Low prevalence of circulating anti-type 6 human herpes virus IgG-antibodies in Spanish children



Low prevalence of circulating anti-type 6 human herpes virus IgG-antibodies in Spanish children

C. Roldan, J. Gutiérrez*, A. de la Higuera and C. Maroto

Department of Microbiology, University of Granada, Hospital Universitario San Cecilio, Granada, Spain (*Reprint address)

Key words: human herpes virus type 6, antibody, prevalence, IgG

Abstract

The prevalence of circulating anti-HHV-6 IgG-antibodies in an infant population, was investigated to assess the evolution of antibody titres from birth to adulthood. Endpoint titration was done by indirect immunofluorescence, in 525 samples of serum from children, healthy adults and pregnant women. In the children, seropositivity increased from the age of 6 months, and was highest (56.52%) between 7 months and 1 year, suggesting that the initial infection occurred between 6 and 12 months of age.

Introduction

10

Salahuddin et al. (1986) described the type 6 human herpes virus (HHV-6), and since then many studies have analysed its molecular structure, pathogenesis, epidemiological characteristics, and the diagnosis of infection. The virus, now known to be ubiquitous and to affect a large part of the world's population, is regarded as the agent responsible for sudden exanthema in newborns. In the acute phase of the disease, acute hepatitis and mononuclear syndrome, among other syndromes, can occur. Infection by HHV-6 is also associated with chronic aesthenia and lymphoproliferative syndromes.

In the present work we studied the prevalence of circulating anti-HHV-6 IgG-antibodies in an infant population to assess the evolution of antibody titres from birth to adulthood in Granada (Spain).

Material and methods

IgG antibody to HHV-6 was determined by an indirect immuno-fluorescent-antibody assay which used twofold dilutions (starting at 1:40) of serum and HSB-2 cells infected with an HHV-6 isolate containing both the HHV-6A and HHV-6B genomes (Hall *et al.*, 1994). In 525 samples of serum 271 were from healthy children (group 1), 154 samples were from healthy adults aged 30 to 50 years (77 men, 77 women; group 2), and 100 samples were from healthy pregnant women aged 20 to 30 years (group 3). Informed consent to take part in the investigation was obtained for each participant.

Table 1 Distribution of titres according to groups and sex

Age	Sex	1/40 n	: %	1/80 n	: %	1/16 n	% %	1/32 n	% %	1/64 n	10: %
0–6 m	М	0	0.0	0	0.0	0	0.0	2	14.28	1	7.14
0 0	F	4	16.0	2	8.0	0	0.0	2	8.0	1	4.0
7 m–1 y	M	1	6.25	2	12.5	4	25.0	2	12.5	0	0.0
·	F	3	42.86	0	0.0	0	0.0	0	0.0	1	14.28
2 –5 y	M	9	18.37	7	14.29	2	4.07	8	16.33	0	0.0
·	F	3	11.11	1	3.7	5	18.53	6	22.22	0	0.0
6 –10 y	M	10	29.41	6	17.65	3	8.82	1	2.94	2	5.88
•	F	6	16.67	4	11.11	2	5.55	3	8.33	1	2.78
11 –15 y	М	3	9.37	2	6.25	5	15.62	2	6.25	1	3.23
•	F	2	6.45	7	22.58	5	16.13	2	6.45	1	2.78
Adults*	М	9	11.69	1	1.3	1	1.3	0	0.0	2	2.6
	F	20	25.96	4	5.19	2	2.6	0	0.0	4	5.19
Pregnant	F	20	20.0	14	14.0	2	2.0	2	2.0	1	1.0

^{*}p <0.05 for results by χ^2 test; and all the other results were p <0.01. M, male; F, female; m, month; y, year; n, number.

Results and discussion

The overall prevalence of circulating anti-HHV-6 antibodies in group 1 was 49.45%, distributed according to age subgroups as shown in Table 1. The corresponding value in group 2 was 27.92%, with a higher prevalence of seropositivity in women than in men (p <0.05; χ^2). In group 3, 39% of the population was seropositive. When antibody titres between groups, age and sex were compared, the only statistically significant difference was that between group 1 and each of the other two groups (p <0.001; χ^2) (Table 1 and Figure 1).

