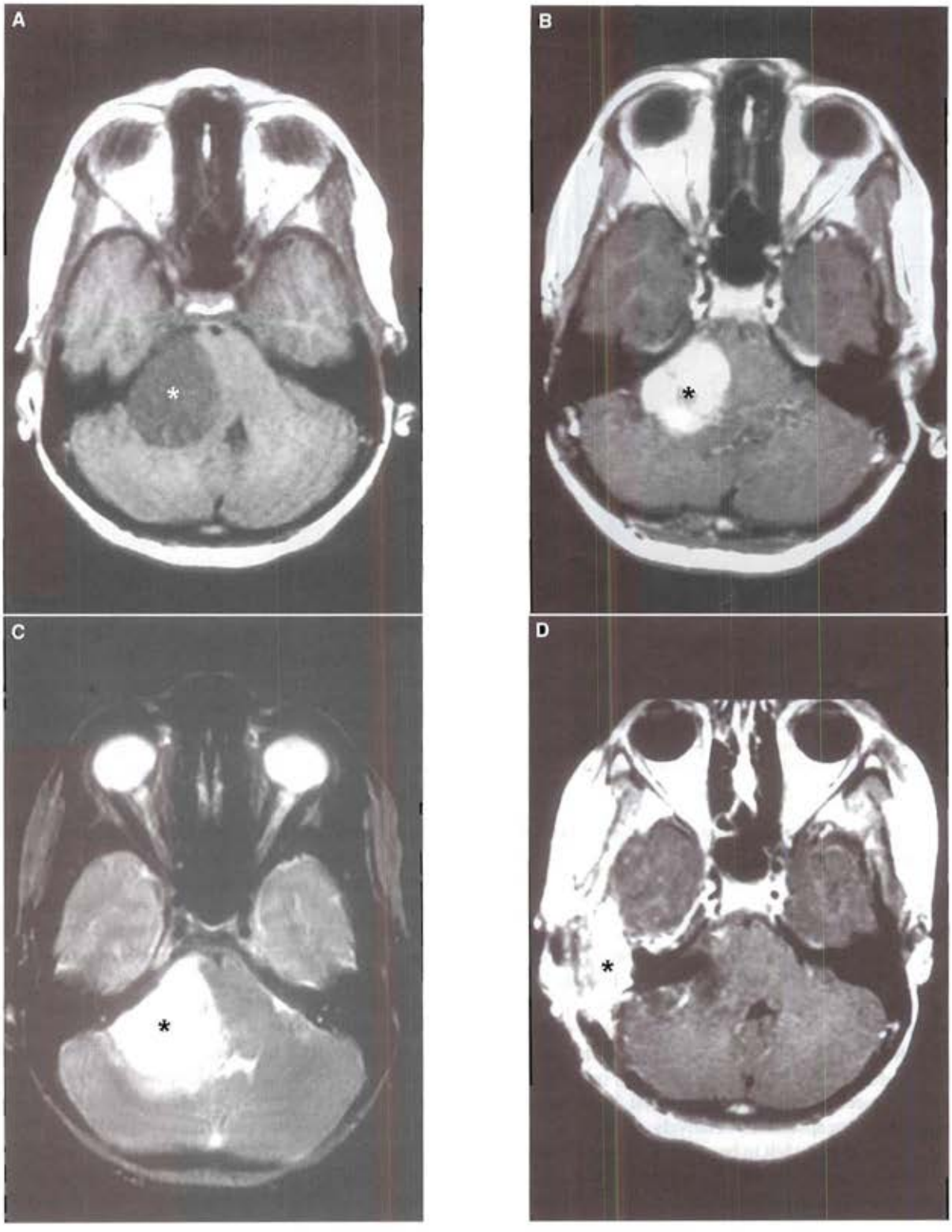


Figure 2a–d.

