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Case Report Open Access

Plasmocytoid Dendritic Cells Leukemia: A Rare Presentation

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Abstract

The plasmacytoid dendritic cells leukemia is a rare hematolymphoid neoplasm with a very poor prognosis, where skin involvement is common. It is a malignant proliferation developed at the expense of hematopoietic cells of the white blood cells, proximate to normal plasmacytoid dendritic cells. The phenotype of tumor cells initially described was CD4 + CD56 +, without T marker expression. CD56- forms have also been reported, even fewer without skin involvement. More specific markers are expressed by tumor cells: CD123, BDCA2, BDCA4.

We report an unusual presentation of this entity, but without skin lesions. The diagnosis of plasmacytoid dendritic cells leukemia was made on the cytological and immunophenotypic data given.

Keywords: Acute leukemia; Plasmocytoid dendritic cells; Bone marrow biopsy; Imunophenotyping

Introduction

Leukemia with plasmacytoid dendritic cells (LpDC) is a distinct entity in the recent classification of the World Health Organization (WHO 2008). It was not entirely characterized until recently [1].

This leukemia is characterized by a systemic proliferation of plasmacytoid dendritic cells (PDC), with Immunophenotyping of surface coexpressing mostly CD4 and CD56. Its evolution is very aggressive with 16 months as median survival [2]. We present for discussion the rare and interesting case of patient presenting a LpDC after physical and biological exploration.

Observation

The subject of this report is an 65 years old, male who presented to consultation with anemia, gingivorrhagia and chronic fatigue. Physical examination showed purpuric tasks at level of the chest, bruising at level of the two superior members and an hepatosplenomegaly.

Hematologic parameters indicate a bicytopenia: a normochromic normocytic aplastic anemia with blood hemoglobin (Hb): 5,4 g/dl and thrombocytopenia, platelet count: 13000/mm^3. The white blood cells totaled (WBC): 39 000 /mm^3 with lymphocytosis (Ly): 18 470/mm^3. Blood smear reveals the presence of medium blasts consisting of regular core, bypassed, with delicate chromatin and nucleoli. The cytoplasm is moderately abundant, basophil and presents sometimes vacuoles or extensions (Figure 1). These leukemic cells represent 40% of all white blood cells. Hepatic enzymes showed: Glutamo Oxaloacetate Transferase (GOT): 135 UI/L, Glutamo Pyruvate Transferase (GPT): 186 UI/L, Gamma Glutamyl Transferase (GGT): 369 UI/L and Phosphatase Alcaline (PAL): 253 UI/L. The C-Reactive Protein (CRP) was 31 mg/l, the sedimentation rate was 80 mm at the first hour. Viral serologies (hepatitis B and C and HIV) were negative. The research of Koch Bacillus in sputum was also negative. Thoraco-abdominal-pelvic CT showed hepatosplenomegaly with hilar lymphadenopathy liver. Bone marrow biopsy revealed sheets of leukemic cells replacing marrow estimated to 80%. These blasts had identical features to the leukemic cells from the blood (Figure 1). Immunophenotyping of these cells objectified the low presence of CD45+, they express strongly CD4, CD56, CD123 and HLA-DR. They are also CD43+, CD36+ and BDCA2+. Myeloid and pan- T or pan-B lymphoid markers were negative except CD2. No recurrent cytogenetic abnormalities were identified in the karyotype. Based on the accumulated data from this case with recent research findings, this hematolymphoid tumor has been assigned a designation of "leukemia not T not B, CD4 + /CD56+" (Figure 2).

