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Case report

Newly diagnosed AIDS with neurosyphilis, Kaposi sarcoma, pancytopenia, oropharyngeal candidiasis, and pseudomonal pneumonia: We shouldn't be seeing this anymore

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ABSTRACT

The incidence of new human immunodeficiency virus (HIV) infections is declining and is half of what it was in the mid 1990s. We present a case of newly diagnosed HIV with acquired immune deficiency syndrome (AIDS), Neurosyphilis, Kaposi Sarcoma, and multiple opportunistic infections. Although this type of patient was not uncommon in the pre-antiretroviral era, we do not often see such a constellation of conditions in a single individual. The significance of this case lies not in the diagnosis, but rather in the number of the diagnoses and the thought process used to attain them.

Introduction

The incidence of new human immunodeficiency virus (HIV) infections is declining and is half of what it was in the mid 1990s [1]. Similarly, syphilis had been steadily decreasing, reaching its lowest point around 2000, but has been increasing in incidence since. Men who have sex with men accounted for 80.6% of all primary and secondary syphilis cases in 2016, and almost half were co-infected with HIV [2]. Data on 3° syphilis in HIV infected patients are not nationally collected or reported in the U.S.

We present a case of a 62-year-old man with newly diagnosed HIV with acquired immune deficiency syndrome (AIDS), neurosyphilis, Kaposi sarcoma and multiple opportunistic infections. Although this type of patient was not uncommon in the pre-antiretroviral era, we do not often see such a constellation of conditions in a single individual. We review the numerous differential diagnoses for each of our patient's problems.

Case presentation

A 62-year-old male with no known medical history was brought to our hospital after having been found by his coworkers on the floor at work earlier that morning. The patient had no recollection of falling, was confused, and was unable to recognize his coworkers. He only complained of new right shoulder pain. The patient worked in a telemarketing office. He became homeless 1 year previously, sleeping at work intermittently or staying with friends. The patient occasionally used marijuana, and did not smoke cigarettes, use injected drugs or drink alcohol. The patient was bisexual with his last sexual encounter 2 years previously.

The patient presented with subjective fevers, loss of appetite with significant weight loss, and fatigue for the previous few months. He noted a flaky full, body rash, episodic dizziness, confusion, worsening vision and frequent falls. He also had non-productive cough, episodic diarrhea and urinary incontinence for several months.

In the Emergency Department, the temperature was 101.9° F, and heart rate was 106 beats per minute. Physical examination revealed a cachectic man with depressed affect. The patient had areas of dry scaly skin on the head, trunk, and extremities. There were multiple violaceous papules of the extremities and trunk (Fig. 1). Oral examination revealed poor dentition and oral thrush.

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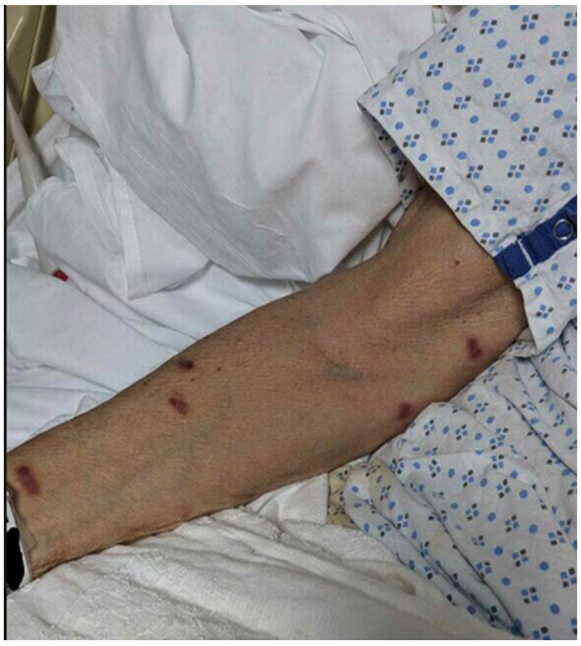

Fig. 1. Skin lesions.

There were rales on auscultation of the right lung. Cardiovascular and abdominal examinations were unremarkable. There was mild edema of the bilateral lower extremities and pain and limitation to range of motion of the right shoulder.

The leukocyte count was 2600 u L, hemoglobin 10.6 gm/dL, and international normalized ratio was 1.4. Venous blood gas showed pH 7.464 and lactic acid 1.9 mmol/L. Creatine kinase -MB was 2726 IU/L. Liver function tests showed an albumin of 2.7 g/dL, direct bilirubin of 0.5 mg/dL, aspartate aminotransferase of 88 IU/L and alkaline phosphatase of 883 IU/L. HIV-1/2 EIA was reactive. Radiograph of the right shoulder showed a non-displaced midshaft fracture of the right clavicle. Chest radiograph (CXR) revealed a right middle lobe pneumonia. Computed tomography (CT) of the head showed no mass, acute hemorrhage or acute infarct. Treatment with ceftriaxone and azithromycin was begun.

