

Case Report

Leukemia B Lymphoblastic Lymphoma in a Child: With t (9.22) and Hyperdiploidy

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Abstract: Introduction: Non-Hodgkin's lymphoblastic B lymphoma with lymph node location is exceptional in children. Unlike acute lymphoblastic leukemia, which is the first cancer in children around the age of 3 with a favorable prognosis with a survival of 5 years in 90%. Observation: child, 15 years old. The hospital admission examination showed a febrile patient (40°C), bilateral cervical and inguinal polyadenopathies, the absence of hepatosplenomegaly. The hemogram at entry found bicytopenia made up of angrogenic anemia and thrombocytopenia. On the haematological level, there has been an evolution towards pancytopenia. A lymph node biopsy showed medullary infiltration with lymphoma cells of phenotype B. The karyotype found hyper diploidy with t (9.22). The patient was put on corticosteroid therapy, hyperhydration and (Allopurinol) followed by COP type chemotherapy (Cyclophosphamide, Oncovin, Prednisone) with good tolerance. A year later the patient presented with a feverish peak (40°C). Only a hematological relapse in the form of acute leukemia. Therapeutically, it was decided to re-induce the patient according to the GRAALL catch-up protocol (Idarubicin-Aracytine) and to propose it for an allograft of bone marrow, but unfortunately the patient died. Conclusion: Lymphoblastic lymphoma / Acute lymphoblastic leukemia B, associated with t (9; 22) and hyperdiploidy in children is an exceptional hemopathy and has a negative diagnosis.

Keywords: Lymphoblastic Lymphoma, Acute Lymphoblastic Leukemia B, t (9.22), Hyperdiploidy, Child

1. Introduction

Malignant lymphomas correspond to lymphomatous proliferations, which group together all the tumor affections linked to a clone of the lymphoid or extraganglionic lymphoid tissue cells. The classification of lymphomas specifies Hodgkin's lymphoma (HL) and non-Hodgkin's lymphomas (NHL), the two entities can occur at any age. NHL represents approximately 10% of pediatric cancers with geographic variations (frequency of Burkitt lymphomas in equatorial Africa) and according to age (from 15 years, we

mainly note NHL with large cells either B or anaplastic) [1-3].

In fact, non-Hodgkin's lymphoblastic B lymphoma with lymph node localization with t (9.22) is reputed to be very aggressive and exceptional in children compared to acute lymphoblastic leukemia which constitutes the first cancer of children around the age of 3 years with a favorable prognosis (5 years survival in 90%) [4-6]. Through this clinical case, we report an exceptional observation of very malignant NHL in a child.

