COVID-19 associated renal artery stenosis in infancy - A report of two cases

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ABSTRACT

Organ-specific vasculitis is an uncommon, delayed complication of COVID-19 infection. It is usually seen in mildly symptomatic or asymptomatic patients. Underlying endothelitis is the most likely pathophysiological mechanism for such a manifestation. We report two infants with renal artery stenosis, most likely consequent to COVID-19 infection.

Keywords: COVID-19, renal artery stenosis, thrombosis, vasculitis

INTRODUCTION

COVID-19 infection among children is usually mild with only 3.3% of children requiring admission in the intensive care unit.[1] Delayed immune-related manifestations of COVID-19 in children include multisystem inflammatory syndrome in children (MIS-C) and organ-specific vasculitis[2] that occur days to weeks after the index episode of COVID-19 infection and are mostly reported in those with mild or asymptomatic COVID-19 infection. In this report, we describe two cases of renal artery stenosis in infancy following COVID-19 infection.

CASE REPORTS

Case 1

A 13-month-old boy who was previously well presented with fast breathing, failure to thrive, and decreased activity for the preceding 5 months. The child had worsening breathlessness and fever for the last 10 days. The parents also complained of generalized swelling and decreased urine output for the last 3 days. There was no history of recent COVID-19 infection in the family. At presentation, he had severe respiratory distress and acute decompensated heart failure requiring mechanical ventilation. He was febrile (102°F) with heart rate of 166 beats/min and blood pressure (BP) of 134/95 mm Hg (>95th percentile) in his right upper arm. He weighed 9 kg (WHO Z-score-0.85) and his length measured 75 cm (WHO Z-score-0.80). Physical examination was negative for conjunctivitis, skin rash, skin peeling, absent pulses, and renal bruit. Echocardiogram showed dilated left ventricle (LV), mild left ventricular hypertrophy (LVH), severe LV systolic dysfunction (LV ejection fraction [EF] 20%), normal coronary arteries, and moderate mitral regurgitation. Laboratory investigations [Table 1] showed polymorphic leukocytosis, normal C-reactive protein (CRP), and erythrocyte sedimentation rate level but elevated interleukin-6 level. COVID-19 reverse transcriptase–polymerase chain reaction (RT-PCR) was negative, but immunoglobulin G (IgG) antibodies were positive. Initially, we managed the child with intravenous (IV) nitroglycerine, dobutamine, furosemide, and empirical

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broad-spectrum IV antibiotics. The blood and urine cultures returned negative.

We considered a provisional diagnosis of MIS-C and the child was treated with IV Ig and IV methylprednisolone. Fever subsided and acute-phase reactants declined after 5 days of steroid therapy, but BP remained at 95th percentile. Ultrasound examination of the kidneys showed a normal right kidney (6.8 mm × 2.7 mm) but a small left kidney (5.1 cm × 2.4 cm) with normal corticomedullary differentiation. Renal Doppler examination was normal while computed tomography (CT) angiogram revealed complete occlusion of the left renal artery approximately 3-mm postostium. Aorta and its other branches, coronary arteries, and pulmonary arteries were normal [Figure 1]. Renal angiogram revealed totally occluded left renal artery [Figure 2], which could be partially recanalized with the establishment of flow using an 0.014-inch guidewire. Further, balloon dilatation of the occluded segment, however, could not be achieved due to technical failure. Nonetheless, the child could be extubated after 2 days with better control of hypertension. Renal angioplasty was successfully performed after 10 days of the initial procedure using sequential dilatation of the left renal artery using 1.5 mm × 10 mm and 3.0 mm × 10 mm size balloons. There was no residual renal artery stenosis. Postprocedure, BP control improved rapidly and permitted reduction in antihypertensive medications. At the time of discharge, the echocardiogram showed improvement in LV EF to 30%. Heart failure therapy with carvedilol (0.2 mg/kg/day) and enalapril (0.2 mg/kg/day) was optimized. LVEF improved to 40%, and BP was controlled <50th percentile at 1-year follow-up.

