

Acute Cytomegalovirus Infection in an Immune-Competent Host: An Atypical Presentation

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Cytomegalovirus can cause multi-organ severe and even fatal disease in immune-compromised patients. The clinical syndromes observed in this setting include encephalitis, pneumonitis, hepatitis, uveitis, retinitis, colitis, and graft rejection [1]. However, CMV infection in immune-competent hosts has traditionally been considered to have a benign self-limited course as it is usually asymptomatic or presents as a mononucleosis-like syndrome. Severe CMV infection in immune-competent patients has been described only rarely. Moreover, the indications for antiviral treatment in immune-competent patients with severe CMV infection have not been elucidated [1].

In this communication we present an immune-competent patient who developed a severe prolonged CMV infection with multiorgan involvement. We review the literature regarding severe CMV infections in immune-competent patients as well as the role of antiviral treatment.

PATIENT DESCRIPTION

A 54 year old woman, a smoker (16 pack-years) but otherwise healthy kindergarten teacher, presented with fever (39°C),

CMV = cytomegalovirus

sore throat, dry cough, loose stools and dyspnea during the previous 12 days. A diagnosis of probable pneumonia had been made in the community clinic where she was treated with several antibiotics, but since her condition was not improving she was referred to our hospital. Physical examination on admission revealed a good general condition, but with pertinent findings of fever 38.1°C, tachycardia (100/min), bilateral cervical lymphadenopathy (5–10 mm), and non-palpable purpura on the lower limbs. There was no apparent hepatosplenomegaly. Laboratory tests showed increased C-reactive protein (43 mg/L) with normal complete blood count. Urinalysis revealed 5–10 red blood cells, 15–20 leukocytes, 2–5 hyaline casts, 0–2 granular casts and 0–1 waxy cast, and the biochemical profile showed hepatitis (elevated alanine aminotransferase 54 U/L, aspartate aminotransferase 63 U/L, alkaline phosphatase 167 U/L, gamma-glutamyl transpeptidase 267 U/L and lactate dehydrogenase 638 U/L). A diagnosis of primary CMV infection was made by positive immunoglobulin M CMV, positive IgG CMV (which was significantly increased from 7 to 79 units after 2 months) and a highly positive polymerase chain reaction for CMV (9390 copies/ml). Other tests for infectious causes (Epstein-Barr virus, Mycoplasma, Q fever, Bartonella, Coxsackie, Enterovirus, urine and blood cultures) and tests for antinuclear antibodies, antineutrophil cytoplasmic antibodies, smooth muscle antibodies, liver kidney microsomal antibodies and mitochondrial antibodies were all nega-

Ig = immunoglobulin

tive. Initial C3, C4 and immunoglobulin levels were normal. Chest X-ray and electrocardiogram were normal on admission.

Despite the primary CMV infection in a patient with prior good health, the course of her disease was complicated by very prolonged fever (2 months) and multiorgan involvement, including severe pneumonitis, pericarditis, colitis [Figure], hepatitis, lymphadenopathy, hepatosplenomegaly, bilateral +3 ankle pitting edema, proteinuria (up to 2.1 g/24 hours) and hypoalbuminemia (29 g/L). In addition, she developed anemia (10 g/dl) and thrombocytopenia (10^5 platelets/ μ l). Moreover, she developed paraproteinemia with high IgM (3.1 g/L) and high free kappa chains (30 mg/L), hypocomplementemia (C4 < 0.6 g/L, C3 = 0.2 g/L) and cryoglobulinemia (1.3%). Due to the severe and protracted disease, treatment was initiated on hospitalization day 13 of with intravenous gancyclovir for a total of 10 days and the patient was discharged with valgancyclovir for another month – a total treatment time of 40 days. Three months after onset of the symptoms, the patient recovered fully with disappearance of all symptoms and signs of disease. Laboratory data revealed a complete resolution of the anemia, hepatitis, paraproteinemia, hypocomplementemia and proteinuria.

COMMENT

We present the case of a previously healthy woman who developed a severe complicated prolonged primary



Computed tomography scan of the abdomen showing colitis

CMV infection involving multiple organ systems. Although complications such as fever, colitis, hepatitis and pneumonitis are well described in immune-compromised hosts with CMV infection [1], the occurrence of these complications in immune-competent patients is rare. A review of 89 articles reporting on severe CMV infection in 290 immune-competent adults summarizes the known data regarding severe life-threatening complications of CMV infection in immune-competent adults [1]. Among these reports, the gastrointestinal tract (colitis) and the central nervous system (meningitis, encephalitis, transverse myelitis) were the most frequent sites of severe CMV infection. Involvement of other organ systems, as evidenced by our patient, included hematological disorders (hemolytic anemia, thrombocytopenia) and pneumonitis.

