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# Craniocervical Arterial Dissection in Children: Diagnosis and Treatment

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### Keywords

Craniocervical arterial dissection; Arterial ischemic stroke; Children; Pediatric; Diagnosis; Treatment; Imaging; Angiography

## Introduction

Craniocervical arterial dissection (CCAD) in childhood usually presents with symptoms of acute ischemic stroke (AIS) or transient ischemic attack (TIA). It occurs in 2.5 children per 100,000 per year [1]. Separation between the intimal layers of the vessel wall creates an area of damaged endothelium with exposure of collagen, activated tissue factor, and exposed von Willebrand factor. These factors generate secondary fibrin and platelet adhesion, leading to thrombus propagation. Once a clot has formed, ischemia occurs from vessel occlusion at the site of dissection or from clot embolus downstream [2]. Aneurysmal dilatation, which can occur secondary to impaired integrity of the vessel wall and persistent arterial pressure occlusion, frequently appears in the C1-C2 vertebral circulation in children [2,3].

Risk factors for dissection in children include head and neck injury, connective tissue disorders (such as Ehlers-Danlos syndrome), and male gender [4–6, Class IV]. Other well-known childhood AIS risk factors (e.g., thrombophilia) may theoretically contribute to risk of AIS in the presence of CCAD. Patients with arterial abnormalities have a high risk of recurrent AIS [7, Class III].

There are two types of CCAD in childhood: extracranial dissection and intracranial dissection. These entities have differing risk factors and management. Extracranial dissections account for 5% to 25% of childhood-onset AIS [4,8••, 9••] and are often preceded by trauma [4–6, Class IV]. Typically, anterior circulation dissection presents with focal neurologic symptoms such as hemiparesis or aphasia. Posterior circulation events from vertebral or basilar dissection are more challenging to diagnose because their symptoms and signs can range from dizziness to coma. Clues to this diagnosis include history of recent trauma and/or cranial nerve abnormalities. Early evidence suggests that dissection is more prevalent in the posterior than the anterior circulation of children with AIS [8••, Class IV]. Interestingly, although neck pain is a common sign of dissection in adult AIS, diffuse headache is more common in children [4,6].

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Because of imprecise classification and challenges in definitive diagnosis, the prevalence of intracranial dissection in childhood is unknown. Recent literature in childhood AIS has focused upon intracranial focal cerebral arteriopathy, which occurs in up to 80% of previously healthy children with AIS [10, Class IV]. Although many of these transient narrowings within the intracranial cerebral vasculature are likely to be associated with an infectious or parainfectious phenomenon rather than dissections [11•, Class IV], recent case reports suggest that some of these lesions may indeed be dissections [12].

## Diagnosis

Diagnosis of childhood CCAD and AIS relies upon the appropriate clinical suspicion. Improvement in clinical suspicion and community awareness will help address the concerning observation that median time to diagnosis for childhood-onset AIS is 25 hours from time of symptom onset [13].

The International Pediatric Stroke Study defines CCAD as "(1) angiographic double lumen, intimal flap, or pseudo aneurysm, or, on axial T1 fat saturation MRI images, a "bright crescent sign" in the arterial wall [as seen in Fig. 1, Case 1]; (2) cervical or cranial trauma, or neck pain, less than 6 weeks preceding angiographic findings of segmental arterial narrowing (or occlusion) located in the cervical arteries; (3) angiographic segmental narrowing (or occlusion) of the vertebral artery at the level of the C2 vertebral body, even without known traumatic history" [14, Class IV].

Spontaneous CCAD occurs with no preceding history of significant trauma, or after seemingly innocuous trauma (examples from our experience include neck torsion during rugby, chiropractor manipulation, climbing over a wall, landing on the head when playing on a trampoline, and falling off of a skateboard). At the same time, it is appreciated that many children without dissection also report a recent prior history of minor trauma, and some "background" level of minor trauma is expected in the healthy pediatric population. Well-designed case-control studies are lacking on this issue. In one series of CCAD in children, minor trauma occurred prior to presentation in 25% [4]. Most children with spontaneous CCAD present with nonspecific, often transient, neurologic symptoms including headache, vomiting, dizziness, vertigo, diplopia, confusion, and neck pain. Other presenting symptoms and signs include altered level of consciousness (25%), Horner's syndrome, and/or seizures (12.5%) [15].

