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Case report

A rare case of AIDS co-infected with COVID-19 presenting with disseminated Herpes Zoster complicated with CMV and Varicella Zoster virus Meningoencephalitis

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Abstract. During the COVID-19 pandemic, numerous co-infections have been reported, with some studies indicating that patients with HIV/AIDS have worse outcomes when co-infected with COVID-19. Here, we present the case of a young adult male who presented with disseminated Varicella and was simultaneously diagnosed with AIDS and COVID-19 virus with several infection-related complications. A 25-year-old African-American male presented to the Emergency Department with vesicular, blistering rashes in multiple dermatomes including his eyelids. The screening test in the ED was positive for COVID-19. Given his high-risk sexual history, he was tested for HIV which returned positive with a CD4 count of zero. He was started on IV antivirals for disseminated varicella with zoster ophthalmicus. The patient was intubated for worsening respiratory failure and required intensive care. During the hospital course, he developed worsening encephalopathy and CSF analysis was positive for CMV and VZV. The patient had a prolonged hospital stay and exhibited evidence of infectious CNS vasculitis and HIV myelopathy. Anti-retroviral therapy was started after the acute period and the patient showed slow but definite clinical improvement. To the best of our knowledge, this is the first case report of a patient with AIDS with COVID-19 and disseminated VZV and with multiple complex infection-related complications (www.actabiomedica.it)

Key words: COVID-19, Disseminated Varicella, HIV, CMV meningitis, CMV vasculitis, Varicella meningitis

Introduction

Since the beginning of the COVID-19 pandemic, there have been 525 million infections and 6.2 million deaths as of May 2022 (1). There have been many reports describing various concomitant infections in patients with COVID-19. COVID-19 and its treatment(s) are associated with higher risks for other infections including varicella-zoster virus (VZV) infection (2).

HIV/AIDS continues to be a pandemic and the continuity of both HIV and COVID-19 pandemics has taken a serious toll on the global public health (3). Several studies also demonstrate that people living with HIV have an increased risk of dying from COVID-19 and/or related complications (4).

We report a challenging case of an adult male patient who was diagnosed with concomitant infection with HIV, SARS.CoV2, VZV, and Cytomegalovirus (CMV) exhibiting different infection-related complications.

Case report

The patient is a 25-year-old male with a past medical history of asthma and childhood chickenpox who presented with maculopapular rashes in the arms,

legs, and face. He also reported a 3-day history of diaphoresis, dizziness, loose stools, and loss of taste sensation. In the ED, he tested positive for COVID-19. Due to high-risk sexual history, he was also tested for HIV which returned positive. With the new diagnosis of HIV, COVID-19, and the rash, he was admitted to the hospitalist service, and infectious disease was consulted.

In the hospital, HIV RNA was detected at 999,908 viral copies/mL and a CD4 count of zero. On further examination, it was also noted that the patient has vesicular lesions on different parts of his body (Fig. 1), including his eyelids, and it was difficult to fully open his eye due to the swelling (Fig. 1 E). Disseminated Varicella Zoster with zoster ophthalmicus was suspected. A punch biopsy of the skin lesion was obtained and Tzanck smeared to confirm the lesions were herpetic in nature. Tzanck smear showed intracorneal necrosis and debris with viral cytopathic effect. Intravenous acyclovir 10mg/kg every 8 hours was started for disseminated Varicella-Zoster and ophthalmology was consulted. Eye examination revealed ocular involvement with a hazy cornea (keratitis), elevated intraocular pressure (HZO glaucoma), and intraocular inflammation (uveitis). The ophthalmologist started polysporin brimonidine, cyclopentolate, and latanoprost eye drops for zoster ophthalmicus.

The patient had ongoing oxygen requirements on the floor. A chest X-Ray showed infiltrates concerning for COVID-19 pneumonia. He was started on dexamethasone and baricitinib. Infectious disease recommended postponing the initiation of antiretroviral therapy (ART) at that stage and treating acute COVID-19 first. He was started on Mycobacterium avium and PJP prophylaxis with azithromycin 1200mg weekly and trimethoprim-sulfamethoxazole, respectively.

