Aetiology of Kawasaki disease

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SUMMARY Thirteen serum samples from nine children with Kawasaki disease and 23 control samples gave negative results on screening for antibodies to hog cholera virus, border disease of sheep, bovine diarrhoea virus, and equine arteritis virus. The sera from two children with Kawasaki disease were cytotoxic; a possible link with cytotoxin from *Propionibacterium acnes* is considered.

Kawasaki disease is characterised by vasculitis and accompanying thrombocythaemia, and it usually affects young children. The tendency for cases to appear in clusters and for the occurrence of 'epidemic years' suggests an infectious aetiology.[1] Many of the clinical features of Kawasaki disease have been described in infectious vasculitic diseases of animals, including acute hog cholera (synonymous with swine fever) in pigs[2] and equine viral arteritis.[3] We therefore undertook a small study of children with Kawasaki disease to seek serological evidence of infection with the causal viruses of these conditions or with related viruses of ruminants.

Patients and methods

Recent cases of Kawasaki disease were identified using the British Paediatric Surveillance Unit (BPSU) reporting system.[4] Reporting paediatricians were asked to provide sera from both the acute and convalescent stage of the disease from their cases. Control sera were obtained from age matched patients with a variety of acute infectious diseases. Thirteen sera from nine patients with Kawasaki disease and 23 control sera were examined.

Collected sera were coded, then frozen at −40°C until being examined 'blind'. Thawed sera were heat treated at 56°C for 30 minutes. Microtitre serum virus neutralisation tests were then carried out in duplicate using the following virus and cell culture combinations: (a) hog cholera virus (Baker A strain) with a porcine kidney cell line (PK 15); (b) an antigenically distinct isolate of hog cholera virus (1987) with PK 15; (c) border disease virus of sheep with bovine turbinate cells; (d) bovine viral diarrhoea virus with bovine turbinate cells; and (e) equine arteritis virus with a rabbit kidney cell line (RK 13).

All five viruses are classified as non-arthropod borne togaviridae, the first four in the genus pestivirus and the last as arterivirus. Virus growth in systems (d) and (e) was detected by cytopathic effect and in (a), (b), and (c) by the neutralising peroxidase linked assay of Holm Jensen to determine the 50% neutralisation end points.[5]

Results

The mean age of the nine cases was 3·3 years (range 1 to 9 years) and of the 23 controls 3·3 years (range 11 months to 9 years). No neutralisation effect was shown with sera from either the children with Kawasaki disease or the controls.

Two of the sera were cytotoxic to a dilution of 1:10—one from a boy aged 1 and the other from a girl aged 6 years. Both these samples were from convalescent patients who had fulfilled the BPSU criteria for Kawasaki disease. This is of some interest as recent work from Japan has suggested that lymph nodes from patients with Kawasaki disease may be infected with a strain of *Propionibacterium acnes* that produces a cytopathogenic substance.[6] Some children with Kawasaki disease have persisting high titres of antibodies to this substance; could our two patients have persisting cytotoxin in their circulation? Unfortunately, no further serum is available from either patient.

Discussion

This small study suggests that there is no direct relationship between Kawasaki disease of children and viral vasculitis diseases of farm animals. The cytotoxicity found in serum samples from two patients convalescing from Kawasaki disease, but not in samples from controls, may be relevant and deserves further study.

Sera from patients with Kawasaki disease were kindly submitted for test by paediatricians at the following hospitals: Airedale General Hospital; Booth Hall Children's Hospital; Bristol Hospitals; Lincoln Hospitals; National Children's Hospital, Dublin; Royal Gwent Hospitals; Saint Mary's Hospital, Newport, Isle of Wight; Scarborough General Hospital; and Glan Clwyd Hospital, Rhyl. We are grateful to G Wibberley for the equine arteritis tests.

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Kawasaki disease in siblings

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SUMMARY We report a case of mucocutaneous lymph node syndrome, which was diagnosed in a 13 month old boy two years after the death of his sister from the same disease.

The aetiology of mucocutaneous lymph node syndrome, or Kawasaki disease, remains elusive, although it was first reported in 1967.[1] Environmental, genetic, and infective causes have all been postulated. We describe the non-contemporaneous occurrence of the disease in two children within the same family.

Case reports

CASE 1

In April 1983 a 6 month old girl was admitted for investigation of a prolonged fever. She had a two week history of ill health including coryzal symptoms, cervical lymphadenopathy, mild conjunctivitis, and a macular rash on her trunk. There had been no contact with infectious disease or travel abroad. Results of investigations are shown in the table.

On day 28 of her admission she developed mucousy diarrhoea and adenovirus type 5 was isolated from the stool. An adenovirus titre before this was negative but subsequently there was a significant rise to a titre of 64.

Her clinical condition deteriorated and nine days later she had a cardiac arrest. Resuscitation was successful and subsequent examination showed cardiac failure and gross cardiomegaly. A diagnosis of viral myocarditis was made. Despite symptomatic treatment there was further deterioration and the child died seven weeks after admission.

Postmortem examination found widespread coronary artery aneurysms with antemortem thrombi and extensive infarction. There was no evidence of pericarditis or myocarditis. The final diagnosis was therefore mucocutaneous lymph node syndrome.

CASE 2

A boy, born to the same parents two years after the death of his sister (case 1), was well until 13 months of age. He was seen with coryza, prolonged fever, cervical lymphadenopathy, conjunctivitis, and a macular rash over the trunk. Results of investigations are shown in the table. Echocardiography showed an area of echodensity at the origin of the

Table *Results of investigations*

Investigation	*Case 1*	*Case 2*
Haemoglobin (g/l)	100	113
White cell count ($\times 10^9$ g/l)	16·8	15·3
Neutrophil (%)	60	54
Lymphocytes (%)	29	44
Platelets ($\times 10^9$/l)	414	430
Erythrocyte sedimentation rate (mm in first hour)	116	66
Alanine aminotransferase (IU/l)*	264	30
Blood cultures	Negative	Negative
Complement fixation test:		
Respiratory syncytial virus	Negative	Negative
Adenovirus	Positive	Negative
Mycoplasma	Negative	Negative
Herpes simplex	Negative	Negative
Measles	Negative	—
Rubella	Negative	—
Neutralisation test:		
Coxsackie B	Negative	—
Paul-Bunnell	Negative	Negative
Throat swab	Negative	Negative

*Normal range 0–45 IU/l.