Multiple concomitanti infezioni opportunistiche e linfomi aggressivi in una persona con HIV/AIDS che non assumeva la terapia antiretrovirale: un esito fatale nonostante le cure intensive.

Multiple concurrent opportunistic infections and aggressive lymphomas in a person with HIV/AIDS not taking antiretroviral therapy: a fatal outcome despite intensive care.

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Riassunto

Nonostante la marcata riduzione della mortalità per malattie correlate all'AIDS tra le persone che vivono con l'HIV (PWH) durante l'era della terapia antiretrovirale (ART), l'incidenza dell'AIDS nel mondo è ancora significativa. Le infezioni opportunistiche e i tumori correlati all'HIV si verificano soprattutto nelle persone che non ricevono l'ART e rappresentano una sfida significativa per la gestione dei pazienti.

Riportiamo il caso di un paziente con HIV e scarsa aderenza alla ART che si presenta alla nostra attenzione con una grave compromissione dello stato di salute generale e molteplici condizioni AIDS definenti. Questo caso evidenzia le sfide delle persone che vivono con HIV e hanno difficoltà ad aderire al trattamento ed è emblematico di come ci si imbatta ancora oggi in forme di AIDS estremamente aggressive e difficili da curare. In questi casi, a volte, nemmeno la diagnosi precoce, il trattamento adeguato e la massima assistenza fino al ricovero in terapia intensiva garantiscono un esito favorevole.

Abstract

Despite the marked reduction of mortality from AIDS-related illnesses among people living with HIV (PWH) during the antiretroviral therapy (ART) era, the incidence of AIDS worldwide is still significant.

Opportunistic infections and HIV-related tumors occur particularly in patients not receiving ART and pose a significant challenge for patient management.

Here we present the case of a patient with HIV and poor adherence to ART who comes to our attention with a severe impairment of general health status and multiple AIDS-defining conditions.

This case highlights the challenges of those individuals who have difficulty engaging in care and is emblematic of how we still encounter extremely aggressive and difficult to treat forms of AIDS.

In these cases, sometimes, not even early diagnosis, adequate treatment, and maximal supportive care up to intensive care unit guarantee a favorable outcome.

Introduction

Prior to introduction and widespread use of combination antiretroviral therapy (ART), AIDS-associated illnesses were the principal cause of morbidity and mortality associated with HIV infection. Nowadays, survival of people with HIV (PWH) has significantly improved and AIDS-related deaths sharply decreased among EU/EEA countries of the World Health Organization (WHO) European Region (1).

Despite marked improvement since the beginning of the HIV/AIDS epidemic, worldwide mortality from HIV-related conditions is still considerable. The WHO African Region remains most severely

affected, but even in Western world the incidence of AIDS is still significant. In 2021, 44 countries in WHO Europe reported 8,194 cases of AIDS with an incidence of 1.2 per 100,000 persons (1).
While mortality from opportunistic illnesses has become much less common with the widespread use of effective ART, death from AIDS still occurs in individuals with late diagnosis and those who have difficulty engaging in care or adhering to ART (2, 4).
Here we report the paradigmatic case of a patient with poor adherence to ART who developed multiple AIDS-defining conditions that led to his death, despite the access to proper treatment and intensive care.