Traumatic CCAD, in contrast, occurs after generalized major trauma, such as a motor vehicle accident. It can present with similar signs and symptoms but is increasingly recognized via screening imaging studies in asymptomatic patients with major trauma.

The cornerstone of diagnosing CCAD is imaging of the cervical and intracranial vasculature. The imaging modalities available for diagnosis of CCAD—conventional angiography (CA), CT angiography (CTA), magnetic resonance angiography (MRA), and Doppler ultrasound (DUS)—possess complementary strengths and weaknesses. Our suggested algorithm for diagnostic evaluation is shown in Figure 2, but it should be recognized that individual clinical circumstances warrant careful, case-by-case consideration.

In the past 10 to 20 years, advances in technology have made MRI/MRA and CT/CTA increasingly sensitive and specific, although CA remains the gold standard for equivocal cases. In general, imaging modalities can be divided into those that can analyze the arterial lumen (CA), and those that can depict both the lumen and mural arterial thrombus (MRA with MRI, CTA, and DUS).

**Anatomic Site of Involvement—**Some authors have hypothesized that the extracranial carotid and vertebral arteries are more vulnerable to dissection than other arteries in the body because of their mobility and proximity to bony projections of the cervical spine [16]. The vertebral artery is particularly vulnerable at its tortuous course around the C1-C2 lateral masses and through the transverse foramina [3]. As a result, two thirds of vertebral artery CCADs occur at these sites [17]. The most common location for carotid CCAD is 2 to 3 centimeters above the carotid bulb [16].

**Conventional Angiography—**CA is still widely considered the gold standard for diagnosis of adult and childhood CCAD, but the risks of this technique may outweigh its benefits in many clinical scenarios [18••]. CA depicts intraluminal findings of CCAD with very high spatial resolution through direct intra-arterial injection of contrast. The most common findings of extracranial CCAD on CA are arterial stenosis, aneurysm formation, or occlusion [19,20]. An intimal flap or double lumen is indicative of CCAD, but these findings are detected in fewer than 10% of dissected arteries, and less commonly in the vertebral arteries [19]. A relative drawback of CA is that intramural hematoma or periarterial findings cannot be directly visualized [21].

Increasingly, CA is supplanted by MRI/MRA for the primary diagnosis of CCAD [21–23]. This trend is due to increased availability of MRI/MRA, potential complications of CA (e.g. femoral hematoma, femoral arterial pseudoaneurysm, recurrent AIS, and radiation exposure), and the need for sedation in CA [22]. Additionally, as noninvasive techniques like MRI/MRA become more prevalent, fewer physicians are trained in CA, resulting in fewer experienced angiographers [24]. Although concern for CA complications is one of the primary factors in limiting CA, several recent papers have documented an excellent safety record for CA in children in the hands of experienced angiographers [25,26]. However, because CA carries a higher risk of complications in patients with connective tissue disease, especially Ehlers-Danlos or an undiagnosed collagen abnormality, CA should be used with caution in this population [27].

**MRI and MRA—**In most centers, MRI/MRA has become the first-line imaging modality for patients with suspected dissection [21,22]. MRI/MRA is noninvasive, uses no radiation, and simultaneously images for dissection and stroke.

Arterial luminal findings of CCAD on either time of flight (TOF) MRA or contrast-enhanced MRA are similar to findings of CA in both adults and children, including arterial stenosis, intimal flap, dissecting aneurysm, or occlusion [4,28,29]. A tapered stenosis (“flame sign”) or a thin, segmented stenosis (“string sign”) is a less common sign of CCAD [28,30]. Intimal flaps and dissecting aneurysms are two specific luminal findings for CCAD, but they are infrequently visualized on MRI/MRA [28,31,32].

Although CA is the gold standard for diagnosis, one advantage of MRI/MRA (TOF or contrast-enhanced) over CA is the ability to directly visualize the intramural hematoma with T1 or T2 fat-saturated imaging as a crescentic hyperintensity along the vessel wall [28,33] (as seen in Fig. 1, Case 1).

