CASE REPORT

Human parvovirus B19 associated dilated cardiomyopathy

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SUMMARY

We describe two children presenting with acute left ventricular dysfunction. Both cases had evidence of dilated cardiomyopathy, requiring inotropic support and were tested for cardiotropic viruses by conventional or real-time polymerase chain reaction using specific primers for enteroviruses, human parvovirus B19, Adenoviruses, Epstein-Barr virus (EBV), herpes simplex viruses 1 and 2 (HSV), human herpes virus-6 (HHV-6) and cytomegalovirus (CMV). IgG and IgM antibodies against parvovirus B19, EBV, HSV and CMV were also tested by ELISA. One case tested positive for parvovirus B19 infection and recovered completely within 6 months in absence of any specific therapy. The other case tested positive for parvovirus B19 infection in association with hypocalcaemia and was cured following standard heart failure therapy along with calcium and vitamin D supplementation. Sequence analysis of DNA products from both patients revealed genotype 3. To best of our knowledge this is first report of circulating genotype 3 from India.

BACKGROUND

Human parvovirus B19 has been associated with a wide spectrum of diseases ranging from erythema Infectiosum, a mild childhood illness characterised by slapped cheek appearance and reticular rash over face, trunks and limbs to complications during pregnancy, acute arthropathy, chronic anaemia in immuno-compromised patients and transient aplastic crisis. Genotypes 1 and 2 of human parvovirus B19 have so far been associated with dilated cardiomyopathy (DCM)^{1–2} but reports of genotype 3 are scarce from all over the world. This manuscript has been written to highlight the role of parvovirus B19 in causation of DCM in children and circulation of genotype 3 in India.

CASE 1**Case presentation**

A 2-year-old male patient was admitted to the paediatric department with high-grade fever with non-productive cough and myalgia for 10 days, respiratory distress, irritability, abdominal pain and refusal to feed since 4 days. On examination, the child was tachypnoeic (respiratory rate 58/min), tachycardic (heart rate 180 bpm), hypotensive (blood pressure 82/58 mm Hg) and had a high grade fever (temperature of 41°C).

Investigations

Two-dimensional echocardiography showed DCM, biventricular involvement with globally hypokinetic

left ventricle with moderate-to-severe systolic dysfunction, severely decreased left ventricular ejection fraction of 15–20% (normal 50–65%), right ventricular systolic dysfunction, moderate mitral valve regurgitation, moderate pulmonary artery hypertension, mild-to-moderate tricuspid regurgitation, moderate pulmonary regurgitation and bilateral dilatation. Left atrial appendage filled with thrombus was seen protruding into left atrial cavity as mobile ball thrombus. There was no evidence of pericardial effusion.

Laboratory investigations showed Haemoglobin level of 9.3 g/mL, leucocyte count of 21 000/mm³ (78% neutrophils), packed cell volume of 34.6, platelet count of 96 000/mm³, erythrocyte count 3.63 × 10⁶/mm³, mean corpuscular volume 74.7 fL, mean corpuscular haemoglobin 24.4 pg/cell, mean corpuscular haemoglobin concentration 32.7 Hb/cell. Serum sodium levels were 140 mEq/L, potassium levels were 4.2 mEq/L, calcium levels were 8.9 mEq/dL, serum protein 5.7 gm%, and albumin 2.9 gm% (table 1).

The patient tested positive for parvovirus DNA by conventional polymerase chain reaction (PCR), and for antiparvovirus IgM antibodies by ELISA though antiparvovirus IgG antibodies were negative. Sequence analysis of VP1/VP2 overlapping region (from nt 3271 to nt 3558) of parvovirus B19 demonstrated genotype 3 (figure 1). Blood culture was negative for bacterial or fungal growth. The patient also tested negative for other cardiotropic viruses (enterovirus, HSV-1, HSV-2, Adenovirus, EBV, CMV and HHV-6) by ELISA and/or PCR.

