Aseptic meningitis caused by human parvovirus B19

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Abstract
Reports on aseptic meningitis caused by human parvovirus B19 are extremely rare. A case of aseptic meningitis is described in which human parvovirus B19 DNA was detected in the acute phase in cerebrospinal fluid by the polymerase chain reaction.

(Arch Dis Child 1993; 68: 784–785)

Erythema infectiosum is generally a benign, self-limiting disease. In 1983 Anderson et al found that it was caused by human parvovirus B19, and other pathological manifestations such as aplastic crisis, arthritis, and myocarditis have subsequently been proved to be associated with this virus. We report a case of aseptic meningitis after erythema infectiosum in which virological examination, including the polymerase chain reaction (PCR), for human parvovirus B19 was performed.

Case report
A 7 year old boy developed a bright lacy rash on the cheeks on 28 June 1992; he was afebrile at that time and had no other symptoms. The rash disappeared within a few days. On 4 July, he became febrile and developed a headache. On 7 July, he began to vomit and was admitted to Tokai Chuo Hospital on 8 July.

On admission he was alert. His temperature was 37.5°C and slight neck stiffness was present. There were no skin eruptions. His peripheral white cell count was 4.7×10⁹/l, with 20% band cells, 45% segmented cells, 26% lymphocytes, and 9% monocytes. C reactive protein was 12 mg/l. Cerebrospinal fluid analysis showed a moderate pleocytosis (leucocyte count 112×10⁶/l, neutrophils 61%, mononuclear cells 39%) with a protein concentration of 0.58 g/l, and glucose of 3.3 mmol/l. Routine culture of the cerebrospinal fluid and a throat swab yielded no growth of pathogens. In a few days the boy became afebrile as well as free of headache and vomiting. Analysis of his cerebrospinal fluid showed a leucocyte count of 9×10⁹/l with 1×10⁹/µl neutrophils and 8×10⁹/µl lymphocytes; the protein concentration was 0.19 g/l and glucose 3.6 mmol/l. He was discharged on 14 July, and no neurological sequelae have been noted during follow up to October 1992.

SEROLOGICAL STUDIES
Serum and cerebrospinal fluid collected from the patient on 8 and 13 July were tested for human parvovirus B19 (HPV-B19) by enzyme linked immunosorbent assay (ELISA) and the PCR. Blood contamination was not found at either spinal tap. The table summarises the ELISA and PCR findings. Serum IgM and IgG antibody against HPV-B19 were positive in both specimens.
HPV-B19 DNA was also positive in serum and cerebrospinal fluid. However, in the cerebrospinal fluid HPV-B19 DNA was positive on 8 July but became negative on 13 July (see figure).

Discussion
In 1983, HPV-B19 was identified as the cause of erythema infectiosum by Anderson et al. Therefore various pathological manifestations have been reported to be caused by HPV-B19. Dijkmans et al detected HPV-B19 DNA in the synovial fluid of a 33 year old woman with arthritis. Saint-Martin et al reported a 1 year old boy with myocarditis caused by HPV-B19. They found HPV-B19 structural proteins in the patient's myocardial tissue. In addition, aplastic crisis is a well known complication of HPV-B19 infection.

Central nervous system involvement, as in encephalitis and aseptic meningitis, is a rare complication of HPV-B19 infection, and there have been only a few reports of central nervous system involvement associated with erythema infectiosum. Three case reports of encephalitis and one report of meningitis were found in a review of the recent literature. None of them, however, demonstrated direct evidence of central nervous system involvement by HPV-B19. The detection of HPV-B19 DNA in the cerebrospinal fluid of our patient by the PCR suggests that central nervous system invasion by the virus had occurred. To the best of our knowledge, this is the first report of the detection of HPV-B19 DNA in cerebrospinal fluid of a patient with a serologically probed HPV-B19 meningitis. The prognosis of aseptic meningitis due to HPV-B19 appears to be good, judging from our experience and a previous case report.

The widespread use of the PCR should help to determine the spectrum of HPV-B19 infection. Similar cases to ours will probably be detected and as yet unknown clinical manifestations may also be found.


Serum interleukin-1α and soluble interleukin-2 receptor concentrations in cystic fibrosis

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Abstract
Interleukin (IL)-1 and IL-2 may participate in the systemic inflammatory response and hypergammaglobulinaemia observed in patients with cystic fibrosis. Thirty seven patients with cystic fibrosis were compared with 25 normal controls. High IgG and IgM concentrations were associated with more severe pulmonary disease. IL-1α and soluble IL-2 receptor concentrations were higher in the cystic fibrosis group than in the controls and also correlated with concentrations of IgG and IgM. These results suggest that these cytokines may contribute to enhanced immunoglobulin synthesis and silent inflammatory activity in clinically stable patients with cystic fibrosis.

(Arch Dis Child 1993; 68: 785–787)

Bacterial adherence occurs in the lung of those with cystic fibrosis despite the presence of intact local immune defences. Continuous bacterial exposure leads to the systemic spread of these vigorous, yet ineffective, local responses. This process may result in hypergammaglobulinemia, which often correlates with the progression of pulmonary disease. The vigorous inflammatory response, in which granulocytes predominate, may produce immunologically mediated pulmonary injury.

Interleukin (IL)-1 and IL-2 are cytokines derived respectively from mononuclear phagocytes and T lymphocytes. They may participate in the initial immune responses to infectious stimuli and immunoglobulin production. Soluble IL-2 receptor (sIL-2R) is released after activation of mononuclear cells by IL-2 and is one indicator of T cell activation. We investigated whether these cytokines were participating in the heightened systemic inflammatory response in cystic fibrosis and whether there was