Intramural hematomas have been reported in up to 76% to 91% of dissected vessels [28,31,32]. On MRI, the appearance of the intramural hematoma in CCAD changes over time: it has been reported as isointense to nearby tissues for the first day or two, then T1 isointense and T2 hyperintense, and finally T1 hyperintense after several more days [21,28,33,34]. T1 and T2 hyperintensity in an intramural hematoma can persist for months [21,33]. The combination of mural hematoma and flowing blood on TOF MRA can lead to an apparent increase in vessel diameter on both source images and maximum intensity

projection (MIP) images. This increase in vessel diameter on TOF MRA was 99% specific for CCAD in one study of carotid and vertebral CCAD [33].

Several studies of CCAD in adults that were published between 1994 and 2002 compared MRI/MRA(TOF) versus CA. MRI/MRA had 50% to 100% sensitivity and 29% to 100% specificity [33,35–39]. In a more recent study of CCAD in adults, contrast-enhanced MRA was 89% sensitive for detection of CCAD, versus 50% for TOF MRA [40]. This finding mimics our clinical experience. MRI/MRA can perform favorably compared with CA, and contrast-enhanced MRA is superior to TOF MRA. Compared with TOF MRA, contrast-enhanced MRA possesses several advantages in detecting arterial stenosis and dissection: imaging of the entire course of the cervical arteries in one acquisition [41], decreased overestimation of stenosis or occlusion due to slow flow [40], and fewer motion artifacts [42].

Limited studies in childhood AIS have demonstrated a 100% correlation between MRA (TOF) and CA in large-artery intracranial abnormalities [43, Class III]; other studies have shown that CA is more sensitive in intracranial abnormalities than extracranial abnormalities of the large vessels [44, Class IV]. Pediatric literature remains limited.

Several common artifacts can make the diagnosis of CCAD by MRA difficult, especially in the vertebral arteries. Examples include turbulent flow [45,46] and venous plexus artifact [47].

High-resolution MRI with specialized cervical surface coils is on the horizon for diagnosis of intramural hematoma in cases of CCAD in adults [48,49••,50, Class IV]. This promising technique could increase sensitivity for intramural hematoma and overcome the artifact related to confounding perivertebral venous plexus enhancement.

**CT Angiography—**Recent studies report a high sensitivity of CTA (98–100%) for diagnosis of spontaneous and traumatic CCAD in adults [51–53]. Other advantages of CTA include widespread availability, speed of examination, noninvasiveness, and ability to be performed as part of an initial trauma screening. The great disadvantage of CTA, especially for children, is the high radiation burden [54]. Furthermore, the diagnostic performance of CTA for CCAD in children has not been extensively studied.

The signs of dissection on CTA are similar to those on both MRA and CA. As in those modalities, the most common findings are stenosis or occlusion at a typical location [45,53,55,56]. The characteristic CCAD luminal findings of intimal flaps and dissecting aneurysms can also be visualized on CTA [55,56] more often than on MRA [45,57].

Artifacts associated with CTA include bone artifact near the skull base and artifact from dental amalgam [55,56]. High-quality CTA examinations also require excellent bolus timing and high injection rates, both of which can be more difficult to accomplish in children. References on CTA techniques in children have been published that address bolus timing and injection rates [58].

**Duplex and Doppler Ultrasound—**In adults, DUS in the diagnosis of spontaneous CCAD has reported sensitivities ranging from 66% to 96% [51,59–62]. Advantages of DUS are that it is relatively inexpensive, uses no radiation, and can be performed emergently at the bedside, but its sensitivity is highly dependent on the operator [63].

Compared with the anterior circulation, DUS is less sensitive in evaluating the vertebral arteries because of their location within the transverse foramina [64], their deeper and more

irregular course, and their small diameter [63]. DUS also has reduced sensitivity for focal disease of the carotid arteries near the skull base because of the limited window [62].

Because of its limited utility in evaluating the vertebral arteries, DUS has not yet been widely studied in children with CCAD.

**Diagnosis of Arterial Injury Following Trauma—**Recent adult trauma literature cites a prevalence of blunt cervical arterial injury (BCAI) following major trauma as high as 1.1% to 1.2% [65,66], although a recent survey of the National Pediatric Trauma registry estimated the prevalence in pediatric trauma at 0.03%. Presumably, BCAI is either underdiagnosed in pediatric patients or its prevalence is lower than in adults [67].

