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ABSTRACT

BACKGROUND AND PURPOSE: Pediatric vertebral artery dissecting aneurysm is a subtype of vertebral artery dissection that can be challenging to diagnose and may be associated with stroke recurrence. This study examines the presenting features, clinical outcomes, and recurrence risk in a cohort of children with vertebral artery dissection, comparing those with aneurysms with those without.

MATERIALS AND METHODS: The medical records of children evaluated for vertebral artery dissection were retrospectively reviewed for neurologic presentation, treatment, stroke recurrence, and angiographic appearance of dissection. Cohort patients were categorized into 2 groups based on the presence or absence of a vertebral artery dissecting aneurysm and compared via the Fisher exact test, Student *t* test, and log-rank analyses. $P < .05$ was deemed statistically significant.

RESULTS: Thirty-two patients met the inclusion criteria, including 13 with vertebral artery dissecting aneurysms. Five cases of vertebral artery dissecting aneurysm were missed on the initial evaluation and diagnosed retrospectively. All patients received antiplatelet or anticoagulation therapy at the time of diagnosis. Children in the vertebral artery dissecting aneurysm group were more likely to present with stroke ($P = .059$), present at a younger age ($P < .001$), and have recurrent stroke ($P < .001$) compared with the group of children with vertebral artery dissection without an aneurysm. After surgery, no patients with vertebral artery dissecting aneurysm experienced recurrent stroke ($P = .02$).

CONCLUSIONS: Vertebral artery dissecting aneurysm is often missed on the initial diagnostic evaluation of children presenting with stroke. In children with vertebral artery dissection, the presence of an aneurysm is associated with stroke presentation at a younger age and stroke recurrence.

ABBREVIATIONS: PCAIS = posterior circulation arterial ischemic stroke; RVAC = rotational vertebral artery compression; VAD = vertebral artery dissection; VADA = vertebral artery dissecting aneurysm

In children who present with posterior circulation arterial ischemic stroke (PCAIS), vertebral artery dissecting aneurysms (VADAs) are a rare and often challenging-to-diagnose subtype of vertebral artery dissection (VAD) that can be detected on angiography. These types of aneurysms are also sometimes referred to as pseudoaneurysms or dissecting pseudoaneurysms, but for clarity in this article and to avoid confusion with the more common colloquial use of the term pseudoaneurysm for post-arterial access lesions, the term VADA will be used. Literature regarding VAD with aneurysm formation is sparse, especially in children.[1-5] The few published cases of pediatric VADA are often grouped together with cases of carotid artery dissection, making it difficult to determine how the study findings relate to this specific patient population. Preceding trauma is a common risk factor for children with VAD or VADA, similar to adults,[4] though a traumatic history is not always elicited. Associations between pediatric VAD and congenital cervical anomalies, eg, odontoid anatomic variants and Klippel-Feil syndrome, have also been reported.[5]

Moreover, several studies have described patients with VAD in the V3 region associated with occlusion of the artery during head-turning, which is sometimes termed rotational vertebral

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artery compression (RVAC) or pediatric bowhunter syndrome. These studies note a high recurrence risk, presumably secondary to chronic recurrent trauma from dynamic compression of the injured portion of the vertebral artery.[6,7] These articles also described the presumed pathophysiology of pediatric bowhunter syndrome, the male predominance in this condition, and the lack of recurrent stroke after surgical interventions, such as endovascular occlusion of the vertebral artery, decompression of the vertebral artery canal, and/or C1–C2 fusion. However, no previous study has compared the clinical course and outcomes in patients with VAD on the basis of the presence or absence of VADA. In our experience, patients with VAD with imaging findings of VADA experience a more malignant clinical course. Thus, the purpose of this study was to report the presenting features, clinical outcomes, and recurrence risk in a cohort of children with VAD, comparing those with VADA with those without.

MATERIALS AND METHODS

This single-center, Health Insurance Portability and Accountability Act–compliant retrospective study was approved by the Children's Hospital of Colorado institutional review board. The medical records of children (younger than 18 years of age at symptom onset) evaluated for PCAIS between 2000 and 2020 were reviewed for inclusion criteria: 1) neurologic deficit suspicious for PCAIS at presentation, and 2) VAD confirmed on angiography. Identification of patients included in our study was facilitated by a PACS keyword search using different combinations of the terms "vertebral," "vertebral artery," "dissection," and "aneurysm." In addition, most patients in our study were already indexed in pre-existing stroke research data-bases maintained by the authors. Initial diagnostic evaluation at the time of presentation involved a combination of head and neck CT, MR imaging, CTA, MRA, and cerebral angiography studies. Head-turning angiography, which was not routinely performed at this center in the early part of the 20-year study period, was also performed in later selected cases. Follow-up imaging, typically MR imaging/MRA, was routinely performed in patients followed at our institution 3 months after presentation and at 1-year intervals thereafter, and sometimes more frequently following stroke recurrence or change in therapy.