An ophthalmology examination was negative for retinitis but revealed bilateral cataracts. A punch biopsy was performed of the skin lesions, which confirmed Kaposi sarcoma. A peripheral smear showed dysplastic neutrophils and toxic granulation. The red blood cells had poikilocytosis and there were rare schistocytes seen. The platelet count was adequate. CT scan of the chest/abdomen/pelvis with IV contrast showed moderate consolidation in right middle and upper lobes. There were faint ground glass densities in the left upper lobe as well as mild emphysematous changes throughout (Fig. 2). The scan also showed a moderate-sized multi-loculated right distal perirectal and proximal right perianal abscess with rim enhancement. The abscess was drained, and cultures grew *Pseudomonas aeruginosa* and *Escherichia coli*.

Bronchoscopy performed on hospital day 5 showed oropharyngeal candidiasis and thick viscous secretions in right middle and lower lobe. IV fluconazole was started. The bronchial washings were negative for malignant cells or acid-fast bacilli (AFB). Respiratory culture and smear grew Pseudomonas aeruginosa. Urine chlamydia and gonorrhea were both not detected, cytomegalovirus (CMV) IgM antibody was negative and QuantiFeron TB Gold (QIAGEN, Hilden, Germany) was also negative. The HIV viral load was 551,166 copies/mL, the absolute CD4 count was 6 cells/mcL and the CD4 percentage was 2%. Syphilis antibody was positive. Reflex rapid plasma reagin (RPR) was reactive, and the titer was 1:32. Lumbar puncture (LP) was performed on hospital day 8 and cerebrospinal fluid (CSF) venereal disease research laboratory (VDRL) was positive. The cell count was normal, protein was 72 mg/dL, glucose was 50 mg/dL and Cryptococcal antigen was negative. Intravenous penicillin G was started, as was antiretroviral therapy (ART) with tenofovir/emtricitabine and dolutegravir. On hospital day 9, bone marrow biopsy was performed. Core biopsy sections were normocellular with normal appearing hematopoiesis. AFB and Gomori-Grocott methenamine silver stains showed no organisms. Immunohistochemical stains showed almost exclusively T-cells (CD3+) and rare B-cells (CD20+).

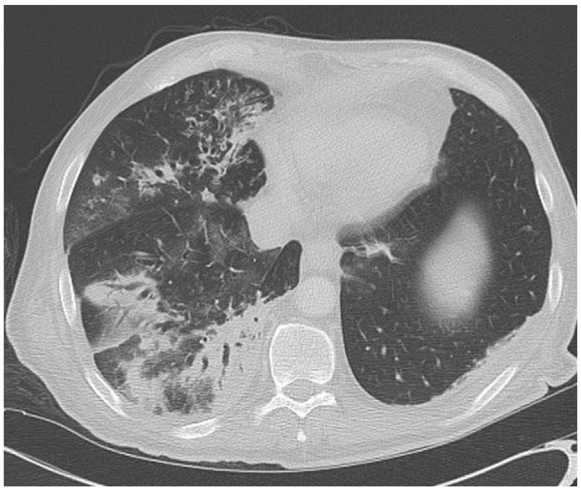

Fig. 2. CT showing right sided pneumonia.

The patient was discharged on hospital day 32 on the following oral medications; trimethoprim/sulfamethoxazole for PJP primary prophylaxis and antiretroviral therapy.

Discussion

AIDS is defined as HIV infection with a CD4 cell count of <200 cells/mcL or the presence of AIDS defining conditions [1]. There are many well recognized opportunistic infections in patients with AIDS. Our patient presented with multiple opportunistic diseases.

Cutaneous lesions: Kaposi sarcoma vs. bacillary angiomatosis

Kaposi sarcoma is the most common neoplasm associated with HIV infection [3]. It is a vascular tumor involving blood vessels, which can affect the skin, lymph nodes and visceral organs. Its incidence has steadily decreased since the 1990s with the widespread use of antiretroviral therapy [4]. Our patient presented with numerous non-blanching purple skin lesions on the upper and lower extremities. Skin biopsy confirmed Kaposi sarcoma. HIV therapy was initiated and the patient responded well to treatment with crusting and fading of all lesions within 3 weeks. Treatment beyond HIV with chemotherapy is chosen based on various criteria, including the extent of the disease, rapidity of growth, HIV viral load and CD4 count [5].

