

Case Report

Severe course of HIV-related Kaposi's sarcoma with cutaneous, visceral and oral manifestations in a late-presenting patient

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ABSTRACT

Kaposi's sarcoma is a soft tissue tumor caused by human herpesvirus 8 (HHV-8). One of its forms is associated with human immunodeficiency virus (HIV) and is characterized by involvement of the skin and internal organs. We present a case of a 42-year-old male diagnosed with acquired immunodeficiency syndrome (AIDS) and disseminated Kaposi's sarcoma with cutaneous, oral and visceral manifestations. During the months of hospitalization the patient suffered from neutropenic fever, gastrointestinal bleedings and required multiple blood transfusions. The patient was started on antiretroviral treatment followed by chemotherapy with paclitaxel. The skin lesions regressed, the patient gained weight and there was an improvement in performance status. This case demonstrates how severe HIV-related Kaposi's sarcoma can be and the effectiveness of antiretroviral treatment combined with chemotherapy in combating the disease. The authors believe that great effort must be made to prevent new HIV infections and all the negative implications that may follow.

KEYWORDS: HIV, AIDS, Kaposi's sarcoma, HHV-8, chemotherapy.

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1. Introduction

Kaposi's sarcoma is a soft tissue tumor associated with human herpesvirus 8 (HHV-8) infection. It occurs, among others, in populations of patients with immunosuppression, for example in patients with acquired immunodeficiency syndrome (AIDS) [1]. It is considered an AIDS-defining illness and the second most common tumor in human immunodeficiency virus (HIV)-positive patients with CD4 lymphocyte count below 200 cells/ μ L [2]. The HIV-related form of Kaposi's sarcoma is characterized by diffuse involvement of the skin and internal organs. On the skin or mucocutaneous surfaces it usually has a presentation of a violaceous pink to purple plaque. The lesions can be associated with lymphedema, pain, and secondary infection. Involvement of the internal organs may result in gastrointestinal or respiratory symptoms. The latter may cause respiratory distress and lead to death [1]. Oral manifestation occurs in up to 65% of HIV-positive individuals and is considered to be a negative prognostic factor [3].

Patients with HIV-related form of the disease tend to have a good response to antiretroviral (ARV) treatment. However, in more severe cases, an addition of systemic chemotherapy may be necessary [4]. The prognosis of the HIV-related form depends on variables such as CD4 lymphocyte count and opportunistic infections [1]. Here we describe a case of a severe course of advanced Kaposi's sarcoma in an HIV-positive patient, who responded well to ARV treatment combined with chemotherapy.

2. Case Report

In June 2021 a 42-year-old male was admitted to our department due to a newly diagnosed HIV infection. The patient was complaining of skin lesions that had started to appear on the chest 4 months prior to the admission. What concerned the patient the most was losing 20 kilograms of weight in 1.5 months. Furthermore, since April 2021, the patient had been experiencing considerable gait disturbances. During that time new skin

lesions in other regions appeared and were accompanied by dysphagia, hearing deterioration in the left ear, tooth loss and ulceration of the oral cavity. In June 2021 there were episodes of low-grade fever and the patient was forced to spend most of the time in bed due to fatigue and needed assistance in the daily activities. The patient also complained of elevated blood pressure. The patient had a history of risky sexual behavior and drug use. The patient also reported having a sexual intercourse with an individual in early stage of an HIV-1 infection in 2015, yet the patient's last HIV test done 2-3 years prior to the admission was negative. The patient's medical history included nephrolithiasis, asymptomatic myocardial infarction and two known cases of lymphoma in the family.

At the time of admission the patient was cachectic. The physical examination revealed multiple raised purple lesions on the face, torso, upper and lower extremities (Figure 1) and in the left ear canal. A generalized lymphadenopathy was also observed. The palatine tonsils were covered with a coating, the hard palate and gingivae were ulcerated, tooth decay was present (Figure 2). There was also a spastic paresis of the left lower limb, which forced the patient to use a wheelchair. Without assistance the patient was only able to walk a distance of only a few meters. The patient's performance status in the Eastern Cooperative Oncology Group (ECOG) score was 4 (completely disabled; cannot carry out any selfcare; totally confined to bed or chair) [5].