Case 2

A 12-month-old girl presented with fever and fast breathing of 15-day duration. She also had poor weight gain for the preceding 3 months. There was a history of symptomatic COVID-19 infection in the grandfather 3 months back. At presentation, she was febrile (102°F) with tachycardia (heart rate

Table 1: Laboratory findings at admission

Investigations	Case 1	Case 2	Reference range*
Hemoglobin	9.8	9.7	10.5–13.5 g/dL
MCV	72.5	65.6	70–86 fL
White blood cell	15.7×10^3	16.5×10^3	6.0–17.0×10^3/μL
Differential count (%)	Neutrophils 69, lymphocytes 27	Neutrophils 45, lymphocytes 45	
Platelet count	352×10^3	587×10^3	150–350×10^3/μL
Ferritin	39.4	--	7–140 ng/mL
C-reactive protein	0.3	8.2	0–0.5 mg/dL
Procalcitonin	3.61	--	0–0.07 ng/mL
Erythrocyte sedimentation rate	10	41	0–10 mm/h
IL-6	25 pg/mL	--	<17 pg/mL
Troponin T-hs	--	38.3	12.7–24.9 pg/mL
CK-MB (activity)	140.3	104.4	0–25 U/L
Creatinine	0.5	0.3	0.2–0.4 mg/dL
ANA	Negative	Negative	
ANCA (p, c)	Negative	Negative	

*Reference values for one year child. (--): Test not done. MCV: Mean corpuscular volume, IL-6: Interleukin-6, CK: Creatine kinase, ANA: Antinuclear antibody, ANCA: Antineutrophil cytoplasmic antibodies, HS: Highly sensitive, NAD: No abnormality detected

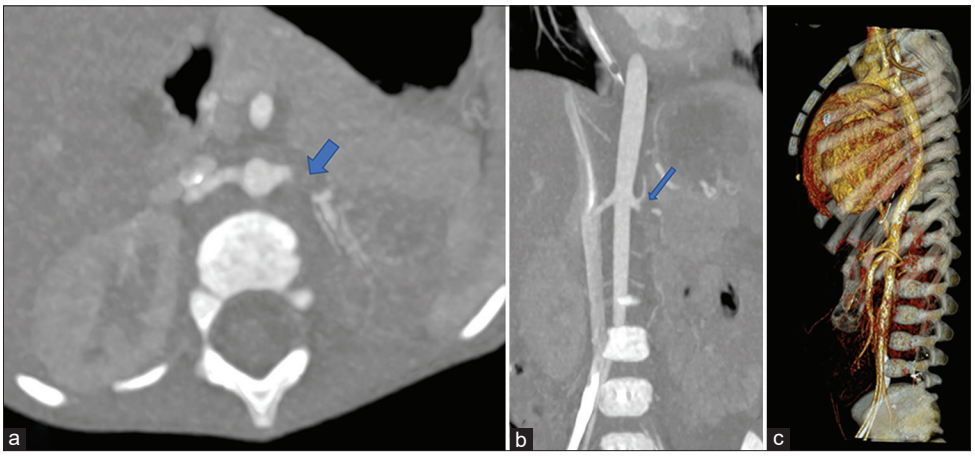

Figure 1: Axial, (a) and coronal, (b) CT angiograms of showing complete short segment occlusion of proximal left renal artery with extra-hilar reformation (arrow). (c) Sagittal volume rendering technique showing normal thoraco-abdominal aorta, arch vessels origin and origin coeliac and superior mesenteric artery. CT: Computed tomography

130 beats/min) and tachypnea (respiratory rate 36/min). She weighed 6 kg (WHO Z score-3.5) and her length was 72 cm (WHO Z score-0.8). Her BP measured 140/98 mm of Hg (>95th percentile) in her left upper arm. Physical examination was suggestive of congestive cardiac failure with normal perfusion. There was no mucocutaneous involvement. Blood investigations showed anemia, leukocytosis, and elevated inflammatory markers [Table 1]. Echocardiogram showed dilated LV, normal coronary arteries, severe LV systolic dysfunction (LVEF 15%), and mild LVH. RT-PCR for COVID-19 was negative but IgG antibodies against severe acute respiratory syndrome coronavirus 2 were detected. Furosemide was started for heart failure. Hypertension was managed with three antihypertensives, namely, amlodipine, metoprolol, and IV nitroglycerine. She also received empirical ceftriaxone. Ultrasonography and Doppler interrogation revealed a small right kidney (5 cm × 2.1 cm) with parvus tardus pattern in the renal artery suggesting right renal artery stenosis and a normal left kidney. CT angiogram confirmed ostioproximal occlusion of the right renal artery with mural thickening [Figure 3]. In addition, there was a long segment concentric mural thickening in juxtarenal abdominal aorta with narrowing of the middle segment of the left subclavian artery. Other aortic branches, coronary arteries, and pulmonary arteries were normal.

She was started on oral prednisolone at a dose of 1 mg/kg/day. After 7 days of steroid therapy, fever subsided, and CRP reduced albeit with poorly controlled hypertension. Renal artery angiogram demonstrated complete occlusion of the ostioproximal segment right renal artery. Renal angioplasty was attempted but could not be done successfully despite multiple attempts. Nevertheless, BP control below the 90th centile was achieved over the next few days with enalapril and metoprolol. LVEF improved to 25%. Repeat attempt at renal angioplasty at 6-week follow-up was also unsuccessful. Further, antihypertensive (enalapril, metoprolol, and amlodipine) was titrated to achieve BP <50th percentile. LVEF was normal at 1-year follow-up.