A board-certified pediatric neuroradiologist with 14 years of experience evaluated each case for the presence of cervical VAD and associated features, including the presence of intraluminal thrombus, luminal irregularity, stenosis, occlusion, dissecting aneurysm, and cervical spine abnormalities. Dissecting aneurysms specifically were defined as either fusiform or saccular focal enlargement of a vertebral artery segment. In cases in which an infarct was definitively visualized on initial imaging, a pediatric neuroradiologist and a pediatric neurologist independently confirmed the diagnosis of PCAIS in each patient and classified the causes of stroke using the Childhood AIS Standardized Classification and Diagnostic Evaluation criteria, which is in essence a consensus classification system for childhood arterial ischemic stroke established by the International Pediatric Stroke Study consortium.[8] Cases with any diagnostic uncertainty or with imaging that was thought to be nondiagnostic were excluded. Demographic and clinical information, including age at presentation, sex, race, ethnicity, presenting signs and symptoms, neurologic symptoms at follow-up, and treatment was recorded via chart review. When applicable, testing for thrombophilia and connective tissue disorders was also documented. Children diagnosed with VAD were separated into 2 comparison groups based on the presence (VADA) or absence (non-VADA) of dissecting aneurysm.

Data analyses were performed by the Fisher exact test and the 2-tailed Student t test using GraphPad software (http://www.graphpad.com/quickcalcs). In addition, the Kaplan-Meier (log-rank) test was used to compare pre- and postsurgery stroke recurrence in the patients who underwent surgical treatment. $P < .05$ was deemed statistically significant. The data sets generated during the current study are available from the corresponding author on request.

RESULTS

Patients and Presentation

Thirty-two patients met the inclusion criteria, including 13 with VADA. Five cases of VADA were diagnosed on retrospective review because the aneurysm was not described in the initial angiography report. Most of the cohort was male, with a greater male prevalence in the VADA group (Table). If one compared the average age at presentation, patients in the VADA group tended to be younger (4.7 years of age) than those in the non-VADA group (11.8 years of age, $P < .001$).

Common presenting signs and symptoms, similar in incidence between both VADA and non-VADA groups, included headache, hemiparesis, altered mental status, vision change, dysarthria, ataxia, emesis, and seizure. Preceding trauma, eg, trampoline fall, sports injury, or motor vehicle collision, was commonly reported at presentation and not statistically different between groups (7/13 in the VADA group, 10/19 in the non-VADA group, $P = 1.00$).

Imaging

The initial diagnosis was made on CTA in 16 patients and on MRA in the other 16. Bilateral injuries were seen in 4 total cases, 3 of which were in the VADA group. There were 2 cases with congenital cervical spine anomalies. One patient in the non-VADA group had an anomalous bone spur identified at the C2 level, and the other in the VADA group had an os odontoideum. An additional 5 patients, all in the non-VADA group, presented after traumatic fractures of the cervical spine, and the vertebral artery abnormalities began at the level of fracture in these cases.

In the non-VADA group, the injury most often consisted of a tapered stenosis in the V2 or V3 segments leading to complete or near-complete occlusion of the more upstream segments of the vertebral artery, including the V4 segments. In contrast to injuries in the non-VADA group, VADA occurred almost exclusively in the proximal V3 segment, just after the vertebral artery exit from the transverse foramen. Common imaging features of VADA are summarized in Fig 1. Acutely in these patients with a VADA, the areas of intraluminal narrowing and/or irregularity were seen in combination with focally dilated arterial segments. Intraluminal thrombus was commonly identified in the dilated arterial segments in the setting of acute infarction. Often, a focal outpouching was seen projecting from the proximal V3 segment either anteriorly on axial images or superiorly on coronal images. In contrast to patients without VADA, the vertebral artery lumen in most (12/13) patients with VADA was not completely occluded either at or downstream from the aneurysmally dilated V3 segment. Typically, after

