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CASE REPORT

Cytomegalovirus reinfection in a patient with chronic hepatitis C

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Abstract

Cytomegalovirus(CMV) infection remains latent throughout life, recurrent in evolution. Recurrent infection includes both reinfection and reactivation and manifest as CMV disease which frequently develops in immunocompromised patients. We describe a case of chronic active hepatitis C, activation produced by reinfection with CMV in a patient with low immunity secondary to splenectomy, chronic VHC infection. CMV infection is sustained by purple lesions, oral aphthae and ulcerations, mononucleosis syndrome, lymphocytes with nuclear inclusions, inflammatory syndrome, hepatitis, nephritis, inflammatory lymphadenopathy, reactive IgG CMV. Recent CMV infection is sustained by 5- fold increase in IgG CMV titers.

Keywords: Cytomegalovirus, chronic hepatitis C, mononucleosis syndrome.

INTORODUCTION

CMV usually causes an asymptomatic infection or produces mild flulike symptoms; it remains latent throughout life and may reactivate.(12,17).
Reactivation of previously latent infection or newly acquired infection manifest as a CMV disease. Clinically significant CMV disease frequently develops in patients immunocompromised by HIV infection, solid-organ transplantation, or bone marrow transplantation, as well as in those receiving high-dose steroids, tumor necrosis antagonists, or other immunosuppressing medications (7, 20).

Symptomatic CMV disease in immunocompromised individuals can affect almost every organ of the body, resulting in cutaneous vasculitis, fever of unknown origin, pneumonia, hepatitis, encephalitis, myelitis, colitis, uveitis, retinitis, and neuropathy(5). CMV may infect the GI tract from the oral cavity through the colon. The typical manifestation of the disease is ulcerative lesions. In immunocompromised individuals, laboratory tests show a mononucleosis syndrome, lymphocytosis plus atypical lymphocytosis(3, 10, 18).

CMV is a lytic virus that causes a cytopathic effect in vitro and in vivo. The pathologic hallmark of CMV infection is an enlarged cell with viral inclusion bodies.

Intracellular inclusions surrounded by a clear halo may be demonstrated with various stains (Giemsa, Wright, hematoxylin-eosin, Papanicolaou). This gives the appearance of an "owl's eye.

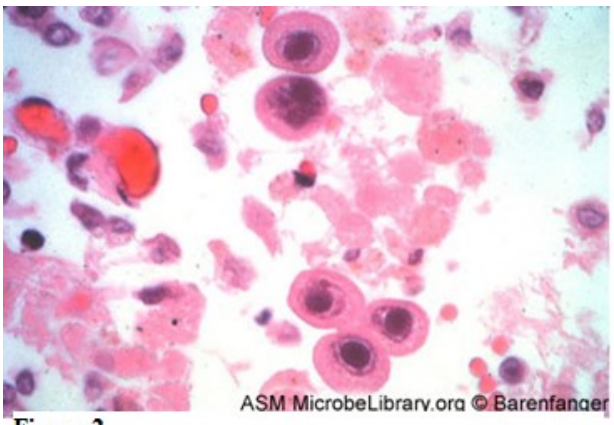


Figure 2.
H&E stain of CMV-infected cell in lungs of AIDS pacient. Nuclear inclusions can be seen

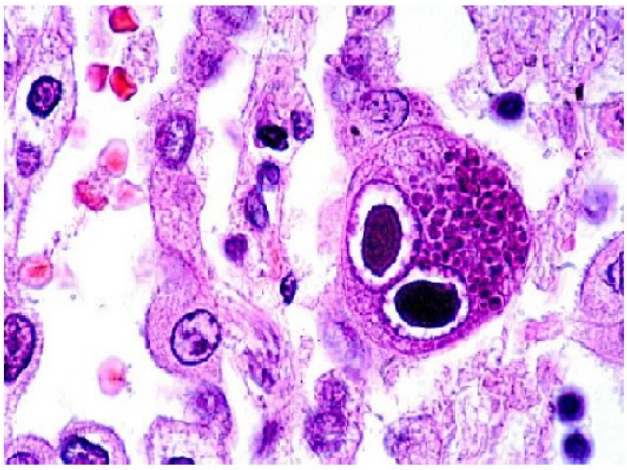


Figure 1.
Hematoxylin-eosin–stained lung section showing typical owl-eye inclusions (480X). Courtesy of Danny L Wiedbrauk, PhD, Scientific Director, Virology & Molecular Biology, Warde Medical Laboratory, Ann Arbor, Michigan.(9)