Recent adult surgical and trauma literature advocates CTA as a screening tool for BCAI following major blunt trauma [65,66]. Controversy exists regarding the sensitivity of CTA in this setting, with sensitivities that range from 54% to 97.7% [52,68]. One pediatric study reported a sensitivity of 88% and a specificity of 100% in CTA in this setting [69].

Given the current recommendations in the trauma literature and the advantages of CTA in this setting (speed, 24/7 availability, and ability to scan multiple body parts at once), CTA is often used for BCAI screening in both children and adults, but given the relative lack of data on BCAI specifically in children and concerns over radiation exposure, MRI/MRA should be considered as an alternative screening tool when appropriate [70].

## Treatment

- Treatment of adult extracranial CCAD has become more controversial over the past 2 to 3 years, with some experts advocating less aggressive therapy such as aspirin, and others using more invasive techniques such as stenting. Although anticoagulation is the recommended (and the most commonly used) treatment for childhood AIS [18••, 71••, Class IV], there are no randomized controlled trials comparing antiplatelet therapy versus anticoagulation in adults or children with CCAD, and this practice is based upon less evidence in children with AIS than in adults. In the absence of an evidence-based treatment strategy, management relies largely upon consensus-based recommendations, patient education about risks and benefits, and physician experience.
- Considerable variability of treatment recommendations is evident across international pediatric stroke centers and even within the United States [9••]. Recently published childhood stroke guidelines recommend treatment of extracranial CCAD with anticoagulation, such as unfractionated heparin (UFH), low-molecular-weight heparin (LMWH), or warfarin. The American Heart Association (AHA) Scientific Statement says, “In children with extracranial CCAD, it is reasonable to begin either UFH or LMWH as a bridge to oral anticoagulation. It is reasonable to treat a child with an extracranial [CAD] with either subcutaneous LMWH or warfarin for 3 to 6 months” [18••]. The American College of Chest Physicians suggests “for AIS secondary to dissection … anticoagulant therapy with LMWH or vitamin K antagonists for at least 6 weeks, with ongoing treatment dependent on radiologic assessment” [71••].
- Recent adult literature suggests that antiplatelet therapy may be as effective as anticoagulation in preventing recurrent stroke, death, or disability in extracranial carotid artery dissection, but this conclusion is controversial. A Cochrane meta-analysis of 36 observational studies in 2010 concluded that there was no statistically significant difference between antiplatelet or anticoagulation therapy when considering recurrent stroke (OR, 0.63; 95% CI, 0.21–1.86) or death (OR,

2.02; 95% CI, 0.62–6.60) [72••, Class II]. In a subanalysis of 26 studies, however, there was a strong but nonsignificant trend favoring the use of anticoagulation in preventing death or disability (OR, 1.77; 95% CI, 0.98–3.22; $P = 0.06$) [72••]. Given the recent data, AHA guidelines suggest, "Alternatively [in children with CCAD], an antiplatelet agent may be substituted for LMWH or warfarin" [18••].

- Interventional procedures to stent or balloon extracranial dissection are typically reserved for patients who fail medical therapies. AHA recommendations suggest that surgical procedures are reasonable in children who continue to have symptoms from an extracranial CCAD despite aggressive medical therapy [18••].
- The use of anticoagulation in intracranial dissection is discouraged by AHA guidelines because of the risk of subarachnoid hemorrhage [18••].
- Follow-up imaging is necessary for patients with CCAD, typically at 3 to 6 months after their initial presentation. In addition, children with vertebral dissections should be evaluated with appropriate neck imaging, to assess for a cervical skeletal abnormality [73,74].