During the hospital stay, the patient had an unwitnessed fall and was found to be confused. A head CT demonstrated left-sided subdural hematoma measuring up to 3 mm in thickness with mild mass effect in the left cerebral hemisphere and a remote left parietal infarction. Neurosurgery was consulted and recommended withholding surgical intervention at that time. The patient had progressive worsening hypoxia and had a sudden increase in O_2 supplementation, with his O_2 requirement going from nasal cannula to a non-rebreather and Optiflow in a few minutes. He was intubated and transferred to the intensive care unit (ICU) where he required mechanical ventilation and vasopressor support. Echocardiography demonstrated a hyperdynamic left ventricle with an ejection fraction of 70% and an elevated right ventricular systolic pressure at 65-70 mm Hg. A CT angiogram chest showed multifocal pulmonary emboli with a significant embolic burden and evidence of right heart strain. The CTA chest also reported patchy and nodular parenchymal opacities along with focal parenchymal nodularity concerning for possible infectious and/or inflammatory sequela. Initially, anticoagulation was held due to the presence of subdural hematomas. However, following further discussion with neurosurgery, intravenous heparin was cautiously started. Given the patients massive pulmonary embolism, the benefits outweighed the risks. The patient's subdural hematoma was monitored with serial head CTs while he was on intravenous heparin, and it remained stable. In the ICU, the patient became febrile and tachycardic. Pan-cultures were obtained, and the patient was empirically started on vancomycin and piperacillin-tazobactam. A lumbar puncture was considered but was not done at this time due to low platelets. At this time, he was started on highly active antiretroviral therapy (HAART) with Biktarvy (bictegravir/emtricitabine/tenofovir alafenamide) by infectious disease. Antibiotics were discontinued after 2 days as cultures did not show any bacterial growth. He self-extubated during a coughing episode after 10 days of intubation.

He was later transferred to the intermediate unit as his respiratory status remained stable on oxygen via nasal cannula. Two days later, the patient was noted to have worsening encephalopathy with fever, tachycardia, and tachypnea. There was a concern for IRIS (immune reconstitution inflammatory syndrome. Repeat cultures were sent and the patient was started on vancomycin and piperacillin-tazobactum. Procalcitonin was low at 0.08 and the chest x-ray was clear making IRIS less likely.

A repeat head CT was suggestive of an interval increase in his SDH with increased midline shift. Neurosurgery was consulted and recommendations were made to take the patient to the OR for burr hole

