IMPORTANCE OF PSYCHOLOGICAL INTERVENTION IN THE MANAGEMENT OF A PATIENT WITH NON-HODGKIN LYMPHOMA AND STAGE C3 AIDS DISEASE

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IMPORTANCE OF PSYCHOLOGICAL INTERVENTION IN THE MANAGEMENT OF A PATIENT WITH NON-HODGKIN LYMPHOMA AND STAGE C3 AIDS DISEASE (Abstract): Long-term evolution of HIV because of noncompliance and nonadherence to antiretroviral therapy favors the occurrence of difficult to treat HIV-related malignancies. We present the case of a female patient in “the pediatric cohort” registered at the Iași Regional HIV/AIDS Center since year 2000, now with stage C3 AIDS. In 2014, a Burkitt lymphoma was pathologically confirmed, and chemotherapy was initiated as recommended by the hematologist. The clinical course was characterized by multiple complications: hematologic and hepatic toxicities, opportunistic infections and depressive episodes. Highly active antiretroviral therapy associated with sustained psychological support resulted in stabilization of the patient’s clinical course (lower HIV viral load and higher CD4 lymphocyte cell counts), anticancer therapy being better tolerated. Currently, patient’s clinical-biological status is quasi-normal. The depressive episodes in this HIV-positive cancer patient undergoing chemotherapy contributed to her non-adherence and non-compliance to treatment, with serious consequences both on clinical and viroimmunological status. Therapeutic strategy in this patient with AIDS and Burkitt lymphoma raised management difficulties as both the drug interactions and cumulative adverse effects had to be considered. Multidisciplinary collaboration and especially psychological intervention are essential for creating a functional team, effective communication being key to achieving long-term adherence to treatment and diagnosis acceptance. Keywords: HIV/AIDS PSYCHOLOGICAL COUNSELING, NONCOMPLIANCE, NONADHERENCE, NEOPLASIA.

In Romania, the late 80s and early 90s marked the onset of a HIV epidemic characterized by perinatal transmission of the virus to many children (1). Changes over time in the guidelines for antiretroviral therapy in the patients included in the “pediatric cohort” were determinants of non-adherence and non-compliance. Maintaining low CD4 cell counts for a long period in advanced stage HIV-positive patients predisposes to opportunistic infections, particularly tuberculosis, and HIV-related neoplasms (2, 3).

From a statistical point of view, there
was an increase in the number of non-Hodgkin lymphoma at the same time with the number of AIDS cases (4). For most lymphomas, a specific cause was not identified, however, some distinct non-Hodgkin lymphomas are associated with a viral infection (4, 5). According to some studies, patients infected with HIV are 59 to 104 times more likely to develop lymphomas, particularly the aggressive type (Burkitt or Burkitt-like lymphoma) with central nervous system damages (20-30%), and have a poor prognosis (6).

Non-Hodgkin lymphoma in patients with AIDS is often characterized by extra nodal involvement and severe course. Patients are treated with chemotherapy specific for non-Hodgkin lymphoma, though there are several potential risks: overgrowth of opportunistic pathogens and discontinuation of treatment in the context of the commonly associated depressive episodes (6, 7). The disease burden experienced by patients determines changes in self-perception with significant decline in self-esteem and motivation for a good adherence and compliance to antiretroviral and antineoplastic therapy, thus the role of the psychologist in the of HIV/AIDS department being essential (8).

**CASE REPORT**

We present the case of a 27-years-old woman registered to the Iaşi Regional HIV/AIDS Center since year 2000, currently with stage C3 AIDS. During patient monitoring a progressive decrease in CD4 count was found and the viral immunology tests showed moderate to severe immunosuppression (fig.1, fig.2) because of non-compliance and non-adhesion to treatment. In 2013 the patient was referred to the gynecology department for irregular periods and lower abdominal pain. Continuing the investigations, an abdominal-pelvic CT scan revealed an expansive tumor mass of 7/3/2.5 cm, located on the right ovary. A salpingo-oophorectomy was performed and pathological examination and immunohistochemical tests made the diagnosis of Burkitt lymphoma. Due to a depressive episode, the patient decided to delay the investigations for malignant non-Hodgkin lymphoma (NHL), during which time she received counseling and antiretroviral therapy consisting in combinations of Darunavir/Ritonavir, Etravirine and Raltegravir. Compliance and adherence to HAART were influenced by psychological support, the CD4 cell counts increasing from 33 cells/mm$^3$ (fig. 1), value recorded at the time of neoplasia diagnosis, to 165 cells/mm$^3$ (fig. 1) and the viral load decreasing to $VL = 10,730$ copies/ml (fig. 2). In January 2014, after repeated discussions with the infectious disease doctor, while benefiting of sustained psychological counseling, the patient was referred to the hematology department. Physical examination at the admission to the Regional Cancer Institute confirmed the presence of bilateral painless submandibular lymph nodes of about 2 cm in diameter. Bone marrow biopsy and CT scan of the thorax, abdomen and pelvis confirmed the diagnosis of stage III A Burkitt lymphoma, per ANN ARBOR staging. Hyper-CVAD (Cyclophosphamide, Adriamycin, Vincristine, and Dexamethasone) chemotherapy protocol was initiated, being subsequently associated with Rituximab. Secondary hematologic toxicity required granulocyte growth factor support and prophylactic antimicrobial therapy (acyclovir and cotrimoxazole). The patient received psychological support throughout the hospital stay, resulting in
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Improved adherence to antiretroviral and antineoplastic therapy. In November 2014, she had an emergency admission to our clinic for: vertigo, nystagmus, abnormal gait, with onset in the context of fever and marked anxiety. Biological exams revealed thrombocytopenia (Tr=84,000/mm$^3$), hepatic cytolysis syndrome (TGO=108 IU/L; ALT = 84 UI/L) and cholestasis syndrome (FA =134 IU/L; GGT =72 IU/L). Laboratory exams were supplemented by lumbar puncture, which ruled out lymphomatous meningitis and other causes, and cranio-cerebral MRI, which both invalidated the presence of tumor masses and brain infil-trates. Biological changes were considered secondary to oncologic therapy and to HIV infection. Following psychiatric and psychological evaluation the patient was diagnosed with generalized anxiety disorder for which antidepressant and anxiolytic therapy was initiated. Daily psychology sessions were resumed. In December, the same year, CD$_4$ cell count increased to 466 cells/mm$^3$ (fig. 1) and the viral load was undetectable (fig. 2).

