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Case Report

Fulminant VZV infection in an adult AIDS patient treated with steroids: A case report

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ABSTRACT

Varicella zoster virus (VZV) typically causes a benign disease in childhood. However, VZV can lead to severe complication in immunocompromised patients, involving skin and nearly every organ system, with significant morbidity and mortality. VZV infection occurs more frequently in patients treated with steroids.

Herein, we describe a case of rapidly fatal disseminated VZV infection with cutaneous and visceral involvement in an adult AIDS patient treated with steroids.

1. Why this case is important

Herein we discuss a case of fulminant infection with cutaneous and visceral involvement in an AIDS patient treated with corticosteroids.

Our patient, treated with methylprednisolone along with trimethoprim–sulfamethoxazole for *Pneumocystis jirovecii* pneumonia (PJP) in a newly diagnosed HIV infection, rapidly succumbed for disseminated VZV infection, with cutaneous, pulmonary and gastrointestinal involvement.

Both immunosuppression and steroid therapy represent major risk factors for the development of VZV infection and their interaction might lead to the severe clinical picture observed, with rapidly progressive disease and death.

Therefore, immunosuppressed patients with clinical suspicion of VZV disease should promptly start antiviral treatment against VZV in order to prevent a fatal outcome. Even antiretroviral therapy should be started early, according with international guidelines addressing treatment of opportunistic infection in HIV patients [1].

2. Case description

On March 2012, an Asian 43-year-old man complaining with high fever, cough and shortness of breath, was admitted to our Hospital.

He had no significant individual or familiar medical history, neither reported drugs or alcohol abuse. He reported unprotected homosexual intercourses.

On admission the clinical condition was poor. The body temperature was 39 °C, with a pulse rate of 180 beats/min, and a respiratory rate of 44 breaths/min. The physical examination revealed oropharyngeal candidiasis and a harsher vesicular breath sound on auscultation.

Blood examination showed 17,700 white blood cells (WBC)/μl (neutrophils 95%, lymphocytes 3.4%, monocytes 1.1%), hemoglobin 9.1 g/dl, C-reactive protein (CRP) 2 mg/dl, fibrinogen 449.9 mg/dl, gamma glutamil transferases (gamma GT) 73 mU/ml, lactate dehydrogenase (LDH) 718 U/l. Other blood exams were in the normal range.

HIV 1–2 antibodies/antigen assay was positive with a plasmatic viral load of 599,385 copies/ml. CD4 cell count was 29 cells/cmm (3.5%) and CD8 cells were 337/cmm (49.5%).

Serology for Toxoplasma, Cytomegalovirus (CMV) and Epstein Barr Virus (EBV) showed past infection.

Syphilis serology was negative.

Blood gas analysis on oxygen therapy showed hypoxemia (pO_2 77 mmHg with 100% oxygen supply).

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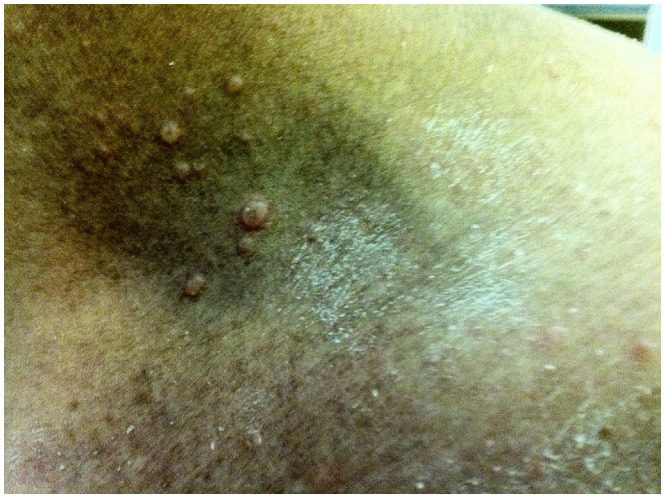

Fig. 1. Cutaneous eruption.

Chest CT scan showed bilateral diffuse interstitial pulmonary infiltrates, suggestive for PJP and treatment with trimethoprim–sulfamethoxazole (15 mg/kg/die of trimethoprim every 8 h) and methylprednisolone (80 mg every 12 h) was promptly started.

Urinary antigens for *Legionella* and *Streptococcus pneumoniae* were negative.

In a week of treatment the clinical condition improved with reduction of dyspnea and fever. The blood gas analysis parameters gradually improved and the oxygen supply was reduced to 50%. Methylprednisolone dosage was tapered to 40 mg twice a day and then further reduced to 20 mg twice a day.

Antiretroviral treatment with Atazanavir, Ritonavir and Tenofovir-emtricitabine was started after two weeks from the beginning of PJP therapy.