## Pharmacologic treatment

- Antiplatelet therapy for CCAD is aimed at preventing arterial thrombus propagation. The most common antiplatelet agent is aspirin, typically dosed at 2 to 5 mg/kg per day. Clopidogrel is sometimes prescribed, although dosing in pediatric patients older than 2 years is not well established. With aspirin, contraindications include aspirin hypersensitivity and known bleeding disorder. Aspirin has few drug interactions, and its main side effect is an increased bleeding tendency, particularly risk of hemorrhage during trauma [71••]. Although rare, patients and their families also need to be aware of the risk of Reye syndrome, especially with concomitant influenza [75]. A yearly flu shot is recommended. Nasal flu vaccination is not recommended. The cost of aspirin is minimal.
- Anticoagulation treatment for extracranial CCAD is also aimed at preventing clot propagation. Usually, UFH is the initial medication of choice for acute treatment, given its short half-life. At the Children's Hospital Colorado, UFH is managed with the abbreviated protocol shown in Table 1. UFH should be administered by a physician experienced with its use.
- A large area of ischemia (typically the size of more than one third to one half the territory of the middle cerebral artery) is a relative contraindication to anticoagulation, as is the presence of subarachnoid hemorrhage. Patients with known intracranial CCAD should be treated with anticoagulation only if other therapies have failed.
- Side effects of anticoagulation include increased bleeding risk, with a variable incidence of 2% to 26% [76,77]. In our experience, clinically significant bleeds are limited (5% risk at a mean follow-up of 3 years) in patients with AIS and arteriopathy who are treated with anticoagulation [78].
- Side effects of heparin include bleeding and heparin-induced thrombocytopenia (HIT). Well-designed, large prospective studies of HIT incidence in children are lacking, but the estimated frequency in non-neonates ranges from 0.5% to 2% and is likely to be higher following cardiac surgery [79,80].
- When a patient is stable and beyond the high-risk period for hemorrhagic conversion or intracranial swelling, transition to LMWH or warfarin is considered.

- According to the American College of Chest Physicians (ACCP) guidelines, target levels for LMWH are an anti-FXa level of 0.50 to 1.0 U/mL in a sample taken 4 to 6 hours after administration [71••]. Side effects of LMWH are similar to those of UFH, although the risk of HIT is thought to be lower with LMWH.
- The ACCP suggests adjusting the warfarin dosage to attain a target International Normalized Ratio (INR) of 2.0 to 3.0. The main adverse effect of warfarin is bleeding. Some evidence suggests that long-term use may be associated with osteoporosis, but this link is by no means definitive [81].
- Long-term management of LMWH and warfarin are best conducted with the assistance of a pediatric hematologist.

## Interventional procedures

- Endovascular therapies have been successful in multiple case reports in childhood AIS and specifically in CCAD [82,83]. The risk-benefit analysis of interventional therapies is uncertain. Adverse events have also been described, such as the failure of a Merci clot retrieval device in a 14-year-old with presumed intracranial dissection [84]. These adverse events are likely to be underreported [85•, Class IV]. For these reasons, patients should be selected for interventional therapies on a case-by-case basis, ideally with the input of a clinician with pediatric stroke expertise. In the setting of extracranial CCAD, interventional therapies such as stenting or selective occlusion with coils should be entertained only if patients fail aggressive medical management (as seen in Fig. 1, Case 2). Intra-arterial thrombolytic devices or devices that mechanically retrieve the clot are also controversial, and should be used (if at all) only within evidence-based adult time windows for treatment.

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## Opinion statement

Diagnosis of craniocervical arterial dissection (CCAD) in children begins with a careful history and physical in a child with a transient ischemic attack (TIA) or arterial ischemic stroke (AIS). The extent of radiologic evaluation for suspected CCAD is based upon careful consideration of the risks associated with the best imaging techniques, weighed against the benefits of enhanced vascular imaging with better diagnostic sensitivity. Although conventional angiography (CA) and CT angiography (CTA) have a higher sensitivity than magnetic resonance angiography (MRA), they are accompanied by risks: for CA, femoral hematoma, femoral arterial pseudoaneurysm, recurrent AIS, and radiation exposure; for CTA, radiation.

For children (non-neonates) with suspected CCAD, MRI with MRA is recommended as the first-line imaging study. MRI usually includes diffusion-weighted, FLAIR, and T1 images of the brain, and T1 or T2 fat-saturation axial imaging through the neck. MRA should include 3D time-of-flight MRA of the head and neck (from the aortic arch through the circle of Willis). Contrast-enhanced MRA should be highly considered in neck imaging. If MRI/MRA is equivocal, CCAD is strongly suspected but not detected on MRI/MRA (especially in the posterior circulation), or the child has recurrent events, additional imaging of the craniocervical vasculature is likely warranted. Individual clinical circumstances warrant careful, case-by-case consideration.

