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A rare pediatric case of cluster headaches after cardiac catheterization in a patient with an isolated innominate artery

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Abstract

While cluster headaches are classified and considered a primary headache disorder, secondary causes of cluster headaches have been reported and may provide insight into cluster headaches' potential pathophysiology. The mechanisms underlying this headache phenotype are poorly understood, and several theories have been proposed that range from the activation within the posterior hypothalamus to autonomic tone dysfunction. We provide a review of reported cases in the literature describing secondary causes after cardiac procedures. We will present a novel pediatric case report of a 16-year-old boy with an isolated innominate artery who presented with acute new-onset headaches 8 h following cardiac catheterization of the aortic arch with arteriography and left pulmonary artery stent placement. The headaches were characterized by attacks of excruciating pain behind the left eye and jaw associated with ipsilateral photophobia, conjunctival injection, rhinorrhea, with severe agitation and restlessness. These met the *International Classification of Headache Disorders*-3 criteria for episodic cluster headaches. The headaches failed to respond to non-steroidal anti-inflammatory medications, dopamine antagonists, and steroids. He showed an immediate response to treatment with oxygen. This unique case of cluster headaches following cardiac catheterization in a pediatric patient with an isolated innominate artery may provide new insight into cluster headaches' pathogenesis. We hypothesize that the cardiac catheterization induced cardiac autonomic changes that contributed to the development of his cluster headaches. The role of aortic arch anomalies and procedures in potential disruption of the autonomic tone and the causation of cluster headaches is an area requiring further study.

Keywords

Child, pediatric, cluster headache, post-catheterization, cardiac catheterization

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Introduction

Cluster headaches are a primary headache disorder characterized by five or more severe, unilateral orbital, supraorbital attacks, with temporal pain lasting 15–180 min (when untreated) with associated ipsilateral conjunctival injection, lacrimation, rhinorrhea, and/or other cranial autonomic symptoms.[1] The age at onset is usually 20–40 years, with the male to female ratio at about 3:1. These headaches are very severe and are associated with agitation and high suicidality.[2]

The pathogenesis of cluster headaches is not fully understood. The trigeminovascular system, the parasympathetic nerve fibers (trigeminal autonomic reflex), and the posterior hypothalamus are all involved in the initiation of cluster headache attacks. These lead to subsequent activation of cortical central nervous system (CNS) involved in pain processing and perception.[3] Unilateral activation in the area of the ophthalmic division of the trigeminal nerve is postulated to trigger perivascular afferents to release CGRP (calcitonin gene-related peptide). This potent vasodilator modulates nociceptive trigeminal neurons. Parasympathetic activation mediated through the trigeminal nerve leads to autonomic symptoms such as conjunctival injection, lacrimation, rhinorrhea, and cranial and extracranial vasodilation, comprising the trigeminal autonomic reflex. Finally, cluster

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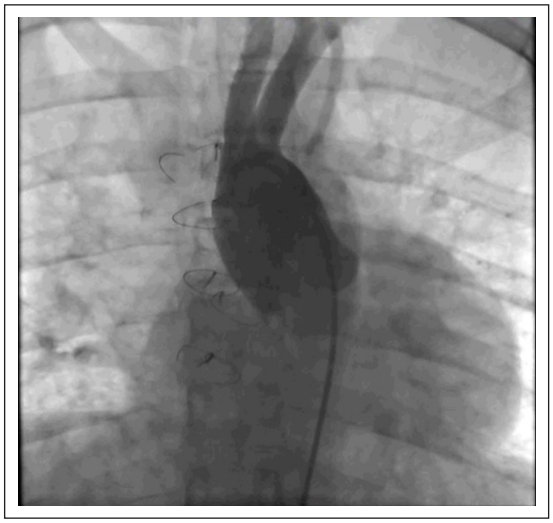

Figure 1. Aortic arch arteriography: injection of contrast through a catheter advanced to the aortic arch revealed no antegrade flow to the innominate artery, which appeared to fill via collateral vessels and via retrograde flow. Unobstructed antegrade flow through the left carotid artery and the left subclavian artery was visualized.

headaches' circadian periodicity suggests a prominent role of the hypothalamus in the pathophysiology of cluster headaches.

While cluster headaches are, by definition, a primary headache disorder, many cluster-like headache cases secondary to other causes have been reported, including vascular causes (aneurysms, arteriovenous malformations, venous sinus thrombosis, carotid/vertebral dissection, and carotid endarterectomy), pituitary tumors, other brain lesions, dental extractions, cataract surgery, and inflammation/infection.[4] We now present a case of new-onset cluster headaches, occurring 8 h after cardiac catheterization with aortic arch arteriography and left pulmonary artery stent placement, in a patient with an isolated innominate artery.