After three weeks of treatment with sulfamethoxazole–trimethoprim, a cutaneous eruption of little papular/vesicular umbilicated lesions was noticed on the neck and legs (Fig. 1). In one day these lesions, with the same features, extended to the trunk and the face. Serology for Varicella Zoster Virus (VZV), Herpes simplex virus (HSV) 1–2, and cryptococcus antigen on blood was performed. Viral swabs for polymerase chain reaction (PCR) for VZV, Poxvirus and HSV on vesicular fluid were performed.

On the next day the clinical condition worsened quickly for the appearance of diffuse abdominal pain, tachycardia (150 beats/min), dyspnea (respiratory rate of 32 breaths/min) and general malaise. The physical examination revealed diffuse crackles on lung auscultation, tender abdomen with epigastric pain, and widespread of the vesicular lesions throughout the body, including ulcerative lesion of oral cavity.

Laboratory tests revealed: WBC 16,600/μl (neutrophils 91%, lymphocytes 5.8%, monocytes 0.8%), ALT 48 UI/l, AST 68 UI/l, gamma glutamine transpeptidase (γGT) 56 U/l, alkaline phosphatasis 134 (U/l); amylasis 293 (mU/ml), lipasis 103 (UI/l).

A lung CT scan performed in the same day showed a radiological picture compatible with Acute Respiratory Distress Syndrome (ARDS).

Empiric treatment with meropenem and vancomycin was started and the methylprednisolone dosage was further lowered at 20 mg/day. High doses of oxygen therapy were administered. Intravenous acyclovir (10 mg/kg three times a day) was started in the suspect of disseminated infection due to VZV. However, on the same day the patient died.

Serology for HSV and PCR for HSV 1–2 on the vesicular lesions were negative. Serology for VZV showed positive IgG and negative IgM. PCR for VZV performed on the vesicular lesions was positive.

3. Post-mortem examination

A full postmortem examination including neuropathological examination was carried out.

The macroscopic examination showed disseminated clear small vesicles throughout the body and some pustules on the face.

Tissue samples were taken from all organs. Histological examination of the cutaneous lesions and esophagus revealed pseudoepitheliomatous hyperplasia and cytopathic effects in infected epidermal cells, such as multinucleated giant cells (Tzanck cells), eosinophilic intranuclear inclusions and ballooning degeneration (Fig. 2a).

Mild neutrophilic/lymphocytic inflammatory infiltrate underlied the lesions. The Immunohistochemistry (IHC) showed a positive signal for polyclonal antibodies anti-HSV 1 and 2 (Cell Marque, Rocklin, USA), that cross react with VZV antigens (Fig. 2b). Polymerase Chain Reaction was performed to specify the etiological agent, resulting positive for VZV. Multiple areas of consolidation with poorly defined necrotizing nodular lesions were present in the lungs. Necrotizing pneumonia with karyorrhectic neutrophils was associated to features of diffuse alveolar damage consisting with hyaline membranes, interstitial edema and pneumocyte hyperplasia. Abundant fibrin, cellular debris and acute inflammation were noted within the necrotic areas. Viable lung parenchyma cells, alveolar lining cells and alveolar macrophages revealed intranuclear viral inclusions (Cowdry type A) (Fig. 2c). Multinucleated giant cells with eosinophilic nuclear inclusions were also seen.

Alveolar froth containing pneumocystis outlined by GMS stain (Fig. 2e, f) was observed, too.

Liver was enlarged and mottled; microscopical examination showed multiple areas of coagulative necrosis without an inflammatory response (Fig. 2a). No ground-glass hepatocytes were seen on light microscopy or with immunohistochemistry.

Samples from skin, lung, esophagus and liver were all VZV positive by PCR.

Brain parenchyma showed scanty inflammation with perivascular lymphocyte cuffing without evidence of HSV or VZV encephalitis.

4. Other similar and contrasting cases in the literature and discussion

Infection with Varicella Zoster virus (VZV) is usually considered a benign infection, however severe complications can occur with fatal or long term disabling outcome, even in normal hosts [2].

VZV infection in immunosuppressed patients may affect nearly every organ system, with significant morbidity and mortality. The visceral disease may occur concurrently or after the skin involvement, although sometimes it may precede cutaneous manifestations or develop without any skin lesions [2–4]. Various organ involvement were described in the literature, including liver, lung, stomach, and esophagus [2,4,5].

Adjunctive corticosteroid to the standard treatment for PJP is recommended, in order to prevent the worsening of respiratory function and to decrease mortality in such patients [6].

High dose or prolonged corticosteroid therapy variously affects the host immunity. Patients treated with steroid are at substantially increased risk for developing disseminated varicella. Dowell and Bresee showed that patients treated with steroid have a 178 fold greater risk for developing varicella complications compared with untreated patients [7].