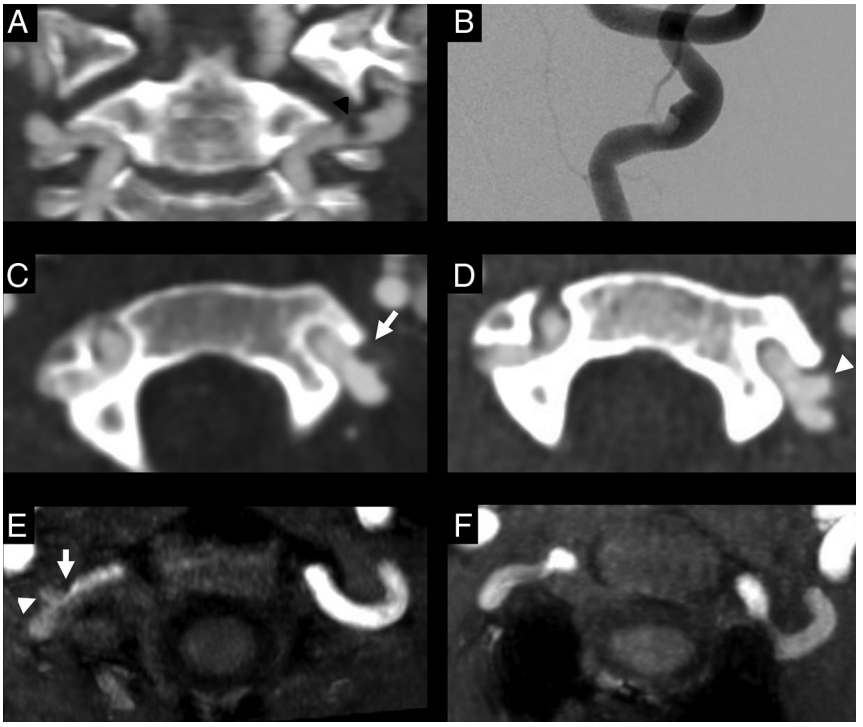

FIG 1. Imaging features of VADA. A 6-year-old boy with recurrent posterior circulation infarctions. Coronal CTA (*A*) and an anterior-posterior image from conventional angiography (*B*) demonstrate a focal filling defect in a fusiform dilation of the proximal left V3 segment (*black arrowhead*). *C* and *D*, A 7-year-old boy with recurrent posterior circulation infarctions. Axial CTA (*C*) from presentation shows a focally dilated proximal left V3 segment with a small filling defect (*white arrow*). Axial CTA (*D*) after several months of anticoagulation shows that the filling defect has resolved, leaving a saccular outpouching of the same proximal V3 segment (*white arrowhead*) that was best seen in the axial plane. *E* and *F*, Another 7-year-old boy with recurrent posterior infarctions. Axial MRA (*E*) at presentation shows the focal filling defect in the proximal right V3 segment (*white arrow*) with focal dilation downstream (*white arrowhead*). Flow-related enhancement in the entire right vertebral artery was decreased. Axial MRA (*F*) several months after cervical fusion shows that the filling defect has resolved and the focal dilation is no longer apparent.

anticoagulation or antiplatelet therapy, follow-up imaging showed that the intraluminal thrombus resolved and the areas of outpouching remodeled into more normal-appearing segments.

Thirteen of the 19 patients (68%) in the non-VADA group presented with PCAIS (the other 6 were diagnosed with TIA), while all 13 patients with VADA presented with stroke as confirmed by initial imaging ($P = .059$). There were no cases of recurrent stroke in the non-VADA group (0/19), while the incidence of recurrent stroke was found to be statistically significant in the VADA group (9/13, $P < .001$. Stroke recurrence over time for all patients in the VADA group is presented in a Kaplan-Meier curve in Fig. 3).

Treatment

All 32 patients in the non-VADA and VADA groups received antiplatelet or anticoagulation therapy at the time of diagnosis with either aspirin or unfractionated heparin. Initial treatment with anticoagulation or antiplatelet therapy was relatively homogeneous between the VADA and non-VADA groups. Beginning in 2021, hard cervical collars were used for cervical spine stabilization in patients with VADA per another institution's recommendations,[7] with no stroke recurrence for the 2 patients in whom they were used. Five patients, all in the VADA group, had definitive surgical treatment following a stroke recurrence after initiation of medical therapy, with 2 of these patients undergoing cervical fusion and 2 undergoing endovascular vertebral artery occlusion (Fig 2). The fifth patient was treated with vertebral artery decompression, as originally described by Fox et al.[6] Pre- and postsurgery stroke recurrence was statistically significant in these 5 patients with VADA ($P = .02$) because none of them had subsequent stroke after surgical intervention.