Case presentation

The patient is a 16-year-old boy with a history of double-inlet left ventricle and interrupted aortic arch who underwent staged reconstruction heart surgery involving Norwood palliation with a central shunt as a neonate, a bidirectional Glenn procedure as an infant, and an extracardiac fenestrated Fontan procedure at age 3. He was noted during these procedures to have a friable proximal innominate artery. At age 16, he underwent a retrograde left heart catheterization for routine surveillance of his congenital heart defect and prior cardiac procedures. Contrast injection through a catheter advanced to the aortic arch demonstrated no antegrade flow to the innominate artery (Figure 1), which appeared to fill via collateral vessels and via retrograde flow. The unobstructed flow was visualized through the aortic arch, left carotid artery, left subclavian artery, and descending aorta without discrete narrowing. Separately, a 10- to 16-mm stenosis of the left pulmonary artery was identified and intervened with balloon angioplasty and stent placement.

Eight hours postoperatively, the patient began experiencing repeated 15- to 90-min attacks of excruciating headaches characterized by pain behind the left eye and left jaw associated with ipsilateral photophobia, conjunctival injection, rhinorrhea, and restlessness. His attacks were frequent, with three to five episodes occurring most mornings after the procedure and then daily after that. According to the *International Classification of Headache Disorders*, his presentation met diagnostic criteria for cluster headaches according to the *International Classification of Headache Disorders*–Third Edition (ICHD-3).[1] The patient was at his baseline with no pain between attacks. A head computed tomography (CT) showed no acute pathology. He was referred to Magnetic Resonance Imaging of the brain and cerebral and neck arteries. He was doing well without recurrence, so the family elected to defer this due to the isolation precautions associated with COVID-19. He did eventually get imaging done about a year later when he presented for different reasons. He had no acute or subacute structural abnormalities of concern within his brain, and his vessel imaging showed stable and known absence of flow-related enhancement within the right innominate, right common, internal, and external carotid arteries, and right vertebral artery.

The patient's headaches were unresponsive to non-specific treatments like acetaminophen, ketorolac, metoclopramide, magnesium, valproate, gabapentin, nasal lidocaine, and methylprednisolone, but found to be responsive to 100% oxygen by nasal cannula. Additional preventive and acute treatments were discussed. His cardiologist recommended that we avoided the use of triptans or verapamil (which would have been the first choice) given his cardiac comorbidities. Given the apparent relationship of his headaches with his reports of poor sleep quality, melatonin 9 mg for prophylaxis failed to prevent the episodes. This is a therapy that has been shown effective in some primary headache syndromes, such as cluster headache.[5] With oxygen therapy, the attacks reduced in frequency and duration, with episodes lasting less than 5 min. He had one attack each day after this therapy began. The patient was discharged after 4 days with home oxygen as needed for future exacerbations. During a follow-up appointment by phone a month later, the patient reported that his cluster episodes had continued to respond to oxygen and were now infrequent, occurring at most once a week. At follow-up 3 months later, he reported resolution of his cluster headaches.

The patient notably had no prior history of cluster headaches. Over the previous 2 years, he did have rare sporadic episodic throbbing headaches lasting 4–72 h and associated with vomiting, photophobia, and preceding visual disturbances consistent with migraines. His migraines were triggered by poor sleep and stress, and had been slowly growing

Table 1. Literature review with cases of cluster headaches induced by cardiovascular procedures.

Authors	Patient(s) attributes	Procedure
Dirkx and Koehler 2017[17]	**Two patients:** 1. 67-year-old man who developed bifrontal headache 2 days after surgery that later changed to cluster headaches a few days later. 2. 63-year-old man who developed cluster headaches 7 days postoperatively.	Carotid endarterectomy
Messert and Black 1978[18]	**Two patients:** 1. 56-year-old man who developed cluster headaches 2 days postoperatively. 2. 57-year-old man who developed delayed cluster headaches 2 months postoperatively.	Carotid endarterectomy
Björne et al., 1994[19]	55-year-old man with history of resolved cluster headaches who experienced recurrence of cluster headaches 20 years later on the first post-operative day after carotid endarterectomy.	Carotid endarterectomy

in frequency to about once per week prior to his cardiac catheterization. However, they were never as severe as his cluster headaches. Unlike the episodes following his cardiac catheterization, the patient's migraines were quickly responsive to a single dose of ibuprofen at 600 mg or taking a nap. These headaches were not associated with any agitation or restlessness.

