Association of cerebellopontine angle atypical teratoid/rhabdoid tumors with acute facial nerve palsy in infants

Report of 3 cases

ALAN SIU, M.D.,1 MICHAELA LEE, M.D.,1 ROBERT RICE, M.D.,2 AND JOHN S. MYSEROS, M.D.1,3

1Department of Neurological Surgery, George Washington University; 2Department of Neurological Surgery, Georgetown University School of Medicine; and 3Department of Neurological Surgery, Children’s National Medical Center, Washington, DC

Atypical teratoid/rhabdoid tumors (AT/RTs) are highly malignant CNS tumors found almost exclusively in childhood. Although essentially universally fatal when incompletely resected, prompt diagnosis followed by early chemoradiation can improve outcomes. An AT/RT can occur extraaxially at the cerebellopontine angle (CPA) and cause acute cranial nerve deficits as the presenting sign. The authors report a series of 3 children who presented with isolated acute facial nerve palsies and in whom subsequent diagnosis of a CPA AT/RT was made. The authors propose that in young children whose presenting symptom is an acute facial nerve palsy with a CPA tumor, AT/RT should be highly suspected.

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Case Reports

Case 1

This 4-month-old girl presented with acute left facial hemiplegia, and was found on MRI to have a left CPA mass extending into the internal auditory canal (IAC), measuring 9 × 14 mm, and adjacent enhancement into the proximal aspect of the facial nerve (Fig. 1). There was no disease dissemination. She underwent a left suboccipital craniectomy to obtain a biopsy specimen of the lesion, without complication. Pathological investigation demonstrated a primitive malignant tumor composed of round blue cells with focal areas of rhabdoid cells that were positive for smooth-muscle actin and epithelial membrane antigen, with a loss of INI1 that was consistent with AT/RT (Fig. 2). Also noted were positive staining for vimen-
tin, synaptophysin, and glial fibrillary acidic protein (data not shown). She was subsequently treated with high-dose chemotherapy with peripheral stem cell rescue. She then received focal radiation therapy followed by 6 months of metronomic maintenance chemotherapy. Follow-up MRI at 5 years indicated no residual enhancement. She continued to have a left facial palsy.

Case 2

This 6-month-old boy presented with acute left facial weakness. Admission MRI studies demonstrated an 8-mm enhancing, lobulated, extraaxial tumor in the left CPA that filled the left IAC (Fig. 3). Results of a hearing test were normal, and a lumbar puncture revealed tumor cells without a clear pathological type. He was thus taken to the operating room for biopsy sampling of this probably malignant tumor. Complete resection was not possible given its infiltration into the porus acusticus. Pathological findings were consistent with AT/RT. Considering the dissemination, a ventricular access device was placed for initiation of intrathecal and systemic chemotherapy in addition to proton beam radiation. Despite these treatments, his dissemination persisted, with a 6-month MRI study indicating new lesion in the left lateral ventricle and right choroidal fissure. He died 8 months after initial diagnosis.

Case 3

This 12-month-old girl presented with facial weakness consistent with a facial nerve palsy, in addition to head tilt and vomiting that on ophthalmological examination confirmed a right fourth and sixth cranial nerve palsy. Admission MRI demonstrated a 26 × 15-mm right CPA heterogeneously enhancing cystic mass, consistent with a high-grade lesion (Fig. 4). Lumbar puncture demonstrated dissemination. She was taken to the operating room to drain the cyst and obtain a biopsy specimen of the lesion, which was well tolerated. Pathological findings were consistent with AT/RT. Subsequently, she received high-dose chemotherapy with stem cell rescue, and proton beam therapy. At 2 months postradiation, she developed progressive lethargy, with an MRI study that was significant for new infiltration into the pons and midbrain, which was of concern for tumor progression or treatment-related change. As she continued to decline, the family elected to withdraw care. She died 8 months after the initial diagnosis. At autopsy, she was found to have multifocal necrotizing leukoencephalopathy, a known complication of aggressive treatment for AT/RT.7

Discussion

Cerebellopontine angle tumors in children are rare,
Facial nerve palsy in CPA atypical teratoid/rhabdoid tumors

Fig. 3. Admission MRI obtained with contrast in a 6-month-old boy with an acute left facial weakness. Imaging shows a left CPA mass and an enlarged IAC. Pathological findings were consistent with AT/RT.

