Our work is important because it investigates the specificity of HHV-6 as aetiological factor for cause of death in four children with initial diagnosis of HHV-6 infection. It suggests caution in implicating HHV-6 in the cause of death. The issue of how immunocompetency is present in a ill child is a good one, but it is difficult to answer. In an attempt to answer this question we thoroughly re-examined both clinical data and anatomo-pathological findings including mucosa-associated lymphatic tissue of our four cases. To the best of our knowledge, patients were immunocompetent, or at least did not show any commonly diagnosable immunodeficiency. However, this affirmation is based on both clinical and pathological data (T- and B-cell markers by immunohistochemistry) for patients who died after hospital admission and on pathological data only (T- and B-cell markers by immunohistochemistry) for the infant with cot death.

It cannot be excluded that HHV-6 may cause a permanent latent infection in early childhood, but, in our opinion and in consideration of the transcriptome analysis results, there is no convincing evidence for a lethal outcome. Probably, HHV-6 may be able to function as a synergistic cofactor in lung infections by other pathogens. Similar to other herpesviruses, HHV-6 can be reactivated at any time and may cause lung disease if host defence mechanisms become defective. However, transcriptome and ultrastructural analysis should be able to exclude its reactivation even if a morphological finding would indicate the contrary. This has great importance for quality assurance and standard policies in intensive care units aiming to support better diagnostic procedures for the future.

Thus, in consideration of our data, we question a participation of HHV-6 in the deaths of our patients and strongly suggest performing transcriptome analysis and/or transmission electron microscopy before making this diagnosis. It can be judged a quite restrictive procedure, but our data suggest a likely uncertainty of diagnosis with immunohistochemistry, in situ hybridisation or PCR only. We agree that every effort must be made to set up promising approaches for monitoring HHV-6 infection in immunocompromised patients. The only suitable approach for fully solving the above raised questions should involve clinical studies to compare the abilities of whole-blood and plasma assays to specifically and accurately detect HHV-6 infection as early as possible.

Acknowledgements

We thank Professor Dr G van Kaick, German Cancer Research Institute, Heidelberg, Germany, for iron measurement of liver tissue (case 1); the Institute of Clinical Immunology and Medical Transfusion, University of Giessen, Germany, for the data provided about HHV-6; Dr F Neipel for transcriptome primer sequences and RT-PCR conditions; and Mrs G Gmeiner (Central Medical Institute of German Federal Armed Forces, Koblenz, Germany) for expert technical assistance. Permission was given for these case reports.

Consolato Sergi

Institute of Pathology, Medical University of Innsbruck, Austria

Edith Daum

Department of Virology, University Hospital, Heidelberg, Germany

Ingo Pedal

Institute of Forensic Medicine, University Hospital, Heidelberg, Germany

Bärbel Hauröder

Central Medical Institute of Federal Armed Forces, Koblenz, Germany

Paul Schnitzler

Department of Virology, University Hospital, Heidelberg, Germany

Correspondence to: Professor Consolato Sergi, Medical University Innsbruck, Muellerstrasse 44, AT-6020 Innsbruck, Austria; consolato.sergi@i-med.ac.at

doi: 10.1136/jcp.2007.048264

Accepted 18 May 2007

Published Online First 1 June 2007

This study was partly funded by the Peripro charity and partly by intramural financial support (Medical University of Innsbruck). No private companies were involved in this study.

Competing interests: None.

References

- 1 Zerr DM. Human herpesvirus 6: a clinical update. *Herpes* 2006;**13**:20–4.
- 2 Wang J, Huff K, McMasters R, et al. Sudden unexpected death associated with HHV-6 in an adolescent with tuberous sclerosis. *Pediatr Neurol* 1999;**21**:488–91.
- 3 Hoang MP, Ross KF, Dawson DB, et al. Human herpesvirus-6 and sudden death in infancy: report of a case and review of the literature. *J Forensic Sci* 1999;**44**:432–7.
- 4 Coumbe A, Fox JD, Briggs M, et al. Cytomegalovirus and human herpesvirus-6 in sudden infant death syndrome: an in situ hybridization study. *Pediatr Pathol* 1990;**10**:483–90.
- 5 Knox KK, Pietryga D, Harrington DJ, et al. Progressive immunodeficiency and fatal pneumonitis associated with human herpesvirus 6 infection in an infant. *Clin Infect Dis* 1995;**20**:406–13.
- 6 Fujiwara N, Namba H, Ohuchi R, et al. Monitoring of human herpesvirus-6 and -7 genomes in saliva samples of healthy adults by competitive quantitative PCR. *J Med Virol* 2000;**61**:208–13.
- 7 Ogata M, Kikuchi H, Satou T, et al. Human herpesvirus 6 DNA load in plasma after allogeneic stem cell transplantation: incidence and clinical significance. *J Infect Dis* 2006;**193**:68–79.
- 8 Boutolleau D, Fernandez C, Andre' E, et al. Human herpesvirus (HHV)-6 and HHV-7: two closely related viruses with different infection profiles in stem cell transplantation recipients. *J Infect Dis* 2003;**187**:179–86.
- 9 Clark DA, Nacheva EP, Leong HN, et al. Transmission of integrated human herpesvirus 6 through stem cell transplantation: implications for laboratory diagnosis. *J Infect Dis* 2006;**193**:912–16.

