ESGAR 2019

The Abdominal Manifestations of Kawasaki Disease in Children: A Pictorial Essay

Eu Leong Harvey James TEO

Department of Diagnostic Imaging and Intervention
KK Women's and Children's Hospital, Singapore

Background

Kawasaki Disease (KD) is a systemic vasculitis in children occurring usually between the ages of 6 months and 5 years. The cause is unknown and common symptoms include fever for >5 days, enlarged lymph nodes, rash, sore throat and diarrhea. KD has a tendency to involve the coronary vessels, and in severe cases, coronary artery aneurysms may develop. The abdominal manifestations of KD are less common and not as well recognized but are important because failure to recognize these findings may cause confusion in diagnosing these patients. Abdominal vessels such as, but not limited to, the aorta, coeliac trunk, superior mesenteric artery and renal arteries may be involved. Areas of vessel wall thickening due to inflammation, stenosis and aneurysms develop in these vessels. Involvement of these vessels gives rise to complications in the abdominal organs resulting in gallbladder hydrops, enteritis, bowel obstruction, portal venous gas, hepatic dysfunction, hepatomegaly, renal scarring and impairment and Kawasaki shock syndrome with ascites.

This poster will familiarize the reader with the diagnostic criteria for KD and illustrate the abdominal manifestations of KD on multi-modality imaging such as plain radiographs, sonography, nuclear medicine, CT, MRI and MRA.

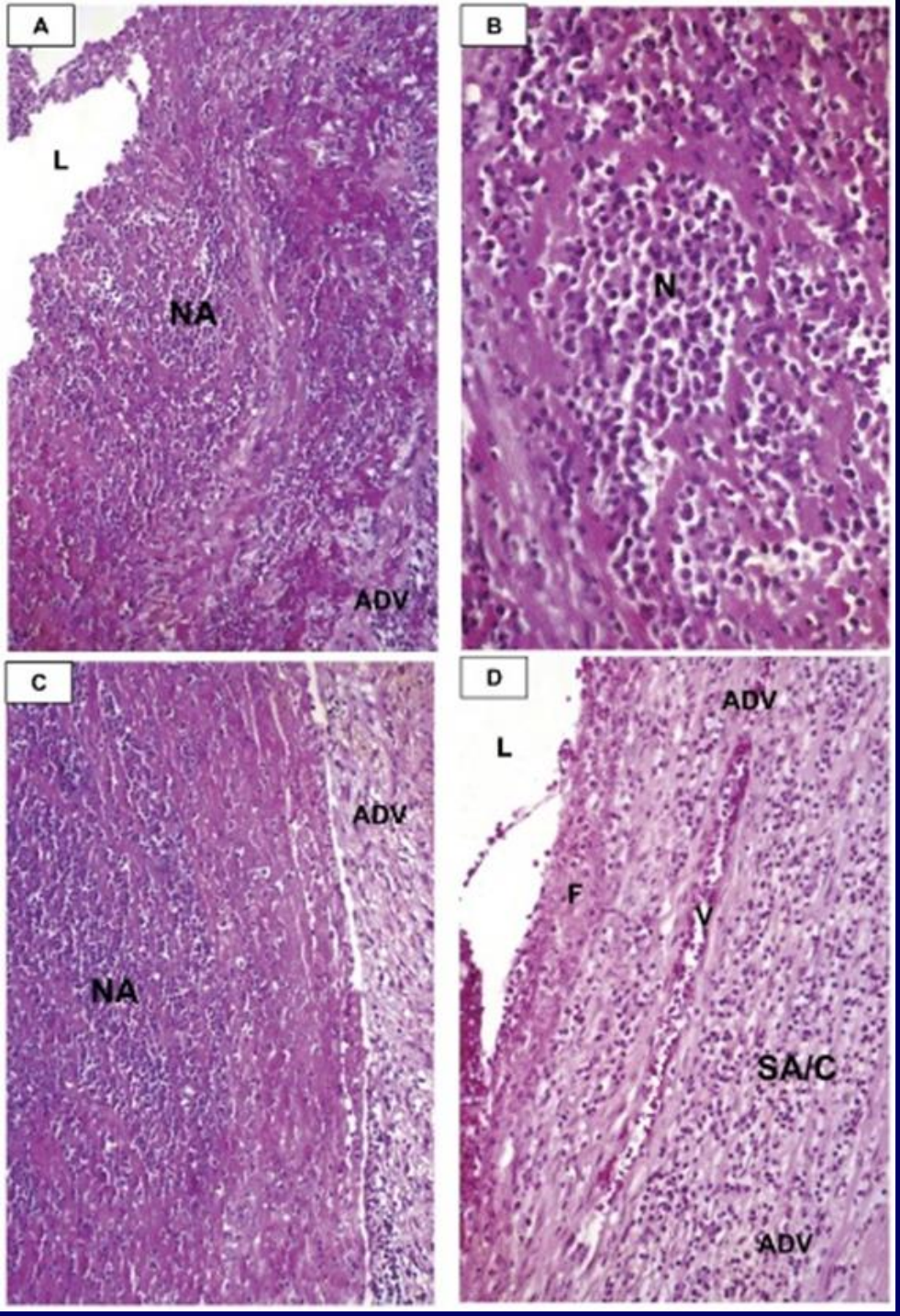
Pathology

- Unknown cause, but likely infectious aetiology
- Systemic vasculitis involving medium and small-sized vessels eg Coronary arteries
- Acute, subacute and chronic arteritis leads to concentric wall thickening, fibrosis and damage. Affected vessels may develop stenosis, thrombi and aneurysms.

Epidemiology

- Ranges from 10-308/100,000 per year worldwide
- Children of Asian ethnicity have a higher incidence
- Highest in Japan and South Korea
- Males > Females, Most are < 5 years old

Takahashi et al. Clin Exp Immuno. 2011 May;164 Suppl 1:20-2 Rowley et al. Front Pediatr 2018;6:374



A. Portion of a CA undergoing NA. The friable fragmenting wall is a mixture of neutrophils and debris. The adventitia is virtually obscured by inflammation and RBCs. H&E, case 2, original magnification 16×.

B. Higher magnification of an area of CA NA predominantly of neutrophils. H&E, case 2, original magnification 63×.

C. The necrotizing process has reached into the adventitia, which is only mildly inflamed. H&E, case 2, original magnification 16×.

D. An area of CAA consistent with having undergone severe SA/C pan-arteritis, leaving only adventitia rich in SA/C inflammatory cells, almost exclusively small lymphocytes. Note the longitudinally sectioned vessel and fibrin/RBC lining the luminal surface. H&E, case 11, original magnification 40×. L=lumen, ADV=adventitia, V=vessel, F=fibrin, NA=necrotizing arteritis, N=neutrophils.

