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ABSTRACT

A 53-year-old male diagnosed with HIV, SARS-CoV-2 and Kaposi sarcoma developed a purple-brown maculopapular rash on the left calf approximately 6 months before hospitalization and was diagnosed with venous ulcer. The lesions grew in size, spread on the whole body and also appeared on the palate. During this time the patient did not ask for a second opinion and was not monitored by a medical specialist. In December 2020, he developed a severe form of COVID-19 with acute respiratory failure and was admitted to the hospital. He was simultaneously diagnosed with HIV and severe immunosuppression. The skin biopsy confirmed Kaposi sarcoma in the nodular stage. Antiretroviral therapy (ART) was initiated and the patient later received liposomal doxorubicin chemotherapy. The patient slowly recovered whilst showing improvement of his clinical condition and immunological status.

Keywords: COVID-19, HIV, Kaposi sarcoma, antiretroviral treatment

INTRODUCTION

The first SARS-CoV-2 cases were reported in December 2019 in the Wuhan province in China. This disease was named COVID-19 by the World Health Organization starting from February 2020 [1].

According to CDC one of the clinical conditions that could potentially determine the patients to develop severe cases of COVID-19 is HIV infection. The clinical progress of those infected with HIV and SARS-CoV-2, with good immunological status and undetectable viral load, seems to be similar to those without HIV. However, the data we have at this point is inconclusive [2,3].

Kaposi sarcoma (KS) is an angioproliferative multicentric tumor originating in the endothelial cells infected with Human Herpesvirus-8 (HHV-8). KS is classified into 4 types: epidemic, associated with HIV infection, iatrogenic, associated with immunosuppressive treatment, endemic (African) and classic

(sporadic). In the epidemic type the lesions usually develop on the skin and mucosae but, in the more advanced forms, they can also affect the viscera. Pulmonary involvement occurs in 80-90% of patients, usually in those with severe immunosuppression who also associate extensive skin and mucous lesions, but it can also present as the main site of involvement in 15% of cases [4,5].

AIM

The purpose of this case report is to highlight the early signs of Kaposi sarcoma and the importance of early diagnosis in HIV infected patients.

CASE PRESENTATION

A 53-year-old male was seen in the emergency department of this hospital because of dyspnea and severe dry cough. The symptoms began approximately



FIGURE 5. Cardio-pulmonary radiography: bilateral pleural effusion and mixed infiltrates in the inferior 2/3 of the left lung and the right base



FIGURE 6. Pulmonary CT: bilateral pleural effusion; thickening of the intra- and inter-septa; the collapse of the right lung

sitions, with eosinophilic cytoplasm, irregular margins and vesicular nuclei, rare mitosis, frequent intracytoplasmic spaces; numerous vesicular spaces of small sizes of flattened endothelial cells containing red blood cells; frequent hematic extravasation, frequent capillary vessels and vascular ectasia, small hemosiderin deposits and minimal lymphocyte infiltration. It confirmed the diagnosis of Kaposi sarcoma (nodular stage).

Differential diagnosis

With regard to the pulmonary affliction, seeing as the patient was severely immunosuppressed, with HIV infection and an AIDS defining illness, we firstly considered other infectious causes. Pulmonary tuberculosis can develop in HIV infected patients 100 times more frequently than in the normal population. The clinical signs and symptoms can vary depending

on the number of CD4⁺ T cells. Immunosuppressed patients usually develop atypical or paucisymptomatic tuberculosis, frequently with remote locations, seeing as the typical symptoms of TB become apparent because of the host's immune response. Those afflicted, with an acceptable immunological status, can develop typical forms of TB, whereas those with severe immunosuppression, with a CD4⁺ count under 200/mm³, could potentially only display adenopathies as the singular clinical sign with normal or atypical imaging chest studies. Tuberculosis was disproved after the analysis of the cultures and smears from the sputum and pleural fluid [4].

Another possible etiology is *Pneumocystis jirovecii* pneumonia. The clinical symptoms and the imaging studies can be similar with those in COVID-19. The ground glass opacity on CT scans can be present in both. One difference between the two is the location of the lesions. SARS-CoV-2 has been showed to affect predominantly the periphery of the pulmonary fields whilst in pneumocystosis the lesions are mainly dispersed in the central region. This disease was ruled out since there were no characteristic cysts found in bronchoalveolar lavage. Other bacterial or fungal pathologies were ruled out after the analysis of the sputum and pleural fluid [1,4,6].

Other non-infectious causes of pulmonary disease (other types of cancer, pulmonary thrombo-embolism, collagen afflictions etc.) were excluded with the help of the imaging and laboratory studies.

We considered Castleman's disease and acroangiokeratosis for the differential diagnosis of the skin lesions. Castleman's disease is a lymphoproliferative disorder associated with HHV-8 infection that can appear in HIV infected patients. In the multicentric type the skin lesions usually appear as hyperpigmented plaques. The skin biopsy was not evocative of this disease. Acroangiokeratosis is a rare benign angioproliferative disease where purple-brown nodules or plaques appear on the inferior limbs usually in association with chronic venous disease. As opposed to the lesions in KS, they are painful, itching, with a tendency for bleeding and ulceration and are not expanding in nature [7,8].

