Accepted Manuscript

Atypical Presentation of Giant Aneurysm in a Pediatric Patient with Duane Syndrome

Chao-Hung Kuo, M.D., Lynn B. McGrath, M.D., Joseph A. Carnevale, M.D., Neena I. Marupudi, M.D., M.S., Jeffery G. Ojemann, M.D., Richard G. Ellenbogen, M.D., Anthony C. Wang, M.D.

PII: S1878-8750(18)31006-4

DOI: 10.1016/j.wneu.2018.05.053

Reference: WNEU 8114

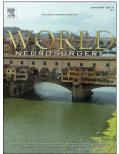
To appear in: World Neurosurgery

Received Date: 5 April 2018

Accepted Date: 8 May 2018

Please cite this article as: Kuo C-H, McGrath LB, Carnevale JA, Marupudi NI, Ojemann JG, Ellenbogen RG, Wang AC, Atypical Presentation of Giant Aneurysm in a Pediatric Patient with Duane Syndrome, *World Neurosurgery* (2018), doi: 10.1016/j.wneu.2018.05.053.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



Atypical Presentation of Giant Aneurysm

in a Pediatric Patient with Duane Syndrome

Chao-Hung Kuo, M.D.^{1,2,3}, Lynn B. McGrath, M.D.¹, Joseph A. Carnevale, M.D.^{4,5}, Neena I. Marupudi, M.D., M.S.^{1,6}

Jeffery G. Ojemann, M.D.^{1,6,7,8}, Richard G. Ellenbogen, M.D.^{1,6}, Anthony C. Wang, M.D.⁶⁹

Corresponding Author

Chao-Hung Kuo, MD

Department of Neurological Surgery, University of Washington Box 359766, 325 Ninth Avenue, Seattle, WA, USA

E-mail: chaohungk@gmail.com

Tel.: +1-206-744-9321; Fax: +1-206-744-9942

*Running title: Giant Pediatric Aneurysm in Child with Duane Syndrome

*Conflict of Interest/ Financial Support: none

¹Department of Neurological Surgery, University of Washington, Seattle, WA, USA

²Department of Neurosurgery, Neurological Institute, Taipei Veterans General Hospital, Taiwan

³School of Medicine, National Yang-Ming University, Taipei, Taiwan

⁴Department of Neurological Surgery, Weill Cornell Medical Center, New York, NY, USA

⁵Department of Neurosurgery, Warren Alpert Medical School of Brown University, Providence, RI, USA

⁶Department of Pediatric Neurosurgery, Seattle Children's Hospital, Seattle, WA, USA

⁷Center for Sensorimotor Neural Engineering, University of Washington, Seattle, WA, USA

⁸Graduate Program in Neuroscience, University of Washington, Seattle WA, USA

⁹Department of Neurosurgery, Ronald Reagan UCLA Medical Center, Santa Monica, CA, USA

Keywords: Duane syndrome; Cerebral aneurysm; Vasculopathy; Congenital disorder

Abbreviation

- CT = computed tomography
- MRI = magnetic resonance image
- MRA = magnetic resonance angiography

Abstract

Background

Duane syndrome is a congenital eye movement disorder characterized by congenital malformation of the abducens nucleus. Thrombogenic conditions during development may lead to vascular anomalies in Duane syndrome, however, the presence of a giant aneurysm in this patient population is a rarely documented phenomenon.

Case Description

We reported a case of a large cerebral aneurysm in a pediatric patient with Duane syndrome, and performed a review of the literatures to identify other potential cases and associations. The pathophysiologic hallmarks of Duane syndrome that lead to alterations in the fetal cerebral vasculature, and which may form the basis for a potential mechanism for aneurysm formation were reviewed in this study.

The patient was an 11-year-old female with Duane syndrome who presented with seizures. CT and MRI demonstrated a large heterogeneously enhancing right temporal mass. Intra-operatively the mass was revealed to be a partially-thrombosed giant middle cerebral artery (MCA) aneurysm. After surgery, the patient had an uneventful postoperative course without residual aneurysm presented on postoperative angiogram. No clinical or radiographic appearance of recurrent aneurysm was evident at her 6-month follow-up.

Conclusions

The pathophysiology of vascular anomalies with Duane syndrome may be related to thrombogenic conditions during development leading to alterations in cerebral fetal vasculature. Strong consideration for vascular anomaly should be given when evaluating cerebral masses in patients with Duane syndrome.