In the USA, Japan and Europe, the percentage of individuals with HHV-6 infection ranged from 60% to 90% of the population; the mean for Spain was 35% (Robert et al., 1990; Levy et al., 1990; Okuno et al., 1991; Lozano de León et al., 1992; Civeira et al., 1989). This

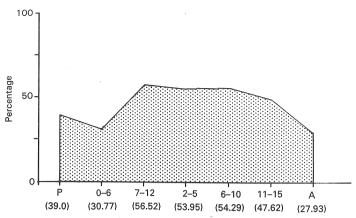


Figure 1 Variation of seroprevalence to HHV-6 according to age. P, pregnant; 0–6, and 7–12 in months, remainder in years; A, adult; average % shown in parentheses.

percentage varied with age and socio-economic conditions (Briggs et al., 1988). The seroprevalence of anti-HHV-6 antibodies in the present work is lower than previously reported results, possibly because of geographical differences and the use of different initial dilutions of the sample. In our study population, the seropositivity was higher among women than among men, which was a finding also noted by Briggs et al. (1988).

In group 1 (children) the seropositivity increased from the age of 6 months, and was highest (56.52%) between 7 months and 1 year. Knowles and Gardner (1988) has described similar results. The prevalence remained close to 50% until adolescence, suggesting that the initial infection occurred between 6 and 12 months of age. This observation has also been reported by Okuno *et al.* (1989) although the rate of seroprevalence in their work was higher (83% for children aged 6 months).

It is suggested that an initial HHV-6 virus infection should be ruled out in children between 7 months and 1 year of age in whom a febrile syndrome is suspected.

References

BRIGGS M., Fox J. and Tedder R. S. 1988. Age prevalence of antibody to human herpes virus 6. *Lancet* 333 1058.

CIVEIRA M. P., Cuende I., Castillo A. and Prieto J. 1989. Prevalencia de anticuerpos frente al virus herpes humano tipo 6 (VHH-6 o HBLV) en la población general. *Med. Clin.* **92** 199. HALL C. B., Long C. E., Schnabel K. C., Caserta M. T., McIntyre K. M., Costanzo M. A., Knott A., Dewhurst S., Insel R. and Epstein L. G. 1994. Human herpes virus-6 infection in children. *N. Engl. J. Med.* **331** 432–8.

KNOWLES W. A. and Gardner S. 1988. High prevalence of antibody to human herpes virus 6 and seroconversion associated with rash in two infants. Lancet 333 912-3.

LEVY J. A., Ferro F., Greenspan D. and Lenette E. T. 1990. Frequent isolation of HHV-6 from saliva and high seroprevalence of the virus in the population. Lancet 335 1047-50. LOZANO DE LEON F., Iglesias C., Lucio-Villegas M. E., Lozano M. C., Corzo J. E., Martin E. and Garcia F. 1992. Estudio seroepidemiológico del virus herpes humano 6 en adictos a drogas por via intravenosa, con y sin infección por el virus de la inmunodeficiencia humana tipo 1. Med. Clin. 99 210-2.

OKUNO T., Takahashi K., Balachandra K., Shiraki K., Yamanishi K., Takahashi M. and Baba K. 1989. Seroepidemiology of human herpes virus 6 infection in normal children and adults. J. clin. Microbiol. 27 651-3.

OKUNO T., Mukais T., Baba K., Ohsumi Y., Takahashi M. and Yamanishi K. 1991. Outbreak of exanthem subitum in an orphanage. *J. Pediat.* **119** 759–61.

ROBERT C., Agut H. and Aubin J. T. 1990. Detection of antibodies to human herpes virus

6 using immunofluorescence assay. Res. Virol. 141 545–55.
SALAHUDDIN S. Z., Ablashi D. V., Markham P. D., Josephs S. F., Sturzenegger S., Kaplan M., Halligan G., Vevverfeld P., Wong Staal F., Kramarsky B. and Gallo R. C. 1986. Isolation of a new virus, HBLV, in patients with lymphoproliferative disorders. Science 234 596-601.

Accepted 14 April 1996

236 Microbios

C. Roldan et al.

News to authors

Manuscripts will be refereed, processed and published rapidly providing the typescript and illustrations have been carefully and accurately prepared in the correct style of each journal.

By following the style of our biomedical journals meticulously you can obtain the advantages of some of the most rapid publication rates for research papers available anywhere. However, a prerequisite is that manuscripts must be impeccably presented in the journal style.