Orenstein et al. PloS One. 2012;7(6):e38998

Clinical Features and Diagnostic Criteria

- Four of the Five criteria below and Fever > 5 days

- Conjunctiva
  - Bilateral, painless, non-exudative
- Lymphadenopathy
  - Cervical > 1.5cm, usually unilateral
- Skin Rash
  - Commonly Maculopapular
- Extremity changes
  - Acute: erythema, induration hands/feet.
  - Subacute: periungal desquamation may follow
- Mucosal changes

  Red cracked lips, Glossitis, Erythema oral mucosa

Ramphul et al, Arch med Sci Atheroscler Di 2018; 3:e41-e45

Diagnosis of Atypical KD

- Laboratory tests
  - Markers for inflammation, anaemia, leukocytosis, thrombocytosis, hypoalbuminaemia, elevated liver enzymes and sterile pyuria
- Echocardiography
  - Early coronary artery abnormalities or involvement

Differential Diagnosis

- Drug hypersensitivity, Stevens Johnson syndrome, staphylococcal scaled skin syndrome, JIA, toxic shock syndrome, viral infection, streptococcal scarlet fever

Ramphul et al, Arch med Sci Atheroscler Di 2018; 3:e41-e45

Abdominal symptoms

- Well-recognized but uncommon manifestation occurring in only 2.3% of cases[1]
- Diarrhea, vomiting are commonest symptoms[2]
- Reported abdominal manifestations include:
  - Gallbladder hydrops (21% of all KD patients), splenic infarcts, pancreatitis, ascites
  - Pseudo-obstruction, duodenal infarction, jejunal stricture, ischaemic colitis, bowel oedema, intussusception, paralytic ileus, liver necrosis,

1. Lone et al, J Indian Assoc Pediatr Surg 2017 22(3): 170-172. 2. Colomba et al J Pediatr 2018;202:186-93

Gallbladder Hydrops

Fig 1: 18 month old boy presented with abdominal pain, found to have GB hydrops on US and subsequently diagnosed with KD.

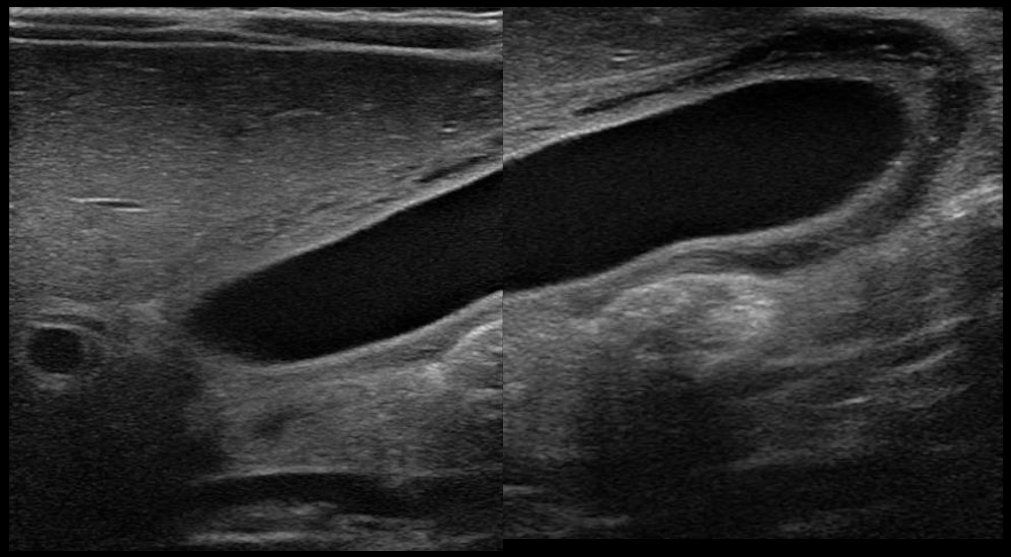
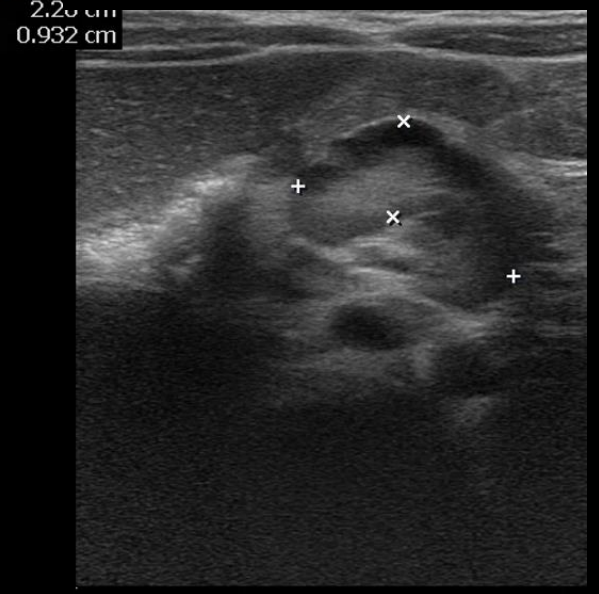


Fig 2: lymph nodes noted in the porta hepatis



GB hydrops is marked dilatation (>6cm length) of the GB (Fig 1) due to chronic obstruction of the cystic duct (Fig 2 usually lymph nodes causing the obstruction) or vasculitis and inflammation. Wall thickening is also noted in the GB wall. The prognosis is good and the condition is self-limiting in the majority of cases.

Sun et al. GB Hydrops associated with KD. Clinical Pediatrics 2018; 57(3) 341

Liver dysfunction and Hepatomegaly

Fig 1: 2yr 6 month old boy presented with hepatomegaly and features of KD. Liver function tests showed raised liver enzymes