Introduction

Duane syndrome, a congenital eye movement disorder, is characterized by co-contraction of the ipsilateral medial and lateral rectus muscles.⁵ The symptoms are a result of a maldeveloped abducens nucleus and aberrant innervation of the lateral rectus muscle by branches of the inferior division of the oculomotor nerve.^{12,15} Based on Huber classification system, there are three subtypes classified by clinical presentation: type (I) impaired abduction with normal adduction; type (II) impaired adduction with normal abduction; and type (III) impaired abduction and adduction.¹⁰ Associated findings in Duane retraction syndrome include gustatory-lacrimal synkinesis, sensorineural deafness, Klippel-Feil spinal anomaly, cervico-oculo-acoustic syndrome, and thenar hypoplasia.

Association of Duane syndrome with intracranial aneurysms is rarely reported. Our review of the literature produced only one case report of an adult patient with Duane retraction syndrome associated with a large intracranial aneurysm at the vertebral-basilar junction.⁸ Vascular insults to the sixth nerve trunk results in axonal degeneration during development. These results can then promote substitutive innervation from third nerve axons to the lateral rectus muscle. If fibrin clots are the causative agent for the vascular insults, other embolic occlusion can alter hemodynamic pressure gradients in developmental stages, leading to compensatory enlargement and persistence of fetal vasculature.¹⁶ In this report, we present a pediatric patient with Duane syndrome with a large intracranial aneurysm.

Case Description

An eleven-year-old girl with sensorineural loss related to Duane syndrome presented with a twomonth history of progressively worsening headaches and seizures. She had developed an

ACCEPTED MANUSCRIPT

increased frequency of impaired awareness (previous called complex partial seizures)⁶, characterized by difficulty breathing and a feeling of panic that progressed to facial twitching and ultimately to loss of consciousness.

Diagnosis

Because of her cochlear implant, a computed tomography (CT) scan of the head was initially performed in lieu of a magnetic resonance image (MRI). CT revealed a 4.5x 3.3x 4.1cm hyperattenuating mass with peripheral calcification in the right anterior temporal lobe (Figure 1A). MRI and magnetic resonance angiography (MRA) of the brain was then performed. MRI demonstrated a right insular intraparenchymal mass, measuring 4.8x 4x 2.8cm, with foci of nodular enhancement in the insular region (Figure 1B and C). Diffusion-weighted imaging and MRA were significantly distorted due to artifact from the child's cochlear implant, and no parent vessel concerning for a thrombosed aneurysm was evident on the initial imaging (Figure 1D). With overall features suggestive of a low-grade tumor, surgical resection was planned.

Management

A right pterional craniotomy was performed. Upon Sylvian fissure dissection, a firm, pulsatile mass was identified. Circumferential inspection of the smooth-walled mass revealed a thrombosed aneurysm. The aneurysm was found to arise from the MCA bifurcation, and circumferentially involved the superior M2 branch. The inferior M2 branch was adherent to the wall of the aneurysm and was dissected free. No neck was identifiable, as the aneurysm had grown to encompass the parent vessel. The thrombosed aneurysm was then circumferentially dissected. There were no patent distal exiting vessels from the aneurysm. The superior M2 branch was sacrificed just proximal to the aneurysm, thereby excising the aneurysm, and the stump of the parent vessel was sutured closed (Figure 2A).

5

Prognosis and Outcomes

No residual aneurysm was identified on postoperative angiogram (Figure 2B and C). Patient had an uneventful postoperative course. Headaches were resolved and seizures were controlled at 6month follow-up visit. No clinical or radiographic appearance of recurrent aneurysm was evident at her 6-month follow-up.

Discussion

In the present case, an intracranial aneurysm in a patient with Duane syndrome was revealed by headache and impaired awareness. Radiographic examination revealed features suggesting a low-grade tumor. However, a thrombosed aneurysm was identified arising from right middle cerebral artery during surgery. After clipping and excising the aneurysm, postoperative radiologic examination revealed no residual or recurrent aneurysm, and clinical recovery was uneventful.

