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Case Report

Focal cerebral arteriopathy-inflammatory type in a child – MR diagnosis using vessel wall imaging technique with review of classification and diagnostic evaluation criteria ☆

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ABSTRACT

Acute ischemic stroke (AIS) in childhood is defined by a stroke occurring after 28 days of life to 18 years of age. This presents a distinct clinical challenge in terms of both diagnosis and treatment. The overlapping clinical presentations of acute ischemic stroke and its mimics such as migraine with aura, seizure with Todd paresis and encephalitis renders early accurate diagnosis of this time-sensitive condition difficult, with a change in the final diagnosis in up to 40% of patients. Identification of the etiology after establishing the diagnosis of ischemic stroke is paramount for prognostication and treatment decisions. These include cardioembolic, arteriopathy, thrombophilia and inflammatory causes.

Magnetic resonance imaging (MRI) plays an indispensable role towards tackling the initial diagnostic dilemma and subsequent evaluation of the underlying etiology, particularly in patients with arteriopathy.

Here we present the MRI findings including vessel wall imaging with longitudinal follow-up, which support the diagnosis of focal cerebral arteriopathy-inflammatory type (FCAi) in a pediatric patient.

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Introduction

Acute ischemic stroke (AIS) in childhood is defined by a stroke occurring after 28 days of life to 18 years of age [1]. This presents a distinct clinical challenge in terms of both diagnosis and treatment. The overlapping clinical presentations of acute ischemic stroke and its mimics such as migraine with aura, seizure with Todd paresis and encephalitis renders early accurate diagnosis of this time-sensitive condition difficult, with a change in the final diagnosis in up to 40% of patients [2].

Identification of the etiology after establishing the diagnosis of ischemic stroke is paramount for prognostication and treatment decisions. These include cardioembolic, arteriopathy, thrombophilia and inflammatory causes.

Magnetic resonance imaging (MRI) plays an indispensable role towards tackling the initial diagnostic dilemma and subsequent evaluation of the underlying etiology, particularly in patients with arteriopathy [3].

Here we present the MRI findings including vessel wall imaging with longitudinal follow-up, which support the diagnosis of focal cerebral arteriopathy-inflammatory type (FCA-i) in a pediatric patient.

Case report

A 14-year-old boy presented acutely symptoms of syncope, right-sided pulsatile headache and left-sided weakness. He sustained a fall with minor injury to the face and developed left-sided limb twitching lasting for 5 minutes. He was immediately attended by his parents and admitted to the Emergency department for further assessment. There was no episode of febrile illness or trauma prior to the presentation. He had no other significant medical history apart from attention deficit hyperactivity disorder.

Initial physical examination showed unremarkable vital signs including his temperature, blood pressure, heart rate and Oxygen saturation. He was drowsy but able to carry out conversations and orientated. His Glasgow Coma Scale score was 15/15.

There was weakness in the left upper and lower limb with muscle power assessment (MRC) grading of 2 out of 5, as well as loss of nasolabial fold in the left face. He demonstrated left pyramidal signs including brisk reflex of the left upper and lower limbs with positive Babinski sign. No significant injury was identified on physical examination.

Initial blood tests including complete blood count, clotting profile, liver and renal function tests were unremarkable.

An urgent computed tomography (CT) brain and cerebral angiogram was arranged (Fig. 1), demonstrating early ischemic infarcts in the right frontal and anterior temporal lobe. There was occlusion of the corresponding right middle cerebral artery (MCA) terminal branches supplying the aforementioned territories but no other proximal large vessel occlusion.