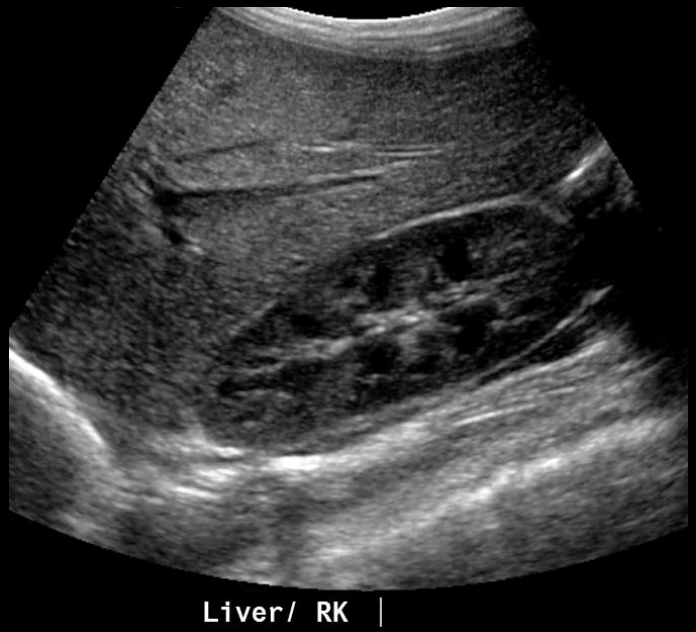


Fig 2: GB hydrops with wall thickening

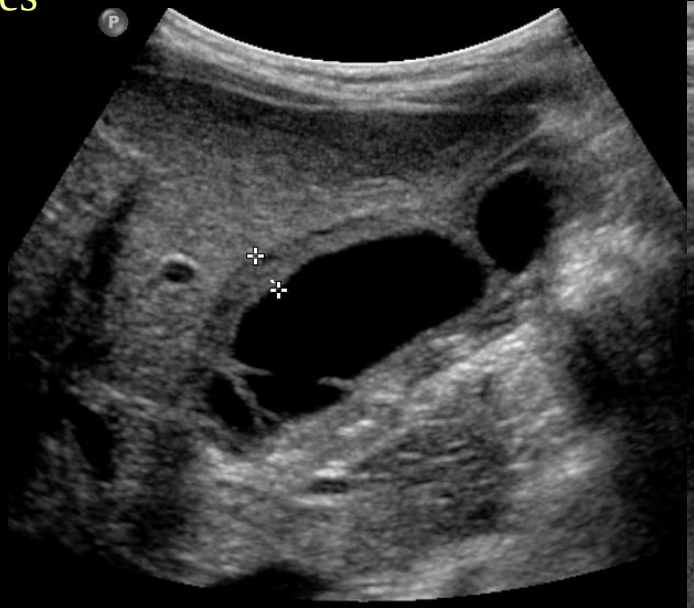
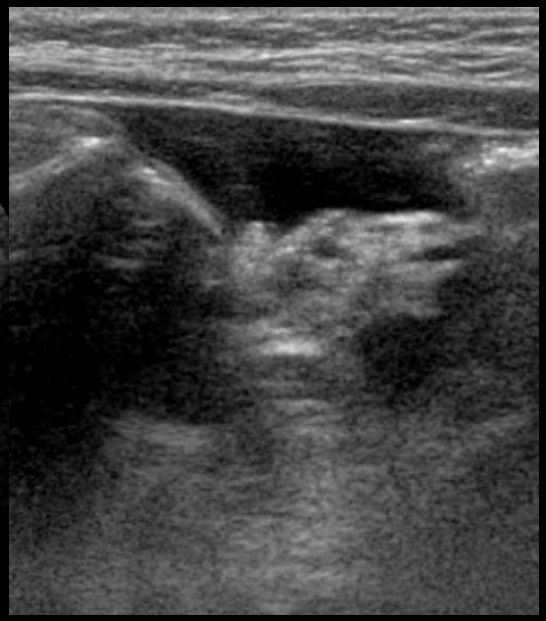


Fig 3: Ascites in the lower abdomen was detected



KD patients frequently have raised liver enzymes and bilirubin. This is associated with IV IG unresponsiveness in KD patients. Hepatomegaly is a frequent non-specific finding in KD (Fig 1). This patient also had GB hydrops with wall thickening (Fig 2) and ascites likely due to third spacing (Fig 3).

Liu et al. The prognostic role of abnormal liver function in IVIG uresponsiveness in KD. Inflamm Res 2016; 65(2) 161

Splenomegaly

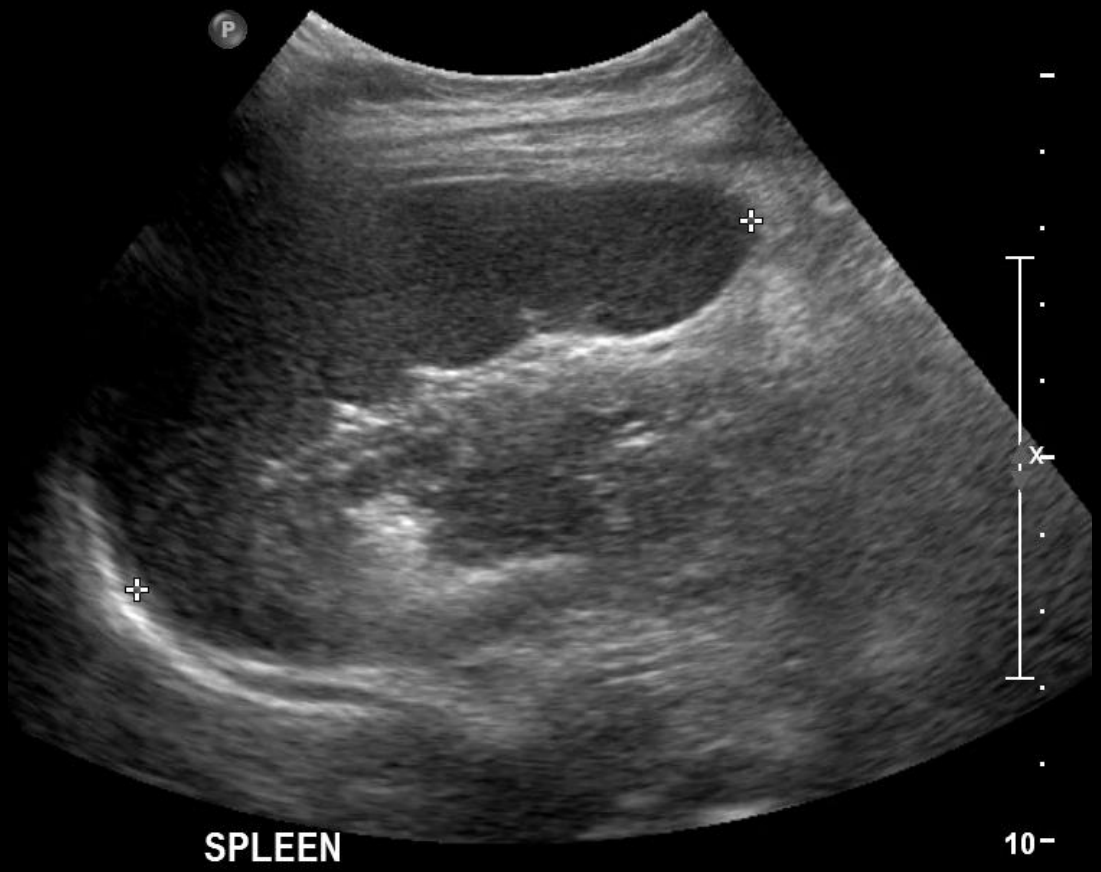


Fig 1: 3yr old boy presented with abdominal pain and suspected KD. US abdomen showed GB hydops (not shown) and splenomegaly. Of 9.6cm which is > 2SD above the norm for a child of this age.

Splenomegaly is hypothesized to be due to haemophagocytic lymphohistiocytosis and macrophage activation. Splenomegaly is a positive predictive factor for coronary artery lesions. Patients with Splenomegaly belonged to more complete KD, had a longer fever duration, more frequent cervical lymphadenopathy and polymorphous rash, higher neutrophil percentage, ALA levels and higher incidence of coronary artery lesions than patients without splenomegaly.