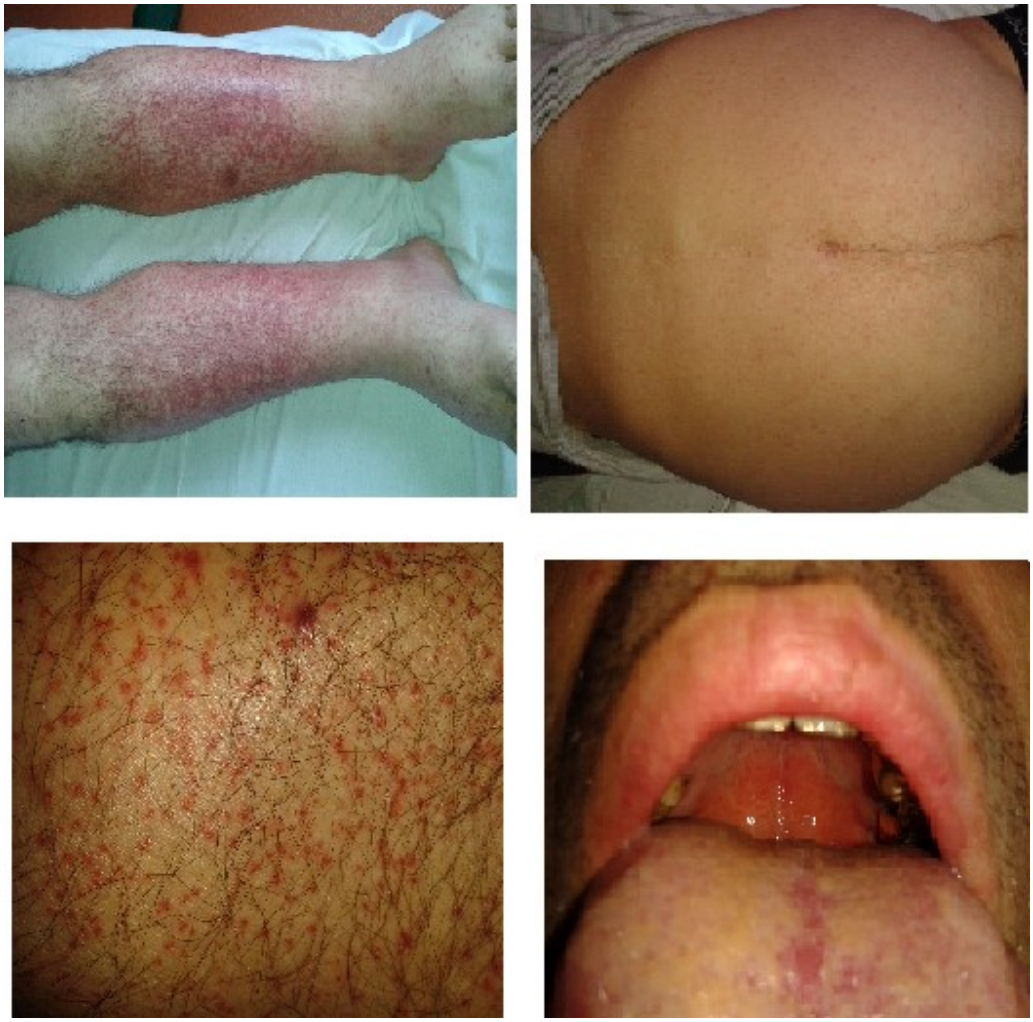
Immune response cytomegalovirus involves the synthesis of specific antibodies in the IgM class a few weeks after contracting the infection, followed a week later by the appearance of IgG antibodies. Primary CMV infection is defined as infection in an individual who was previously CMV seronegative. In these patients, CMV immunoglobulin M (IgM) antibodies may be found as early as 4-7 weeks after initial infection and may persist as long as 16-20 weeks. Determination of IgM antibodies is an important tool in the diagnosis of acute cytomegalovirus infection. Naturally acquired immunity to the virus does not seem to prevent reinfection or the duration of viral shedding(2, 8,16).

Reactivation of the virus is not uncommon, sometimes occurring with viremia and a positive IgM result in the presence of IgG antibody. This is usually observed during intercurrent infections or at times of patient stress. However, it is difficult to distinguish between primary and secondary infection.