MRI of the brain was performed on day 2 of presentation (Fig. 2). There were large areas of restricted diffusion and hyperintensity on the fluid attenuated inversion recovery (FLAIR) images in the right frontal and temporal lobes with involvement of the basal ganglia, again consistent with an acute infarct in the right MCA territory. Time-of-flight

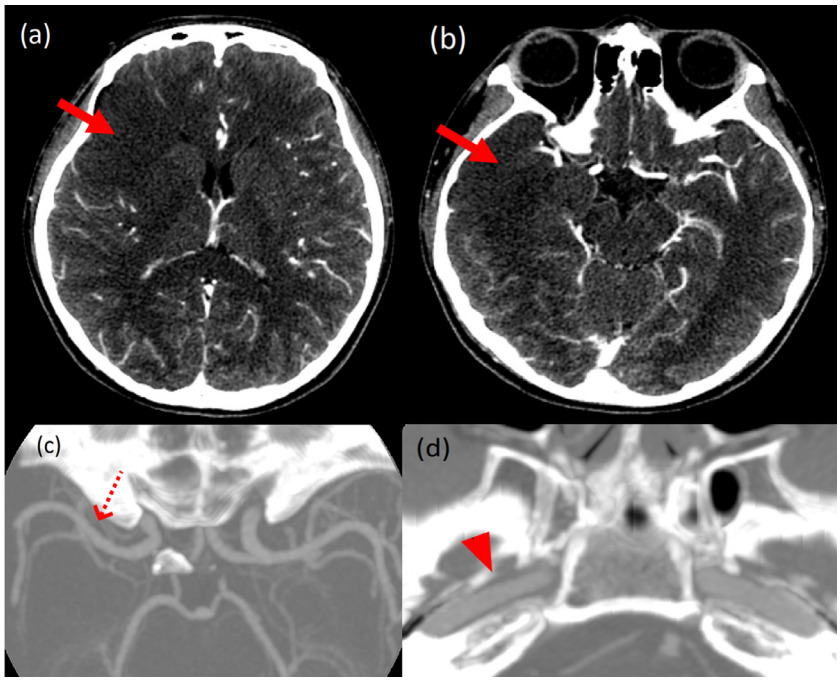

Fig. 1 – CT brain with cerebral angiogram demonstrating loss of gray-white differentiation (*red arrows*) in the right frontal (A) and anterior temporal lobe (B) with involvement of the basal ganglia consistent with acute infarcts in the right MCA territory. Maximum-intensity projection (MIP) demonstrating the patency (*red dashed arrow*) of the right proximal MCA (C) and petrous segment of the right ICA (D). Note the relative reduction of the right ICA (*red arrowhead*) compared to the contralateral left side.

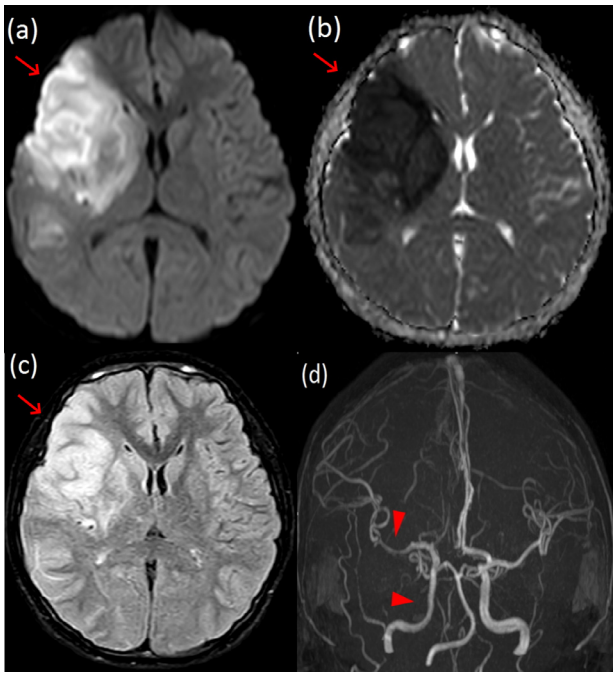

Fig. 2 – MRI performed on day 2 of presentation with diffusion-weighted imaging (A), apparent diffusion coefficient map (B) and FLAIR images (C) demonstrating restricted diffusion and cytotoxic edema (*red arrows*) in the right frontal and parietal lobes consistent with an acute infarct in the right MCA territory. The TOF-MRA images (D) demonstrating reduced caliber of the right ICA and MCA (*red arrowheads*).