The patient's father reported having headaches in his adolescence that were not severe and were managed conservatively as migraines. These were associated with light and sound sensitivity, and he reported that they often required sleep for complete resolution.

Discussion

To our knowledge, this is the first reported case of cluster headaches following cardiac catheterization in a patient with an isolated innominate artery. Isolation of the innominate artery from the aortic arch is a very rare anatomic defect with few reported cases.[6,7] We postulate that the patient's unique anatomy coupled with sympathetic stimulation and possible injury from cardiac catheterization and aortic arch arteriography led to his acute onset of cluster headaches 8 h postoperatively. A case of cluster headache remission after correction of an atherosclerotic narrowing at the origin of the innominate artery has been reported,[8] leading us to postulate that our patient's isolated innominate artery predisposed him to cluster headaches. Furthermore, isolation of the innominate artery has been associated with the development of subclavian steal, cerebral ischemia, and headaches.[6,7] Interestingly, our patient had been noted to have friability of the proximal innominate artery as a neonate, and in the 2 years before his onset of cluster headaches, he had been having increasingly frequent migraines. We speculate that his innominate artery's isolation could have contributed to his increasingly frequent headaches due to other case reports of headache associated with an isolated innominate artery[6] or an anomalous origin of an internal carotid artery.[9] Finally, it is notable that cluster headaches are more prevalent in patients with cardiovascular risk factors, including structural heart disease,[10] such as right-to-left shunt.[11,12]

In addition to the patient's unique anatomy increasing his susceptibility, we hypothesize that the patient's procedure triggered the onset of cluster headaches due to sympathetic stimulation and possible vascular injury. There is literature supporting dysregulation of cardiovascular autonomic control in cluster headache, notably ictal parasympathetic hyperactivation and sympathetic hypoactivation, with subclinical autonomic dysregulation persisting in the pain-free state.[13–15] Barloese et al.[16] report that low-frequency sphenopalatine ganglion stimulation induces increased cardiac sympathetic tone and decreased parasympathetic tone, measured via heart rate variability analysis, in cluster headache, leading to the theory that rebound parasympathetic hyperactivity after withdrawal of increased sympathetic tone during sphenopalatine ganglion stimulation could trigger cluster headache attacks. We, therefore, theorize that our patient's cardiac catheterization could have caused increased cardiac sympathetic tone with rebound parasympathetic hyperactivity that triggered his new-onset cluster headaches.

It is also quite possible that vascular injury from our patient's cardiac catheterization could have contributed to his cluster headaches. Cluster headaches have been reported after carotid endarterectomy, perhaps due to damage to the internal carotid artery, which carries trigeminal nerve roots (Table 1).[17–19] In addition, there have been multiple reports of cluster-like headaches secondary to other vascular causes such as aneurysms, arteriovenous malformations, venous sinus thrombosis, and carotid/vertebral dissection.[4] In the same family of trigeminal autonomic cephalalgias as cluster headaches, recurrent hemicrania has been reported to be triggered by aortic dissection,[20] possibly due to the referral of aortic wall pain signals to the trigeminal ganglion via the cardiac plexus, first cervical ganglion, and the internal carotid nerve. Vascular complications of cardiac catheterization include pseudoaneurysm, arteriovenous fistula, thromboembolism, infection, and other bleeding.[21] While our patient did not develop symptoms supporting a significant vascular complication, it is still possible that minor vascular injury contributed to his symptoms.

Finally, it is possible that this patient developed primary cluster headaches incidentally after his cardiac catheterization,

but this is unlikely given his acute presentation of new cluster headaches only 8 h postoperatively.

Conclusion

Headaches are a common complaint in children, but it is very rare to have children describe headaches that meet ICHD-3 criteria for cluster headaches.[22] Cluster headaches have been described in adults following cardiovascular procedures and after neck trauma in adults and children. We describe a novel pediatric case of new cluster headaches following cardiac catheterization, aortic arch arteriography, and left pulmonary artery stent placement in a 16-year-old boy with an isolated innominate artery and underlying structural heart disease. We theorize that abnormal aortic arch anatomy, combined with intervention causing sympathetic stimulation and rebound parasympathetic hyperactivity, and possible vascular injury, could have contributed to our patient's development of new cluster headaches. The role of aortic arch anomalies and interventions in the causation and palliation of cluster headaches remains an area that requires further study. Clinicians should consider excluding secondary causes in children presenting with cluster-like headaches.

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Statement of ethics

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article. Our institution does not require approval by institutional review board (IRB) for this case report.

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