2. Observation

Child, aged 15, with no significant history. The history of his illness dates back to 2 months before his hospitalization by the installation of an intermittent fever estimated at 39°C. He was admitted to the clinical hematology service of the Military Instruction Mohamed V hospital for the exploration of cervical polyadenopathies associated with an infectious syndrome made of fever and chills all in a context of deterioration of the general state. The admission examination showed a febrile patient (40°C), a tumor syndrome made up of bilateral cervical and inguinal polyadenopathies, the absence of hepatosplenomegaly, an infectious syndrome without a clinical infectious call point. The hemogram at entry found a bicytopenia made up of angrogenic anemia and a thrombocytopenia (Hb=12,1 g / dl, reticulocytes=93,000 / mm³, platelets=33,000 / mm³), the rate of GB has normal summer of 4500 / mm³. The blood smear showed only a few hyperbasophilic cells. The EBV and CMV PCR as well as the HBV, HCV, toxoplasmosis, HIV, HTLV-1 and 2, TPHA-VDRL serologies were all negative. Both the malaria test and the ECU were negative. Blood culture has isolated *Salmonella enteritidis*. The patient was put on antibiotic (piperacillin / tazobactam). Antibiotic therapy completely reduced cervical and inguinal lymphadenopathy with a normalization of fever at 37°C, but on the haematological level there was an evolution towards pancytopenia (GB=800 / mm³, PNN=100 / mm³, Hb=10.3 g / dl, platelets=17,000 / mm³). The hemostasis assessment found a TP=90%, a TCA ratio=1.17, a fibrinogen level=4.74 g / l. The biochemical assessment revealed a high CRP=49.3 mg / l, an LDH of 278 IU / L, a high TG level of 2.26 g / l with a ferritinemia of 2029 ng / ml, and a uric acid level of 93 mg / l. In front of this clinical-biological table, a myelogram was made which revealed a marrow invaded 92% by lymphomatous cells (Figure 1a). Myeloperoxidase was negative. A lymph node biopsy objectified a histological aspect and an immunohistochemical profile of a medullary infiltration by lymphomatous cells of phenotype B (Figure 1b). Immunohistochemical cells expressed the markers: CD20, CD10, Bcl2 and Tdt. Immunophenotyping on peripheral blood has been in favor of B proliferation but with the unique expression of the B markers CD19 and CD10. CD45 expression was moderate on the cells studied. The karyotype found hyper diploidy with t (9.22) linked to the BCR-ABL molecular transcript. The patient was put on corticosteroid therapy in front of the large tumor mass, under hyperhydration and (Allopurinol) followed by COP type chemotherapy (Cyclophosphamide, Oncovin, Prednisone) with good tolerance. A year later the patient presented with a feverish peak (40°C). A relapse only haematological (without affecting the central nervous system) in the form of acute leukemia revealed by the following biological table: GB=21200 / mm³, plate=48,000 mm³, blood smear at 67% of blasts, myelogram invades at 94% of blasts. CIVD's assessment was negative. Therapeutically, it was decided to re-induce the patient according to the GRAALL catch-up protocol

(Idarubicin-Aracytine) and to propose it for an allograft of bone marrow, but unfortunately the patient died.

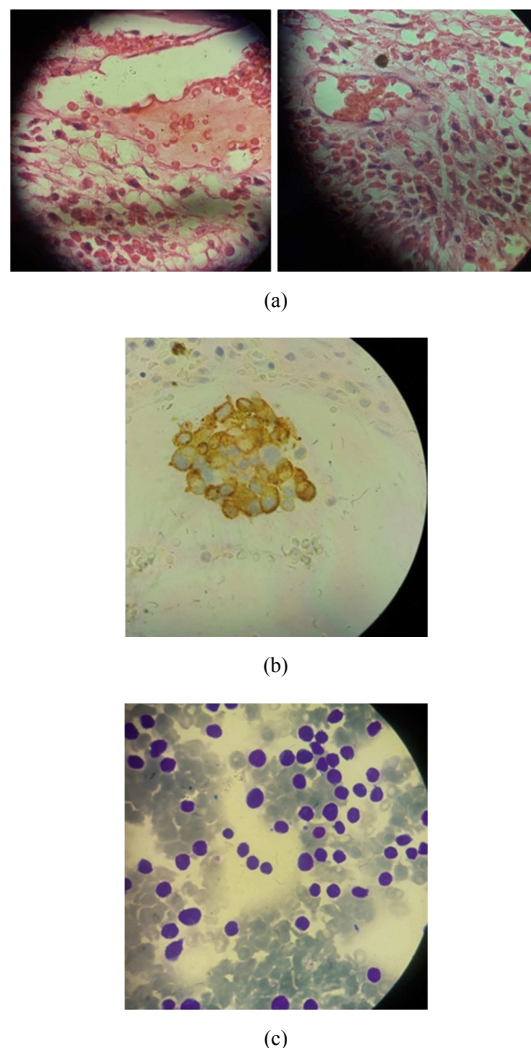


Figure 1. Lymph node biopsy finding a histological (a) aspect and an immunohistochemical (b) profile of a medullary infiltration by a lymphoblastic lymphoma of phenotype B. Medullary smear stained with MGG, showing lymphoma cell invasion, x100 (c).