Treatment of CCAD in children is challenging and differs for intracranial and extracranial dissections. In extracranial CCAD, we most commonly use anticoagulation for 6 weeks to 6 months in patients with TIA or AIS. Typically, unfractionated heparin is used in the acutely ill patient at heightened risk for bleeding (because of its short half-life), whereas low-molecular-weight heparin (LMWH) or warfarin are reserved for the stable patient. If the history is suspicious for dissection (head and neck trauma, recent cervical chiropractic manipulation, recent car accident, or neck pain), we consider treatment for dissection even with normal MRI/MRA. For patients with CCAD with a stroke size greater than one third to one half of the middle cerebral artery territory (or other bleeding risk factors) and extracranial CCAD, in whom there is concern about heightened risk for hemorrhagic conversion, we commonly use aspirin therapy during the acute phase. Regardless of their treatment in the initial weeks to months, we subsequently treat all patients with aspirin for 1 year after their event, and sometimes longer if they have other risk factors. Interventional techniques, such as extracranial cerebral arterial stent placement or selective occlusion, are understudied in children. Interventional techniques are typically reserved for patients who fail aggressive medical management and have recurrent TIA or AIS.

The diagnosis and treatment of intracranial dissection is extraordinarily challenging in children, in whom inflammatory intracranial arteriopathies are common. When intracranial arteriopathy is clearly associated with dissection, the clinician should look for the presence of subarachnoid hemorrhage and/or dissecting aneurysm. Treatment decisions should be made by a multidisciplinary pediatric stroke team, given the lack of data in this area. Intracranial cerebral artery stent placement carries high risk and is not recommended for intracranial CCAD in children.

Most importantly, we educate all children with CCAD and their parents about the paucity of evidence in the treatment of this disease, the risks of enhanced imaging techniques such as CTA or CA, and the challenges involved in weighing the risks of aggressive therapies and interventions against the costs of unclear diagnosis and potentially ineffective treatments. We also educate our patients with CCAD about the signs and symptoms of recurrence and the importance of emergent evaluation.

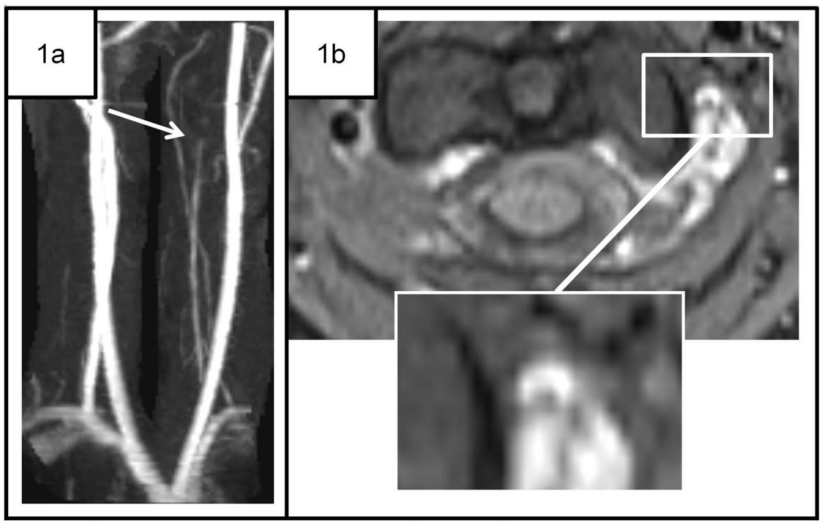


**Figure 1.**

Selected cases of childhood spontaneous craniocervical arterial dissection (CCAD). **Case 1.** 12-year-old girl with transient ischemic attack (TIA) and CCAD. One hour after incidental neck trauma, the patient had left facial droop that spontaneously resolved. **1a** Maximum intensity projection (MIP) images using time of flight (TOF) magnetic resonance angiography (MRA), ordered at the initial neurology visit (1 month later) shows slow flow through a small left vertebral artery, with abrupt cutoff at C2-C3 (*white arrow*). **1b** T1 fat saturation images reveal a "crescent sign" at C1–C2 (*inset*). MRI of the brain was normal. **Case 2.** 4-year-old boy with dissecting aneurysm and right visual field cut. MRI/MRA and CT angiography showed left posterior cerebral artery infarct but were equivocal for the diagnosis of CCAD. **2a** Conventional angiography revealed a dissecting aneurysm of the left vertebral artery at the C2-C3 level (*white arrow*). The patient failed medical management with aspirin and low-molecular-weight heparin. **2b** He has been symptom-free for 14 months after interventional coiling of left vertebral artery (*black arrow*).