Our case was unique in the occurrence of many rare complications in a single patient. In the setting of anemia, IgM paraproteinemia, lymphadenopathy and hepatosplenomegaly, the presence of an underlying lymphoproliferative disease was considered. In a report of 24 immune-competent patients aged 17–62 years (mean age 31.8 years) with acute or recent (within 1–3 months) primary CMV infection,

M component was detected in 40% of the patients [2]. However, the production of M protein was transient, and by 6 weeks only 1 of 10 patients in that study retained the M component [2], as occurred in our patient.

In the setting of proteinuria, nephritic urine, hypoalbuminemia and pitting edema, as in our patient, the possibility of a nephrotic/nephritic underlying syndrome was considered. Although CMV is secreted in the urine during infection, acute renal failure, mostly due to interstitial nephritis, has previously been described in a few cases [3]. The present case was unique since the patient developed nephritic syndrome that resolved completely after 3 months.

Another distinctive complication in the present case was the detection of low complement and cryoglobulinemia. Similarly, a study of 115 immune-competent CMV patients showed high immunoglobulin levels in 56% of the cases and monoclonal antibodies in 8% [4]. Of the 115 patients 10 (8.7%) demonstrated at least one immunological abnormality: antinuclear antibodies, smooth muscle antibodies, cryoglobulinemia, rheumatoid factor, and low complement.

The indications for treatment of CMV infection in immune-competent hosts have not been established.

However, in the case of severe or complicated CMV infection, early treatment with ganciclovir is recommended [5]. In our case, early antiviral treatment resulted in complete recovery. We suggest that despite the lack of evidence, in complicated cases and in particular in patients with significant multiorgan involvement, early antiviral treatment is mandatory. However, more clinical experience is needed to evaluate the potential role of antiviral therapy in this setting.

In conclusion, we describe an immune-competent previously healthy woman with acute primary CMV infection. The case was distinctive for the multiple and uncommon complications in a single patient. Thus, primary CMV infection may have an atypical presentation with severe prolonged and multiorgan involvement in an immune-competent patient. It is suggested that antiviral treatment be initiated early in the course of similar cases.

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Phototoxic Response to *Ficus carica* Leaf and Shoot Saps

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Photocontact dermatitis due to figs, though well known by dermatologists, is poorly recognized by the general physician. The approach to a patient presenting to the Emergency Department with a skin reaction is based on the pathogenesis of his or her reaction. In the case described here, the contact with shoot and leaf sap, rich in photoactive psoralens, was the cause of the severe phototoxic response.

PATIENT DESCRIPTION

A 55 year old white male presented to the Emergency Department with a 3 day history of generalized erythematous and edematous rash with vesicles and bullae especially on the trunk and extremities. These symptoms emerged several hours after the patient had pruned the branches of a fig tree while working in his garden without a shirt. He denied eating any figs or coming into contact with any other fruit or plant. His past medical history was not clinically significant.

On physical examination the patient was alert. Vital signs were normal. Examination of head, eyes, ears, nose and throat were normal with no swelling of the lips, palate, uvula, face or neck. Examination of the chest, abdomen, back and extremities showed patches of erythema, with clear vesicles

and bullae [Figure]. Cardiac, pulmonary and neurological examinations were normal. The results of chest X-ray examination and laboratory investigations were normal.

The differential diagnosis of the patient's illness was allergic contact dermatitis (phytophoto) or chemical burn. He was therefore treated with intravenous promethazine 50 mg to alleviate pruritus, and intravenous hydrocortisone 300 mg, administered over 30 minutes, to suppress progression and later recurrence of symptoms.

The patient was admitted to the Internal Medicine ward for continued treatment and follow-up. The drug regimen included oral antihistamine and prednisone 40 mg per day. The patient's general condition improved:

the erythema, vesicles and bullae regressed and the pruritus subsided. He was discharged on prednisone tablets in a tapering dosage, with recommendations to avoid scratching and secondarily infecting the skin lesion and also to avoid exposure of the afflicted body parts to sunlight.

COMMENT

A literature survey revealed a wide spectrum of reactions. These include a relatively self-limited reaction of oral allergy syndrome [1], and photocontact dermatitis as an acute skin reaction that may be easily confused with other causes of contact dermatitis and is termed phytophotodermatitis. It is characterized by sunburn, blis-



Patches of erythema, with clear vesicles and bullae on the abdomen