DISCUSSION

Renal artery stenosis in infancy is extremely rare.[3] The presentation with fever and elevated biochemical

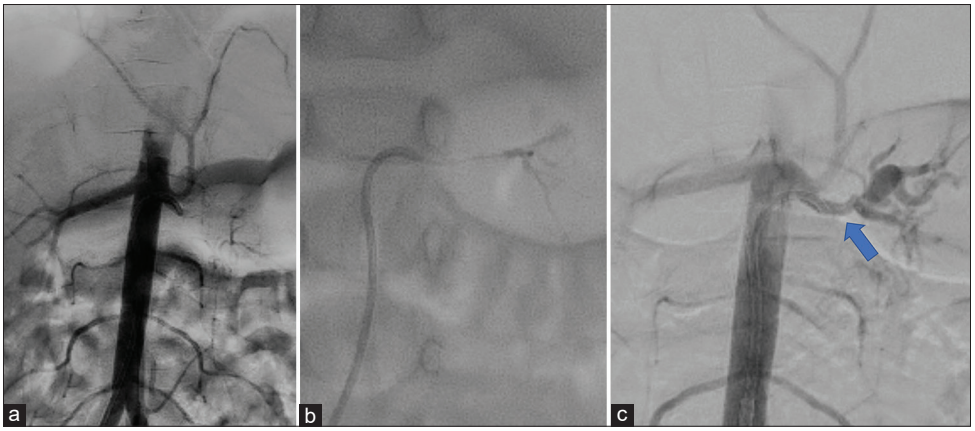

Figure 2: Digital subtraction angiograms, (a and b) showing total occlusion of left renal artery, (c) post angioplasty angiogram showing good recanalization of left main renal artery (blue arrow)

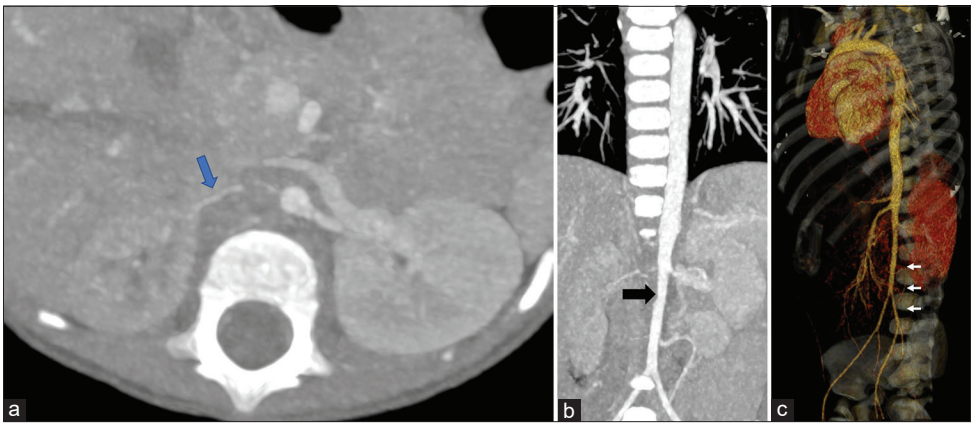

Figure 3: Axial, (a) and coronal (b) CT angiograms showing near total ostioproximal occlusion of right renal artery (blue arrow). (c) Reformatted VRT images mild narrowing of juxtarenal aorta (black and white arrow). CT: Computed tomography, VRT: Volume rendering technique

markers indicates an inflammatory etiology. Although these children fulfilled the European League Against Rheumatism/Paediatric Rheumatology International Trials Organization criteria for Takayasu arteritis (fever, hypertension, positive inflammatory markers, and angiographic abnormalities, including subclavian artery involvement), infantile Takayasu arteritis or middle aortic syndrome is rare and is a diagnosis of exclusion.[4,5] Other causes of renal artery stenosis in children include fibromuscular dysplasia, syndromes such as William's syndrome, neurofibromatosis, and other vasculitides such as polyarteritis nodosa.

COVID-19, on the other hand, is known to have caused organ-specific vasculitis.[2,6-8] The presence of COVID-19 antibodies during the early phase of pandemic favored the diagnosis of COVID-19-related vasculitis. Moreover, complete thrombotic occlusion of the renal artery in our patients early in the course of illness possibly indicate COVID-19 infection as the etiology. However, there was no way by which we could completely rule out infantile Takayasu arteritis in these patients. More accurate tests such as pentraxin-3 and tissue biopsy were not available.