Kang et al Clinical aspects of splenomegaly as a possible predictive factor of coronary artery changed in KD. Cardio Young. 2018;21:1-6

Pseudo-obstruction (PO)

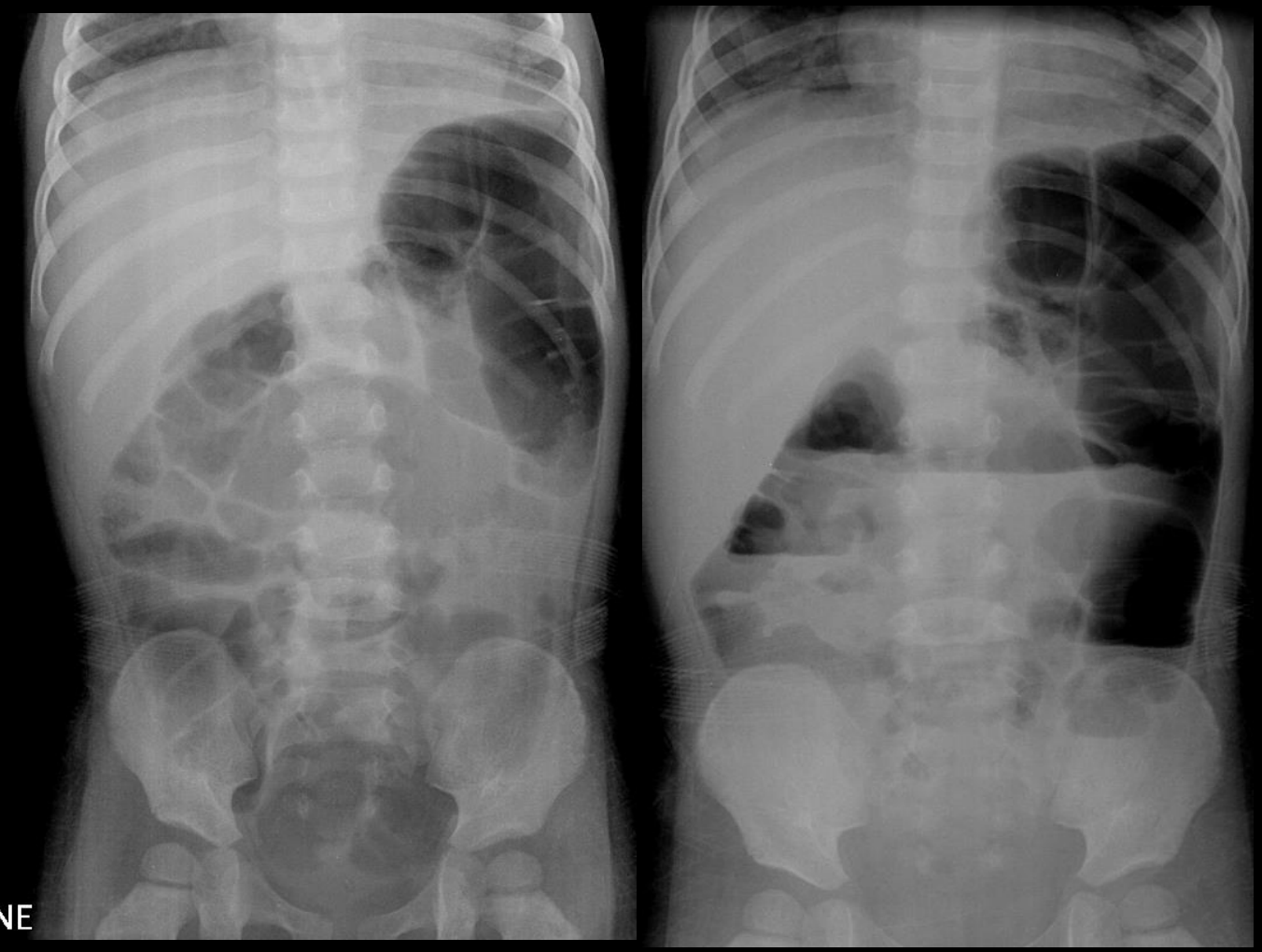
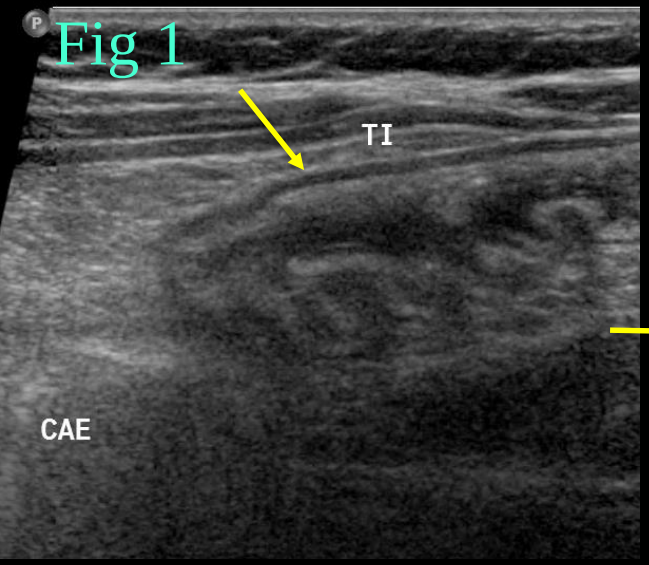


Fig 1: 2yr 3mth boy presented with abdominal pain , vomiting and distension. Supine and erect AXR shows generalized bowel dilatation. The patient was subsequently diagnosed with KD.

PO is felt to be related to mesenteric artery vasculitis with ischaemia and dysfunction of the myenteric plexus. However, no abnormalities are found on vessel imaging suggesting small bowel disease. Treatment is bowel rest and of the underlying KD.

Colomba et al J Pediatr 2018;202:186-93

Terminal ileitis (TI) and Colitis



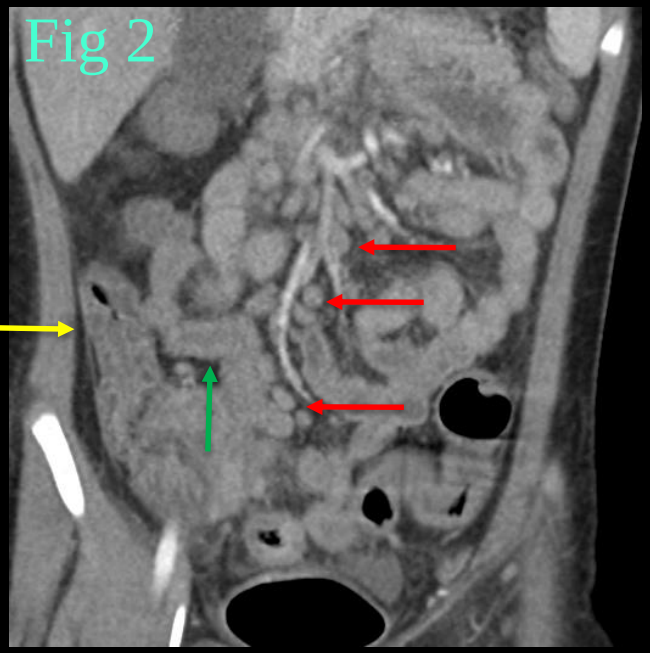
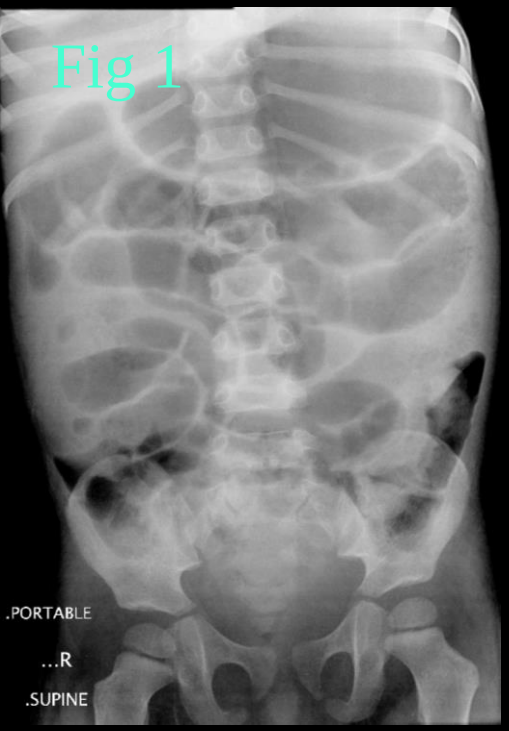