Final diagnosis

The laboratory and imaging studies established the diagnoses of interstitial and alveolar pneumonia with acute respiratory failure of mixed origin, severe

SARS-CoV-2 infection, disseminated Kaposi sarcoma (with mucosal, cutaneous and visceral involvement), bilateral serous hemorrhagic pleurisy (due to KS) and HIV-AIDS infection with severe immunosuppression (C3 stage), moderate normocytic normochromic anemia and secondary hypoalbuminemia.

Therapeutic focus and assessment

The treatment for COVID-19 was administered in accordance with the national guidelines. He received oxygen therapy (with a maximum flow of 10L per minute), corticotherapy with intravenous dexamethasone, prophylaxis for thrombo-embolic incidents with subcutaneous enoxaparin. Also, given the extension and appearance of the pulmonary lesions and the fact that the patient was severely immunosuppressed, a bacterial suprainfection could not have been excluded at first; therefore, he received wide spectrum antibiotic therapy with intravenous meropenem until the results of the cultures were done. Prophylaxis for *Pneumocystis jirovecii* pneumonia with Trimethoprim /sulfamethoxazole was initiated. He also received bronchodilators, antitussives, antihistamines, anxiolytics, pain-killers, diuretics and albumin.

Regarding the HIV infection, initiation of combined antiretroviral therapy is the main method of treatment, that could potentially lead to the clinical regression of the KS lesions and slow down the progress of the disease. Some patients with severe symptoms, visceral involvement and rapid dissemination are also indicated to receive systemic chemotherapy. The drug of choice in these situations is liposomal doxorubicin (in the absence of cardiovascular contraindications) [5].

Antiretroviral therapy was initiated in accordance with the EACS guidelines with an integrase inhibitor – Raltegravir in doses of 400 mg – 2 times/day, and 2 reverse-transcriptase inhibitors – Tenofovir and Emtricitabine in doses of 200 mg/245 mg – 1 time/day. The patient was later seen in an oncology department where he was administered chemotherapy with liposomal doxorubicin (Caelix).

The patient's clinical progress, initially unfavourable, was ameliorated. The respiratory insufficiency and the inflammatory syndrome disappeared, the skin lesions showed signs of regression and the cellular immunity improved (CD4+ T cells = 396/mm³). He has discharged after one month of hospitalization

with a good clinical status, without need oxygen therapy, with good cardio-respiratory and digestive functions, with the recommendation of continuation of the antiretroviral and cytostatic drugs.

DISCUSSION

Epidemic Kaposi sarcoma (KS) associated with HIV infection is the most common form of KS. The induction of antiretroviral therapy lowered the incidence of the disease and diminished the mortality rates in the whole world, although they remain high in some regions (such as sub-saharan Africa). The progression rate of the disease is usually fast, leading to visceral dissemination and, in the cases with the worst clinical outcomes, the involvement of the respiratory or digestive systems [9,10].

Studies showed that approximately 10-20% of the patients diagnosed with Kaposi sarcoma are identified with advanced forms of disease and that a percent of 6,6% develop IRIS (immune reconstitution inflammatory syndrome). IRIS develops after the initiation of effective antiretroviral therapy, along with the amelioration of the host's immune status and the reduction of the viral load, revealing itself through the paradoxically worsening of the patient's previous infections [4,11].

The available data regarding the risks of SARS-CoV-2 infection in patients with HIV are still inconclusive. Multiple studies didn't reveal a more unfavourable clinical outcome in hospitalized patients with HIV and COVID-19 compared to the general population. One factor which was proven to negatively influence the mortality in patients with HIV and SARS-CoV-2 is pulmonary tuberculosis. Other risks factors associated with more severe outcomes were the ones previously proven to worsen the prognosis of COVID-19 patients (advanced age, cardiovascular diseases, diabetes mellitus, chronic pulmonary disease, obesity etc.) [12-17].

CONCLUSIONS

The particularities of this case consist in the following: the patient was simultaneously diagnosed with HIV, SARS-CoV-2 and Kaposi sarcoma; he was a late presenter (CD4+ T cells <350/mm³); he was identified with an AIDS defining disease; he developed a severe form of disseminated Kaposi sarcoma (with cutaneous, mucous and visceral involvement)

and COVID-19 with acute respiratory insufficiency; he was a MSM patient.

We want to emphasize the importance of HIV early diagnosis. This can easily be done through periodical screening of the individuals at higher risk of contracting the virus. Also, as physicians, we should

be able to recognize the early signs KS in our patients so that to avoid the development of advanced forms and severe complications. All those cases require an interdisciplinary approach in order to manage the disease progression and to institute a proper treatment plan.

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