Case report

A 52-year-old man received his HIV diagnosis in 2009: he started antiretroviral therapy, but he discontinued it after one month and interrupted the attendance of HIV clinic (he was lost to follow-up). He came to our attention 14 years later, when he was hospitalized for poor general conditions, weight loss, fever, dyspnea, and lymphadenopathy. Laboratory tests at admission showed an elevated viral load (HIV RNA 2,540,000 copies/ml) and a low CD4+ T lymphocyte count (14 cells/mm3), Ebstein-Barr Virus-DNA on blood 2,400 copies/ml, Cytomegalovirus-DNA on blood 2,200 gEq/ml. Chest-abdomen computed tomography (CT) scans and Positron Emission Tomography (PET) scans performed at admission raised the suspicion of lymphoproliferative disease (tracer uptake at multiple supra- and sub-diaphragmatic lymph nodes bilaterally, spleen, multifocal skeleton, bone marrow). In addition, the chest CT scan showed a left interstitial pneumonia with 2.5 cm thickening of irregular morphology in the left upper perihilar region. A bronchoscopy with bronchoalveolar lavage revealed Pneumocystis jirovecii, Cytomegalovirus (CMV DNA 38,000 copies/ml) and Mycobacterium avium complex (MAC).
Treatment with cotrimoxazole, ganciclovir, and methylprednisolone was started.
The patient's AIDS-defining conditions also included cutaneous Kaposi's sarcoma, confirmed by histologic examination of a lesion on the left lower limb, and esophageal candidiasis evidenced at esophagogastroduodenoscopy, whereby fluconazole was added in therapy.
On radiological suspicion of lymphoproliferative disease, the patient underwent a lymph node biopsy and a bone marrow evaluation (bone marrow aspirate and osteomedullary biopsy) for the histological diagnosis, which revealed two different types of lymphoma.
Anaplastic T-cell lymphoma was found in the lymph node specimen while diffuse large B-cell lymphoma (DLBCL) transformed from marginal lymphoma was found in the bone marrow specimen.
During the biopsy procedure, the worsening of respiratory failure required intubation and transfer to the intensive care unit (ICU), where respiratory distress was managed and resolved.
On return to the ward, chest CT scan showed improvement in the interstitial pneumonia, but also a peri-bronchial nodular thickening at the right lung, possible expression of mycobacteriosis in the early stage. In the meantime, the onset of pancytopenia required a dose reduction of cotrimoxazole and ganciclovir, after fourteen days of treatment and the evidence of undetectable blood CMV DNA.
Antiretroviral therapy with tenofovir alafenamide, emtricitabine, dolutegravir, and anti-MAC therapy with clarithromycin, ethambutol, amikacin were started. Rifamycin could not be introduced due to drug interactions with anti-blastic agents. Concurrently, indeed, the first cycle of chemotherapy according to the reduced-dose CHOP schedule (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) was started.
The post-chemotherapy course was complicated by an episode of febrile neutropenia, treated with a one-week course of piperacillin/tazobactam, and a marked worsening of pre-existing pancytopenia that required the use of granulocyte colony-stimulating factor and transfusion of red cells and platelets.
Ten days after the first cycle of chemotherapy, the patient experienced a new worsening of respiratory function with CT signs of fungal pneumonia and concomitant elevation of serum galactomannan, so that intravenous isavuconazole was started. A new diagnostic bronchoalveolar lavage was not performed because of the poor respiratory status.
Over the next few days, there was a progressive decline in general conditions with persistent diarrhea, hyporexia, poor recovery of bone marrow activity and respiratory function. Therefore, the second cycle of chemotherapy was postponed.

On the 40th day post-chemotherapy, new febrile episode occurred with isolation of Enterococcus faecium on blood and rapid evolution into septic shock, despite adequate antibiotic therapy introduced at the onset of fever, so the patient was again transferred to the ICU.
Within few hours after admission to the ICU, a multi-organ failure developed, leading to the patient's death the same day, despite maximal care.

Conclusions

Opportunistic infections (OIs) and HIV-associated tumors were a major source of morbidity and mortality in patients with HIV before the ART era, but still occur today, mostly in patients who are not receiving ART. Our patient's case is emblematic of how clinicians may still encounter extremely aggressive and difficult to treat forms of AIDS today. The dramatic impairment of the individual health status, despite the availability of proper diagnostic and therapeutic tools, reduces the chances of survival: even prompt initiation of antiretroviral therapy, adequate care of OIs and HIV-related tumors, and maximal supportive care up to ICU, do not guarantee a favorable outcome. This case highlights the importance of early HIV diagnosis and early initiation of ART, while also addressing the challenges of those individuals who have difficulty engaging in care. ■

