on 04/28/23: lymph node enlargement in the inguinal, iliac, pericaval, left paraaortic, retrocrural regions, in pulmonary hila and various compartments of the mediastinum, axillary and cervical, in addition to diffuse hypermetabolism in the bone marrow and splenomegaly. Performed inguinal lymph node biopsy on 05/05/23 – Immunohistochemistry released on 05/21/23 – Pathological cells positive for BCL2 CD10 CD4 CD5 CD7 CD8 Tdt, KI67+100%, diffuse CD3+, cytoplasmic pattern. Evolved with progressive worsening of the clinical condition and pancytopenia. Bone marrow aspirate collected on 05/26/23 for Immunophenotyping showing: 4.1% CD56+ CD3(-) CD8-/+ CD4(-) NK CELLS; 15% MATURE (CD45++) POLYCLONAL T LYMPHOID CELLS (CD3++): . 3.8% CD4+ TCRALFA/BETA+ (TCRCBETA1+ 50%); . 8.8% CD8+ TCRALFA/BETA+ (TCRCBETA1+ 20%); . 0.5% CD8+ TCRGAMA/DELTA+; . 1.3% CD4+CD8+ TCRALFA/BETA+ (TCRCBETA1+ 30%); . 0.6% DOUBLE-NEGATIVE: 0.1% TCRALPHA/BETA+ AND 0.5% TCRGAMA/DELTA+ 11.3% MATURE CD8+ LYMPHOID CELLS (CD45++), WITH PARTIAL EXPRESSION OF SURFACE CD4 AND CD3, EXPRESSION OF CYTOPLASMIC CD3+ (EPSILON CHAIN), T MARKERS (CD2+ CD5+ CD7+) AND CYTOTOXIC/NK ANTIGENS (CD56+ CD16-/+ CD94+ Perforin+), and effector T cell phenotype (CCR7(-) CD27-/+ CD28-/+ CD45RA+ homogeneous). NK profile stage 4: CD56++ CD16-/+ and CD57(-) (Figure 1).

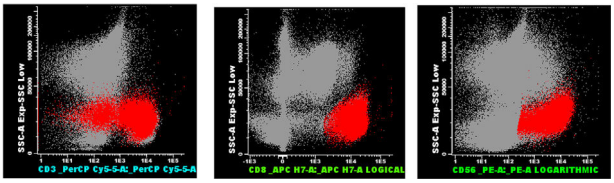

Figure 1: Mature CD8+ lymphoid cells, with partial expression of surface CD3, NK profile CD56++.

Negative antigens: CD25 CD57 CCR7 CD11C CD45RO CD1A CD117 CD30 TCRAlpha/Beta TCRCBeta1 TCRGama/Delta HLA-DR TDT and CD10. At that time, the patient presented skin lesions on the chest and face (Figures 2 and 3), his clinical condition worsened and he was admitted to the ICU. A cerebrospinal fluid sample was also infiltrated by T/NK cells. The phenotypic findings associated with the clinical condition led to the diagnostic conclusion of T/NK Cell Lymphoma. Serology tests for EBV were negative. He did not present clinical improvement, developed Mucormycosis and died.

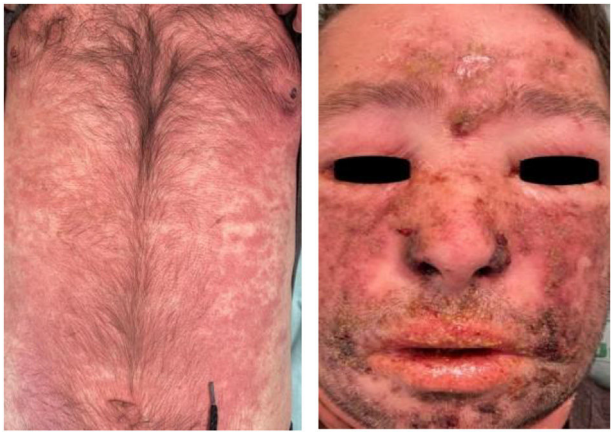

Figure 2: Skin lesions on the chest. Figure 3: Skin lesions on the face.

Comments: Flow cytometry was indispensable in the diagnostic elucidation, in the separation of normal and pathological T and NK cell subpopulations of the sample, and in the rapid definition of lymphoma with a severe and aggressive clinical course.

