

# Cytomegalovirus mononucleosis: risk for fathers of young children

GIUSEPPE BIGNARDI

MARK ATKINS

JANICE MAIN

**SUMMARY.** A case of pyrexia of unknown origin in a 35-year-old man, who had become a father nine months earlier, is presented. A diagnosis of cytomegalovirus mononucleosis was achieved only after extensive investigations. It is suggested that cytomegalovirus mononucleosis should be added to the differential diagnosis when investigating pyrexia of unknown origin in fathers of young children.

**Keywords:** infectious mononucleosis; cytomegaloviruses; differential diagnosis; communicable diseases.

## Introduction

A MAJOR clinical concern in relation to cytomegalovirus infection is that of mothers contracting a primary infection when pregnant, because of the possible consequences to the fetus. However, fathers should not be forgotten, as those who are seronegative are at risk of acquiring a primary infection from their offspring.

## Case report

A 35-year-old man, who was a senior registrar in microbiology, developed a febrile illness 11 weeks after a holiday in Italy. He complained of malaise and headache, which were worse in the late afternoon, and of intermittent sore throat. His neck was painful during the first few days of his illness. His temperature often rose to 38.5 °C in the evening; this was relieved by paracetamol. There was no significant past medical history. He had had mumps and rubella as a child. There was no history of recent needlestick injuries and he had received a course of hepatitis B vaccine followed by a satisfactory immune response. His wife and their nine month old son were well when he first developed the illness; one week later, however, his son developed a febrile illness with coryza and cough which lasted for one week and was followed by an episode of otitis media. On the ninth day of illness the father's full blood count showed  $5.3 \times 10^9$  white cells per litre of which  $3.4 \times 10^9$  were neutrophils and  $1.5 \times 10^9$  lymphocytes. The erythrocyte sedimentation rate was 4 mm hour<sup>-1</sup>.

After two weeks of illness the opinion of a consultant in infectious diseases was sought. On examination the patient was found to have no lymphadenopathy, no splenomegaly, his liver was just palpable, his chest was clear, his throat was normal, his pulse was regular and his heart sounds were normal. A chest x-ray was normal. Specimens were taken for routine biochemistry, blood culture and a variety of serological tests.

---

G Bignardi, MRCPATH, senior registrar in microbiology; M Atkins, MB, senior registrar in virology; and J Main, MRCP, senior lecturer in infectious diseases and general medicine, St Mary's Hospital, London. Submitted: 25 May 1992; accepted: 26 June 1992.

Twenty four days after the onset of symptoms a repeat full blood count showed lymphocytosis with atypical lymphocytes present (total white cell count  $7.2 \times 10^9$  l<sup>-1</sup> of which  $1.2 \times 10^9$  were neutrophils and  $5.1 \times 10^9$  lymphocytes).

The level of aspartate aminotransferase was slightly increased (56 IU l<sup>-1</sup>). Two blood cultures were negative as were bacterial cultures from urine and throat swabs. Serology tests for brucella, toxoplasma, *Mycoplasma pneumoniae*, *Coxiella burnetii*, adenovirus and hepatitis A, B and C viruses were all negative. Monospot tests were done at nine and 24 days after the onset of symptoms and were both negative. No drugs were taken by the patient except paracetamol.

Cytomegalovirus serology was positive both for immunoglobulin G (IgG) and for immunoglobulin M (IgM) on multiple specimens taken from day 15 of the illness onwards. The methods used for cytomegalovirus serology were Behring enzyme immunoassay for IgG and IgM, and Mercia IgM capture enzyme immunoassay. Both cytomegalovirus IgG and IgM tests were confirmed by a reference laboratory. A buffy coat culture gave a cytomegalovirus-like cytopathic effect in human embryo lung fibroblasts after 18 days. A serum specimen taken from the patient's nine month old son was positive for cytomegalovirus IgG antibodies but negative for IgM antibodies using the same methods as for the father; a urine specimen grew cytomegalovirus after only 24 hours in tissue culture (which suggests a very high viral titre). A serum specimen taken from the patient's wife was positive for cytomegalovirus IgG but negative for IgM antibodies, again by the same methods. The father improved and became afebrile between five and six weeks after the onset of symptoms.

The patient was off work for a total of three weeks and was a hospital inpatient for two days. A diagnosis of cytomegalovirus mononucleosis was eventually made.