No patients in the cohort died during their initial hospitalization. All were discharged home in stable condition. Patients in the VADA group were followed for an average of 1914 days following presentation, while the group of patients without VADA were followed for an average of 899 days. At last clinical follow-up, persistent neurologic deficits were common in both the VADA and the non-VADA groups.

DISCUSSION

To our knowledge, this is the first study to describe the unique differences in long-term outcome between children with VAD involving aneurysms (VADA group) and those without aneurysms (non-VADA group). Despite the rarity of pediatric VADA in the literature, approximately 41% of our cohort demonstrated VAD with associated aneurysms.

We also believe that this is the first article to clearly describe the high recurrence risk (69%) in pediatric patients with VADA, irrespective of RVAC. Recurrent stroke in these patients tends to occur within the first 6–12 months, as demonstrated by these data. Thus, early treatment of patients with VADA with measures to prevent recurrent injury of the aneurysm is likely warranted, possibly even without an initial trial of medical management. Short-term treatment regimens can consist of antithrombotic therapy and cervical spine stabilization with a hard collar to prevent recurrent injury, as suggested by Braga et al.[7] Indeed, medical management failures in our patients with VADA all occurred while they were treated with a soft collar or no collar. We began using hard collars in 2021 as an additional precaution per the recommendations of Braga et al, and we have observed no stroke recurrences in the 2 patients stabilized in this way.

It remains unclear whether patients with VADA without stroke recurrence, or even with a single recurrent event, benefit from surgical therapy, especially since recurrent events after 1