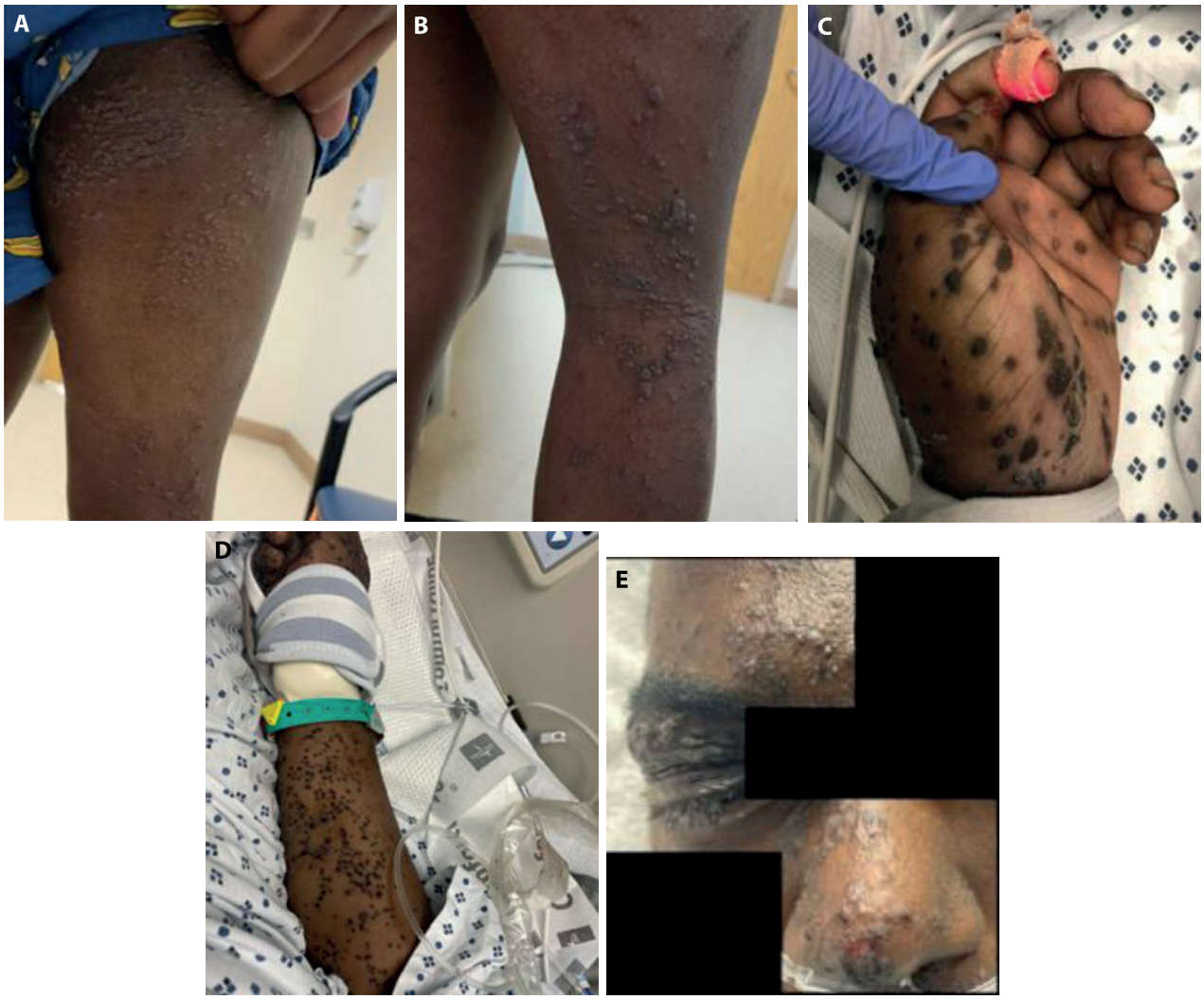

Figure 1. Maculopapular rash and crusted vesicular rashes involving multiple dermatomes (A-E). Vesicular rash involving V1 dermatome, with ptosis indicating zoster ophthalmicus. Note the Hutchison sign on the nose tip (E).

and SDH evacuation. CSF fluid was obtained during the burr hole procedure. CSF showed pleocytosis with encephalitis panel (AFB, fungal, bacterial, and cryptococcal antigen, viral) positive for both CMV (cytomegalovirus) and VZV. Blood was also positive for both CMV and VZV. Given that the patient had received a prolonged course of acyclovir, treatment was switched to intravenous ganciclovir (5 mg/kg IV every 12 hours), which covers both CMV and VZV. A follow-up CTA head showed multifocal irregularity and narrowing of bilateral MCA, ACA, and PCA branches including the distal right M1 and distal right A1 segments (Fig 2), consistent with vasculitis which can be seen in both VZV and CMV. Intravenous methylprednisolone was started at 1 gram daily for 5 days to treat the CNS vasculitis. For CMV CNS disease there are no clear guidelines on the optimal length of therapy, but infectious disease recommended 2 weeks of intravenous ganciclovir. Repeat LP after 2 weeks showed a drastic drop in CMV.

During the hospitalization, the patient remained paraplegic. Differential diagnoses included critical illness myopathy, VZV/CMV induced myelitis, and HIV myelopathy. Thoracic spine MRI showed multifocal patchy