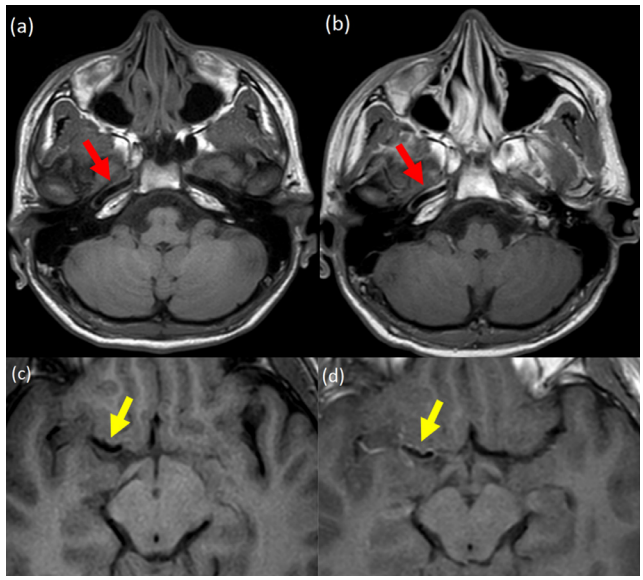

Fig. 3 – MR vessel wall imaging performed at day 2 of presentation with an 1.5T MRI scanner (Ingenia; Philips Healthcare, Best, The Netherlands) with pre- and postcontrast 3D black-blood T1-weighted sequence with volumetric isotropic turbo spin echo acquisition with the following parameters with: Repetition time (TR) = 400 ms; Echo time (TE) = 25 ms; Flip angle = 90 degrees; Voxel size = 0.5 mm x 0.5 mm x 1.8 mm; Matrix size = 400 x 400. This demonstrated concentric wall thickening (*red arrows*) at the petrous segment of the right ICA (A) with avid contrast enhancement (B). Similar findings (*yellow arrows*) of concentric vessel wall thickening (C) with enhancement (D) are also observed in the right proximal MCA.

magnetic resonance angiography (TOF-MRA) demonstrated patency of the right ICA and proximal MCA but with relatively reduced calibers.

Further investigation using pre- and postcontrast intracranial vessel wall imaging (Fig. 3) was performed at the same setting using 3D black-blood T1-weighted sequence with volumetric isotropic turbo spin echo acquisition (VISTA). This demonstrated concentric wall thickening with avid enhancement over the right internal carotid artery (ICA), M1 and M2 segments of the right MCA, and A1 segment of the right anterior cerebral artery (ACA). The above features are characteristics of vasculitis.

The patient was treated with hypertonic saline for his cerebral edema and remained conscious with left hemiplegia. He developed a sudden episode of clinical deterioration on day 7 of admission with increased drowsiness and headache. Repeated CT brain showed a new infarction in the right parietal lobe with increased midline shift. He then received emergency right decompressive craniectomy and remained clinically stable.

Follow-up MR vessel wall imaging was performed approximately 1 month after the initial presentation (Fig. 4). This demonstrated progression of the concentric enhancing wall thickening in the previously involved regions.

Extensive additional work-up for the patient was unremarkable. Infectious workup including polymerase chain reaction testing in CSF and serology for VZV and HSV infections were negative. Nasopharyngeal and throat swabs were negative for SARS-CoV-2. Transthoracic echocardiogram was unremarkable. Workup for thrombophilia, autoimmune and metabolic conditions including MELAS were also unrevealing.

Based on the clinical presentation and imaging findings, a consensus diagnosis of FCA-i was made after multidisciplinary team meeting with pediatric rheumatologists and pediatric neurologists. The patient was treated with antiplatelet therapy, steroids and intensive rehabilitation.

Further follow-up MRI at 4 months, 7 months, and 10 months showed persistent but stable appearances of the concentric enhancing wall thickening involving the right ICA, proximal MCA and ACA (Fig. 4).

At 1 year of clinical follow-up, there were no further recurrent episodes of ischemic stroke. His activity of daily livings remained independent with residual weakness of the left upper and lower limbs with MRC grading of 4 of 5.