Treatment

The patient was started on standard heart failure medicines including diuretics, anticoagulants and inotropic support.

Outcome and follow-up

The child remained stable and improved gradually over a period of 2 weeks when finally he was discharged from the hospital; though he was advised follow-up to monitor recurrence or development of chronic heart failure. The child was followed till 6 months and recovered completely.

CASE 2**Case presentation**

A 4-month-old male child born full term after spontaneous vaginal delivery with a birth weight of 2.8 kg and no medical problem at the time of discharge from the hospital, was admitted to the Department of Paediatrics with the symptoms of sluggishness and sweating during feeding for the past 4 days, mild-to-moderate fever for

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Table 1 Laboratory findings of case 1

Serial number	Biochemical parameters	Result	Normal range
1	Haemoglobin	9.3 g/dL	(14–20) g/dL
2	Total leucocyte count	21 000/mm ³	(4.3–10.8)×10 ³ /mm ³
3	Neutrophils	78%	(40–60)%
4	Platelet count	96 000/mm ³	(15 000–350 000)/mL
5	Packed-cell volume	34.6%	(31–44)%
6	MCV	74.7 fL	(90–100) fL
7	Erythrocyte count	3.63×10 ⁶ /mm ³	(4.2–5.4)×10 ⁶ /mm ³
8	MCH	24.4 pg/cell	(25.4–34.6) pg/cell
9	MCHC	32.7 Hb/cell	(32–36) Hb/cell
10	Serum sodium	140 mEq/L	(133–146) mEq/L
11	Serum potassium	4.2 mEq/L	(3.5–5.4) mEq/L
12	Serum calcium	8.9 mEq/L	(8.5–10.3) mEq/L
13	Serum protein	5.7 g%	(6.0–8.5) g%
14	Albumin	2.9 g%	(3.2–5.0) g%

MCH, Mean corpuscular haemoglobin; MCHC, Mean corpuscular haemoglobin concentration; MCV, Mean corpuscular volume.

3 days along with groaning and marked respiratory distress for 3 days. The patient developed erythematous rash on face, abdomen and chest on the day of admission to the hospital. Physical examination revealed tachycardia (heart rate of 150 bpm); tachypnoea (respiratory rate of 56 breaths/min), mild fever (temperature of 39°C) and hypotension (blood pressure 86/60 mm Hg). Cardiopulmonary examination revealed that the heart sounds were muffled.

Investigations

Chest X-ray showed cardiomegaly. An urgent echocardiography of the patient was carried out that showed left ventricular hypokinesia, severely decreased left ventricular ejection fraction of 34% (normal 50–65%), moderately abnormal fractional shortening of 21% (normal: 27–45%), moderate-to-severe mitral valve regurgitation and mild tricuspid regurgitation. These findings suggested DCM. No clot or vegetation on the valves was seen. There was no coarctation of aorta or patent ductus arteriosus.

Laboratory investigations showed; haemoglobin: 12.7 g/mL, TLC 8500/mm³, neutrophils 70%, platelet count of 1,16,000/mm³; normal serum creatinine (0.7 mg/dL), serum sodium (138 mEq/L), serum potassium (3.7 mEq/L) and serum magnesium (1.9 mg/dL) levels; raised serum urea levels 31 mg/dL; low serum calcium levels 5.5 mg/dL and raised serum parathormone 267.1 pg/ml (table 2). Blood culture was negative for aerobic bacteria and fungi and smear and antigen test for malaria was negative. PCR and serology for enterovirus, HSV-1, HSV-2,