Reactivation of the virus - infection with the same CMV strain previously involved- is diagnosed by positive IgM CMV in the presence of IgG antibodies, reinfection - new aquired infection- refers to the detection of a CMV strain different from the one that caused primary infection, elevated IgM CMV levels or 4-fold increase of IgG titers respectively(14,15,19)

MATERIA AND METHODS

A 41 years old man admitted for palpable, purple lesions localized on legs, bilaterally, symmetrically, lower abdomen, accompanied by leg oedema, 2 days onset. History reveals splenectomy(1975), chronic C hepatitis(2009). In general clinical examination we find oral mucosa aphthae, hepatomegaly. Alcohol abuse is denied. Primary dermatological diagnosis is cutaneous vasculitis.



RESULTS AND DISCUSSION

Leucocytosis, lymphocytosis, inflammatory syndrome, hepatocytolysis, elevated GGT, hyperbilirubinemia. Peripheral blood smear: atypical lymphocytes, with nuclear inclusions (mononucleosis syndrome). IgM and IgG for EBV- nonreactive, serum testing for HIV antibody – negative, Anti-Toxoplasma immunoglobulin G (IgG) titres negative, IgG CMV-5 folds the normal levels, IgM CMV nonreactive. Rheumatoid Factor-negative, negative cryoglobulins. Negative pharyngeal exudate, normal levels for ASLO. ANA, ANCA negative.

Abdominal ultrasound examination reveals fibrotic liver for chronic hepatitis, no signs for hepatocelular carcinoma, hepatic hilar lymphadenopathy-inflammatory .

Platelet count is mandatory for differential diagnosis of purple lesions in a splenectomised patient. Normal platelet count excludes thrombocytopenic purpura secondary to splenectomy. Presence of palpable purpura in a patient with chronic C hepatitis offers multiple differential diagnosis, leukocytoclastic vasculitis (LCV) first of all. Hepatitis type C is a commonly recognized cause of LCV, likely through the presence of cryoglobulins. Leukocytoclastic vasculitis is a necrotizing small vessel vasculitis of the skin , kidneys, joints,

and eyes. Disorders of this type belong to a group termed mixed cryoglobulinemia syndrome. These disorders display palpable purpura of the legs (which is worse distally and inferiorly), livido reticularis, ulcerations, urticaria, symmetric polyarthritis, myalgias, cutis marmorata, and fatigue(1).

Medication intake: antibiotics - particularly beta-lactam drugs, nonsteroidal anti-inflammatory drugs, diuretics may be implied in etiology of vasculitis, as well as upper respiratory tract infections -particularly with beta-hemolytic streptococci, HIV infection, bacterial endocarditis, enteroviruses.

Rheumatoid Factor negative, negative cryoglobulins – exclude leukocytoclastic vasculitis in active hepatitis type C, negative HIV excludes HIV infection as potential etiological factor for vasculitis, negative pharyngeal exudate asociated to normal levels for ASLO excludes beta-hemolytic streptococcal upper respiratory tract infection, no new medication intake from those involved were detected.

Regarding hepatocitolysis, autoimmune hepatitis might be another possibility. ANA, ANCA negative – exclude autoimmune hepatitis(6). Existence of oral aphthous lesions, no genital ones exclude Behcet Disease. Co-existence of oral aphthous lesions and ulcerations with palpable purple lesions imposes another possible diagnosis: Cytomegalovirus infection.

This supposition is sustained by clinical signs, as well as lab signs, atypical lymphocytes, with nuclear inclusions. Mononucleosis syndrome may be also caused by Epstein-Barr virus (EBV) infection IgM and IgG for EBV- nonreactive, primary toxoplasmosis (Anti-Toxoplasma immunoglobulin G (IgG) titres negative), or acute HIV seroconversion(11). - testing for HIV antibody – negative. 5- fold increase in IgG CMV titres demonstrates recent CMV infection, a reinfection.

CONCLUSIONS

Final diagnosis is active chronic hepatitis type C, activation produced by reinfection with CMV in a patient with low immunity secondary to splenectomy, chronic VHC infection. CMV infection is sustained by purple lesions, oral aphthae and ulcerations, mononucleosis syndrome, lymphocytes with nuclear inclusions, inflammatory syndrome, hepatitis, inflammatory lymphadenopathy, reactive IgG CMV - . 5- fold increase in IgG CMV titers.

We did find interesting this case for the complexity of diagnosis as well as for underlying that monitoring the dynamics of the level of CMV IgG antibodies is an important means of detecting acute CMV infection besides determination of CMV IgM antibodies, meaning a reinfection and it requires the establishment of specific antiviral therapy.

We consider necessary monitoring CMV IgG in immunosuppressed patients.

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