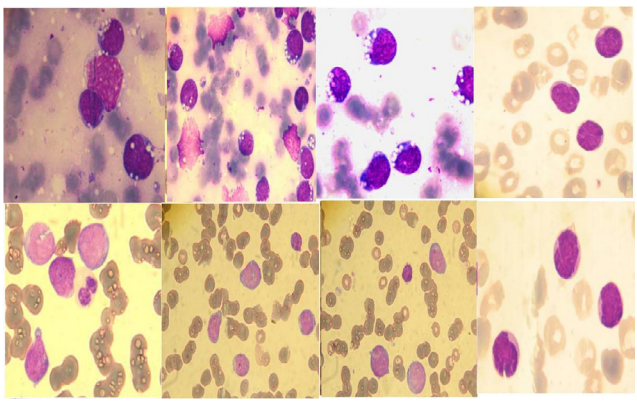

Figure 1: Medullar aspect of a medium blasts with a regular core, bypassed, and a delicate chromatin and nucleoli. Cytoplasm is moderately abundant, basophil and presents vacuoles and sometimes cytoplasmic extensions.

The patient refused treatment and left hospital against medical advice. He returned four weeks later to emergency in an array of septic shock, he died a few hours after admission.

Discussion

The nomenclature used to describe this entity (Blastic Dendritic Plasmacytoïd Cell Neoplasm (BPDCN) or derived leukemia of

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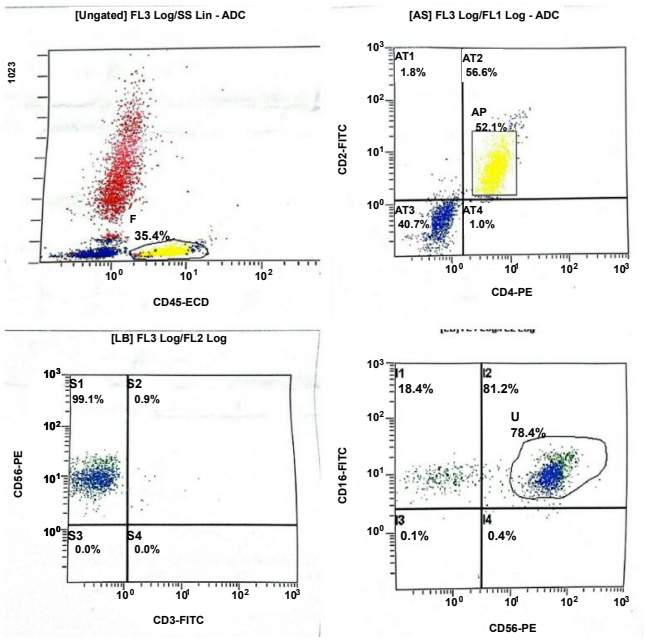

Figure 2: Immunophenotyping of the leukemic cells: CD45+ low, CD4+ bright, CD56+ bright.

pasmacytoid dendritic cells (LpdC)) evolved during years until the underlying biology has improved. This leukemia was initially described in 1995 as acute leukemia with agranular cells CD4+ (NK : Natural Killer). After the apparition of blasts CD56+, the expression "Lymphoma with NK blastic cells" was used. Thereafter, the term "CD4+/CD56+ hematodermic neoplasm" was invented basing on the immunophenotyping and a predilection for cutaneous involvement. However, following the discovery and confirmation that acute leukemia with CD4+/CD56+ cells is derived from plasmacytoid dendritic cells (type 2 of dendritic cells), the current nomenclature, "blast tumor with plasmacytoid dendritic cells", was chosen to describe this entity in the classification WHO 2008 of hematopoietic and lymphoid tissue tumors [1].

Plasmacytoid dendritic cells leukemias (LpDC) are rare and present less than 1% of acute leukemia. They are so frequent after 50 years old but pediatric forms have been also described. The sex ratio is (3/1) with a male predominance [2]. We observe lymphadenopathy and/or splenomegaly in 61% of cases [2,3]. Most of patients present cytopenia due to bone marrow infiltration; it is most often thrombocytopenia [4]. The leukocytosis is infrequent, but the presence of blasts in blood is usually observed. Bone marrow infiltration at diagnosis is found in 87% of cases with very variable rates [5]. This is consistent with data of physical and biological exam of our patient who presents also leukocytosis with lymphocytic predominance and 40% of circulating leukemic cells.

