Scientific Research Publishing

Open Journal of Blood Diseases, 2017, 7, 103-107
http://www.scirp.org/journal/ojbd
ISSN Online: 2164-3199
ISSN Print: 2164-3180

Combination of Haemoglobinopathy and Haemopathy

—(Adult T-Cell Lymphoma/Leukemia and Sickle Cell Disease: A Rare Case of Disease Observed in the Adult Referral Center of Sickle Cell Disease (CRD-A) in Martinique

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How to cite this paper: Kone, D., Atimere, N.Y., Couitchere, L. and Loko, G. (2017) Combination of Haemoglobinopathy and Haemopathy. *Open Journal of Blood Diseases*, **7**, 103-107.
https://doi.org/10.4236/ojbd.2017.74010

Received: November 30, 2017
Accepted: December 25, 2017
Published: December 28, 2017

Abstract

Authors report a case of beta thalassemia combined with hematological malignant (ATLL) in a 40-year-old female, cashier screened HTLV-1 positive; followed since her 10 years old for the account of thalasso-sickle cell disease at the adult referal center of sickle cell disease in Martinique. Therapeutic management consisted of systemic chemotherapy, intrathecally-administered preventive chemotherapy combined with a treatment based on bisphosphonate and corticosteroid.

Keywords

ATLL, Sickle Cell Disease, HTLV1, Martinique

1. Introduction

The combination of main haemoglobinopathy and haemopathy is rare, only two cases had been reported before 1960 [1] and about twenty cases after 1986 [2]. The hypothesis that the red blood cells would have a protective role in the occurrence of haemopathies was abandoned for the most plausible explanation which was the short lifespan of patients suffering from sickle cell disease.

With recorded improvement in patient management, notably with the establishment of the referral centers, the neonatal screening, the antibiotic prophylaxis and the use of hydroxyurea or hydroxycarbamide, the median survival as well as the impact on cancers, and mainly haemopathies has also recorded significant

growth [3] [4].

We report a case of combined beta-thalassemia and adult T-cell lymphoma/leukemia (ATLL) discovered during hospitalization for febrile cough, dyspnoea and chest pain.

2. Observation

Mrs. BC, 40, cashier, had in her medical history, three gestations, two parities and a miscarriage, a crotch in her left eye since the age of 24, ischemic stroke in a context of hyperviscosity, high blood pressure and seroconversion to HTLV1 before 2000. She had been followed up since the age of 10 for the beta-thalassemia. The baseline hemoglobin level was 110 - 120 g/L, HbF = 13.2%, HbA2 = 4.5%, HbA1 = 14.4% and HbS = 67.9%. There was no G6PD deficit.

The patient is admitted for febrile cough, dyspnoea and left upper abdominal pain. The clinical examination reveals a temperature of 38.5˚C, a saturation at 94% in ambient air, an FC = 100 bt/min (heart rate), a regular tachycardia without over-noises. There is no edema in the lower limbs or deep vein thrombosis.

Quiet cracking under pulmonary, small hard and painless axillary and inguinal adenopathies were also recorded. However, there was no skin lesion.

The biological check-up revealed hyperleucocytosis at 38 g/l, normal hemoglobin, hypercalcemia at 3.67 $m{\cdot}mol^{-1}$, an LDH rate 2 times above normal, normal cardiac enzymes, no ECG abnormality detected, a normal hepatic, renal, electrolytic and inflammatory assessment.

The radiological evaluation revealed on lugs x-rays, non-specific opacities of the lugs basis and on abdominal-pelvic scanner the presence of mesenteric, inguinal and retro-peritoneal adenopathies.

The hypothesis of nonspecific pneumonitis, acute chest syndrome related to sickle cell disease and hematopathymphoid were mentioned. The immunophenotypic-lymphocyte study had demonstrated a clonal proliferation of T-lymphocytes CD4+, CD25+, coupled with a CD7phenotypic hole—confirming the ATLL diagnosis.

The treatment included systemic chemotherapy (interferon and zidovudine) and intrathecal injections.

For 3 years now, the patient is in complete remission and benefits from annual clinical and biological monitoring.