Fig. 1. CD$_4$ cell count

Fig. 2. Viral load
Subsequently, in February 2015, the patient was reassessed for cough, chest pain and fever. Laboratory investigations have shown a decrease in CD$_4$ count to 198 cells/mm$^3$ (fig. 1) and a viral load of 89,000 copies/ml (fig.2). A chest X-ray was performed and it described a characteristic appearance of bronchopneumonia. But the etiology of infection could not be determined. Empirical antibiotic therapy was initiated with moxifloxacin and imipenem the clinical course being slowly favorable.

Following discussions with the infectious disease doctor and psychologist the patient admitted that after her general status had improved she started missing doses of HAART, initially 3-4 days a week to complete discontinuation for one month. Remission of lung phenomena allowed patient’s transfer to the hematology department. CT and PET-CT examination confirmed the recurrence of an abdominal lymphadenopathy and thus the relapse of the disease, and therefore antineoplastic therapy was reinitiated. In May 2016, the patient achieved partial remission of the disease, supported by imaging investigations, undetectable viral load (fig.2), and CD$_4$ count of 435 cells/mm$^3$. The viral immunology assessment in October 2016 showed that viral load remained undetectable, and CD$_4$ count increased to 528 cells/mm$^3$ (fig. 1).

**DISCUSSION**

Given the therapeutic advances in the management of HIV/AIDS the prognosis and the quality of life of patients with HIV have improved. However, the association between the diagnosis of HIV infection and a neoplastic disease has a strong psychological impact, causing recurrent depressive episodes that are a favorable factor of therapeutic abandonment. Under these circumstances the psychologist plays an important role in the multidisciplinary team, namely to guide the patient through acceptance of the diagnosis and adapting to challenges of everyday life. Counselling and psychological support, aimed at providing support in managing negative emotions was based on an honest and comfortable exchange of information (9).

Depression is a natural step in accepting the diseases with serious prognosis, characterized by apathy, insomnia, loss of appetite, constant anxiety, and fear of death (10). The recurrent depressive episodes were initially relieved and subsequently overcome by talks with the physician, psychological support, and antidepressant medication. However, the factors that contribute to the degree of patient adherence to therapy are myriad and include the socio-economic status, level of education, family support, and finally motivation. In the here reported case the patient's high level of education and her desire to start a family were all decisive factors for accepting the psychological counseling.

**CONCLUSIONS**

Our case emphasizes the fact that the association of AIDS with a malignant disease predisposes to recurrent depressive episodes leading to nonadherence and noncompliance to antiretroviral therapy. We believe that the role of the psychologist tends to be minimized in favor of drug therapy, but the presented case highlights the important contribution of appropriate psychological support in the multidisciplinary management plan of the HIV-positive patient.
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REFERENCES


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**NEWS**

**HYDROGEN PEROXIDE VASORELAXATION INVOLVES S-GLUTATHIONYLATION OF VOLTAGE-DEPENDENT K CHANNELS**

H₂O₂ is an endothelium-derived hyperpolarizing factor (EDHF), but H₂O₂ effects vary with the vascular bed and experimental conditions. If H₂O₂ relaxes rat mesenteric artery, what is the mechanism? Methods: myography of isolated resistance arteries, patch clamp of mesenteric arterial smooth muscle cells (MASMCs), streptavidin pull-down assays with biotinylated glutathione ethyl ester. Relaxation of precontracted arteries by H₂O₂ was reversed by dithiothreitol, reduced by 4-aminopyridine (4-AP), blocker of voltage-dependent K channels (Kᵥ) channels, but not by blockers of big-conductance Ca²⁺-activated K⁺ channels or of inward rectifier K⁺ channels. H₂O₂ increased Kᵥ currents; this was prevented by glutathione reductase; Kᵥ incorporates glutathione (GSH) in the presence of H₂O₂. Thus, H₂O₂ activates Kᵥ channels (maybe via S-glutathionylation) with artery relaxation, while the basal redox status of MASMCs determines Kᵥ response to H₂O₂ (Park SW, Noh HJ, Sung DJ et al. Hydrogen peroxide induces vasorelaxation by enhancing 4-aminopyridine-sensitive Kᵥ currents through S-glutathionylation. *Pflugers Arch* 2015; 467(2), 285-297).

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