Fig. 4. Admission MRI obtained with contrast in a 12-month-old girl who presented with facial weakness and extracranial deficits. The MRI studies show a highly infiltrating right CPA mass with a cystic component that abuts the fourth ventricle.

accounting for a minority of lesions, representing approximately 1%–3% of pediatric brain tumors. Likewise AT/RTs themselves are also rare, comprising 1%–2% of all pediatric CNS tumors, although this number can rise as high as 20% in patients younger than 3 years. Case studies vary regarding the predominant tumor type, ranging from benign tumors to more malignant phenotypes. Additionally, there is a paucity of data correlating the timing of the presenting symptoms with the diagnosis. One study observed that pediatric CPA tumors frequently caused cranial nerve palsies, but made no mention of duration. Another series showed cranial nerve palsies in 46% of patients with AT/RT as a presenting symptom.

We have observed in our cohort a correlation between acute facial nerve deficits and CPA AT/RT, and suggest that in children whom acute facial palsies and a CPA tumor develop, AT/RT should be highly suspected. Other variables that may assist with differentiating a high-grade lesion are MRI findings of signal voids, vascular encasement, widening of the lateral recess, cerebellar edema, hydrocephalus, and seeding of the neuraxis.

The nature of AT/RT as it relates to cranial nerves, specifically the facial nerve, is unknown. As a distinct tumor entity that was once misdiagnosed as a primitive neuroectodermal tumor, it is very likely that it carries a differential interaction with the tissue types in the CPA that is distinct from the classic medulloblastoma. This is in contrast to classic medulloblastoma in the CPA, which occurs in older patients, and often presents with multiple cranial nerve deficits over the course of months, with facial nerve weakness being uncommon and manifesting later. Although the cell of origin in AT/RT is unknown, some have postulated that the origin of this tumor is a primitive stem cell derived from the neural crest, because the histological studies of AT/RT can manifest neural, epithelial, and mesenchymal staining. In this regard, the typical immunohistochemical staining pattern includes epithelial membrane antigen, S100, and glial fibrillary acidic protein. Additionally, other studies have pointed to similar mutations in the SMARCB1/INI1 gene between familial schwannomas and malignant RTs. The observations of a relationship between the neural crest and AT/RT suggest a propensity for cranial nerve invasion, resulting in acute cranial nerve disorders.

The differential diagnosis in infants with CPA tumors can be quite broad, but in large case series these most commonly are medulloblastoma, schwannoma, ependymoma, and astrocytoma. Although some of the patients with AT/RT may actually have been miscategorized as having medulloblastoma prior to 2006, facial nerve palsy was an uncommon finding for these tumors. A limitation, however, is that these studies did not correlate the specific symptoms with the pathological findings. In this report we highlight a key clinical finding that is highly associated with CPA AT/RT. Acute cranial neuropathies as the presenting symptom may serve as an adjunct that should raise the suspicion and concern for AT/RT in children with CPA lesions. This early consideration is important because the overall survival is quite poor, with a median of 10–17 months. Although the treatment course may not change with high-grade malignancies, earlier diagnosis could guide the treatment course when considering more malignant versus benign lesions, from directing the aggressiveness of resection to the prompt implementation of multimodal therapies, which can improve outcomes. Recent retrospective studies are in conflict in determining the prevalence of malignant versus benign CPA lesions in children. The presence and acuity of facial nerve deficits can serve as an authoritative variable to aid in the determination of the lesion’s pathological features, but we believe that it can define more malignant lesions, especially in very young patients. Future studies are needed to determine the specificity of facial nerve palsies in AT/RT compared with other malignant CPA lesions.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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References


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Address correspondence to: John S. Myseros, M.D., Children’s National Medical Center, 111 Michigan Ave. NW, Washington, DC 20010-2970. email: JMyseros@childrensnational.org.