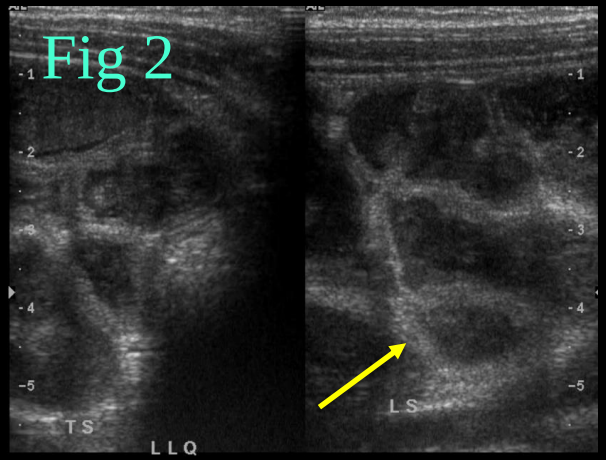
Fig 1: 7-yr old boy presented with abdominal pain. US shows thickening of the wall of the TI (arrow). Fig 2: Coronal CT image shows thickening of the wall of the TI (green arrow), ascending colon (yellow arrow) and multiple abdominal lymph nodes (red arrows). The patient was subsequently diagnosed with KD.

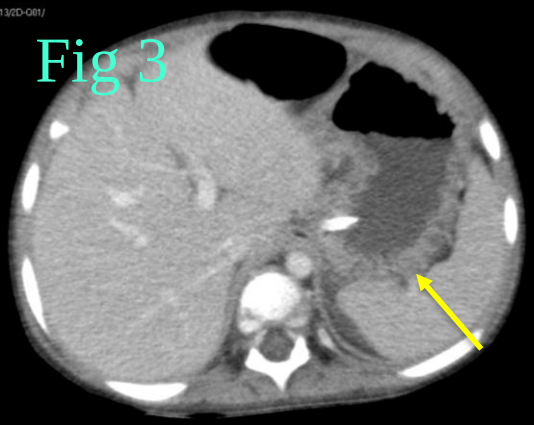
The GIT has been proposed has been proposed as a major site of entry of infectious agents causing KD into the body. GIT involvement may be due to vasculitis and thrombosis of small submucosal arteries involving the intestine resulting in relative ischaemia leading to bowel wall thickening. Effects of bowel ischemia is usually initial hypermotility followed by paralysis. More severe cases may result in nodular areas or obstruction that may need surgical treatment.

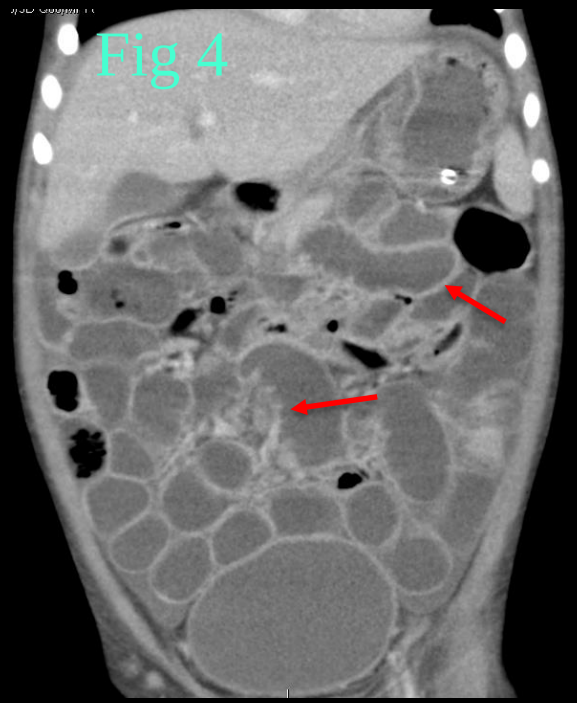
Colomba et al J Pediatr 2018;202:186-93

Generalized Intestinal inflammation









Figs 1&2: 2-yr old boy presented with generalized abdominal pain and suspected KD. AXR and US shows generalized bowel dilatation. US also shows generalized bowel wall thickening (arrow). Figs 3&4: Axial and Coronal CT image shows thickening of the stomach wall (yellow arrow) and small bowel (red arrows) resulting in generalized distended fluid-filled bowel loops. The patient was subsequently diagnosed with KD.

Most cases resolve rapidly with the onset of IVIG treatment supporting the theory that intestinal vasculitis is responsible for the abdominal symptoms in KD.

Colomba et al J Pediatr 2018;202:186-93

Portal Venous Gas

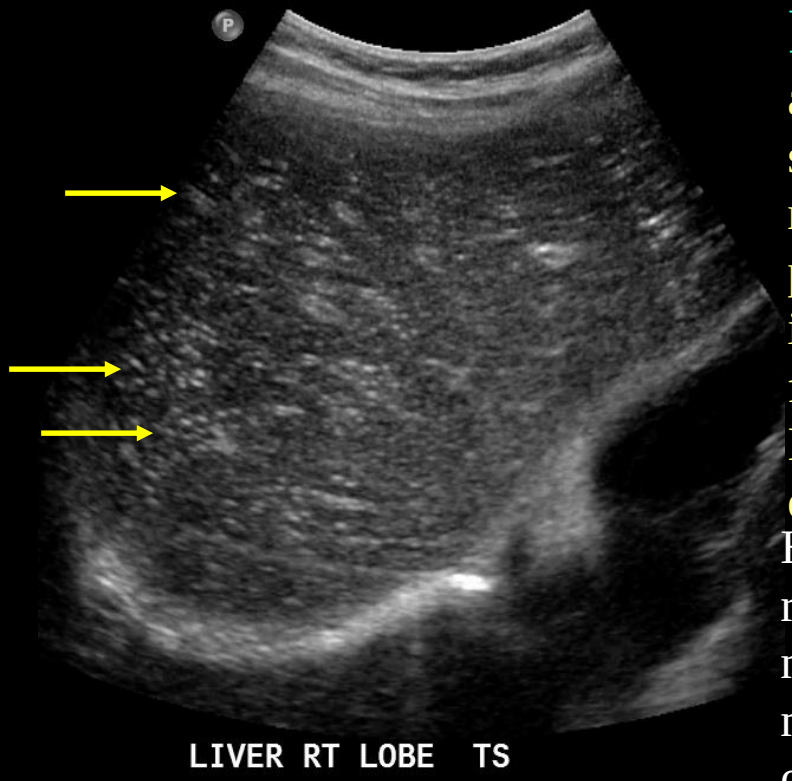


Fig 1: 5 yr old boy with KD complained of abdominal pain. GB hydrops was detected (not shown). Images of the liver show the presence of multiple punctate echogenic foci situated within the portal venous system (arrows). On real time imaging these were mobile and showed continuous flow from the hepatic portal venous system into the IVC – the "Aquarium" sign. No intramural gas was detected.