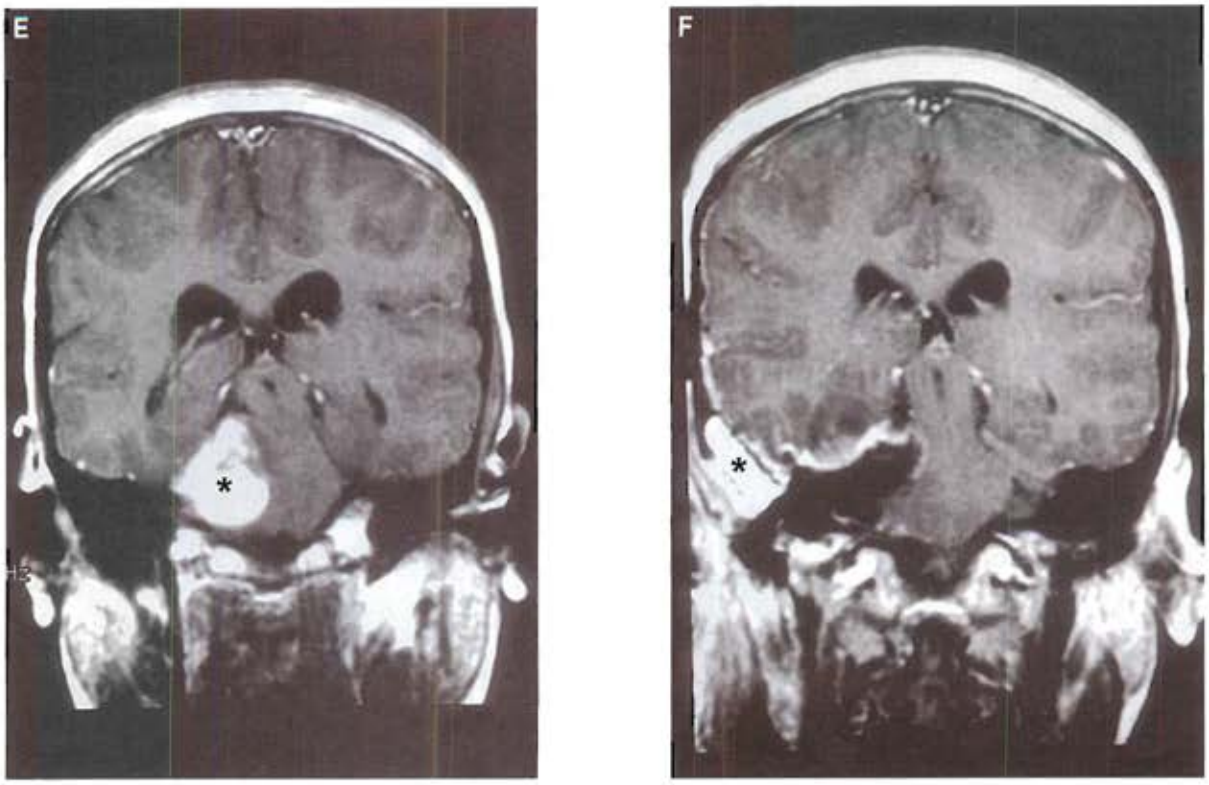


Figure 2e & f. A. Noncontrast axial short TR MR image revealing a hypointense giant right petro-clival CPA tumor (*) (TR 400/TE 16/NEX 1); B: Same image after contrast enhancement revealing a brightly and homogeneously-enhancing tumor (*) (TR 400/TE 16/NEX 1); C: A long TR un-enhanced MR image revealing a hyperintense CPA tumor (*) (TR 2500/TE 30/NEX 0.75); D: Postoperative contrast-enhanced axial MR image demonstrating gross total tumor removal. Note the fat graft (*) placed in position of drilled petrous bone (TR 400/TE 16/NEX 1). E. Coronal contrast-enhanced short TR MR image revealing a brightly homogeneously-enhancing CPA tumor (*). Note the brain stem compression (TR 400/TE 16/NEX 1) F: Post-contrast postoperative coronal short TR MR image confirming gross total tumor removal and relief of brain stem compression. Note the fat graft (*) placed in position of drilled petrous bone (TR 400/TE 16/NEX 1)

transverse/sigmoid sinus. The tumor itself had a faint reticular tumor blush on MRA.

Operative findings

The lesion was approached via a right pre-sigmoid, retro-labyrinthine, sub-temporal, trans-tentorial ('petrosal') approach [2,3] with somatosensory evoked potential (SEP), brain stem auditory evoked response (BAER), and facial nerve electromyography (EMG) intraoperative monitoring. Upon dural opening and tentorial sectioning, we encountered a gray-green, apparently encapsulated, relatively poorly vascularized tumor, grossly felt to be a schwannoma. Preserved arachnoid cistern planes allowed us to successfully separate and elevate the tumor from the cranial nerve IX and X complex, the cranial nerve VII and VII complex, and the anterior inferior cerebellar artery inferiorly. Frozen section biopsy surprisingly returned a diagnosis of 'low grade astrocytoma'.