3. Discussion

Lymphomas are very heterogeneous disease groups, some of which constitute a diagnostic and therapeutic emergency (Burkitt's lymphoma). The occurrence of lymphomas has increased a lot in recent years and this mainly affects developed pay. The incidence currently reaches 13.3 cases per 100,000 men and 7.8 cases per 100,000 women. Tumor diseases are rare in children. HL and NHL rank third, after leukemia and brain cancer. Thus the frequency and distribution of LH and NHL in children and adolescents under the age of 18 differs from that observed in adults. The incidence of NHL is low in children and increases with age, reaching a peak around 80 to 84 years (0.6 cases per 100,000 in children, compared to more than 90 cases per 100,000 in the elderly) [7, 8]. Lymphoma can have any location and therefore a very heterogeneous clinical and biological picture. Some

tables are more important or more frequent. The main tables are defined by peripheral lymphadenopathies, unique or not, associated with an unexplained long-term fever that exceeds 38°C for more than three weeks with unexplained pruritus in some cases [8, 9].

In our patient, the examination of the first blood smear first suggested a mononucleosis syndrome, which was dismissed in the face of the negativity of viral serologies. The immunohistochemical study of an osteomedullary biopsy (BOM) as well as the immunophenotyping of circulating cells made it possible to correct the diagnosis of our patient towards an LAL / LL B. Indeed the last WHO classification of NHL published in 2017, integrated three essential concepts:

-Lymphoma is always developed from a normal cell of the lymphoid tissue, so this proliferation will depend on the criteria of differentiation and activation of the lymphoid cell involved (B or T);

Genetic anomalies that control the malignant transformation by deregulating the homeostasis of the cell;

The identification of lymphomatous proliferation meets specific histopathological, immunophenotypic, cytogenetic, molecular and clinical course criteria [3, 10, 11].

Therefore, lymphomas developed at the expense of B or T precursor lymphoid cells are grouped into LAL / LL B or T, due to the existence of a common precursor and similar management. The terminology leukemia or lymphoma differs depending on the point of departure of the disease, in both cases, it is the same type of malignant cells involved [5, 10, 12]. Lymphoblastic lymphoma is a diagnostic and therapeutic emergency. It represents 30% of pediatric NHL. The median age is 9.5 years. It is more common in boys. Most often it is T lymphoblastic lymphoma [2]. The malignant transformation of B lymphoid cells is often linked to recurrent chromosomal translocations. An oncogene and a gene which codes for the immunoglobulin chains are directly responsible for the cellular modifications in a specific way. The presence of an oncogenic virus also constitutes a malignant cellular deregulation mechanism (HTLV-1, HIV, EBV, etc.). Cytogenetic analysis is of major utility, it provides information on:

Cellulaire the cell clone, to differentiate a reaction proliferation from a malignant proliferation;

The probable type of lymphoma, due to the presence of certain translocations as well as the prognosis [8, 13].

In general, the prognostic factors for lymphoblastic B lymphomas with t (9;22) are linked to the disease, the patient, and the response to treatment:

1. prognostic factors linked to the disease: anemia, elevations in LDH, a large tumor mass, the number of visceral lesions, the Ann Arbor stage [14];
2. prognostic factors related to the patient: age over 60, impairment of the general condition with a WHO score greater than 2 (score 3: bedridden subject more than 50% of the day), fever, weight loss (more than 10% of the weight the last 6 months);
3. prognostic factors linked to the response to treatment: complete remission is the first criterion of good

prognosis, the early normalization of the PET-scan after two or three courses [4].

In this kind of situation, the use of the karyotype is essential before the therapeutic induction phase because it guides the therapeutic scheme. Our patient presented mainly poor prognostic factors related to the disease in a febrile context with a karyotype which showed hyperdiploidy with t (9; 22). In this context the prognosis is then that which is linked to the abnormality of worse prognosis. T (9; 22) is the most common cytogenetic abnormality in adult ALL / LLB with 20% to 30% and only 3-5% in childhood LAL / LLB. Its frequency increases with age up to 50 years and then decreases. The prognosis is poor, which could be improved by a specific inhibitor of the BCR-ABL fusion protein. 5-year survival is less than 15% for patients treated with chemotherapy. Allografting remains the only curative possibility when the latter is impossible, autografting is recommended provided that the graft is free from residual molecular disease [4, 15, 16].