Endothelial injury and spontaneous thrombosis are well-described in COVID-19 infection. Cases of spontaneous thrombosis of the aorta and its branches have been reported even in patients with mild COVID-19 infection.[9] Endothelial injury as a result of viral infection initiates a cascade of inflammation leading to vasculitis, platelet aggregation, and coagulation activation that result in microvascular thrombosis.[10] Although reported earlier, arterial thrombosis is a relatively uncommon presentation of Takayasu arteritis.[11] Acute worsening of symptoms with evidence of shrunken kidneys and difficulties during intervention in our patients may suggest a subacute or acute on chronic vascular pathology. Besides renal artery stenosis, the multi-organ involvement in these patients also resembled MIS-C.[12] A 13-year-old patient diagnosed with MIS-C was reported to have aortoarteritis with renal artery involvement who responded to immunosuppressive therapy.[13] Infantile presentation, the absence of thrombocytopenia, and lymphopenia in our patients were contrary to described features of MIS-C.[12] At around the onset of symptoms in our patients, a nationwide seroprevalence study in August 2020 indicated 5.4% seropositivity in children aged 10–18 years and even lower in younger children.[14,15] Hence, the probability of incidental coexistent COVID-19 infection too was very low in our patients.

These cases highlight unusual cardiovascular manifestations of COVID-19 infection. The clinical details are expected to provide necessary guidance for the management of similar cases in subsequent waves of the ongoing COVID-19 pandemic.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Kachru S, Kaul D. COVID-19 manifestations in children. Curr Med Res Pract 2020;10:186-8.
2. Ramos-Casals M, Brito-Zerón P, Mariette X. Systemic and organ-specific immune-related manifestations of COVID-19. Nat Rev Rheumatol 2021;17:315-32.
3. Kurt-Sukur ED, Brennan E, Davis M, Forman C, Hamilton G, Kessaris N, *et al.* Presentation, treatment, and outcome of renovascular hypertension below 2 years of age. Eur J Pediatr 2022;181:3367-75.
4. de Souza AW, de Carvalho JF. Diagnostic and classification criteria of takayasu arteritis. J Autoimmun 2014;48-49:79-83.
5. Gupta H, Kaur N, Saxena A, Jagia P, Kumar S, Gupta SK, *et al.* Non-specific aortoarteritis (NSAA) in children: A prospective observational study. BMJ Paediatr Open 2021;5:e001106.
6. Quintana-Castanedo L, Feito-Rodríguez M, Fernández-Alcalde C, Granados-Fernández M, Montero-Vega D, Mayor-Ibarguren A, *et al.* Concurrent chilblains and retinal vasculitis in a child with COVID-19. J Eur Acad Dermatol Venereol 2020;34:e764-6.
7. Papa A, Salzano AM, Di Dato MT, Varrassi G. Images in practice: Painful cutaneous vasculitis in a SARS-Cov-2 IgG-positive child. Pain Ther 2020;9:805-7.
8. Regev T, Antebi M, Eytan D, Shachor-Meyouhas Y, Ilivitzki A, Aviel YB, *et al.* Pediatric inflammatory multisystem syndrome with central nervous system involvement and hypocomplementemia following SARS-COV-2 infection. Pediatr Infect Dis J 2020;39:e206-7.
9. Woehl B, Lawson B, Jambert L, Tousch J, Ghassani A, Hamade A. 4 cases of aortic thrombosis in patients with COVID-19. JACC Case Rep 2020;2:1397-401.
10. Becker RC. COVID-19-associated vasculitis and vasculopathy. J Thromb Thrombolysis 2020;50:499-511.
11. Emmi G, Silvestri E, Squatrito D, Amedei A, Niccolai E, D'Elios MM, *et al.* Thrombosis in vasculitis: From pathogenesis to treatment. Thromb J 2015;13:15.

12. Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, *et al.* Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. JAMA 2020;324:259-69.
13. Salman R, Masand P, Huisman TA, Pereira M, Kearney DL, Guillerman RP, *et al.* A novel large-vessel arteritis in SARS-CoV-2-related multisystem inflammatory syndrome in children (MIS-C). Radiol Cardiothorac Imaging 2021;3:e200535.
14. Murhekar MV, Bhatnagar T, Selvaraju S, Saravanakumar V, Thangaraj JW, Shah N, *et al.* SARS-CoV-2 antibody seroprevalence in India, August-September, 2020: Findings from the second nationwide household serosurvey. Lancet Glob Health 2021;9:e257-66.
15. Tönshoff B, Müller B, Elling R, Renk H, Meissner P, Hengel H, *et al.* Prevalence of SARS-CoV-2 infection in children and their parents in Southwest Germany. JAMA Pediatr 2021;175:586-93.