Abstract
Cytomegalovirus (CMV) infection has been involved in vascular disease in immunodeficient adults. Here we report a 6-month-old boy with cytomegalovirus infection who developed medium vessel vasculitis along with coronary aneurysms.

Keywords: Medium vessel vasculitis, Cytomegalovirus.

Introduction
Vasculitis is a systemic disorder characterized by inflammation of all the blood vessels. It is more common in adults but does occur in childhood. It may present as a primary disorder or can be a part of spectrum of a systemic disease. (1) For diagnosis of a vasculitic disorder a detailed history, complete physical examination and focused laboratory investigation are vital. The aim of the work-up is identification of underlying etiology of the disease and determination of the disease activity as well as extent. (2) The medium-size-vessel category includes polyarteritis nodosa (PAN), Kawasaki disease (KD) and cutaneous polyarteritis nodosa. The etiology of medium vessel vasculitis can be immune, infective or remains unknown. The possible involvement of cytomegalovirus (CMV) in the pathogenesis of vascular diseases has been suggested. CMV has been shown to be involved in vascular diseases in a murine model. (3) We report a 6-month-old boy with CMV infection who developed medium vessel vasculitis and coronary aneurysms.

Case Report
A 6-month-old boy with normal antenatal and postnatal period presented with the infrequent passage of black colored stools for 3 months and low grade, continuous fever for 1 month. There was no history of rash, erythema, cracking of lips, strawberry tongue, weight loss or any abnormal movements. Examination revealed pallor and hepatosplenomegaly; there was no dysmorphism, petechiae, icterus or lymphadenopathy. Fundus examination was normal. Investigation showed hemoglobin 8 gm/dl, white cell count (WBC) 20100 cells/cumm (polymorphs 70%, lymphocytes 25%, monocytes 3% and eosinophils 2%), platelet count 1,10,000 cells/cumm, erythrocyte sedimentation rate (ESR) 93 mm in the first hour and C-reactive protein (CRP) 85 mg/dl. Peripheral smear revealed anisopoikilocytosis, microcytic hypochromic anemia with no abnormal cells. Urine microscopy showed 22 WBC/high-power field; however, blood culture and urine culture were sterile. Liver function tests (LFT) showed elevated transaminases and hypoalbuminemia. CMV IgM and Urine CMV PCR were positive. TORCH profile of mother was negative. X-ray skull and chest, ECG were normal. Ultrasound (USG) abdomen shows hepatosplenomegaly with normal echotexture. He was started on intravenous ganciclovir (5 mg/kg twice daily).

On the 15th day of admission, he developed high-grade fever with oropharyngeal and conjunctival congestion without mucopurulent discharge. Three days later he developed edema and erythema of hands. On 23rd day of admission, he developed bluish discoloration of the right forearm just below elbow joint extending to right middle and index finger with absent pulsation of right radial artery. Color Doppler showed fusiform dilatation of bilateral subclavian artery and multiple collaterals of the right brachial artery. There was no color flow in the radial artery. He was started on low molecular weight heparin, however, it progressed to gangrene in next six days. USG abdomen with Doppler showed hepatosplenomegaly with a fusiform aneurysm involving bilateral common iliac artery (right > left). Echocardiography showed aneurysm of right coronary artery, left circumflex and left anterior descending artery; bicuspid aortic valve and moderate pericardial effusion. CT angiography (figure 1) showed mild to moderate pericardial effusion with an aneurysm involving left main coronary artery/ giant aneurysm of left anterior descending artery (12 mm), fusiform dilatation of the bilateral subclavian artery, celiac artery, superior mesenteric artery, renal artery and bilateral common iliac artery. All these features were suggestive of medium vessel vasculitis. ANA, dsDNA, and ANCA were normal. As our index case has three out of five classical criteria’s (fever persisting atleast 5 days, bilateral bulbar conjunctival injection without exudate and erythema of palms and edema of hands) and supplemental criteria (anemia, elevation of alanine aminotransferase, white blood cell count ≥15,000 cells/cumm, and urine WBC ≥10/high-power field) so the possibility of incomplete Kawasaki disease was kept. At that time ESR was 54 mm/hr platelet count was 436,000 cells/cumm. He was given intravenous immunoglobulin (IVIG) and aspirin. Fever subsided after 48 hours of starting therapy however his general condition worsened. He developed shock along with disseminated intravascular coagulation and died on day 29 of admission. An autopsy was done which showed inclusion bodies in the wall of the subclavian and coronary artery.

Figure 1: 3D reconstructed picture of CT angiography showing aneurysm of coronary arteries, iliac arteries and renal arteries.
Discussion

Systemic vasculitis can be caused by viruses of which hepatitis B related polyarteritis nodosa, is most common. Human immunodeficiency virus, human T-cell lymphotrophic virus, CMV and varicella-zoster virus have also been reported to be associated with vasculitides. (6) CMV can directly infect vascular endothelial cells and causes local vasculitis and ischemia or there may be host immune response to cells expressing viral antigen which can act as stimulus for vasculitis. (7)

KD is the second most common childhood vasculitis, accounting for 23% of all vasculitides. (5) The classic diagnosis of KD is based on the presence of fever persisting at least for 5 days and at least 4 of the 5 principal clinical features i.e. changes in extremities, polymorphous exanthema, bilateral bulbar conjunctival injection without exudate, changes in lips and oral cavity and cervical lymphadenopathy. (8) Patients who do not fulfill the classical criteria have been diagnosed as having “incomplete” Kawasaki disease, a diagnosis that is generally based on coronary artery abnormalities on echocardiography and supplemental lab criteria’s (8). Our patient fulfilled criteria’s for atypical Kawasaki disease and fever responded after starting aspirin and immunoglobulin. This child was diagnosed to have CMV infection on histopathology as well as in PCR in urine suggesting that he had medium vessel vasculitis and coronary artery dilatation probably atypical Kawasaki disease associated with CMV. PAN is also associated with CMV infection and was considered initially but our patient doesn’t fulfill American College of Rheumatology (ACR) criteria of PAN. (10) Also on biopsy there was no fibrinoid necrosis or granuloma.

Diagnosis of CMV vasculitis is based on clinical picture of vasculitis, positive serology (IgM) or CMV DNA PCR and CMV inclusion in biopsy specimen if possible. (9) Antiviral therapy is generally given in severe cases and whenever needed it should be started with ganciclovir or valganciclovir. (11) Response of therapy is generally good with few exceptional recurrences. (12)

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References:

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