Persistent parvovirus b19 infection resulting in carpal tunnel syndrome

A woman showing chronic arthropathy after a parvovirus B19 infection was followed for 1 year with quantitative determination of parvoviral DNA, and specific immunoglobulin (Ig)M and IgG in blood. B19 arthropathy resulted in carpal tunnel syndrome, needing surgery, after 8 months of persistent B19 viraemia, when IgM was already cleared but IgG values were still high.

Case history

Carpal tunnel syndrome (CTS) is the most common peripheral compression neuropathy, but many aspects of its aetiology are not at all

clear. CTS is often termed as idiopathic but it has also been attributed to a variety of underlying disorders and processes, and sometimes CTS has been reported as secondary to infectious diseases of bacterial, mycotic and viral origin, including parvovirus B19. Parvovirus B19 in humans can cause acute infections but also persistent infections with continuous virus production both in immunocompetent and in immunosuppressed individuals.¹ Parvovirus B19 is generally associated with erythema infectiosum, arthritis and arthralgias, hydrops fetalis and transient aplastic crisis,¹ but also, in a few reports, it has been suggested to have a role in the development of CTS. In fact, Samii *et al.*² described three cases of acute bilateral CTS associated with B19 infection diagnosed by serological data and, in one case, by detection of B19 DNA in serum by PCR. Moreover Gendi *et al.*³ found three cases of CTS in adults in whom 1 year previously a parvovirus infection had been diagnosed by specific immunoglobulin (Ig)M. Recently, two cases of CTS in two female patients with prolonged arthralgia and chronic fatigue syndrome following a previous acute B19 infection have been described by Kerr *et al.*⁴ Two principal difficulties with the hypothesis that B19 can be an infectious agent which can trigger CTS can arise, however: (1) the causal relationship, as CTS is generally found a long time after laboratory detection of acute infection; and (2) the limitation of the methods of detection of recent or past B19 infections.

In the present report we describe a case of a woman, followed for 1 year with quantitative determination of parvoviral DNA,⁵ specific IgM and IgG in blood,⁶ who showed persistent parvovirus B19 viraemia for 8 months, with chronic B19 arthropathy and occasionally recurrent fugaceous erythemas, which led to CTS, needing surgery. This, apparently immunocompetent, 42-year-old woman was followed for B19 infection markers (fig. 1, table 1) for 12 months after exposure to her child who had B19 infection.

At the onset of the illness, B19 arthritis affecting bilaterally the small joints of the hands, wrists and elbows occurred. Symptoms persisted for 8 months with pain, stiffness and swelling. The patient was always afebrile and no anaemia was observed. At the beginning of the observation period, no rash was observed but, during the 8 months in which the parvovirus was present in the blood, transient rashes occurred. Concomitant with the presence of arthritis symptoms, B19 DNA was always detectable by real-time PCR. B19 IgG was always present, with similar titres throughout the study, while IgM was cleared at month 4. Between month 7 and 8, CTS developed. After month 8, concomitant with CTS surgery, but in our opinion not consequent to it, B19 virus cleared from the patient's blood without any intravenous immunoglobulin (IVIG) treatment, and the patient fully recovered without any other sign of B19 arthralgias.

It is possible to speculate that in this case at month 7–8, cell-mediated immunity finally became effective, or antibody maturation occurred, possibly with transient autoimmunity relevant to CTS development. The hypothesis of a possible role for B19 in CTS is consistent with the fact that a variety of manifestations, similar to CTS, have been reported in subjects with B19 infection such as pain, effects on soft tissues with swelling, persistent finger paraesthesia and slowing of nerve conduction velocities.^{7,8} The prevalence

Figure 1 B19 infection markers (viral load, IgM, IgG) and onset of CTS in the patient.

Table 1 B19 viral load, IgM, IgG and clinical features in the patient

Months	Parvovirus B19		B19 IgM		B19 IgG		Clinical features
	Viral load (geq/ml)	Test result	OD/cut-off	Test ratio result	OD/cut-off ratio	Test result	
0	1.30E+06	Pos	9.44	Pos	16.30	Pos	Arthralgias
1	8.41E+05	Pos	7.64	Pos	15.99	Pos	Arthralgias
2	6.25E+05	Pos	7.00	Pos	11.73	Pos	Arthralgias
3	1.50E+05	Pos	2.62	Pos	13.16	Pos	Arthralgias
4	1.00E+05	Pos	0.86	BL	8.41	Pos	Arthralgias
5	7.23E+04	Pos	0.53	Neg	10.26	Pos	Arthralgias
6	1.61E+04	Pos	0.38	Neg	10.42	Pos	Arthralgias
7	3.02E+04	Pos	0.34	Neg	9.88	Pos	Arthralgias
8	1.24E+04	Pos	0.40	Neg	9.07	Pos	Arthralgias
9	1.00E+00	Neg	0.29	Neg	8.96	Pos	Arthralgias
10	1.00E-01	Neg	0.33	Neg	7.49	Pos	Arthralgias
11	1.00E-01	Neg	0.22	Neg	8.00	Pos	Arthralgias
12	1.00E-01	Neg	0.38	Neg	7.89	Pos	Arthralgias