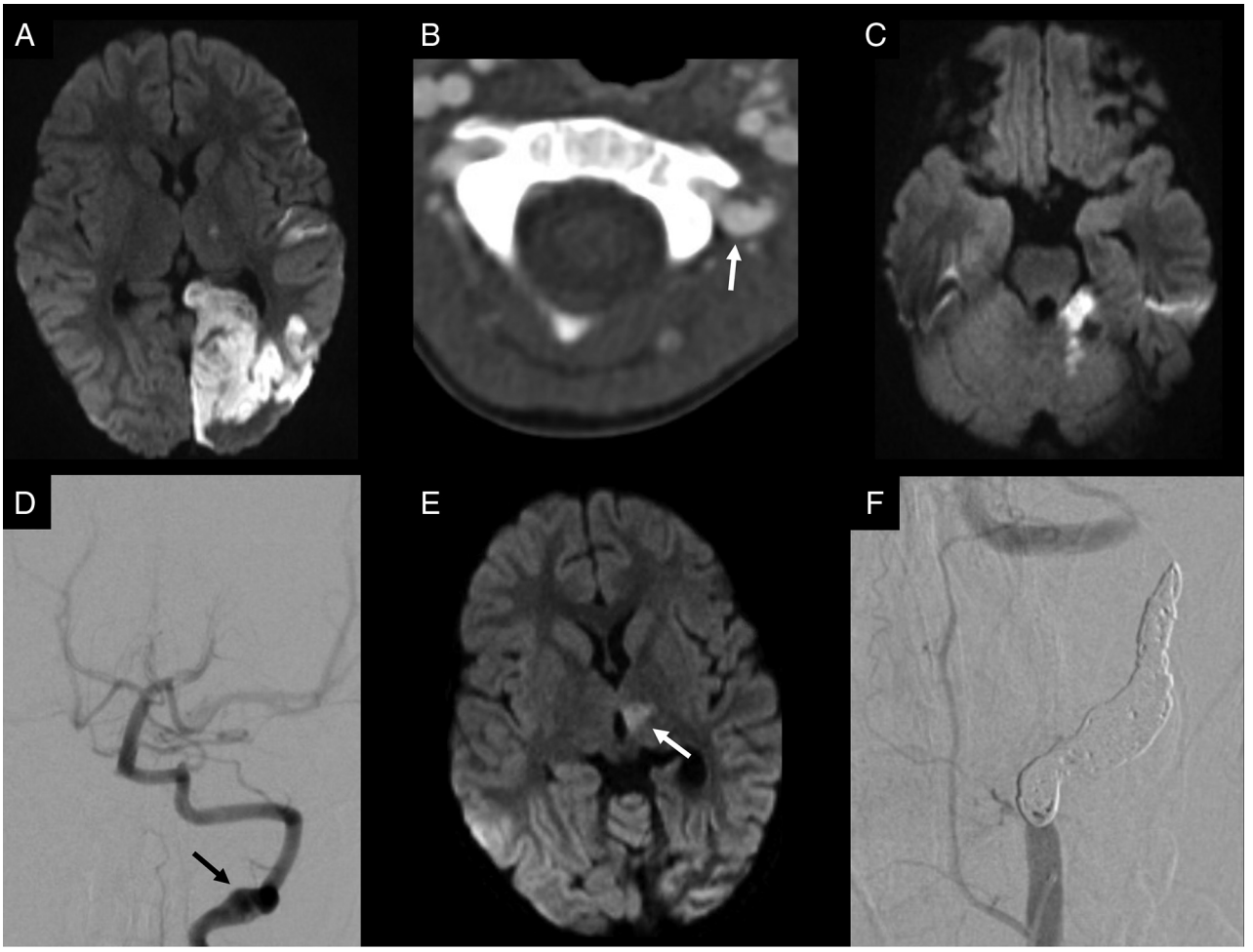

FIG 2. A 3-year-old boy initially presenting with syncope. *A*, Axial DWI demonstrates multiple areas of diffusion restriction in the posterior circulation. Abnormalities were bilateral and of differing signal intensity on ADC maps, implying different ages (not shown). *B*, Axial CTA image from the same day as image *A* shows focal dilation of the left V3 proximal segment (*white arrow*). This abnormality was not diagnosed at the time of imaging. *C*, Repeat DWI 3 weeks after initial presentation following new neurologic symptoms while on aspirin demonstrates a new area of restricted diffusion in the left superior cerebellum. *D*, Conventional angiography, performed 2 days after image *C*, demonstrates the focal area of left proximal V3 segment dilation and irregularity (*black arrow*). This abnormality was only present on a single series due to a misalignment of the lateral camera of the biplane, and it was not diagnosed at the time of the procedure. *E*, Axial DWI obtained 8 weeks after initial presentation following another acute neurologic deterioration while on anticoagulation demonstrates a new area of diffusion restriction in the left thalamus (*white arrow*). *F*, Catheter angiogram demonstrates complete coil occlusion of the abnormal vertebral artery segment. No recurrent symptoms or new areas of infarction occurred following this procedure.

year with or without surgical intervention appear to be rare. None of our 13 patients with VADA had recurrent stroke >12 months after their first event. The high rate of recurrent stroke events in this series of patients with VADA suggests that aggressive therapy such as surgical intervention is reasonable and, if not undertaken, should be highly considered with recurrent stroke events.

Five patients in our VADA group who had stroke recurrence underwent surgical intervention, and none had further events. This result is consistent with prior reports of favorable outcomes in children with VAD who had definitive surgical treatment following failed medical management.[9,10] Currently there is a lack of consensus on which surgical treatment is most appropriate, though at our institution vessel-sparing procedures, ie, cervical decompression or fusion, are typically favored over endovascular coiling, given the lifetime risk of compromise to the contralateral vessel. Generally, we recommend decompression in unilateral cases and fusion in cases of bilateral disease or with findings of cervical spine instability. The alternative of endovascular coiling may be considered when decompression is not feasible, particularly in cases with rapid stroke recurrence and negative findings of RVAC on rotational angiography. However, given the paucity of reported pediatric VADA cases treated by surgery, further multicenter investigation is necessary to determine the efficacy and durability of these techniques.

VADA is commonly acknowledged to be a difficult diagnosis that is sometimes missed on the initial imaging evaluation of children who present with PCAIS or strokelike symptoms. This occurred in 3 of our patients seen between 2000 and 2010.[11] Missed or delayed diagnosis of VADA can lead to inappropriate