Fig 1. Pre-chemotherapy image of the torso showing multiple raised purple lesions.



Fig 2. Pre-chemotherapy image of the mouth showing ulceration of the gingivae and tooth decay.

The patient's laboratory results are presented in Table 1.

Table 1. Baseline immunological and virological data during observation.

Data	06.2021	08.2021	01.2022	05.2022	09.2022	04.2023
CD4 lymphocyte count (cells/μL)	79	241	243	242	308	416
CD8 lymphocyte count (cells/μL)	714	1065	882	661	809	855
CD4/CD8 ratio	0.11	0.23	0.28	0.37	0.38	0.49
HIV-1 VL (copies/ml)	301598	<40	<40	<40	102	50

The HIV-1 infection was confirmed with a western blot and the patient was started on an ARV treatment consisting of dolutegravir, emtricitabine and tenofovir disoproxil fumarate (DTG/FTC/TDF). The patient was also administered intravenous (i.v.) benzylpenicillin due to syphilis. From the upper respiratory tract specimen *Candida spp.* was cultured.

During the hospitalization multiple bleedings from the lower gastrointestinal tract and events of hemoptysis occurred. Pancytopenia with hemoglobin (Hb) level drops to 6.4 g/dl required repeated blood transfusions and the patient developed febrile neutropenia.

In August 2021, control laboratory tests showed signs of immune reconstitution inflammatory syndrome (IRIS): an increase in CD4 and CD8 lymphocyte counts accompanied by a strong decrease of HIV-1 viral load (VL). Kaposi's sarcoma was confirmed histologically in tissues sampled from the skin lesions, lymph nodes and gastrointestinal tract. Additionally, lymphoma was excluded in a trephine biopsy. The patient was started on paclitaxel (PTX). PTX was administered once a week together with dexamethasone, ondansetron, clemastine, omeprazole and hydrocortisone.

An episode of fever with neutropenia occurred and the patient was administered meropenem empirically. The blood culture was positive for non-drug resistant *Escherichia coli*. The procalcitonin level rose to 1.35 ng/mL and the Hb level decreased significantly again. The patient received blood transfusions and was administered filgrastim. In the following days a painful swelling and redness in the right groin region were observed. Neoplastic etiology was suspected, since an abscess was excluded during an ultrasound examination. Due to the neutropenic fever the chemotherapy cycles had to be rescheduled.

Despite chemotherapy, cachexia progressed during the hospitalization - a notable weight loss was observed. The patient had lost 12 kilograms and the lowest observed body weight was 51 kilograms.

After two months of chemotherapy a reduction in ulceration of the oral cavity was noticed (Figure 3), whereas the intensity of skin lesions remained unchanged.



Fig 3. Image of the mouth after 4 months of chemotherapy showing regression of the ulceration.

Three months later, in January 2022, the gait disturbances aggravated and the patient was diagnosed with axonal sensorimotor polyneuropathy. A magnetic resonance imaging (MRI) of the head and an electromyography (EMG) were performed and the patient was consulted by a neurologist - an HIV-related neuropathy, possibly combined with chemotherapy side effects, was suspected. There was also a decrease in the patient's CD4 and CD8 lymphocyte counts. The patient refused to receive any rehabilitation outside the hospital.

In March 2022 a reduction of skin lesions was finally observed (Figure 4). In the following months, the plaques continued to regress. For this reason, and to minimize toxicity, paclitaxel once a week was changed to once every two weeks. In August 2022 the oral cavity was completely free of lesions. Moreover, the patient started to gain weight and continued throughout further observation. However, new red disseminated lesions with swelling were present on the left thigh. Thrombosis was excluded. A month later the new lesions increased in size and the swelling was still present.



Fig 4. Image of the torso after 7 months of chemotherapy showing a notable regression of the skin lesions.

In November 2022 the patient complained of swelling in both lower extremities. Low-molecular-weight heparin (LMWH) injections were administered. The skin lesions on the left thigh regressed slightly. There was also an improvement in gait.