Discussion

FCA-i

FCA-i type, also previously referred as transient cerebral arteriopathy (TCA) in the literature, is thought to be the most

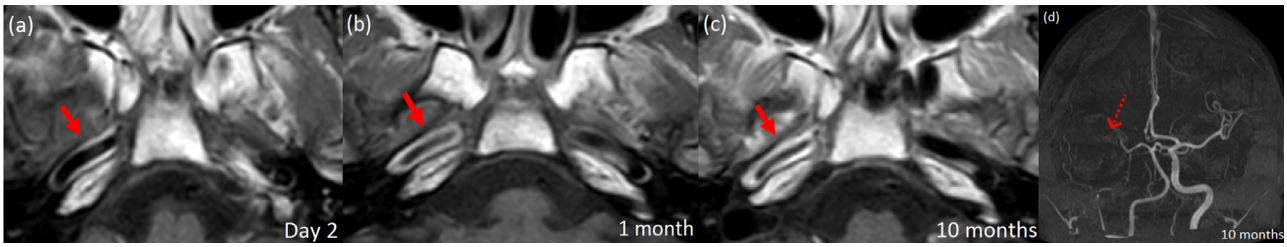

Fig. 4 – Comparison of MR vessel wall imaging performed at day 2 (A) and 1 month of presentation (B), demonstrating progression of the concentric enhancing vessel wall thickening (*red arrows*) in the petrous segment of the right ICA. Further follow-up at 4 months, 7 months, and 10 months (C) demonstrated persistent but stable appearances of the concentric enhancing vessel wall thickening. TOF-MRA performed at 10 months shows persistent signal loss (*red dashed arrow*) of the right ICA and MCA (D) which may be due to slow flow due to the significant vessel stenosis.

common type of arteriopathy in children with acute ischemic strokes [4].

This presumed inflammatory disease affecting the large intracranial arteries (eg, ICA, MCA or ACA) is thought to be most commonly due to a parainfectious process leading to localized vessel inflammation with secondary thrombus formation and ischemic stroke, classically following varicella infection [5]. More recent reports have also suggested links with COVID-19 infection in the recent global pandemic [6].

The typical clinical course is described as a dynamic self-limiting process characterized by progressive arteriopathy early on during the first six months followed by stabilization or improvement, which are consistent with the findings as in this described case.

Banding appearances, caused by intermittent areas of stenoses of the affected large vessels, can be demonstrated with the superior spatial resolution of digital subtraction angiogram is thought to be pathognomonic for this condition. However, this requires an invasive investigation with procedural risks and is only present in approximately a quarter of the cases and is therefore not a sensitive marker [7].

MRI vessel wall imaging is at the forefront of research in the diagnosis and prognostication for this condition [8]. Pre-contrast vessel wall images has been demonstrated to allow direct visualization of hyperintense intramural thrombus in both cases of extracranial and intracranial dissection [8,9]. This potentially allows distinction between this inflammatory condition and focal cerebral arteriopathy – dissection type (FCA-d), which demonstrate similar appearances of intracranial large vessel luminal narrowing or irregularities but nonetheless represents a separate distinct disease process.

Concentric vessel wall enhancement has been described as a characteristic finding for this inflammatory condition in both the pediatric population [8], as well as in the adult literature in analogous conditions [10]. The characteristic appearances would allow differentiation from other etiologies affecting the large intracranial vessels, such as arterial dissection or cardio-embolic events, which would not demonstrate enhancement of the vessel walls.

Vessel wall imaging has been further described as a potential tool for prognostication. Previous case series have demonstrated that presence of strong intensity vessel wall enhancement at presentation was found to be significantly associated with progressive arteriopathy on subsequent follow-up imaging when compared to absence of strong enhancement (83% vs 0%) [11]. Patients with progressive arteriopathy on imaging have also been described in the literature to be associated with up to 19-fold increased risk of recurrent stroke [12]. Therefore, the presence and intensity of vessel wall enhancement on presentation may allow for diagnosis and prompt for intensification of clinical and radiological monitoring for patients identified to be at risk of future deterioration.

