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Real time PCR reconfirmed three novel clinical associations of parvovirus B19: Non-occlusive bowel gangrene, amegakaryocytic thrombocytopenia & myositis

Sir,

Human parvovirus B19 (B19), a single-stranded DNA virus belonging to the genus erythrovirus in the family *Parvoviridae* is an emerging virus[1,2] causing a wide range of clinical infections depending on the patient's immunological and haematological status[3,4]. However, the entire range of infections is not yet known. Earlier we reported three novel clinical associations of B19 namely, non-occlusive bowel gangrene, amegakaryocytic thrombocytopenia and myositis complicating erythema infectiosum[5-7] based on the detection of B19 specific IgM antibodies and B19 DNA by in-house PCR (VP1-VP2 common region primers) and in-house nested-PCR (VP1 unique region primers) besides other clinical and haematological features. To reconfirm that B19 infection caused these three clinical manifestations of B19 virus, the stored DNA (at- 20° C) or samples (at -70° C) which were positive for B19 virus were re-tested with more specific test namely, B19 real-time PCR kit (ZJ Bio-Tech Shanghai, China) wherein real-time PCR amplified (Corbett Rotor-Gene 6000, Australia) (from a different genomic region) sequences of B19 were hybridized with a B19 specific DNA probe making a double check on genomic sequences of B19.

Gangrene of stomach or intestine owing to non-occlusive bowel infarction (NOBI) has an unknown aetiology[8-11] with no further information after our report[5], and same is the status for amegakaryocytic thrombocytopenia due to B19 infection. However, there are couple of reports and a review article on myositis induced by B19 that supports our finding[12-14]. Results of previously reported cases of NOBI had shown B19 genome in serum samples of all eight cases (in three cases resected bowel tissues also) besides anti-B19 antibodies and thrombus in gastric vessels[5]. The second study was on a nine months old male child who had purpura, epistaxis and intra-cerebral haemorrhage and bone marrow showed absence of megakaryocytes. B19 specific IgM, IgG antibodies in serum and B19 DNA in both serum and bone-marrow were detected[6]. The third study was on a nine years old female child who presented with fever, anaemia and generalized erythematous rash later developed arthralgia, myalgia and calf tenderness (myositis) and was unable to walk despite any neurological deficit. Her creatine phosphokinase (CPK) was highly elevated (twice) while Parvovirus B19 specific IgM antibodies and DNA were detected in the serum[7].

On re-testing these positive samples by B19 real-time PCR, consistently positive results were observed and reported here. In cases of bowel gangrene (NOBI) the mean copy numbers of B19 virus were lower in biopsy tissues which ranged from 2.7 to 3.9 x 10^3 in comparison with 1.8 to 7.6 x 10^4 virion/ml in the serum. In the case of myositis due to B19 the virus copy number was little higher 8.3 x 10^4 in serum but the bone-marrow sample from amegakaryocytic thrombocytopenia case had much higher virus load of 3.3 x10^7virion/ml. This again showed that B19 genome was present in patients suffering from these three novel clinical associations of B19 besides anti-B19 IgM antibodies and other clinical and histological features described earlier[5-7]. It may be noted that in acute B19 infection intense viraemia occurs and virus titres may range from 10^{10} to 10^{12}/ml. The lower limit of B19 DNA detection by our in-house PCR was previously determined to be 2.4 x 10^3 virion/ml[15]. Further, bone marrow is the major site where virus replication occurs due to great tropism of B19 virus to erythroid progenitor cells causing destruction of colony forming and blast forming units of red cells resulting in anaemia and reticulocytopenia[16]. Bowel tissues had lower virus

copies/ml since tissue distribution of B19 remains to be determined. However B19 may remain at cryptic sites and infect vascular endothelial cells. The possible mechanisms of these three clinical associations of B19 remain unexplained till date. Further studies on larger number of cases need to be done to substantiate these novel clinical associations of B19 virus.

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