## Discussion

This patient suffered from a protracted illness and was worried about the nature of a pyrexia of unknown origin.

This case highlights the need for repeating a full blood count in patients investigated for pyrexia of unknown origin even after an initial normal result: in this patient the full blood count was normal after nine days but showed lymphocytosis and atypical lymphocytes 24 days after the onset of symptoms. Indeed, lymphocytosis may appear relatively late in the course of both cytomegalovirus<sup>1</sup> and Epstein-Barr virus<sup>2</sup> mononucleosis, while the monospot test also needs to be repeated as delayed appearance of heterophile antibodies can occur and may be associated with a more prolonged duration of illness.<sup>3</sup> In patients with lymphocytosis and atypical lymphocytes a prolonged illness in the absence of lymphadenopathy is more in keeping with cytomegalovirus than Epstein-Barr virus mononucleosis or toxoplasmosis. Although sore throat is common both in patients with cytomegalovirus and Epstein-Barr virus mononucleosis, exudative pharyngitis is less common in cytomegalovirus mononucleosis in children and rare in adults.<sup>4</sup> In this patient the diagnosis was supported by culture and confirmed by serology results. Cytomegalovirus infection in the immunocompetent adult is usually subclinical. It is not known why some adults develop the full blown picture of cytomegalovirus mononucleosis.<sup>5</sup>

From the available results in this case it seems most likely that transmission from the seropositive mother resulted in congenital or perinatal infection of the son and that the father acquired the infection from the son. Between 5% and 15% of cytomegalovirus seropositive women undergo reactivation with endocervical excretion during pregnancy<sup>6,7</sup> and this can be a source of infection for both the children and seronegative fathers. Cytomegalovirus infection of infants may be acquired congenitally, nately or postnatally (via breast milk), but is rarely symptomatic when the source is a mother with reactivation rather than primary infection.<sup>7</sup> In this case the timing of the father's primary infection, when the child was nine months of age, makes acquisition from the child more likely than from his wife. Excretion of cytomegalovirus in the urine of infants with asymptomatic congenital or perinatal infection usually peaks around the age of six to nine months and may persist for years, while pharyngeal shedding is not prolonged.<sup>8</sup> The son of this patient was excreting a high titre of virus in his urine and his father often changed his nappies.

Transmission of infection from infants to seronegative parents is well documented.<sup>9</sup> In a case similar to the one described here the isolate from a six-month-old girl and that from her father were almost identical when compared using restriction endonuclease analysis.<sup>10</sup> The case reported here emphasizes the need to consider cytomegalovirus mononucleosis in the differential diagnosis of pyrexia of unknown origin in fathers of young children.

## References

1. Monto HD. Cytomegalovirus. In: Mandell GL, Douglas RG, Bennett JE (eds). *Principles and practice of infectious diseases*. Edinburgh: Churchill Livingstone, 1990.
2. Schooley RT, Dolin R. Epstein-Barr virus (infectious mononucleosis). In: Mandell GL, Douglas RG, Bennett JE (eds). *Principles and practice of infectious diseases*. Edinburgh: Churchill Livingstone 1990.
3. Chretien JH, Esswein JG, Holland WG, McCauley CE. Predictors of the duration of infectious mononucleosis. *South Med J* 1977; **70**: 437-439.
4. Begovac J, Soldo I, Presecki V. Cytomegalovirus mononucleosis in children compared with the infection in adults and with Epstein-Barr virus mononucleosis. *J Infect* 1988; **17**: 121-125.
5. Jordan MC, Rousseau WE, Stewart JA, et al. Spontaneous cytomegalovirus mononucleosis. *Ann Intern Med* 1973; **79**: 153-160.
6. Knox GE. Cytomegalovirus: patient counselling. *Semin Perinatol* 1983; **7**: 43-46.
7. Betts RF. Cytomegalovirus infection epidemiology and biology in adults. *Semin Perinatol* 1983; **7**: 22-30.
8. Stagno S, Pass RF, Dworsky ME, Alford CA. Congenital and perinatal cytomegalovirus infection. *Semin Perinatol* 1983; **7**: 31-42.
9. Pass RF, Hutto C, Ricks R, Cloud GA. Increased rate of cytomegalovirus infection among parents of children attending day-care centers. *N Engl J Med* 1986; **314**: 1414-1418.
10. Yarrish RL, Wormser GP, Bittker SJ, et al. The febrile father with a cytomegalovirus infection; a family affair. *Postgrad Med* 1989; **85**: 251-254.