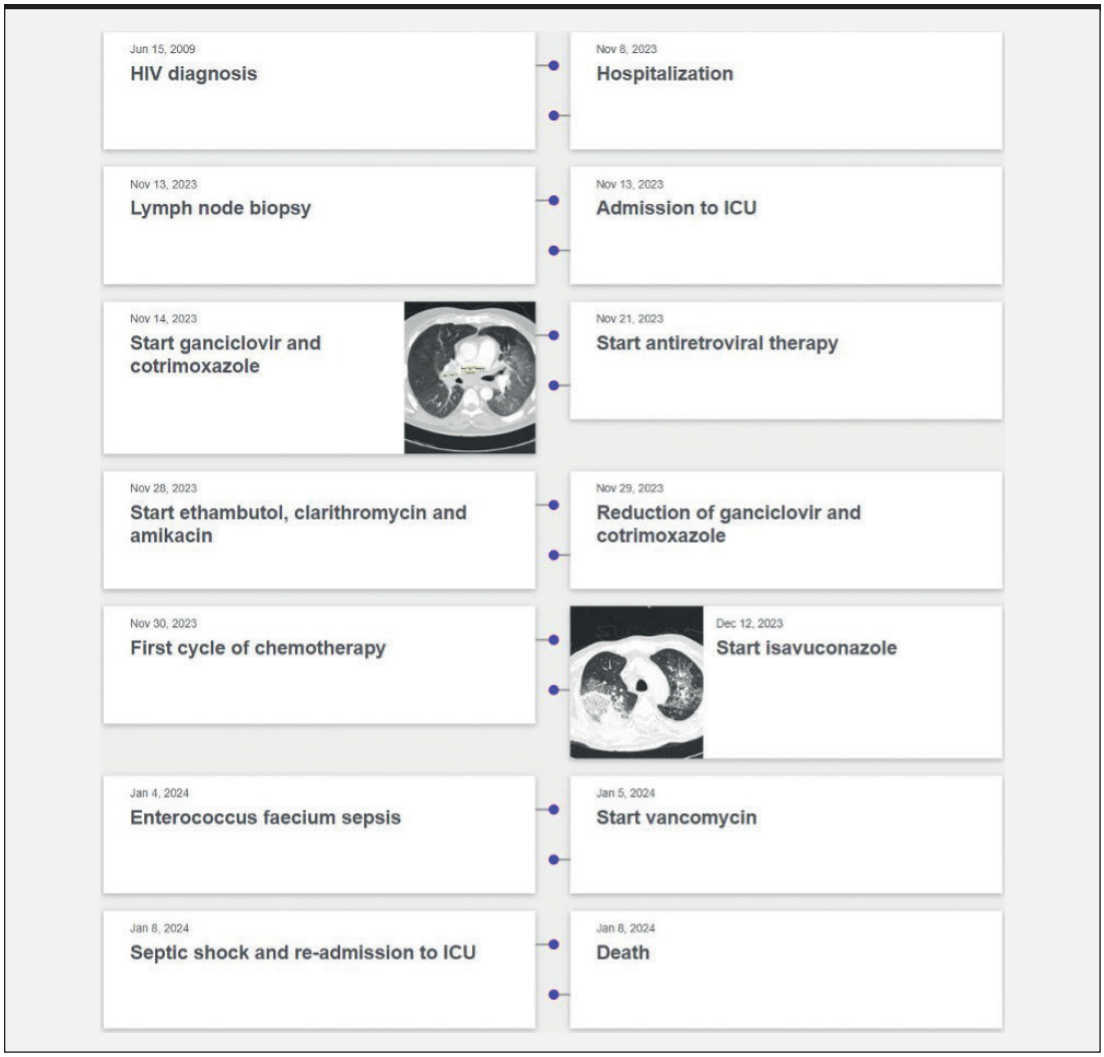

Figure 1. Timeline of major events in the patient's medical history.

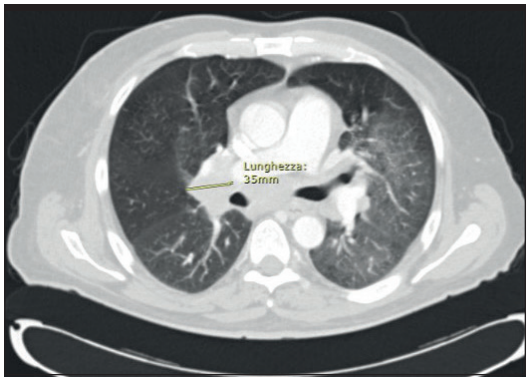

Figure 2. Chest computed tomography (CT) scan (Nov. 2023): ground-glass thickening of the left lung and lymphadenopathy in the hilar site bilaterally (maximum diameter 3.5 cm).

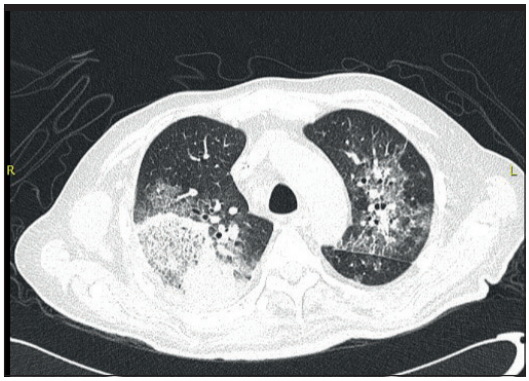

Figure 3. Chest computed tomography (CT) scan (Dec. 2023): consolidation with "reversed halo sign" at the right upper lung lobe.

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