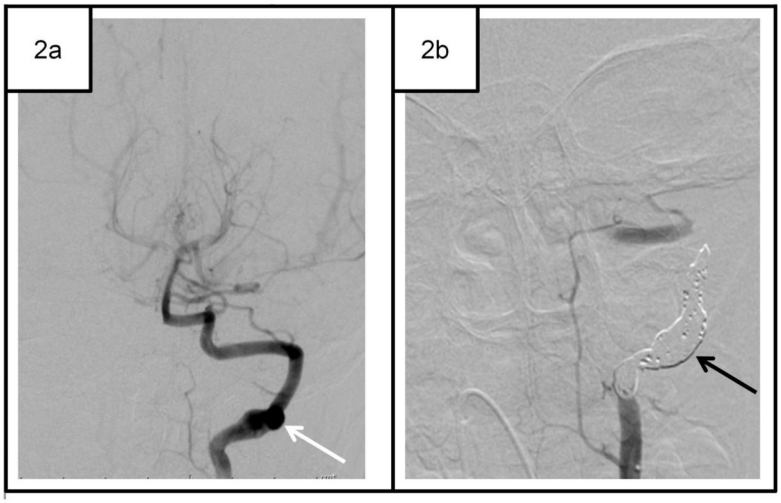


**Figure 2.**

Algorithm for the initial radiologic evaluation of suspected spontaneous craniocervical arterial dissection (CCAD). Evaluation begins with brain MRI with diffusion-weighted imaging (DWI), time-of-flight (noncontrast) MR angiography (MRA) of the head, and contrast-enhanced MRA of the neck with a T1 fat-saturated sequence. *AIS* arterial ischemic stroke; *CA* catheter angiography; *CTA* CT angiography; *TIA* transient ischemic attack.

## Table 1

Protocol for the use of unfractionated heparin in children with acute ischemic stroke

| | |
|---|---|
| **1** | A heparin bolus is typically not recommended in AIS, given concerns for risk of bleeding. |
| **2** | Initial orders |
| | **a.** Order STAT DIC screen (PT, aPTT, fibrinogen, D-dimer) |
| | **b.** Order STAT CBC |
| **3** | Initial maintenance infusion for heparin (for infants and children > 1 month old): 15–20 units/kg per hour |
| **4** | Follow-up orders |
| | **a.** Order an anti-factor Xa level 8 hours after initiation of the heparin infusion, and adjust heparin drip accordingly. |
| | **b.** Standard therapeutic treatment goal is 0.3–0.7 anti-Xa units/mL. |
| | **c.** A peripheral venipuncture for anti-Xa level is preferred. |
| | **d.** When a peripheral venipuncture is not possible, the anti-Xa level should be drawn from a line other than sites used to administer heparin. |
| | **e.** If drawing an anti-Xa level from a line containing heparin, the line should be flushed with saline and 3 to 5 mL of blood discarded prior to obtaining the sample. |
| | **f.** Monitor hemoglobin/hematocrit and platelet count every 5 to 7 days while hospitalized, paying particular attention to evidence of heparin-induced thrombocytopenia (HIT). (More frequent monitoring of platelet counts and hemoglobin/hematocrit may be warranted in a setting of increased bleeding risk or clinical instability.) |
| | **g.** Monitor for signs and symptoms of clinically significant bleeding |
| **5** | Further treatment monitoring of unfractionated heparin |
| | **a.** Order an anti-Xa level 8 hours after every change in infusion rate. |
| | **b.** Monitor anti-Xa level every 24 to 48 hours in the absence of a recent change in infusion rate, when anti-Xa levels are at goal. |

(Protocol from Children's Hospital Colorado, adapted from Monagle P, Chalmers E, Chan A, et al.; American College of Chest Physicians [71••].)