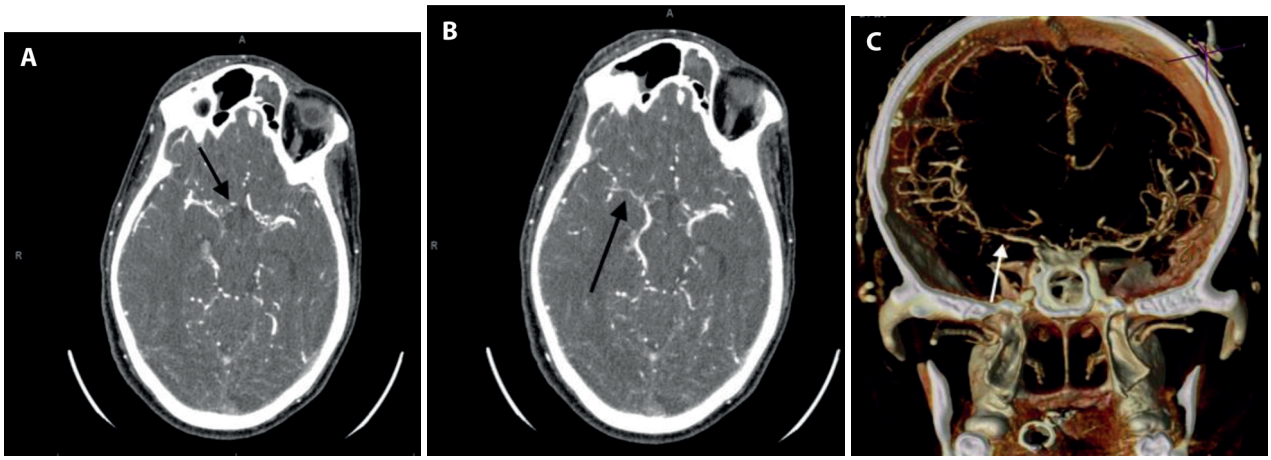

Figure 2. CTA head showing narrowing of ACA (A), and MCA (B); black arrows point to right A1 and distal right M1 segments, concerning for vasculitis. (C) Volume rendered 3-D reformatted image from CTA.

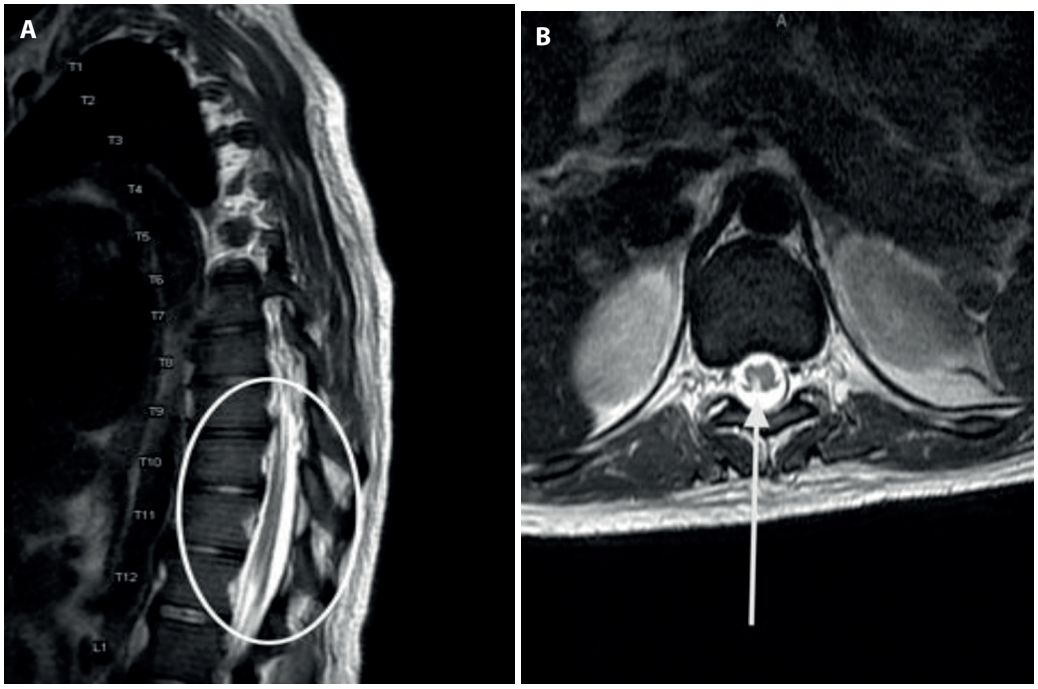

Figure 3. MRI thoracic spine. Multifocal patchy and discontinuous signal abnormality within the thoracic cord: sagittal view (White oval in A) and Transverse View (White Arrow in B). Differential includes HIV vacuolar myelopathy or nonspecific demyelination.

and discontinuous signal abnormalities within the thoracic cord (Fig 3). Similar findings are seen in HIV vacuolar myelopathy and nonspecific demyelination. The patient was transferred to inpatient rehabilitation and he continued to gradually recover his motor activities. His mobility remained impaired and he required assistance with activities of daily living. Three months after initiating HAART, his HIV viral count decreased from 596,000 copies per mL to 124 copies per mL and his CD4 count increased from 0 to 10 cells per cubic mm.

Discussion

In the last two years of the COVID-19 pandemic, several co-infections and superinfections have been observed along with COVID-19. COVID-19 and its treatment(s) have been known to reactivate several latent infections (2). Several studies showed that co-pathogens were encountered in 8% of COVID-19 cases, but Feldman et al commented that this finding is mainly from superinfections in the later stage of COVID-19 rather than initial co-infection (5).

