Case 3

A 25-year-old Thai homosexual man from Bangkok

Chief complaint: chronic dermatomal eruption on anterior and posterior chest for three months

Present illness: Known case AIDS since 2547 with CMV retinitis leading to blindness. He was admitted due to pulmonary PCP with hypoxemia. The eruption initially appeared as vesicles and developed into thick crust which was treated twice with an oral acyclovir 5 times a day approximately 7-10 days on each monthly interval. The lesions seemed to be recalcitrant although asymptomatic. The CMV viral load was extremely high (> 100,000 copies/ml). Therefore, further investigation to exclude systemic CMV was recommended. Bone marrow study was negative. Meanwhile, abnormal liver function test was kept on rising, although upper abdominal ultrasound was not contributory. The liver biopsy was consequentially performed. Unfortunately, he experienced massive postoperative intraabdominal bleeding. This resulted in cardiac arrests and his death afterwards.

Skin examination: multiple discrete dark brown hyperkeratotic, slightly verrucous and crusted papules arranged along left dermatome of T1 and T2 with some area of hypopigmented atrophic scars

Investigation:

CMV insitu hybridization on skin tissue: positive

CD4 level: 3% (19 cells)

CMV viral load (EDTA-blood): > 100,000 Copies/ml

Tzanck smear: positive

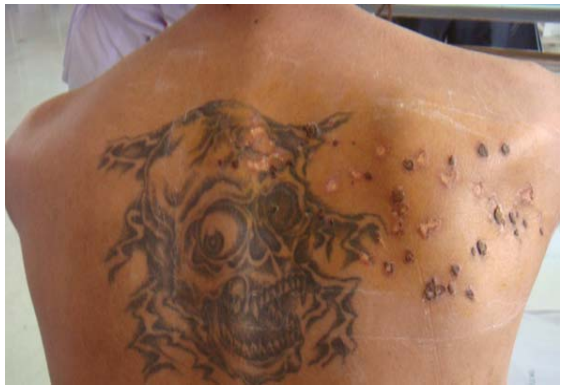
Polymerase Chain Reaction (PCR) on skin tissue: presence of Varicellar zoster virus (VZV).

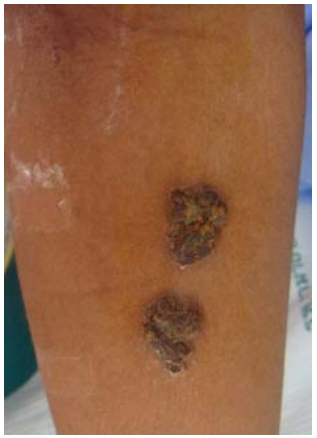
Histopathology (S11-08572)

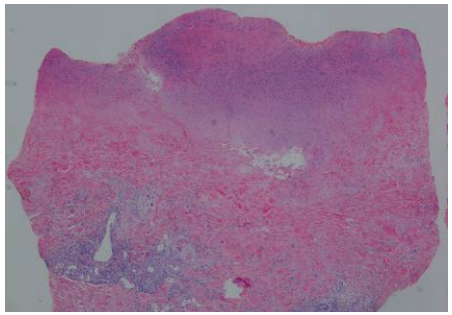
Necrotic ulcer composed necrotic tissues of the upper dermis

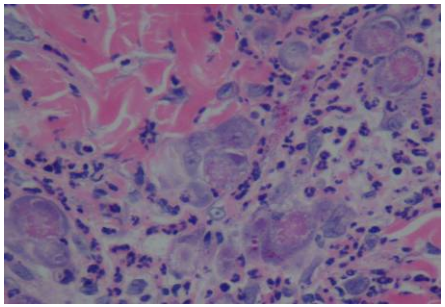
Deep to the ulcer, moderately dense inflammatory-cell infiltrate of neutrophils and multiple large purplish intranuclear and intercytoplasmic inclusions within endothelial cells and histiocytes, which positively stain for cytomegalovirus (immunohistochemistry)