Hepatic portal venous gas is a non-specific radiological finding that may occur when there is mucosal disruption, necrosis of the bowel wall, mechanical distension or sepsis due to a gas forming organism. It has been reported in necrotizing enterocolitis, trauma, endoscopy, intussusception and colitis. The presence of portal venous gas with KD has been reported only once previously in the literature. The reported case was complicated by an ileocolic intussusception. Our case showed no other complication other than portal venous gas which resolved on follow US a few days later. Possible pathogenesis is thought to be due to vasculitis resulting in bowel ischaemia with mucosal necrosis and disruption allowing air to enter the vasculature. The patient recovered on conservative treatment.

Singh et al. Hepatic portal venous gas and the "the aquarium sign" due to intussusception in KD. Echocardiography. 2012; May 29

Abdominal Vasculitis I

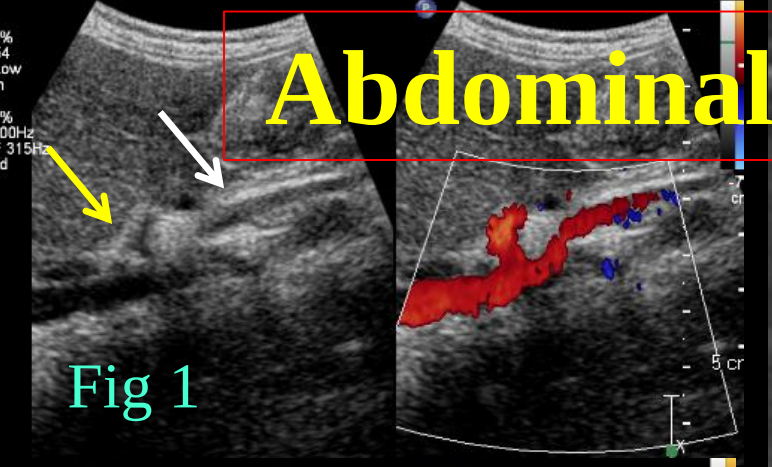


Fig 1

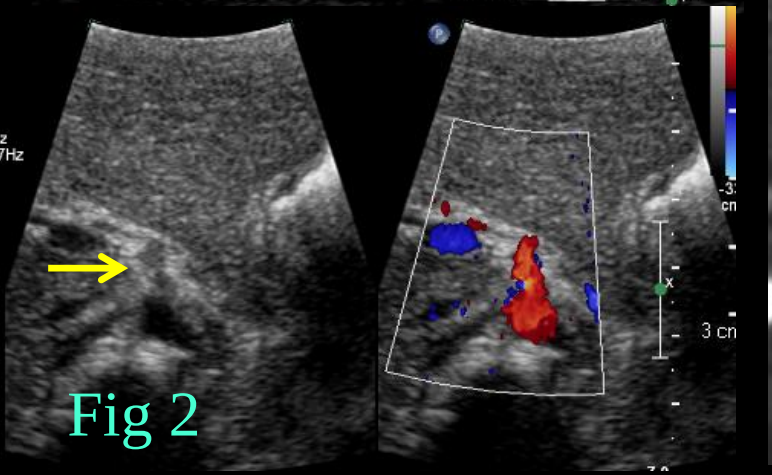


Fig 2

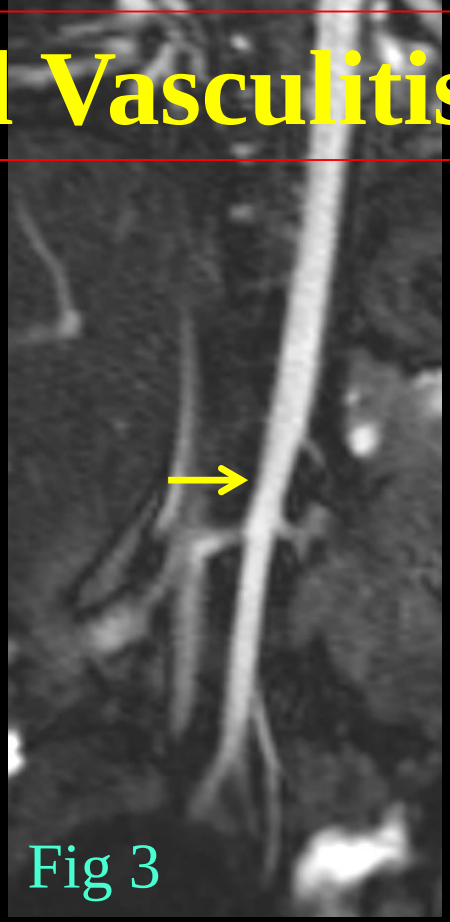


Fig 3

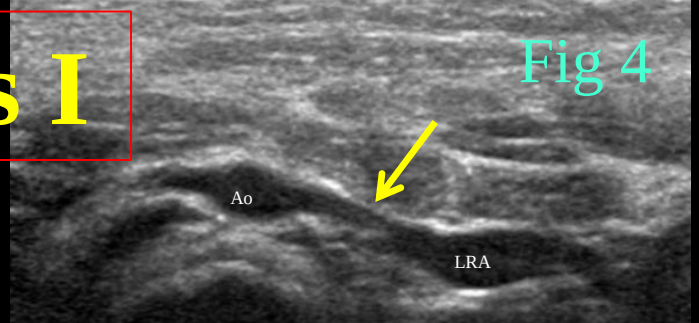


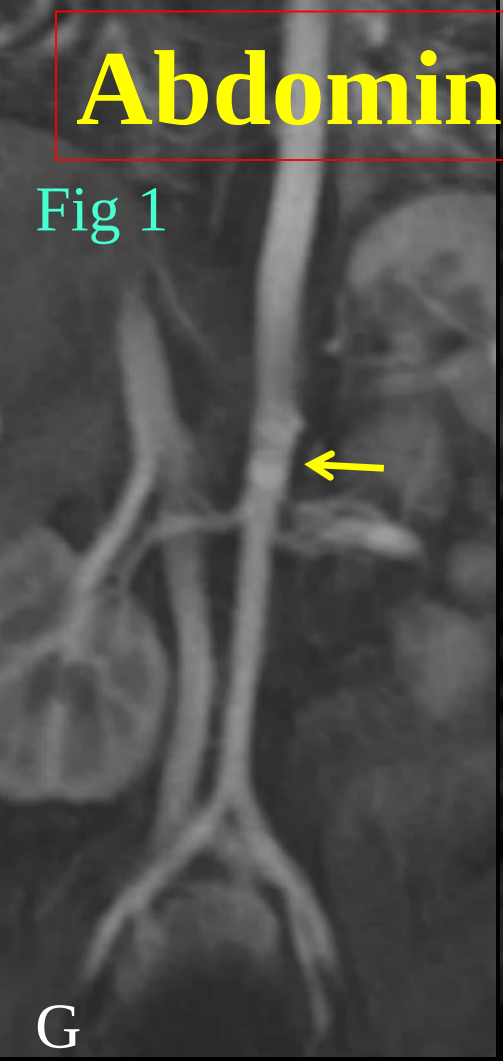
Fig 4