The tumor center was debulked using a cavitron ultrasonic aspirator until the tumor capsule became mobile. A clear arachnoid cleavage plane was present along the interface between tumor and the cerebellum, middle cerebellar peduncle, and the pons. The tumor was found to arise from the proximal trigeminal nerve distal from its brain stem origin. The nerve itself was atrophic and thinned to a widened and diaphanous superior 'cap' over the tumor. A gross total tumor resection was achieved with all surrounding anatomic structures preserved. An abdominal fat graft was harvested and placed in the position of the drilled bone (temporal mastoid). Neurophysiologic monitoring during the surgery remained un-perturbed.

Postoperative course

Her postoperative course was uneventful. Her headache, nystagmus, mild facial nerve dysfunction, and cerebellar findings resolved postoperatively. Her trigeminal function remained intact for motor function, but was worse for light touch and pinprick sensation postoperatively. Her corneal reflex was absent on the right. Eye protection lubricants were prescribed. The remainder of her neurological examination remained normal. She was monitored for two days in the intensive care unit, and discharged home after a total of one week of hospitalization. Postoperative MRI confirmed gross total tumor resection (Figure 2D and F). No recurrence was noted on follow-up MRIs during the past year.

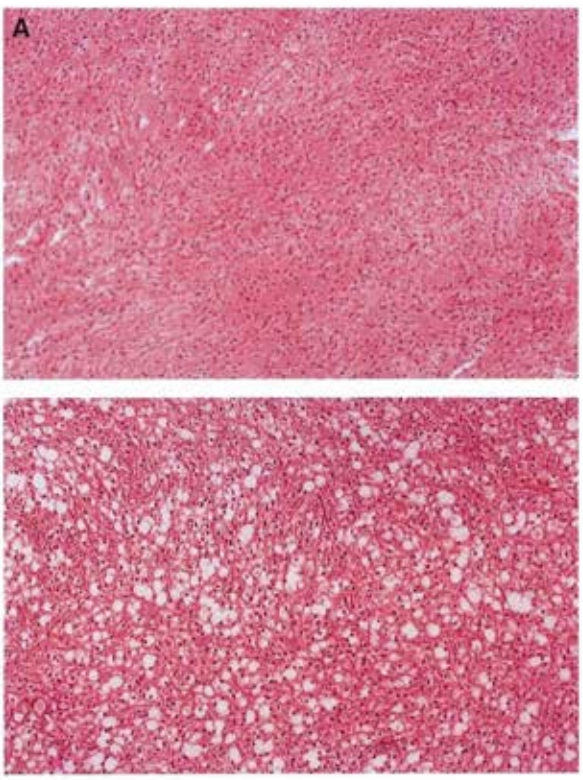
Histological findings

Gross pathological examination revealed multiple small pieces of pale, gray-pink, gelatinous tumor. Microscopic examination revealed a low-grade glial neoplasm. The tumor demonstrated a biphasic pattern composed of bundles of elongated glial cells mixed with areas of microcavitary change. The cells were thin, somewhat elongated, and had small, oval shaped nuclei in the background of fibrillary glia with many Rosenthal fibers. There was no vascular proliferation, mitosis or necrosis. These histopathological features were typical for pilocytic astrocytoma (Figure 3).

Discussion

CPA tumors and primary versus secondary CPA gliomas

CPA tumors represent about 10% of all intracranial tumors in adults. Vestibular schwannomas are the most common (80%) followed by meningiomas (10%). The remaining 10% includes a variety of other lesions including: other cranial nerve schwannomas,