Pediatric intracranial aneurysms are rare, comprising less than 5% of all intracranial aneurysms^{2,14}. The demographic distribution and clinical pattern of pediatric aneurysms are notably different from those of adult aneurysms. Compared with female dominance in adult aneurysms, male was dominant in pediatric aneurysms^{2,3,7,9}. In adult clinical presentations, most patients presented with aneurysm rupture (changed of Fisher and Hunt and Hess grading). The percentage of presenting aneurysm rupture versus neurological symptoms caused by compressing by aneurysm was around 61% versus 8% ^{1,3,11,13}. However, Garg et al. described 62 pediatric patients with intracranial aneurysm. 82% of patients had presenting feature of headache, 21% patient with seizure, and 27% with loss of consciousness⁷. The other study which reviewed 135 publications including 573 pediatric patients with intracranial aneurysms demonstrated the

percentage of presenting aneurysm rupture is about 55%, and 30% with neurological symptoms or compression effect caused by the aneurysms. The localization of pediatric aneurysms was mainly in anterior circulation. The percentage of middle and anterior cerebral artery is similar³. Although Duane syndrome is not associated with a higher prevalence of intracranial vascular malformations, large intracranial masses in patients with Duane syndrome may be more likely vascular in origin than neoplasm. A case report described a 36-year-old male with Duane syndrome a giant aneurysm at the vertebro-basilar junction. The patient dies after developing locked-in syndrome from thrombosis of the basilar artery⁸ The authors suggested that the absence of motor neurons in the abducens nucleus and the sixth cranial nerve was caused by maldevelopment of posterior circulation. Vascular hypofunction due to anomalous formation of the basilar artery and its branches not only causes under-development of the abducens nucleus during important stage of embryogenesis, but could also increase the risk of aneurysm formation from maladaptive hemodynamics from anomalous vasculature development. However, in our case, bilateral posterior circulations were still intact without abnormal vascularity after postoperative follow-up.

In another study, Hernando et al. reported an 18-month-old male with Duane syndrome presenting with right eye strabismus and right-sided hearing loss. Brain MRA revealed right internal carotid artery agenesis and hypoplasia of the right vertebral artery. The patient was ultimately diagnosed with Wildervanck syndrome (cervico-oculo-acoustic syndrome), a syndrome with featured combining Klippel–Feil anomaly, Duane syndrome and congenital deafness⁴. Tischfield et al.¹⁷ previously reported a relationship between Duane syndrome and HOXA1 mutation. HOXA1 mutations can cause horizontal gaze abnormalities, deafness, facial weakness, hypoventilation, and vascular malformations of the internal carotid arteries. More

7

recently, Parsa et al. proposed the pathophysiologic mechanism of fibrin emboli and associated focal hypoperfusion as an explanation for the development of sporadic congenital malformations. Occlusion from such emboli alters local hemodynamic pressure gradients, potentially resulting in enlargement, persistence, or dysregulation of fetal vascular tissue.¹⁶ Because features of Duane syndrome are associated with vascular insults to the sixth nerve trunk or nuclei, circulating emboli could also increase the risk of cerebral vasculopathy and aneurysm formation.

Conclusion

Embryological vascular dysgenesis associated with syndromes may have been the cause of the large aneurysm in our patient with Duane syndrome. In patients with Duane syndrome presenting with large intracranial masses, vascular anomaly should be strongly considered based on putative pathophysiology of the syndrome.

Disclosures

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

References

 Unruptured intracranial aneurysms--risk of rupture and risks of surgical intervention. International Study of Unruptured Intracranial Aneurysms Investigators. N Engl J Med 339:1725-1733, 1998.

- Alawi A, Edgell RC, Elbabaa SK, Callison RC, Khalili YA, Allam H, Alshekhlee A: Treatment of cerebral aneurysms in children: analysis of the Kids' Inpatient Database. J Neurosurg Pediatr 14:23-30, 2014.
- Beez T, Steiger HJ, Hanggi D: Evolution of Management of Intracranial Aneurysms in Children: A Systematic Review of the Modern Literature. J Child Neurol 31:773-783, 2016.
- Braga M, Pederzoli M, Beretta S, Ferrarini M, Canovaro P, Arpaia G, Crespi V: Agenesis of the right internal carotid artery and Klippel-Feil syndrome: case report. Spine (Phila Pa 1976) 34:E740-742, 2009.
- Duane A: Congenital deficiency of abduction, associated with impairment of adduction, retraction movements, contraction of the palpebral fissure and oblique movements of the eye. 1905. Arch Ophthalmol 114:1255-1256; discussion 1257, 1996.
- 6. Fisher RS, Cross JH, D'Souza C, French JA, Haut SR, Higurashi N, Hirsch E, Jansen FE, Lagae L, Moshe SL, Peltola J, Roulet Perez E, Scheffer IE, Schulze-Bonhage A, Somerville E, Sperling M, Yacubian EM, Zuberi SM: Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia 58:531-542, 2017.
- Garg K, Singh PK, Sharma BS, Chandra PS, Suri A, Singh M, Kumar R, Kale SS, Mishra NK, Gaikwad SK, Mahapatra AK: Pediatric intracranial aneurysms--our experience and review of literature. Childs Nerv Syst 30:873-883, 2014.
- 8. Hedera P, Friedland RP: Duane's syndrome with giant aneurysm of the vertebral basilar arterial junction. J Clin Neuroophthalmol 13:271-274, 1993.
- 9. Herman JM, Rekate HL, Spetzler RF: Pediatric intracranial aneurysms: simple and complex cases. Pediatr Neurosurg 17:66-72; discussion 73, 1991.