Figs 1&2: 8-month old child with KD. Sagittal US images of the celiac trunk (yellow arrow) and SMA (white arrow) show irregularity of the calibre of the arteries with increased echogenicity of the surrounding soft tissue indicative of inflammation.

Fig 3: 3D gadolinium enhanced reconstructed image shows a decrease in the caliber of the aorta just above the level of the renal arteries (arrow). The renal arteries appear normal. Fig 4: However, US immediately after the MRI shows narrowing at the origin of the left renal artery (arrow) with post-stenotic dilatation. Evaluation of small vessels is difficult on MRI

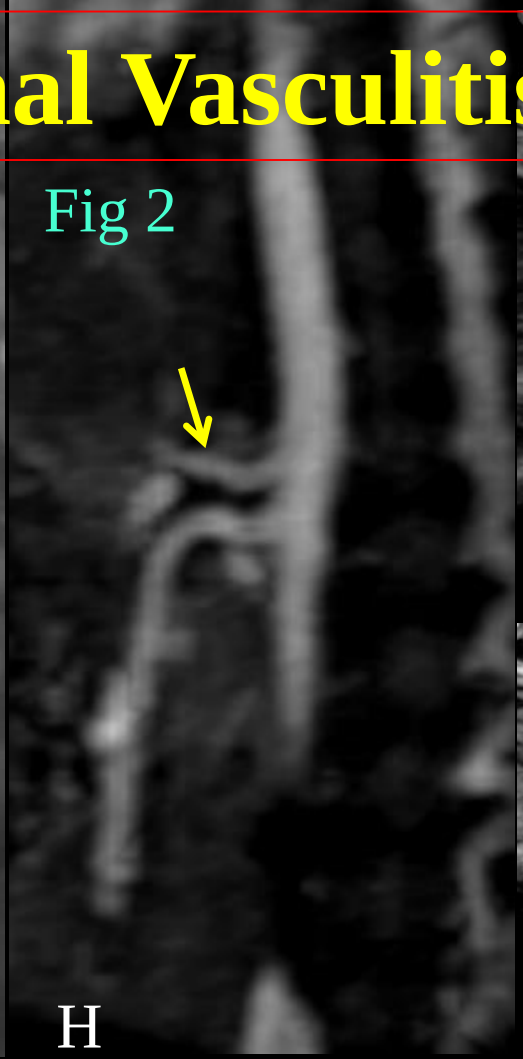
Abdominal Vasculitis II

Fig 1



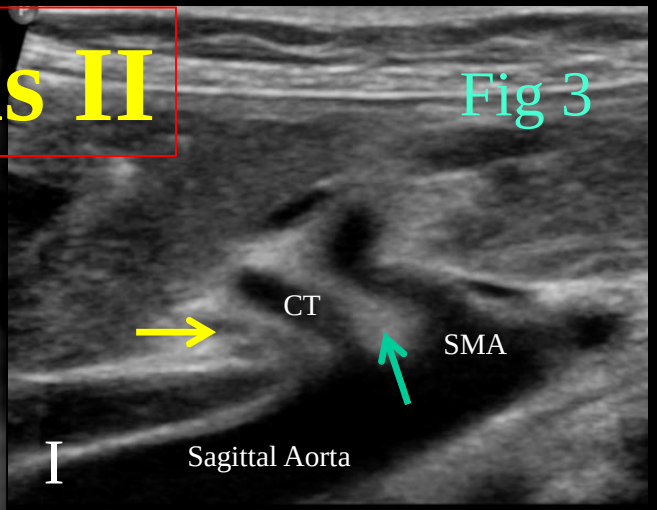
G

Fig 2



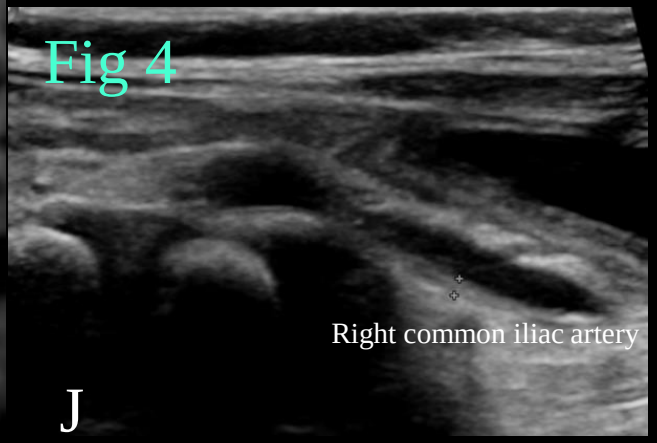
H

Fig 3



I

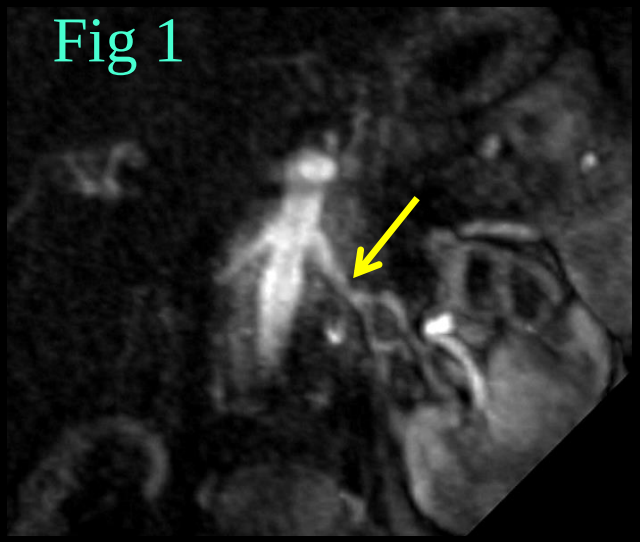
Fig 4



J

Figs 1-4: 3mth old boy with refractory KD (1) 3D gadolinium enhanced reconstructed image shows narrowing of the aorta beginning just above the level of the renal arteries (arrow). (2) Sagittal MIP image shows irregularity of the celiac trunk (CT) (arrow). (3) Sagittal US image shows hyperechogenicity of the soft tissue surrounding the celiac trunk (yellow arrow) and SMA (green arrow) indicating the presence of inflammation. (4) US also shows mural thickening and narrowing involving the right common iliac artery

