

Cytomegalovirus mononucleosis: risk for fathers of young children

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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 5.3×10^9 white cells per litre of which 3.4×10^9 were neutrophils and 1.5×10^9 lymphocytes. The erythrocyte sedimentation rate was 4 mm hour⁻¹.

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.

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Twenty four days after the onset of symptoms a repeat full blood count showed lymphocytosis with atypical lymphocytes present (total white cell count 7.2×10^9 l⁻¹ of which 1.2×10^9 were neutrophils and 5.1×10^9 lymphocytes).

The level of aspartate aminotransferase was slightly increased (56 IU l⁻¹). 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 cytomegalovirus¹ and Epstein-Barr virus² 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.³ 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.⁴ 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.⁵

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^{6,7} and this can be a source of infection for both the children and seronegative fathers. Cytomegalovirus infection of infants may be acquired congenitally, natively or postnatally (via breast milk), but is rarely symptomatic when the source is a mother with reactivation rather than primary infection.⁷ 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.⁸ 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.⁹ 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.¹⁰ 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.

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