3. Discussion

Adult T-cell leukemia/lymphoma is a rare haemopathy with a prevalence of 2 to 5 cases/100000 inhabitants and affects 2% - 3% of subjects infected with the HTLV-1 virus. There are 15 cases per year in Martinique and more than 700 case-years in Japan. [5] [6] [7].

At the adult referral center for sickle cell disease management in Martinique, out of 778 patients followed up, about 30 are HTLV-1 carriers; representing 3.86% of sickle cell patients infected with HTLV1. Only one patient develops an

ATLL *i.e.* 3% of patients infected with HTLV1 or 0.1% of sickle cell patients followed upat the center. It is therefore a rare pathology to record with sickle cell patients. This rarity could be explained by the low life expectancy of sickle cell disease [5] [6]. According to Dearden, the onset median age for ATLL contraction is about 62 years in Japan and 50 years in the Caribbean [7]. Although the appearance of ATLL is just recent in the Caribbean, the median age remains above the life expectancy for patients suffering from sickle cell disease.

The usual modes of transmission of the virus were breastfeeding, which accounts for 95% of transmission followed by blood transfusion and sexual intercourse. Our 40-year-old patient was probably contaminated through the vertical route of transmission of the virus because according to Ohshima there is a latent period of 30 to 50 years after infection by HTLV1 before the appearance of the ATLL [8].

Classically, we recorded four different forms of this disease (acute, lymphomatous, chronic and indolent [8].

The acute form is characterized by a circulating phase of predominant atypical cells and the lymphomatous form is characterized by a minimal circulating phase. They are clinically translated by peripheral lymphadenopathies, possible hepatotoxicosis, wide variety of skin lesions, neurological, gastrointestinal, bone and pulmonary disorders, revealinghypercalcemia, hyperlymphocytosis made up of clover cells with convulsed nuclei with at immunophenotyping, a clonal proliferation of CD4+, CD25+ T-lymphocytes associated with a phenotypic hole CD7– [8] [9] [10] [11] [12].

Chronic forms are slow-onset with T-cell hyper-ammocytosis above 3000/mm^3 without hypercalcemia or organ involvement other than lymph node, pulmonary and cutaneous. Indolent forms are characterized by lymphocytosis < 4000/mm^3 with more than 5% abnormal mature adults T-cells and a common presence of cutaneous lesion [8] [9] [10] [11] [12].

Due to strong hyperlymphocytosis, hypercalcemia, and weakness of the tumor syndrome, our patient was classified suffering from the acute form.

The combination of the interferon Alpha with, the antiretroviral (Zidovudine) and prophylactic intrathecal chemotherapy used for our patient remains an effective treatment of the acute form of ATLL directed against both the abnormal lymphocyte and the HTLV1 virus [13]. Some authors have used a combination of polychemotherapy of CHOP versus VCAP (vincristine, cyclophosphamide, doxorubicin and prednisone), AMP (doxorubicin, ranimustine and prednisone), and VECP (vindesine, etoposide, carboplatin and prednisone) and achieved a higher rate of complete remission but the overall 3 years survival rate was not statistically different from CHOP result [14]. Bone marrow auto-transplantation is another therapeutic option in the management of ATLL in case of full remission.

The disease progression was marked by malignant hypercalcemia treated with corticosteroids and bisphosphonates.

The patient has been in clinical and biological remission for 3 years with the disappearance of the tumor syndrome, the absence of atypical lymphoid cells circulating with immunophenotyping, as well as the normalization of serum calcium and LDH levels.

This good prognosis observed with our patient got contrasted by the observations of some authors for whom the acute form of ATLL would be a poor prognosis and issued overall survival delay of less than 1 year [15] [16]. Is sickle cell ATLL a good prognosis?

A broader and, multi-center study on this rare condition in sickle cell disease may address this concern.

4. Conclusions

The combination of major haemoglobinopathy and hematopathy becomes a frequent concern for physicians because of the considerable gain in life expectancy of this population in relation to an efficient management.

This should allow reviewing the concepts on sickle cell disease mainly focused on growth disorders, chronic anemia, educational and socio-familial problems, chronic cardiovascular complications. Patients with Major Sickle Cell Disease may have cancer and specifically in Martinique, it will be necessary to diagnose ATLL.

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