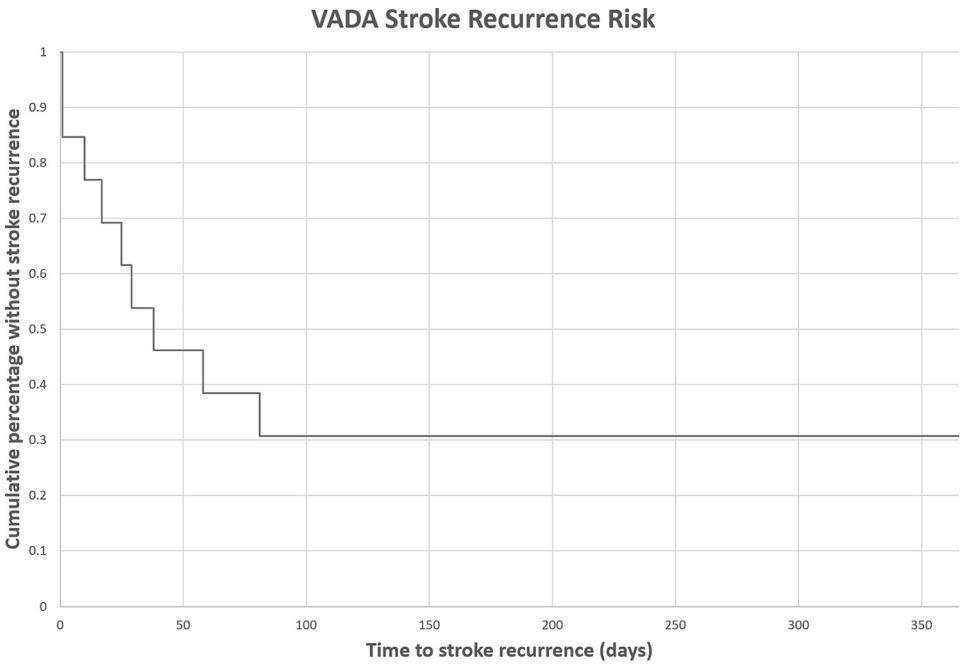

FIG 3. Stroke recurrence in the VADA group.

Comparison of clinical characteristics at presentation

	Cohort	VADA	Non-VADA	*P* Value
Age (yr)	8.9	4.7	11.8	<.001
Sex (No.)				.45
Male	21	10	11	
Female	11	3	8	
Initial diagnosis				.059
Stroke	26	13	13	
TIA	6	0	6	
Signs and symptoms (No.)				
Headache	13	5	8	
Hemiparesis	13	6	7	
Altered mental status	10	4	6	
Vision change	7	4	3	
Ataxia	5	4	1	
Emesis	5	2	3	
Dysarthria	5	1	4	
Seizure	4	2	2	
Nausea	3	1	2	
Numbness	2	0	2	
Abdominal pain	1	1	0	
Vertigo	1	1	0	

treatment and possibly poor outcomes. Antithrombotic and/or antiplatelet therapy was initiated in all patients in our cohort. Unfortunately, even when appropriate therapy was initiated soon after diagnosis, many of our patients with VADA experienced recurrent stroke.

The reason that the presence of a dissecting aneurysm in VAD increases the risk of stroke recurrence in children remains unclear. Possibly the aneurysm causes slow or turbulent blood flow in the vertebral artery that, with time, leads to thrombus formation and embolic stroke. Furthermore, patients with VAD with RVAC, ie, pediatric bowhunter syndrome, may be predisposed to developing VADA. In RVAC, neck rotation causes episodic vertebral artery compression, sometimes in association with a cervical bony abnormality, that can predispose to recurrent vertebral artery injuries and thromboembolism. Although the association between RVAC and pediatric vertebral artery dissection is well documented,[10,12] VADA without RVAC is also seen, and treatment in these cases is uncertain. Currently most institutions do not routinely perform angiography with provocative maneuvers to definitively diagnose RVAC, so the true incidence of pediatric RVAC may be underreported. It is now our practice to perform conventional angiography with head rotation in most of our patients with VADA. In the VADA group of our cohort, only 3 patients, all males, presented with a history and imaging findings consistent with RVAC on rotational angiography.

The limitations of this study include its small sample size, retrospective design, and lack of uniform follow-up. Improvements in neuroimaging quality and increased diagnostic awareness that occurred during the 20-year study period could have impacted the incidence of diagnoses of PCAIS, VAD, and VADA. In addition, there may have been a selection bias toward enrolling patients with more severe symptoms because our cohort was recruited in a tertiary care setting.

CONCLUSIONS

In our cohort of children with VAD, those with VADA were likely to present with recurrent stroke within 12 months of the initial event. VADA was often missed on the initial diagnostic work-up of children presenting with PCAIS or strokelike symptoms. Clinicians and radiologists evaluating children with PCAIS should carefully assess the presence of VADA and be aware of its influence

on stroke recurrence, even when appropriate therapy is initiated at diagnosis. Neck stabilization during the acute phase with a hard collar is likely warranted, and consideration of surgical treatment should be pursued in cases of failed medical management and possibly as first-line therapy in those with RVAC.

Disclosure forms provided by the authors are available with the full text and PDF of this article at www.ajnr.org.

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