In the setting of immunocompromise, bacillary angiomatosis should be excluded as the treatment differs from that of Kaposi sarcoma. Bacillary angiomatosis is caused by the rickettsial organism

Bartonella henselae, also the cause of “Cat Scratch Disease” [6]. It usually presents in either papular or nodular forms. Lesions appear as small red/purple papules that can expand into large pedunculated lesions that may have a vascular appearance [7]. These lesions can be easily differentiated from Kaposi sarcoma based on the histology seen on skin biopsy. Bacillary angiomatosis histology

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shows lobular vascular proliferation surrounded by endothelial cells. Warthin-Starry silver stain can reveal the Bartonella organisms [8]. At least 3 months of treatment with doxycycline or azithromycin is sufficient in treating this infection although other regiments can also be used. If a patient has already been treated but has a relapse, another 3 month course of the same therapy is required. Suppressive therapy can be discontinued after at least 3 months of treatment and the patient's CD4 count over 200 cells/mcL for at least 6 months' time [9]. Kaposi sarcoma has many histologic variants. There is prominent spindle cell proliferation and characteristic scattering of plasma cells and numerous lymphocytes. There may be hyaline globules present intra and extra cellularly, which stain positive with Periodic acid-Schiff stain [8].

Neurocognitive disorders: HIV associated dementia vs. neurosyphilis

Changes in memory, concentration and motor skills are common in advanced HIV-infected patients. HIV-associated dementia is characterized by subcortical dysfunction, attention-concentration impairment, depressive symptoms, and impaired psychomotor symptoms [10].

Cognitive decline in AIDS can also be attributed to central nervous system malignancies, infections such as toxoplasmosis or cryptococcosis, progressive multifocal leukoencephalopathy or nutritional deficiencies. In our case, neurosyphilis was likely to have compounded the patient's cognitive and motor deficits. Bacillary angiomatosis has also been implicated as a treatable cause of neurocognitive decline in HIV.

The association between syphilis and HIV has been well documented. Several studies have described the effect of syphilis, particularly on HIV infected patients. There are known to be transient increases in the viral load and decreases in CD4 cell count. However, the overall course of HIV progression or the risk for syphilis transmission are unknown. Studies have shown variable response of neurosyphilis to penicillin treatment. A case study by Muneoka et al. noted significant improvement in visual cognition, and long-term memory [11]. There was, however a worsening of working memory. It was thought that the improvement in cognition was associated with resolution of the encephalitis as evidenced by improvement on EEG [11]. On the other hand, worsening of cognition was thought to be related to dysfunction in the temporofrontal lobe seen on MRI [11]. Other MRI findings of neurosyphilis may include atrophy, changes in white matter, and localized lesions [12]. Hearing impairment may also be caused by neurosyphilis. Hearing loss can be unilateral or bilateral and either sudden in onset, progressive or fluctuating. The patient may also experience vertigo or loss of balance [13]. Ocular syphilis can also be a manifestation of neurosyphilis. The Centers for Disease Control and Prevention recommends that any patient found to have ocular syphilis have an LP [14].

It is difficult to determine if our patient's neuro-cognitive decline was secondary to the neurosyphilis or secondary to the advanced HIV [15]. Although there is a significant decrease in cases of neurosyphilis, it is important to screen for it especially in HIV infected patients, due to the clinical and public health implications.

Pneumonia: TB vs. PJP vs. Pulmonary Kaposi sarcoma vs. Bacterial pneumonia

Our patient presented with cough, fever, and radiologic evidence of pneumonia. Due to severe immunosuppression, TB had to be excluded because as immunity declines, the cavitation is less likely to be appreciated. As CD4 counts drop below 200 cells/mcL, CXR findings may be atypical, with interstitial infiltrates, and diffuse or mild and lower lung involvement which is unlike the classic upper lobe involvement in TB [16].

PJP, caused by the fungus *Pneumocystis jirovecii*, is an AIDS defining illness that most often occurs in patients with CD4 counts <200 cells/mcL. The onset of this infection in HIV infected patients is indolent. Hypoxemia may be pronounced. Bilateral interstitial and alveolar infiltrates can be seen on radiographs, with CT scan showing ground glass opacities [17]. Diagnosis generally requires bronchoalveolar lavage (BAL).

Since our patient had confirmed Kaposi sarcoma, bronchoscopy was necessary to rule out lung involvement. It is important to keep pulmonary Kaposi in the differential diagnosis in any AIDS patient presenting with cough, hypoxemia and hemoptysis, even in the absence of skin lesions, because treatment with steroids can lead to worsening of the Kaposi sarcoma [18]. Pulmonary Kaposi may present with radiographic findings of reticulonodular opacities, flame lesions with the presence of occasional effusions and adenopathy [18]. Bronchoscopy is necessary for diagnosis. Lesions are red/purple and located in the lower airways and occasionally the trachea. Biopsy should not be performed, as lesions are vascular with a tendency towards bleeding. Instead, PCR for HHV 8 is done on the lavage samples [18]. In our case, BAL demonstrated *Pseudomonas aeruginosa*. This bacterium has been found to cause 5–7% of cases of community-acquired pneumonia in HIV-infected patients [19].