- Huber A: Electrophysiology of the retraction syndromes. Br J Ophthalmol 58:293-300, 1974.
- Investigators UJ, Morita A, Kirino T, Hashi K, Aoki N, Fukuhara S, Hashimoto N, Nakayama T, Sakai M, Teramoto A, Tominari S, Yoshimoto T: The natural course of unruptured cerebral aneurysms in a Japanese cohort. N Engl J Med 366:2474-2482, 2012.
- Kalevar A, Ong Tone S, Flanders M: Duane syndrome: Clinical features and surgical management. Can J Ophthalmol 50:310-313, 2015.
- 13. Molyneux A, Kerr R, International Subarachnoid Aneurysm Trial Collaborative G, Stratton I, Sandercock P, Clarke M, Shrimpton J, Holman R: International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomized trial. J Stroke Cerebrovasc Dis 11:304-314, 2002.
- Ostergaard JR, Voldby B: Intracranial arterial aneurysms in children and adolescents. J Neurosurg 58:832-837, 1983.
- Pagon RA, University of Washington. GeneReviews. Seattle: University of Washington: <u>http://www.ncbi.nlm.nih.gov/books/NBK1116</u>.
- 16. Parsa CF, Robert MP: Thromboembolism and congenital malformations: from Duane syndrome to thalidomide embryopathy. JAMA Ophthalmol 131:439-447, 2013.
- Tischfield MA, Bosley TM, Salih MA, Alorainy IA, Sener EC, Nester MJ, Oystreck DT, Chan WM, Andrews C, Erickson RP, Engle EC: Homozygous HOXA1 mutations disrupt human brainstem, inner ear, cardiovascular and cognitive development. Nat Genet 37:1035-1037, 2005.

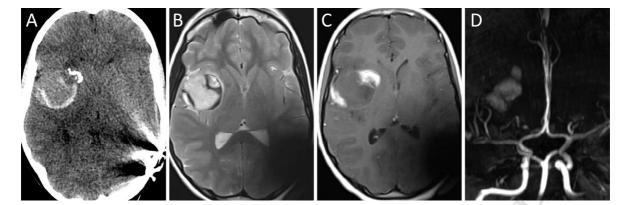
Legend

Figure 1

Illustrate preoperative image. A computed tomography scan revealed a hyperdense mass with peripheral calcification in the right anterior temporal lobe (A). Magnetic resonance image demonstrated a right insular intraparenchymal hemorrhagic mass (B, T2-weighted image), with foci of nodular enhancement in the insular region (C, T1-weighted image with contrast enhanced). Magnetic resonance angiography revealed tumor-flash pattern without parent vessel concerning for an aneurysm (D).

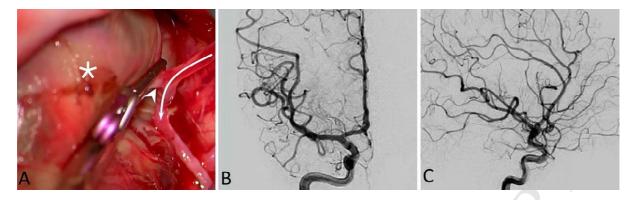
Figure 2

Intraoperative finding was demonstrated a thrombosed aneurysm (A, asterisk) feeding by the middle cerebral artery (A, curved arrow). The stump (A, arrow head) of aneurysm was clipped. The postoperative digital subtraction angiogram was revealed no residual or recurrent aneurysm B: anterio-posterior view; C lateral view).



Ctip the Marine

ACCEPTED MANUSCRIPT



other the second

Highlights

- 1. Atypical presentation of pediatric aneurysm mimicking with tumor was presented.
- 2. Vasculopathy in Duane syndrome may be related fetal development.
- 3. Considering vasculopathy should be given for cerebral masses in Duane syndrome.

A ARA ARA