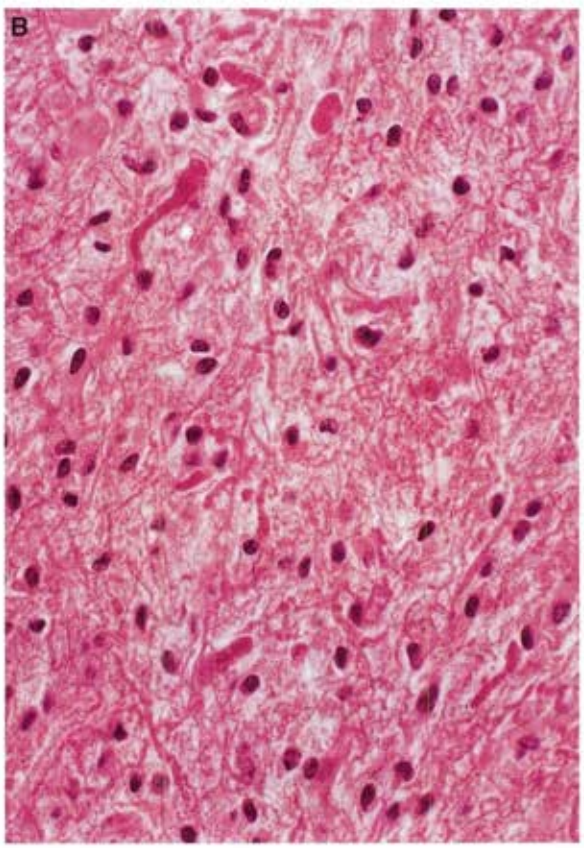


Figure 3. Representative histology; hematoxylin–eosin stain, original magnification ×33; A: Upper half: Solid area of the tumor. Note the occasional Rosenthal fibers which can be seen even at this low magnification; Lower half: Cystic area of a tumor; B: Solid tumor area. Note abundant Rosenthal fibers (original magnification ×132).

metastatic tumors, epidermoid, dermoid and arachnoid cysts, ependymomas, neurofibromas, cholesteatomas, glomus jugulare tumors, choroid plexus papillomas, lipomas, medulloblastomas, ependymoblastomas, and exophytic brain stem gliomas [4,5,7,9–17,19,23,26,31,34,36].

CPA gliomas are very rare and usually only secondarily involve the CPA. They are most often exophytic extensions of primary brain stem fibrillary and gemistocytic astrocytomas [5,14,16,19]. We have been able to find only six cases of truly primary CPA gliomas published in the literature [4,8,17,27,31]. In each case, the glioma arose from the eighth cranial nerve completely separate from the brain stem. All six cases were reported in adult patients, and only one of the six gliomas was a pilocytic astrocytoma [4]. The other five cases were either described non-specifically as 'gliomas' or were fibrillary astrocytomas [8,17,27,31].

Pilocytic astrocytomas

Pilocytic astrocytomas remain the most common solid tumors, brain tumors and posterior fossa tumors in children. Sex distribution is roughly equal. In the posterior fossa, they occur either in the cerebellum or in the brain stem. Regardless of their point of origin, the majority of these lesions remain intrinsic parenchymal tumors. On the rare occasion where they do extend exophytically from their point of origin they usually fungate dorsally, spreading the tonsils of the cerebellum, and only rarely extend into the CPA [1,11,15,18,20,21,28,29,35,36].

An extra-axial pediatric primary CPA pilocytic astrocytoma has not been previously reported. In fact, excluding bilateral vestibular schwannomas in patients with NF2 [24], pediatric CPA tumors are exceedingly rare, and only include several published cases of schwannomas, chordomas, ependymomas and secondary fibrillary and gemistocytic astrocytomas [7,19,23,31]. We have been able to identify only one other previously reported case of primary CPA pilocytic astrocytoma and this tumor arose in an adult patient. It was small in size, and took origin from the VIII cranial nerve complex [4].

The cranial nerve glial segment (root entry zone) as a source for primary CPA gliomas

Cranial nerves contain three histologically distinct segments: the glial segment, a transition zone and a peripheral segment (Figure 4) [6,32,33]. The cranial nerve root entry zone refers to the maximum possible length of proximal cranial nerve where glial axon insulation may still be present, and includes both the glial segment and the transition zone. The glial segment is adjacent to the brain stem and is histologically identical in structure to a central nervous system white matter tract, where nerve axons are supported by neuroglia (both astrocytes and oligodendrocytes). The peripheral segment is histologically similar to a peripheral nerve, where the nerve fibers are insulated and supported exclusively by Schwann cells. Between these two segments lies an intermediate or transition zone of varying length. This transition zone is 'helmet-shaped' in longitudinal cross section, extending for a greater distance within the center of the nerve compared with the circumferential periphery [6]. Even beyond the root entry zone, occasional isolated 'glial islands' have been identified on histological sections of the peripheral segment [6,32,33,37,38]. Studies by Bridger and Farkashidi [6], Lang [22], Skinner [32], Tarlov [33] and Ylikoski et al. [37,28] detailed the histology and systematically measured the extent of glial outgrowth along the various cranial nerves (Table 1). Sensory cranial nerves have longer root entry zones, than motor nerves. Excluding the optic [32,33] and olfactory [32] nerves, which are direct extensions of the central nervous system and have no peripheral segments, the longest glial segment is found in the eighth cranial nerve, followed by the sensory part of the fifth cranial nerve, and then the facial and glossopharyngeal nerves. The remaining cranial nerves have short (< 1.9 mm) glial segments.