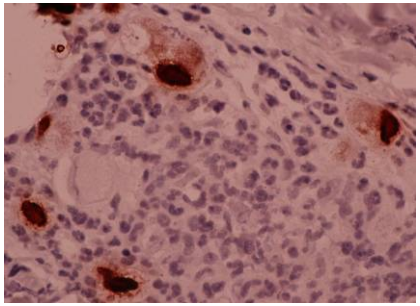
Cluster of large pale keratinocytes and pale vesicular nuclei and necrotic cells, within eccrine sweat glands











Diagnosis: Chronic herpes zoster with concurrent CMV infection
Treatment: intravenous Acyclovir for one week with minimal improvement
Presenter: Marinya Pongpudpunth
Consultant: Ploysyne Rattanakemakorn
Discussion:

Human cytomegalovirus (CMV) is a b-herpesvirus and ubiquitous member of the herpes family of viruses, which also includes herpes simplex virus, varicella-zoster virus, human herpes virus 6 (HHV-6) and Epstein–Barr virus (EBV). More than 80% of healthy adults are CMV seropositive, indicating previous exposure. CMV has recently become as important as an opportunisticinfections in immunosuppressive conditions. After primary infection, CMV, like other herpes viruses, undergoes latency and persistence in the infected individual. The mechanism of reactivation is still unknown. Although primary infections or reactivation of CMV usually remain either subclinical or self-limiting in immunocompetent individuals but in immunocompromised patients, this virus is a major cause of morbidity and mortality especially in acquired immunodeficiency syndrome (AIDS), organ transplant recipients and in those receiving immunosuppressive therapy.[1,2]

Isolated cutaneous CMV disease in immunocompromised patients are rare compared with involvement of other organs. Perianal and rectal ulceration are most common manifestration including indurated hyperpigmented nodules or plaques, papular and purpuric eruptions, vesiculobullous lesions, purpura, petechiae, indurated plaques, and nodules.[3] Cutaneous manifestations of CMV infection are not sufficiently distinctive to diagnoses by clinical findings alone. The diagnosis of cutaneous CMV infection has usually been established by microscopic examinations. Cytomegalic inclusions, CMV antigens, or CMV-DNA detected in skin biopsy specimens have been considered as significant clues to diagnose cutaneous CMV infection. However, it is still controversial whether CMV detected in skin biopsy specimens is responsible for the pathogenesis of cutaneous manifestations, because the characteristic cytomegalic cells from uninvolved skin in AIDS patients have been detected. [4,5]

The coexisting finding of CMV and HSV in mucocutaneous lesion of HIV infected individuals has been rarely reported. [6-9] Most cases presented with mucocutaneous ulcers resembling common herpes infection. Daude´n E, et al[10]published the largest series of coexistence of these viruses in mucocutaneous lesion of 17 AIDs patients (most of the cases with CD4 count less than 100 cells/μL). Most of the patients have perianal and perigenital ulcers. There were 2/17 having disseminated herpes zoster. Most of the cutaneous lesions disappeared after being treated with acyclovir without gancyclovir administration, although some of these cases have other CMV associated organ involvement. Subsequently, CMV particles were found on normal skin (forearm) of these patients even in normal distant area. They concluded that Cytomegalovirus does not play any significant pathogenetic role in cutaneous lesions. Accordingly, we performed normal skin biopsy on forearms which show the absence of CMV bodies. So far, there were very unusual to find concurrent CMV inclusions in a typical herpes zoster lesion like our case. This accidental histologic finding of CMV inclusions in ours raised the suspicion whether these CMV was pathogenic, especially in the setting of a severe compromised host. CMV viral load test shows excessively high titer. There are evidences regarding an association between a high systemic CMV

load and CMV disease in HIV-infected individuals. The CMV viral load is a predictor for the development of CMV disease and response to treatment, also high CMV load is an independent predictor of poor survival in most studies.[10,11] In contrary to previous reports, in our case, due to the high number of CMV particles and high titer of serum CMV viral load, in addition to severe immunocompromised status with previous history of CMV infection, these may be the warning sign for reactivating systemic CMV infection in other organs. In conclusion, we recommend further investigation in appropriate clinical settings with severely immunocompromised host to exclude other lethally associated organ involvement in order to provide early treatment and better outcome.

Reference

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