Although theoretically, HIV can increase the risk of contracting SARS□CoV□2, currently there is no specific data about the risk of COVID□19 in people with HIV (6). During the COVID-19 pandemic, screening for HIV and other sexually transmitted infections has decreased (7). From March-September 2020, there were 5000 fewer HIV-1 diagnoses and 700,000 fewer screening HIV Ag/Ab tests sent compared to the same time period in 2019 (7). COVID-19 presents a risk to HIV patients with low CD4+cell counts, high viral load, and other comorbidities. Studies show the COVID-19 incidence in HIV carriers is found to be equal to that in the general population, but the severity of COVID-19 likely increases with lower CD4 levels (8). Some other studies demonstrate that HIV carriers have an increased risk of dying from COVID-19 or related complications (4). Reasons for their increased risk of poor clinical outcomes in HIV and SARS-CoV2 co-infected patients include a weakened immune system, presence of several co-infections, and side effects of ART drugs (9). Other confounding variables must also be considered when analyzing this population. HIV carriers have a higher prevalence of comorbidities including alcohol use, drug use, as well as poor kidney and bone health (10). In addition, HIV has disproportionately affected individuals in minority racial and ethnic groups. The same systemic structures placing these groups at risk also place them at higher risk of infection with COVID-19.

Herpes zoster (HZ), and reactivation of latent VZV infection, occur commonly in HIV-infected patients and sometimes is the initial presentation (11). HZ is now being reported as a co-infection in COVID-19 patients (12-14). However, there are only a few cases of disseminated VZV infection (involving multiple dermatomes) in COVID-19 patients reported so far (15-17).

This is the first-ever case report of co-infection of HIV, SARS-CoV2, CMV and VZV presenting with AIDS, and disseminated VZV. The patient exhibited multiple infection-related complications during his hospitalization course. The patient was found to have CMV and VZV in his blood and CSF and was treated for infectious meningoencephalitis. CMV reactivation has been seen to be associated with COVID-19 (18), (19), although reports of CMV meningoencephalitis in COVID-19 are rare and is limited to only one case report so far (20). VZV and CMV are known to cause infectious CNS vasculitis as seen in this patient (21). The patient was also found to have a pulmonary embolism. Recent studies do report high risks of DVT and PE in COVID-19 patients (22-24). The patient also exhibited possible HIV- associated vacuolar myelopathy, a rare early presentation in AIDS/HIV infection.

The juxtaposition of AIDS, disseminated VZV and COVID-19 in this patient can be hypothesized due to a skewed CD4+ and CD8+ T cell population. HIV is well known to decrease the lymphocyte cell counts of infected individuals. This pattern was also observed in COVID-19, where studies showed lower CD4+ T cells and CD8+ T cells correlate with the severity of COVID-19 (25), (26), (27). An increased incidence of HZ during the COVID-19 pandemic has also been reported (14). A study reported that CD3+ T cells, CD4+ T cells, and CD8+ T cells were significantly lower in the HZ group compared to a healthy group (28). During the COVID-19 pandemic, the number of HZ cases has increased. In a recent review, Algaadi hypothesized that given the lymphopenia associated with COVID-19 infection, which favors VZV reactivation, there may be a causal relationship between COVID-19 and VZV infection (29). Feldman et al noted that additional infections occur in patients with SARS-CoV2 or HIV that are associated with poor outcomes, but it is not always possible to differentiate true co-infections or superinfections (5).

In summary, this is a rare case of SARS-CoV2 co-infection in an AIDS patient, complicated by disseminated VZV and CNS involvement by CMV and VZV. This case emphasizes the importance of continued STI screening and safe sexual practices even as COVID-19

lockdowns and mandates ease. Many of the symptoms associated with HIV also overlap with symptoms of COVID-19. Although COVID-19 presents many challenges and unknowns, we must maintain our clinical suspicion of HIV infection and other co-infections. This case also highlights the medical advancements that have been made in terms of HIV treatment. Thirty years ago, without anti-retroviral therapy, this patient would have died. Although some antiretroviral agents like lopinavir/ritonavir, boosted darunavir, tenofovir disoproxil fumarate/emtricitabine have been tested to treat or prevent COVID-19 in some clinical trials, none were found to be effective (30, 31). Currently, CDC has authorized COVID-19 vaccines in HIV patients with continued intensive safety monitoring.

Ethical Approval: Not applicable.

Conflicts of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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Consent for Participation: All authors consent to publish this manuscript.

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