Eighty percent of cases of LpDC present nonspecific skin lesions: atypical rash refractory to standard therapy [5]. The primary leukemic presentation, but without skin lesions, has rarely been reported [1,5-7]. In this case, petechial and bruising were related to profound thrombocytopenia.

Currently, it is believed that this leukemic cells are originating from hematopoietic precursor of dendritic cell-type 2 or plasmacytoid, not belonging to myeloid or lymphoid lineage [8]. Two particularities are found in most published cases and can guide diagnosis: the presence of micro-vacuoles arranged on "necklace of pearls" on the periphery of the cytoplasm and the presence of cytoplasmic expansion in form of pseudopodia [5,8,9]. These cytological features are found in our case which prompted us to test specific markers of pasmacytoid dendritic cells. However, the proliferation can take different forms [10,11]. At last, negative cytochemical reactions (myeloperoxidases, esterases) and results of immunophenotyping will allow to exclude other diagnosis hypothesis [12].

Immunophenotyping of these leukemic cells shows the combined expression of CD4+ and CD56+, without specific markers of any lineage: pan-T, pan-B lymphoid or myeloid antigens. The expression of CD45 indicates their hematopoietic origin. The phenotypic profile corresponds to the circulating normal plasmacytoid dendritic cells (pDC). The expression of specific markers of normal pDC exists on the LpDC. Indeed, cells of LpDC express: CD123+ strong (receiver at the IL-3), HLA-DR+, CD45RA+, CD45R0- BDCA-2+ (Blood dendritic cells antigen), BDCA-4+, ILT-3+ (Immunoglobulin like transcrit). In LISG study (Leukemia Immunological Study Group) [5], the LpDC express also frequently CD36 (85 %) and CD68 (92 %) (2 markers associated to myelomonocytic lineage) and some cases express CD2 (9 %) and CD7 (61 %) as normal pDC [5,12,13].

Flow cytometry of the marrow aspirate specimen of our patient showed agranular leukemic cells with a strong expression of CD4, CD56, CD123, HLA-DR at immunophenotyping, and a weaker expression of CD45, CD2, CD43, CD36 and BDCA2. We note the absence of myeloid and pan-T and pan-B lymphoid markers.

Two thirds of patients with LpDC have chromosomal abnormalities [9,11,13]. In most cases, Karyotypes are complex and associate within the same clone an original combination of recurrent anomalies. There are present in lymphoid or myeloid pathologies and none can be considered specific to LpDC, but their association within the same clone is particular [5,9,13]. The karyotype of our patient was normal, but it does not rules out the LpDC diagnosis.

All physical and biological data found are compatible to leukemia derived from plasmacytoid dendritic cells, a distinct entity in the WHO classification 2008, despite the absence of skin lesions, which is usually observed [1,6-8]. Its prognosis is poor, the median survival is less than 16 months, even for patients with pure cutaneous form. Relapses are common and early with frequent neuromeningeal attacks [2,10,11].

There is no prospective randomized data to define optimal first-line chemotherapy. Currently, we adopt acute myeloid or lymphoblastic leukemia protocols, for induction therapy. The bone marrow transplant may be considered from the beginning of the course of the disease, this could result in long-term remissions. However, research efforts are needed to better understand the biology of LpDC and establish treatment algorithms based on evidence that may ultimately improve the overall prognosis of this disease [14].

Conclusion

This case illustrates unusual presentation of LpDC without skin lesions. These Leukemias are defined by their particular cytological and immunophenotypic features of blasts, combining expression of CD4 and CD56, negativity of pan-T or pan-B lymphoid, and myeloid markers. This disease typically presents with a skin lesion (nodule or plaque), frequently with cytopenia but presentation without cutaneous lesions has rarely been reported in the literature. The recent individualization of this entity is probably not reflected an emerging disease. Rather it

reflects the use of advanced diagnostic methods in current practice as flow cytometry to better characterize hematolymphoid neoplasm [2,12,13].

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