Table 2 Laboratory findings of case 2

Serial number	Biochemical parameters	Result	Normal range
1	Haemoglobin	12.7 g/dL	(14–20) g/dL
2	Total leucocyte count	8500/mm ³	(4.3–10.8)×10 ³ /mm ³
3	Neutrophils	70%	(40–60)%
4	Platelet count	1 16 000/mm ³	(150 000–350 000)/mL
5	Serum sodium	138 mEq/L	(133–146) mEq/L
6	Serum creatine	0.7 mg/dL	(0.6–1.2) mg/dL
7	Serum potassium	3.7 mEq/L	(3.5–5.4) mEq/L
8	Serum magnesium	1.9 mEq/L	(1.9–2.7) mEq/L
9	Serum urea	31 mg/dL	(4–15) mg/dL
10	Serum parathormone	267.1 pg/mL	(10–55) pg/mL

adenovirus, EBV, CMV and HHV-6 were negative. The patient tested positive for parvovirus B19 DNA by conventional PCR, though antiparvovirus IgM and IgG antibodies were negative. Genotyping of parvovirus sequence showed genotype 3 (figure 1).

Treatment

The patient was immediately started on decongestive therapy with 0.7 ml furosemide intravenous twice daily (1 mg/kg/day, 1 mL=10 mg) for 3 days, 0.35 mL digoxin intravenous stat (25µg/kg/day, 1 mL=0.25 mg) followed by 0.18 ml stat after every 8 h (12.5µg/kg/day). At the same time the child was managed with continuous intravenous calcium infusion (dose 150 mg/kg/day) until normalisation of serum calcium, after which the patient was switched to oral calcium in a dose of 250 mg twice daily. Vitamin D (cholecalciferol) was given 3000 unit daily orally.

Outcome and follow-up

The child was discharged from the hospital after clinical improvement and normalisation of serum calcium levels on day 5. The child was followed till 4 months and recovered completely.

DISCUSSION

We presented two cases of DCM, with detectable human parvovirus B19 DNA in serum.

Case 1 had detectable parvovirus B19 DNA and anti-parvovirus IgM antibodies in blood without any other cause of DCM. Positive tests for parvovirus B19 and auto-recovery in 6 months in the absence of any specific treatment signal role of parvovirus B19 in causation of DCM. Available literature has few case reports on role of parvovirus B19 in myocarditis in immunocompetent adults³ and children.⁴ Response to specific immunoglobulin therapy in addition to conventional heart failure therapy was shown in previous studies,^{5 6} which supports the causative role of the virus in DCM. Parvovirus B19 is known to cause direct myocardial injury⁷ and can trigger an autoimmune response of the myocardium leading to DCM.⁸ Case 2 had hypocalcaemia along with parvovirus positivity, cardiac function recovered rapidly after receiving treatment with calcium and vitamin D. Tomar *et al*⁹ have also reported in their series of 15 cases the role of hypocalcaemia as a cause of cardiomyopathy in children. Although clinical investigations and response to treatment are suggestive of hypocalcaemia as the cause; contribution of parvovirus B19 infection cannot be ruled out in causing congestive heart failure.

Figure 1 Phylogenetic tree showing genetic relatedness of parvovirus B19 genotype 3 seen in Lucknow, India with strains from other countries (sequences obtained from GenBank, NCBI).

Patients who were parvovirus B19 positive with DCM have shown genotype specific effects on left ventricular function; genotype 2 is associated with more severely disturbed cardiac function as compared to genotype 1.^{1 2} Studies reporting genotype 3 in cardiomyopathies are not available. We have created a phylogenetic tree (figure 1) to study the genetic relatedness of genotype 3 of parvovirus B19 reported from other countries. The Indian strains from our study are not related to any one of them.

Learning points

- ▶ Parvovirus B19 should be considered in the differential diagnosis of dilated cardiomyopathy in children in the absence of other detectable causes.
- ▶ Specific immunoglobulin therapy are now available, consideration should be given to its use that could promptly restore an acute cardiac impairment.
- ▶ Genotype 3 of parvovirus B19 can present as dilated cardiomyopathy.

Contributors PJ was involved in writing the manuscript and literature search. AJ contributed by editing the manuscript and developed the concept of the article. DNK was involved in data collection and literature search. MK was involved in case treatment and data analysis.

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Competing interests None.

Patient consent Obtained.

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