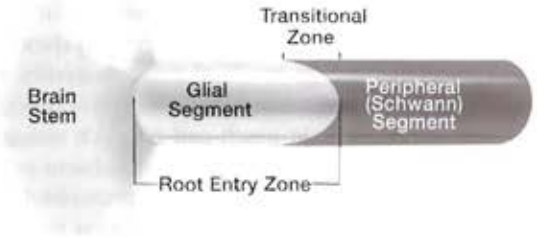


Figure 4. Artist's rendition of the cranial nerve segments demonstrating the location of the glial segment, the location and shape in longitudinal cross section of the transition zone and the location of the peripheral (Schwann) segment. The root entry zone includes both the glial segment and the transition zone (fashioned after references 6,32,33,35, and 36).

Table 1. The mean (range) lengths of cranial nerve root entry zone segments reported by different investigators in millimeters

Cranial nerve	Cranial nerve root entry zone length (mm)			
	Bridger and Farkashidi [6]	Lang [24]	Skinner [35]	Tarlov [36]
I	—	—	Total	0.5
II	—	—	Total	Total
III	—	—	1.2	1.2
IV	—	—	1.9	1.9
V Motor	—	—	—	—
V Sensory	—	3.6 (2–6)	3.0	2.2
VI	—	—	0.5	0.5
VII	—	2.05 (0.5–4)	2.5	0.8
VIII	10.75*	10 (6–15)	8.2 – cochlear 9.0 – vestibular	8.0 – cochlear 8.3 – vestibular
IX	—	—	1.3	1.1
X	—	—	1.0	1.3
XI	—	—	—	<0.5
XII	—	—	—	<0.1

*Bridger and Farkashidi [6] measured the length of the eighth cranial nerve glial segment (mean, 9.75; range, 2–18 mm) separately from the length of the transition zone (mean, 1.0; range, 0.5–3.5 mm).

Schwannomas originate from either the transition zone or the peripheral segment of cranial nerves. A primary GBM of the oculomotor nerve has been reported [30].

We hypothesize that the root entry zone (either the glial segment or the transition zone) of the cranial nerve is the anatomical point of origin for primary CPA gliomas. This hypothesis would explain the predominance of eighth cranial nerve origin for the six previously reported cases [4,8,17,27,31], since the eighth cranial nerve has the longest root entry zone. In addition, the root entry zone length ratio for the eighth *versus* fifth cranial nerves is roughly 4.5 to 1. This ratio, corrected for the larger volume of the fifth nerve, is actually very close to the ratio 6 to 1 encountered comparing the incidence of primary eighth nerve CPA gliomas [4,8,17,27,31] to fifth nerve CPA gliomas (our case). If our hypothesis is correct, it is only a matter of time before the first root entry zone primary CPA oligodendroglioma is identified arising from either the eighth or fifth cranial nerves. While our hypothesis also predicts the eventual recognition of gliomas arising from the root entry zones of other cranial nerves (e.g. facial or glossopharyngeal nerves), their glial segments and transition zones may be too short for a clear intraoperative distinction between primary CPA gliomas and secondary exophytic gliomas arising from the immediately adjacent brain stem.

Conclusion

The authors present a case of a giant trigeminal root entry zone primary CPA pilocytic astrocytoma arising in a nine-year-old girl. The tumor was completely resected via a right pre-sigmoid, retrolabyrinthine, sub-temporal, trans-tentorial ('petrosal') approach with minimal morbidity. This case represents the first reported case of a pediatric primary CPA glioma and the seventh reported case of primary CPA glioma, overall. It represents the second reported case of a primary CPA pilocytic astrocytoma. Given the findings in this case and the six other cases of cranial CPA gliomas reported in the literature, we hypothesize that the point of origin of these rare and unusual tumors is the root entry zone of the involved cranial nerves. The differential diagnosis of primary CPA tumors should be expanded to include cranial nerve root entry zone primary CPA gliomas.

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