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CASE REPORT: PLASMA CELL LEUKEMIA

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A 55-year-old female was referred to the medical hematology service for severe anemia and osteolytic lesions in the spine and skull. At the time of consultation, the hemogram showed "lymphocytosis," with the automated analyzer misidentifying plasma cells as lymphocytes, and the peripheral blood smear revealed cells resembling hairy cells, raising suspicion of hairy cell leukemia or plasma cell leukemia. The patient was requested to undergo a series of laboratory tests to perform a differential diagnosis between the two conditions. Laboratory findings were as follows: Hemoglobin: 6.7 g/dL (normocytic-normochromic anemia); Leukocytes: 48,620 cells/μL (leukocytosis); Platelets: 128,000 cells/μL (thrombocytopenia); Creatinine: 2.6 mg/dL; Calcium: 14.2 mg/dL (hypercalcemia); Beta-2-microglobulin: 42 mg/L; LDH: 146 U/L; Total proteins: 7 g/dL; Albumin: 4 g/dL. Peripheral blood morphology confirmed anemia and thrombocytopenia with 72% plasmacytoid cells. Serum protein electrophoresis revealed a monoclonal band in the mid-gamma region (1.5 g/dL). Immunofixation identified a monoclonal component of free Lambda light chains. Immunoglobulin levels were markedly reduced (IgG: 375 mg/dL, IgA: 10 mg/dL, IgM: 4 mg/dL), and no monoclonal bands were detected in urine. Peripheral blood was examined by multiparametric flow cytometry using first an LST tube and then plasma cell panel with the CytoFLEX BC cytometer. Using CD138/CD38 gating strategy identified 75% circulating leukocytes as plasma cells with a neoplastic phenotype. These cells expressed CD38 and CD138 but lacked CD19, CD45, CD56, CD117, and CD27, with cytoplasmic lambda light chain restriction. Bone marrow examination was deferred at the

time of diagnosis. FISH analysis for IGH/FGFR3 t(4;14), IGH/MAF t(14;16), and p53 gene deletions (17p13.1) showed no abnormalities. Based on international criteria for plasma cell leukemia (PCL)—defined as ≥ 20% and ≥ 2000/μL plasma cells in peripheral blood—the diagnosis of primary PCL was confirmed. The patient's clinical presentation, including hypercalcemia, anemia, and osteolytic lesions, supported the diagnosis. **Discussion:** PCL is a rare and aggressive form of multiple myeloma characterized by circulating plasma cells. Morphological variability of plasma cells can complicate diagnosis; cells may mimic lymphocytes, monocytes, or hairy cells. Key diagnostic tools include bone marrow studies, flow cytometry, and a comprehensive myeloma profile, including serum protein electrophoresis, immunofixation, free light chain assay, and 24-hour urine analysis. **Management and Conclusion:** Given the poor prognosis and aggressive nature of PCL, treatment was initiated promptly with a bortezomib-based regimen. PCL highlights the importance of accurate diagnostic methods to guide timely and appropriate therapy.

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COEXISTENCE OF CHRONIC MYELOMONOCYTIC LEUKEMIA AND LYMPHOPROLIFERATIVE DISORDER: THE DIAGNOSTIC ROLE OF IMMUNOPHENOTYPING IN PERIPHERAL BLOOD