GI infections: Esophageal candidiasis/oral thrush

Oral/esophageal candidiasis is the opportunistic infection most often seen in HIV patients [20]. Our patient had odynophagia and disturbance in taste. Bronchoscopy revealed candidiasis. Diagnosis of oral candidiasis can be made by identifying white plaques in the oral mucosa and pseudohyphae upon KOH preparation. Of note, patients with candida esophagitis may not always have oral thrush. In this case, esophagogastroduodenoscopy (EGD) is necessary to make the diagnosis, with biopsy showing yeast and pseudohyphae [21]. Other infectious causes of esophagitis include herpes simplex virus (HSV) and cytomegalovirus (CMV). On EGD, HSV lesions will classically be well circumscribed with heaped up margins, biopsies of which will reveal multinucleated giant cells [21]. CMV lesions will be linear and deep, with intracytoplasmic or intranuclear inclusion bodies on histology [21]. After the patient received fluconazole and topical clotrimazole, he noted significant improvement in his taste and increased ability to swallow. The treatment of choice for esophageal candidiasis is oral fluconazole with a 400 mg loading dose and then 200 mg daily thereafter for 2–3 weeks [21].

Blurry vision: CMV vs. HSV retinitis

The patient complained of progressive blurry vision for months prior to admission. There was concern for the possibility of CMV or HSV retinitis. Progressive Outer Retinal Necrosis (PORN) is seen in severely immunocompromised individuals with a history of Varicella Zoster Virus, HSV and rarely CMV [22]. There is rapid retinal necrosis resulting in an inflammatory granulomatous reaction and ischemia within the retina [23]. Prognosis is very poor. Ocular syphilis can involve almost any structure in the eye. Uveitis and chorioretinitis are by far the most common manifestation [14]. Long standing uveitis in a patient with syphilis can lead to the formation of cataracts, glaucoma and macular edema [14]. Our patient's ophthalmology examination revealed cataracts bilaterally and ruled out any serious eye infections.

Pancytopenia: Malignancy vs. chronic illness vs. disseminated MAI

Pancytopenia in the setting of HIV can be attributed to the HIV infection itself or to opportunistic infections or malignancy.

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Mycobacterium avium complex (MAC), caused by M. *avium* or M. *intracellulare,* can present as focal or disseminated infection. Disseminated infection can often go undiagnosed and be attributed to worsening of the patient's chronic HIV symptoms. Symptoms are nonspecific and can include fever, night sweats, diarrhea, weight loss and fatigue [23]. Disseminated MAI can be seen in patients with CD4 counts <50 cells/microL. MAI can be isolated from various locations in the body including the gastrointestinal and respiratory tracts, blood, bone marrow, liver and lymph nodes [24]. Survival if not treated ranges from 4 to 5 months. This significant morbidity and mortality, in addition to the nonspecific symptoms of this infection, emphasize the importance of establishing a diagnosis. Laboratory abnormalities include elevations in alkaline phosphatase and lactate dehydrogenase, as well as anemia. Blood cultures may not reveal this bacterium. Bone marrow biopsy should be done in the presence of negative blood cultures. Our patient had negative blood cultures, BAL cultures and negative histology from the bone marrow biopsy, ruling out MAC infection.

The pancytopenia in our patient was likely secondary to the advanced HIV infection, although opportunistic infections could have been contributing factors. With antimicrobials, antifungals and antiretroviral therapy, the patient's pancytopenia gradually improved.

HIV wasting

The patient appeared very cachectic and had significant weight loss over the past year. He described severe weakness to the point where he became unable to walk over the course of a few months' time. HIV wasting syndrome is defined by a weight loss of 10% or more for at least 1 month, associated with diarrhea, weakness and fever not explained by another condition other than HIV [25]. In HIV, wasting can be a result of HIV infection itself but can also be due to opportunistic infections or associated cancers [24].

Conclusion

This significance of this case lies not in the diagnosis, but rather in the number of diagnoses and the thought process used to discern them. This type of patient was quite common in the pre-antiretroviral era. Occam's Razor, i.e that one simple diagnosis should be sought to explain all of a patient's complaints, cannot be used in this case. Having that approach would have led to missed diagnoses [26]. Hickam's Dictum, i.e "patients can have as many diseases as they damn well please" is the more fitting approach [26]. We addressed each of our patient's individual symptoms and compiled a set of differential diagnoses for each. The simplest explanation is not always the most likely. It is important to think broadly and keep all possible differential diagnoses in mind until absolutely ruled out.

Conflicts of interest

None.

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Authors contribution

Daria S. Yunina: Writing, Review and editing.
Natalie Elkayam: Writing.
Shanti Patel: Writing.
Fidelis Okoli: Writing.
Edward Chapnick: Review and editing, Supervision.
Melvin Hecht: Review and editing, Supervision.

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