The patient was last reviewed in April 2023. Currently the patient does not require the use of a wheelchair. The paresis has regressed to a great extent but not completely and the patient is able to walk a distance of a few hundred meters unassisted. The patient was declared unfit to work and is now living with his parents where the patient moved after the first discharge. The patient still requires assistance with daily activities and has an ECOG score of 3 (capable of only limited selfcare, confined to bed or chair more than 50% of waking hours) [5]. The patient's current body weight is 86 kilograms.

3. Discussion

According to a paper by Miranda et al. late presenters account for 40 to 60% of HIV cases in Europe [6]. Late presentation of an HIV infection is defined as a diagnosis of HIV with a CD4 lymphocyte count <350 cells/ μL , or the occurrence of an AIDS-defining event, regardless of the CD4 lymphocyte count, and is associated with adverse clinical outcomes [7]. The presented case serves as a good example of this. The patient was a late-presenter and, as a consequence, the clinical course of the HIV infection and the sarcoma was severe. As it was already mentioned, the patient had to go through multiple blood transfusion, suffered from neutropenic fever, bleedings from the gastrointestinal tract and cachexia. As a result, the patient still requires prolonged chemotherapy and has not fully recovered. Not only was such unfavorable course a terrible burden on the patient, but also obliged the clinicians to put great effort in fighting for his life during long months of hospitalization.

In his meta-analysis Liu et al. [8] prove that HIV-positive men who have sex with men (MSM) have the highest incidence of Kaposi's sarcoma. In addition to this, the incidence is significantly bigger in males than in females and considerably lower in people receiving ARV therapy. Available data suggests that up to 30% of patients without ARV therapy will develop Kaposi's sarcoma [9]. As it can be clearly seen, the featured patient represented the groups of the highest risk of Kaposi's sarcoma. Not only did the patient have multiple sexual contacts with men, but also suffered from AIDS and was not receiving adequate treatment.

The featured patient reached the hospital at the stage when the sarcoma had already disseminated. The patient claimed that it was due to insurance difficulties. However, in the past, the patient also had not sought medical help as often as it would be advised. Despite being aware of belonging to a high-risk group, the patient did not get tested as often as current guidelines suggest. According to Centers for Disease Control and Prevention (CDC), individuals from the risk groups (including MSM) are advised to be screened at least annually [10]. Wurm et al. identified individual risk perception and anxiety regarding stigmatization as the most important barriers in accessing HIV testing services [11]. Furthermore, if the patient had consulted medical professionals more often, it is possible that he would be offered pre-exposure prophylaxis (PrEP), gained knowledge on how to prevent sexually transmitted diseases (STDs) or, in case of infection, received adequate treatment.

Current guidelines suggest that all HIV-positive individuals with Kaposi's sarcoma should be initiated on ARV treatment. Liposomal doxorubicin (LD) and PTX are currently

the most often used first-line chemotherapy agents in these patients. Since HHV-8 cannot be eradicated the purpose of the therapy is long-term control; the number of cycles of chemotherapy and the duration of treatment is determined by clinical response [12]. In the described case these recommendations were followed. First, the patient received ARV agents and then was started on chemotherapy consisting of PTX. Due to the severe course of the disease and its disseminated character, the patient requires chemotherapy to this day.

Involvement of the oral cavity is considered to be a poor prognostic factor [3]. Not only can it suggest an undiagnosed HIV infection, but is also associated with dissemination of the sarcoma. In addition to this, patients with oral manifestations may have a higher mortality rate than those who have only the skin affected [13]. Despite such dreadful estimates, in the featured case the disease seems to be well controlled, lesions in the oral cavity are fully regressed and the patient's performance status improved.

4. Conclusions

HIV-positive patients who present late and suffer from disseminated HIV-related Kaposi's sarcoma can be treated with good clinical outcome only if ARV treatment is administered early and is combined with chemotherapy. Despite the fact that it has been many years since the beginning of HIV epidemic, many patients are still being diagnosed at an advanced stage. Therefore, early detection of an HIV infection and knowledge of what skin lesions can be associated with it is a matter of great importance. Not only can it help prevent severe course of the infection, but also opportunistic infections and other dangerous complications.

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