The particularities of this observation are:

According to the WHO classification, acute leukemias / B lymphoblastic lymphoma with recurrent cytogenetic anomalies are grouped into 9 entities: LAL / LLB with t (9;22) (BCR-ABL1), LAL / LLB with t (v; 11q23) (MLL (now KMT2A) rearranged), LAL / LLB with t (12; 21) (TEL-AML1 (ETV6-RUNX1)), LAL / LLB with hyperdiploidy, LAL / LLB with hypodiploidy, LAL / LLB with t (5; 14) (IL3-IGH), LAL / LLB with t (1; 19) (TCF3 - PBX1), LAL / LLB with BCR-ABL1 - like, LAL / LLB with iAMP21 [3, 4]. Our patient had recurrent translocation (9, 22) with a positive BCR-ABL and hyperdiploidy. The translocation which involves the ABL gene and the BCR gene is responsible, as in LAM or CML, for the production of a mutated protein with tyrosine kinase activity, either p210 or p190 in the other half of the cases. The treatment of this form of acute leukemia / lymphoblastic B lymphoma is more difficult while hyperdiploidy is considered to have a good prognosis. In fact, to our knowledge, this is an association never described before [5, 17].

Primary lymph node involvement, with t (9;22) is a rare association in children. The primary locations in children are most often abdominal, mediastinal and ENT [3].

The good clinical course of the disease before and after chemotherapy despite the seriousness of the biological picture and the context. And an atypical cytology evoking a mononucleosis syndrome on the first blood smears of the first two weeks of admission to the hospital. These are elements that can delay the diagnosis as well as the treatment of this aggressive entity. In fact, ALL / LL B with BCR-ABL is considered to be of high grade malignancy with an unfavorable prognosis in children [1, 4, 6].

According to the data in the literature, remission is complete in young people whose age is <30 years in 90 to 95% of cases with a median of three years of life in approximately 60% of subjects, our patient died after a year [4].

Indeed, the therapeutic scheme depends on the histology, the classification of Ann Arbor and prognostic factors. The

establishment of a central venous pathway (except contraindication) is urgent in B lymphoblastic lymphomas with t (9;22). Due to the corticosteroid sensitivity of NHL, it is recommended not to prescribe corticosteroid therapy before any biopsy because it can modify the anatomopathological aspect. The treatment of non-Hodgkin's B lymphomas is based on chemo-immunotherapy. The latter combines the administration of anti-B monoclonal antibodies with the chemotherapy protocol. The number of courses and the intensity depend on prognostic factors. The place of radiotherapy in the treatment of NHL is no longer of importance compared to chemotherapy, especially in very aggressive entities [6, 11, 18].

4. Conclusion

B lymphoblastic NHL with t (9;22) can be found in children. This entity represents a diagnostic and therapeutic emergency. A table associating peripheral lymphadenopathies with a non-recurrent fever and pruritus in certain cases constitute the first signs of discovery of this type of lymphoma in the majority of cases. You have to know how to look for the three clinical pictures revealing an emergency (an upper cellular syndrome, a rapidly progressing abdominal mass, or a neurological syndrome linked to spinal cord compression). A histological biopsy study of the peripheral ganglion supplemented by a tumor karyotype and immunophenotyping establish the diagnosis and prognosis. The NHL LL / LAL B entity, associated with t (9; 22) and hyperdiploidy in children constitutes an exceptional haemopathy with a derogatory diagnosis. It can pose a diagnostic problem, with a delay in therapeutic management. In this kind of situation an urgent BOM supplemented by a molecular and cytogenetic study are essential [2, 4, 8].

Declaration of Interests

The authors declare that they have no conflicts of interest in connection with this article.

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