Abdominal vasculitis III: Renal scarring



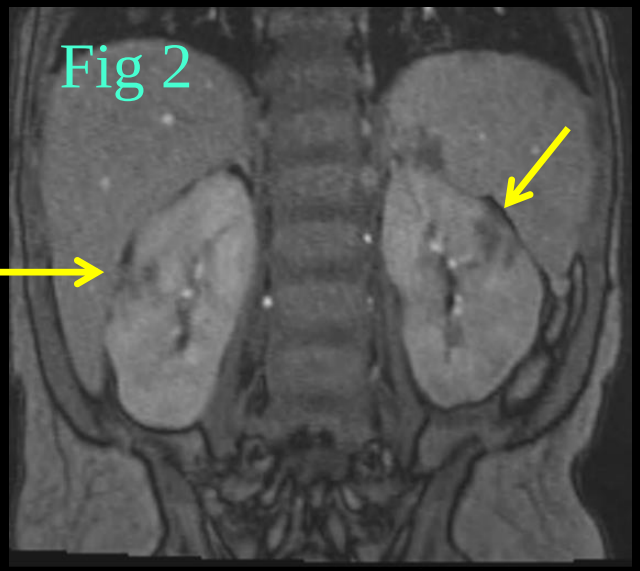


Fig 1: 5mth boy with KD and hypertension. MRA of the renal vessels show possible focal narrowing of the left renal artery (arrow).

Fig 2: Gd enhanced Coronal MRI of the kidneys show focal scarring in both kidneys (arrows)

Renal involvement in KD include pyuria, acute kidney injury, tubule-interstitial nephritis, haemolytic uraemic syndrome, immune-complex nephropathy, shock syndrome, acute nephritic syndrome, nephrotic syndrome, renal tubular abnormalities which may result in renal scarring and failure. The precise pathogenesis of underlying the development of renal problems is unclear. Vasculitis of the arteries in the kidney, immune-complex mediated kidney injuries, and T-cell immune-regulatory abnormalities have been proposed as possible mechanisms.

Watanabe et al. Kidney and urinary tract involvement in KD. Int J Pediar. 2013☹2013):831834

Acute Kidney Injury

Fig 1

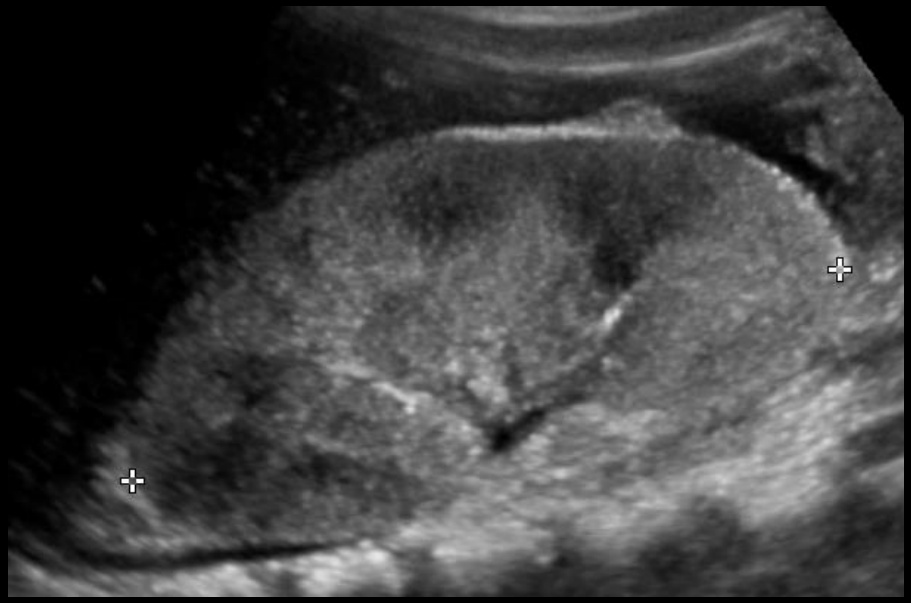
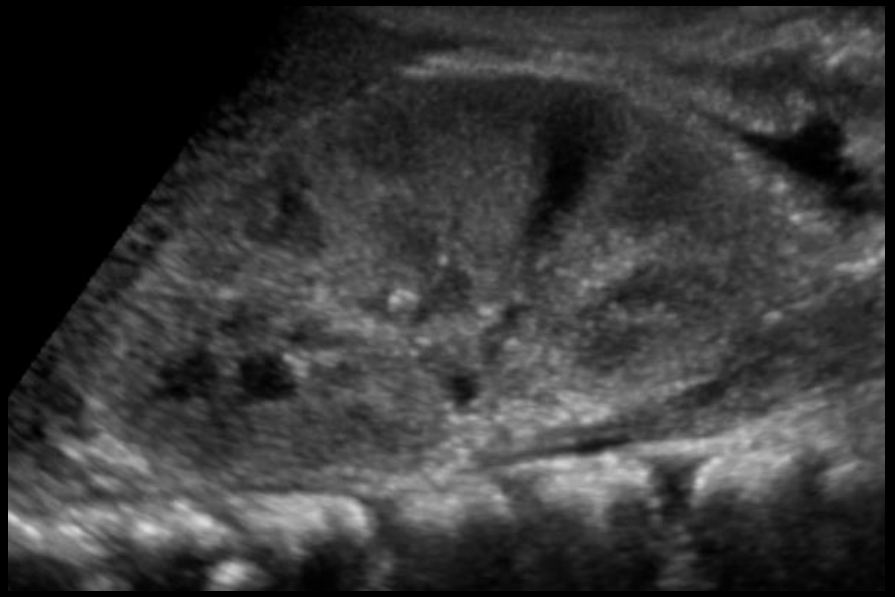


Fig 2



Figs 1&2: 3yr 6mth old boy with KD. He developed nephrotic syndrome, haematuria which eventually progressed to kidney failure. US shows generalized increased in echogenicity in both kidneys.

Imaging features are non-specific and include generalized increased echogenicity, enhanced cortico-medullary differentiation on sonography, enlarged kidneys and renal scarring also seen on other imaging modalities.

Treatment

- IVIG
  - Single dose within 10 days of symptoms
  - reduces incidence of coronary artery aneurysms
- Aspirin
  - modifies the inflammatory state
  - prevents thrombotic risk
- Corticosteriods
  - may be a useful adjunct to IVIG
- TNF-α
  - in patients who do not respond to IVIG

Ramphul K et al. KD: a comprehensive review. Arch med Sci Atheroscler Dis. 2018;3:e41

Conclusion

The diagnosis of KD should be considered in all children with prolonged fever and abdominal pain. A high index of suspicion is necessary particularly in countries where there is a high prevalence of this condition. Early diagnosis may further detect the presence of coronary aneurysms and improve prognosis.