BL, borderline; CTS, carpal tunnel syndrome; geq, genome equivalent; Neg, negative; OD, optical density; Pos, positive.

of B19 arthralgias, moreover, is similar to CTS prevalence, being greater for middle-aged women than for children and men.¹ To establish the role of parvovirus B19 in the development of CTS and to determine if long-lasting B19 infections in patients with chronic arthritis can lead to CTS, it would be important to include research on B19 chronic infections with the presence of low levels of B19 DNA as a concurrent disease which could interact with secondary CTS.

Acknowledgements

We are grateful to Dr Jonathan Kerr for discussion of the data and valuable comments.

Monica Musiani, Elisabetta Manaresi,
Giorgio Gallinella, Marialuisa Zerbini

Department of Clinical and Experimental Medicine,
University of Bologna, Italy

Correspondence to: Professor Monica Musiani,
Department of Clinical and Experimental Medicine,
Division of Microbiology, Via Massarenti 9, 40138
Bologna, Italy; monica.musiani@unibo.it

doi: 10.1136/jcp.2007.048140

Accepted for publication 12 March 2007

Published Online First 30 March 2007

www.jclinpath.com

Competing interests: None declared.

References

- Zerbini M, Musiani M. Human parvoviruses. In: Murray PR, Baron EJ, Pfaller MA, Tenover FC, Tenover RH, eds. *Manual of clinical microbiology*, 8th edition. Washington, DC: American Society for Microbiology, 2003:1534–43.
- Samii K, Cassinotti P, de Freudenreich J, et al. Acute bilateral carpal tunnel syndrome associated with human parvovirus B19 infection. *Clin Infect Dis* 1996;22:162–4.
- Gendi NS, Gibson K, Wordsworth BP. Effect of HLA type and hypocomplementaemia on the expression of parvovirus arthritis: one year follow up of an outbreak. *Ann Rheum Dis* 1996;55:63–65.
- Kerr JR, Bracewell J, Laing I, et al. Chronic fatigue syndrome and arthralgia. *J Rheumatol* 2002;29:595–602.
- Gallinella G, Bonvicini F, Filippone C, et al. Calibrated real-time PCR for evaluation of parvovirus B19 viral load. *Clin Chem* 2004;50:759–762.
- Gallinella G, Zuffi E, Gentilomi G, et al. Relevance of B19 markers in serum samples for a diagnosis of parvovirus B19-related diseases. *J Med Virol* 2003;71:135–139.
- Faden H, Gary GW Jr, Korman M. Numbness and tingling of fingers associated with parvovirus B19 infection. *J Infect Dis* 1990;161:354–355.
- Barah F, Vallety PJ, Cleator GM, et al. Neurological manifestations of human parvovirus B19 infection. *Rev Med Virol* 2003;13:185–99.

An audit of UK pathologists' use of the British Society of Gastroenterology guidelines for the initial biopsy diagnosis of suspected chronic idiopathic inflammatory bowel disease

The original British Society of Gastroenterology (BSG) guidelines for the initial biopsy diagnosis of suspected chronic idiopathic inflammatory bowel disease (CIIBD) were published in 1997 in the *Journal of Clinical Pathology* and by the BSG, and were followed by a supplementary document, also published by the BSG.^{1–3} The guidelines were comprehensive and evidence-based, and included text, figures, proformas and tables.

A need for revision and update of these guidelines has been identified. New clinical and pathological entities have been described, new approaches to diagnosis and management have been adopted, and there has been sufficient time for pathologists to assess the value of the various elements of the original guidelines. Standardisation of reporting has become more prevalent, encouraged by the publication of cancer reporting guidelines and other CIIBD reporting guidelines.⁴ Also, the proportion of gastrointestinal (GI) pathology reported by pathologists with a specialist interest has increased.

As an initial step towards revision, an audit of UK GI pathologists' use of the guidelines was performed in late 2005. The audit aimed to assess awareness of the guidelines, determine their use, identify problems with their application, and gauge support for their revision.

Materials and methods

A one-page questionnaire with a series of questions, and two to four possible replies to each question, was e-mailed to 147 members of the Pathology Section of the BSG, with a reminder 2 months later. Free text replies were also encouraged; 35% of recipients responded. The results were collated and presented by the author to the Pathology Section at the Annual Meeting of the BSG in Birmingham, UK, in March 2006.

Results

Use and value of the guidelines

More than 95% of respondents were aware of the guidelines, and over 95% found them either

Figure 1 Proportion of respondents who found the guidelines useful for various aspects of their work.