In terms of treatment, there is currently limited high-quality evidence regarding the optimal treatment of this condition and randomized controlled trials are being planned regarding the role of steroid use [13].

Classification and nomenclature of childhood ischemic stroke

Classification and nomenclature of arteriopathy in childhood ischemic stroke has evolved over time. Various terms such as transient cerebral arteriopathy (TCA), focal cerebral arteriopathy (FCA) and large-vessel childhood primary angitis of the central nervous system (cPACNS) have been used to describe similar disease processes [14].

The Childhood AIS Standardized Classification and Diagnostic Evaluation (CASCADE) criteria was developed by the International Pediatric Stroke Study (IPSS) aiming to provide an objective classification to promote further research [14].

The primary CASCADE criteria based on the caliber and the distribution of the affected vessels classifies patients into small vessel arteriopathy of childhood, unilateral focal cerebral arteriopathy (FCA) and bilateral cerebral arteriopathy of childhood, aortic / cervical arteriopathy, cardio-embolic or other/multifactorial entities (Table 1). This anatomical-based classification of the CASCADE criteria has been shown to show improved inter-rater reliability compared to standard practice [15].

Retrospective cohort studies based on the CASCADE criteria demonstrated that patients with unilateral focal cerebral arteriopathy (FCA) demonstrate early progression of arteriopathy with a median time to progression of 11 days with up to 40% of patients at risk of recurrent strokes [16], necessitating intensive monitoring in the early period for potential early arteriopathy progression and recurrent stroke as illustrated in the clinical course of this case.

Patients with bilateral cerebral arteriopathy also suffer from an increased 75% risk of recurrent stroke but the progres-

Table 1 – Primary childhood AIS standardized classification and diagnostic evaluation (CASCADE) criteria.

Primary classification	Type of affected vessels	Key features on imaging
Small vessel arteriopathy of childhood	Small caliber intracranial arteries	Multifocal arterial narrowing demonstrated on conventional digital subtraction angiogram.
Unilateral focal cerebral arteriopathy of childhood (FCA)	Unilateral large intracranial arteries (including ICA, MCA, ACA and / or the posterior circulation)	Stenosis or vessel irregularity of the vessel supplying the territory of infarct demonstrated on CT, MR or conventional angiography.
Bilateral cerebral arteriopathy of childhood	Bilateral large intracranial arteries (including ICA, MCA, ACA and / or the posterior circulation)	
Aortic / Cervical Arteriopathy	Aortic and cervical arteries	Double-lumen, intimal flap or pseudoaneurysm demonstrated on CT, MR or conventional angiography. Characteristics hyperintense crescent in the arterial wall may be demonstrated on T1 fat-saturation MRI images.
Cardio-embolic	Any	Abrupt blockage of an artery consistent with a clot, without any surrounding irregularity or stenosis suggestive of arteriopathy.
Other or multifactorial	N/A	N/A

sion of the arteriopathy occurs significantly later at a median of 124 days, emphasizing the need of long-term follow-up for these patients. Conversely, patients with underlying cardio-embolic stroke demonstrated a lower risk of 8% of recurrent stroke in this cohort study.

Therefore, the CASCADE criteria allows for a classification of patients which provides important information of the recurrent stroke risk and also informs the appropriate time-frame for which these patients should be monitored at.

Further efforts have also made to identify typical clinical and imaging features of further subtypes of different arteriopathies in the vascular effects of infection in pediatric stroke (VIPS) study [7], such as unilateral focal cerebral arteriopathy-inflammatory type (FCA-i) and unilateral focal cerebral arteriopathy-dissection type (FCA-d).

In conclusion, we present at a pediatric case of focal cerebral arteriopathy-inflammatory type. Vessel wall imaging is a recent commercially available MR imaging sequence, which is useful for early diagnosis, prognostication and follow-up assessment in inflammatory cerebral arteriopathy. Vessel wall imaging should be considered to be incorporated into the imaging protocol for pediatric AIS as etiology of pediatric stroke is different from the common atherosclerotic stroke in adults.

Patient consent

Written informed consent for publication of this case report has been obtained from the patient.

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