## Acknowledgements

We thank the virology department at St George's Hospital in London for performing confirmatory cytomegalovirus serology.

## Address for correspondence

Dr G Bignardi, Diagnostic Bacteriology, Microbiology Department, St Mary's Hospital, Praed Street, London W2 1NY.

## INFORMATION FOR AUTHORS AND READERS

Papers submitted for publication should not have been published before or be currently submitted to any other journal. They should be typed, on one side of the paper only, in double spacing and with generous margins. A4 is preferred paper size. The first page should contain the title only. To assist in sending out papers blind to referees, the name(s) of author(s) (maximum of eight), degrees, position, town of residence, address for correspondence and acknowledgements should be on a sheet separate from the main text.

Original articles should normally be no longer than 4000 words, arranged in the usual order of summary, introduction, method, results, discussion and references. Letters to the editor should be brief — 400 words maximum — and should be typed in double spacing.

Illustrations of all kinds, including photographs, are welcomed. Graphs and other line drawings need not be submitted as finished artwork — rough drawings are sufficient, provided they are clear and adequately annotated.

Metric units, SI units and the 24-hour clock are preferred. Numerals up to 10 should be spelt, 10 and over as figures. Use the approved names of drugs, though proprietary names may follow in brackets. Avoid abbreviations.

References should be in the Vancouver style as used in the *Journal*. Their accuracy must be checked before submission. The title page, figures, tables, legends and references should all be on separate sheets of paper. If a questionnaire has been used in the study, a copy of it should be enclosed.

Three copies of each article should be submitted and the author should keep a copy. One copy will be returned if the paper is rejected. A covering letter should make it clear that the final manuscript has been seen and approved by all the authors.

All articles and letters are subject to editing.

Papers are refereed before a decision is made.

Published keywords are produced using the *GP-LIT thesaurus*.

More detailed instructions are published annually in the January issue.

### Correspondence and enquiries

All correspondence should be addressed to: The Editor, British Journal of General Practice, Royal College of General Practitioners, 12 Queen Street, Edinburgh EH2 1JE. Telephone (office hours; 24 hour answering service): 031-225 7629. Fax (24 hours): 031-220 6750.

### Copyright

Authors of all articles assign copyright to the *Journal*. However, authors may use minor parts (up to 15%) of their own work after publication without seeking written permission provided they acknowledge the original source. The *Journal* would, however, be grateful to receive notice of when and where such material has been reproduced. Authors may not reproduce substantial parts of their own material without written consent. However, requests to reproduce material are welcomed and consent is usually given. Individuals may photocopy articles for educational purposes without obtaining permission up to a maximum of 25 copies in total over any period of time. Permission should be sought from the editor to reproduce an article for any other purpose.

### Advertising enquiries

Display and classified advertising enquiries should be addressed to: Advertising Sales Executive, Royal College of General Practitioners, 14 Princes Gate, Hyde Park, London SW7 1PU. Telephone: 071-581 3232. Fax: 071-225 3047.

### Circulation and subscriptions

The *British Journal of General Practice* is published monthly and is circulated to all Fellows, Members and Associates of the Royal College of General Practitioners, and to private subscribers. All subscribers receive *Policy statements* and *Reports from general practice* free of charge with the *Journal* when these are published. The 1993 subscription is £105 post free (£115 outside the UK, £16 airmail supplement). Non-members' subscription enquiries should be made to: Bailey Management Services, 127 Sandgate Road, Folkestone, Kent CT20 2BL. Telephone: 0303-850501. Members' enquiries should continue to be made to: The Royal College of General Practitioners, 14 Princes Gate, Hyde Park, London SW7 1PU. Telephone: 071-581 3232.

### Notice to readers

Opinions expressed in the *British Journal of General Practice* and the supplements should not be taken to represent the policy of the Royal College of General Practitioners unless this is specifically stated.

### RCGP Connection

Correspondence concerning the news magazine, *RCGP Connection*, should be addressed to: RCGP Connection Editor, Royal College of General Practitioners, 14 Princes Gate, Hyde Park, London SW7 1PU. Telephone: 071-581 3232.