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Introduction: The association of chronic myelomonocytic leukemia, with bone marrow infiltration by chronic lymphoproliferative diseases has been reported in the literature mainly by case reports, and documented through bone marrow biopsies. More recently, as the diagnosis of CMML can be made by peripheral blood immunophentyping, this association could be detected more frequently. This association has been included in the ICC classification of subtypes of CMML.[1] **Case Description:** Male patient, 72 years old, was hospitalized due to pneumonia. At that time, the peripheral blood (PB) count showed leukocytosis with monocytosis and thrombocytopenia, which did not resolve after the pneumonia was cured. Reviewing former PB counts, monocyte counts >10% could be detected. In 2024, no lymphadenopathy could be observed, but the spleen was 2 cm below the costal margin. **Tests during most recent hospitalization:** Creatinine: 0.9 mg/dL, Ferritin: 46 ng/mL, Serum iron: 67.7 μg/dL, ALT: 34 U/L, Vitamin B12: 794 pg/mL, Folic acid: 6.01 ng/mL, Beta-2 microglobulin: 2244 ng/mL (normal <2164), LDH: 320 U/L (normal), Protein electrophoresis: monoclonal peak of 1.46 g/dL; Serum immunofixation: IgM/Kappa. **Bone marrow aspirate:** Hemodiluted. M:E ratio: 4.28. Lymphocytes: 15%. **Bone marrow biopsy:** markedly hypercellular marrow tissue, granulocytic hyperplasia with maturation arrest. Scattered CD34+ cells. Interstitial infiltration by low-grade lymphoma (lymphocytes and plasma cells) with IgM Kappa on immunohistochemistry. Likely Waldenström macroglobulinemia, with marginal zone lymphoma as differential diagnosis. Immunophenotyping suggested. **Bone marrow immunophenotyping (October 2024):** Monocytosis of 9.1% composed of mature elements. Classical monocytes: 86.1%, Intermediate: 10.8%, Non-classical: 3.1%. Polyclonal plasma cells: 0.15%. Monoclonal B lymphocytes with the following phenotype: CD45+++, CD19++, CD20++, CD43+, CD79b++, CD200++, partial IgM (41%), and predominance of kappa light chain. **Peripheral blood immunophenotyping (November 2024):** Monocytosis of 22.3% composed of mature elements. Classical monocytes: 97.2%, Intermediate: 2.0%, Non-classical: 0.4%. 3.2% monoclonal B lymphocytes with phenotype: CD45+++, CD19++, CD20+++, CD79b++, CD200++, IgM+++, partial CD23 (30%), kappa light chain. **Comments:** In the last years, new strategies for the study of subtypes of monocytes using flow cytometry have been developed. This permitted to better understand the role of these cells in non-neoplastic inflammatory diseases as well as the detection of neoplastic clones. In the present case, the diagnostic work-up in a case with CMML using PB immunophenotyping by multiparametric flow cytometry permitted also the detection of a small lymphoid clone of Waldenström macroglobulinemia. The examination of bone marrow biopsy permitted to diagnose an extensive infiltration of this lymphoproliferative disorder. The patient was treated for macroglobulinemia, and is well and in observation. **Comments:** In this case, peripheral monocytosis detected during infections was known since 2015 but had never been thoroughly investigated. Only during the last infectious episode was the patient referred to a hematologist. After bone marrow immunophenotyping—of which the sample was very diluted—CMML was suspected, and peripheral blood testing confirmed the diagnosis. The monoclonal peak was an incidental finding, but immunophenotyping allowed the diagnosis of chronic lymphoproliferative disease. However, the true extent of this disease in the bone marrow was only assessable through biopsy. The co-existence of myeloproliferative neoplasms or CMML with chronic lymphoproliferative diseases is a rare event (1–2% of chronic myeloproliferative neoplasms). According to limited literature, these appear to be independent neoplasms, not derived from the same stem cell. Immunophenotyping (blood or bone marrow) is the most sensitive technique for detection.

Table 1 The evolution of PB counts.

	11/12/2025	04/16/2019	08/22/2021	01/05/2022	05/02/2024	08/2024	09/2024
RBC	3,81	3,82	3,18	3,89	3,73	3.63	3,7
HB	12,7	12,1	10,2	12,2	12	11,5	12,2
HCT	36,9	37,9	30,70	38,4	36	35,1	36,7
MCV	96,9	99,21	96,4	98,7	96,5	96,6	99,5
LEOCOCYTE	4200	6680	13940	7250	15660	26200	8100
BAND CELLS	42	67	0	73	626	1048	
SEGMENTED	1722	3073	10804	2826	9396	20436	4540
EOSINOPHILS	42	67	0	73	0	0	
BASOPHILS	0	0	42	73	0	0	
TYPICAL LYMPHOCYTES	1680	1536	1450	1740	3289	2620	14600
ATYPICAL LYMPHOCYTES	0	935	0	0	0	0	
MONOCYTES	714 (17%)	1002(15%)	1645 (11,8%)	2538 (35%)	2349 (15%)	2096 (8%)	1780
PLATELETS	140.000	150.000	88.450	121.000	53.280	59.140	101.000