Read the leaflets prepared for authors, entitled *Information for contributors* and *Photographic illustrations*, and send manuscripts for the international biomedical journals MICROBIOS, CYTOBIOS and *BIOMEDICAL LETTERS*, to Dr Stuart Anderson, Executive Editor, The Faculty Press, 88 Regent Street, Cambridge CB2 1DP, England.

- * MICROBIOS is a biomedical research journal, established in 1969, which is concerned with all aspects of Bacteriology and Microbiology. Issues are published every three to four weeks comprising four volumes per annum.
- * BIOMEDICAL LETTERS is an international journal for rapid publication of medical, biomedical, and neuroscience research papers, and was first published in 1976. Issues are despatched bimonthly.
- * CYTOBIOS was founded in 1969, and is a biomedical journal for research papers into all aspects of cell science and genetics. Issues are published monthly in four volumes per annum.
- * Manuscripts are peer reviewed.
- * Fifty reprints are provided free to the first named author, although postage is extra.
- * Worldwide distribution, so authors invariably receive many requests for reprints.
- * Abstracted in CURRENT CONTENTS and all the leading abstracting journals.
- * Subscription rates and leaflets for authors are available from the publishers.

The Faculty Press 88 Regent Street Cambridge CB2 1DP England

MICROBIOS

is an international biomedical research journal, established in 1969, which is devoted to fundamental studies of viruses, bacteria, microfungi, microscopic algae, and protozoa. It is concerned with all aspects of micro-organisms, but lays particular emphasis upon chemical microbiology.

Original observations are accepted on the applications of microbiology in the fields of pharmaceutical and chemical production; food manufacture and spoilage; public health and sanitation; biodeterioration; pharmacology and immunology.

Papers on the organization and metabolic activities of micro-organisms are published, as well as work on cell-virus interactions. Manuscripts which are especially welcome are those dealing with the chemical anatomy of micro-organisms, and the biochemical and biophysical factors that affect microbial activity.

The subscription rate for 1997 will be £395.00 sterling

CYTOBIOS

is a transworld biomedical research journal, established in 1969, which publishes original investigations into all aspects of cell organization. Contributions will be accepted on the behaviour, structure and function of animal and plant cells, including studies on extracellular products and subcellular organelles.

The journal emphasizes work at chemical and molecular levels. It publishes original papers on cytogenetics; cell division and growth; cell physiology and pathology; immunochemistry and immunobiology. Manuscripts are solicited which correlate findings in the biochemical and biophysical fields with morphological, cytological and physiological knowledge.

Discoveries resulting from advances in, and application of, modern biological and medical techniques to cytology are particularly welcome. So also are cytochemical papers which contribute to an understanding of cell organization and to the study of organic fine structure.

The subscription rate for 1997 will be £395.00 sterling

BIOMEDICAL LETTERS

is an international research journal, established in 1976 as *Microbios Letters*, having the fundamental aim of accelerated publication, and distribution to a worldwide readership. It is intended for short and preliminary biomedical communications, but may include some longer papers and reviews. In general manuscripts should not exceed 5,000 words in length and include only one or two Tables and/or Figures.

BIOMEDICAL LETTERS is primarily designed for the publication of medical research papers. Clinical studies will be considered, and papers in such fields as cellular pharmacology, virology, bacteriology, biochemistry, immunology, molecular biology, biochemical genetics, biophysics, haematology, physiology. Manuscripts on neuroscience, radiation biology and cancer research, will be particularly welcome.

The subscription rate for 1997 will be £200.00 sterling

Manuscripts

To enable the Executive Editors to plan the publishing programme of forthcoming issues, the following information will be much appreciated:

(1) Ih	ope to submit a paper for publication in	Tick box				
(a)	MICROBIOS					
(b)	CYTOBIOS					
(c)	BIOMEDICAL LETTERS					
	ase send me a free copy of the leaflet itled 'Information for contributors'					
The pre	bbable title of the paper will be:					
I confirm that this manuscript will be based on original, unpublished research, and I understand that all papers are subject to peer reviewing procedures before acceptance. The approximate date of submission will be:						
Name						
Status						
Addres	s	,				
		• • • • • • • • • • • • • • • • • • • •				
Please	complete and return to the address below:					

THE FACULTY PRESS 88 Regent Street Cambridge CB2 1DP Great Britain