Blastoid Mantle Cell Leukemia: Combined Diagnostic Approach in a Very Rare Entity

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Introduction. Mantle cell lymphoma (MCL) is an rare variant of non-Hodgkin lymphoma (3–10% cases) with characteristic morphology (well-differentiated cells with deeply cleaved nuclei), phenotype (CD5 and Cyclin D1 positivity), genotype (t (11 : 14)/bcl-1) and poor prognosis. In 10–20% patients MCL may transform or initially present as blastoid variant consisting of larger pleomorphic cells with blastic features. Tumour cells are detectable in blood in 40–50% cases of blastoid MCL, but overt blastoid mantle cell leukemia with > 30% leukemic cells are exceedingly rare, only several episodic patients have been described. Such cases may present a great diagnostic challenge, for patients are usually morphologically and clinically indistinguishable from acute leukemia, while treatment options for these two entities are entirely different.

The aim. Morphology and flow cytometry data in the case of leukemic blastoid MCL are presented to increase the awareness of this rare entity and to stress the necessity of combining several diagnostic approaches to ensure the correct diagnosis.

Materials, methods and results. A 54-year-old male patient was hospitalized in Riga Eastern Clinical University Hospital Hematology Department due to generalised lymphadenopathy, B-symptoms and hyperleukocytosis 141E9/l that later raised to 350E9/l. 92% leukocytes were atypical mononuclear cells; 70% being medium-sized and large cells with high nuclear polymorphism including deeply cleaved nuclei, young dispersed chromatin with well-defined nucleoli. The rest were small lymphocytes with broad cytoplasm and cleaved nuclei. Phenotype by flow cytometry was CD45++, CD19 weakly+, CD20++, cytCD79a++, CD5+, CD25+, CD38 weakly+, CD22++, cytIgM+; the cells did not express TdT, CD34, CD10, surface immunoglobulins as well as T-cell and myeloid antigens. The phenotype was incompatible with acute lymphoblastic leukemia and highly suggestive of MCL (prolymphocytic transformation of B-CLL/SLL being a remote second possibility). Bone marrow and lymph node histology revealed diffuse infiltration by small and medium-sized cells with clear pleomorphic nuclei; immunohistochemical staining results were identical: CD20++, CD3-, CD5+, CD10–, CD34-, bcl-2+, Cyclin D1+, Ki67 index below 40%. Phenotype CD20+, CD5+, Cyclin D1+ is pathognomonic, so MCL diagnosis was unquestionably proven. Molecular genetics for bcl-1 rearrangement were not performed.

Conclusion. The case demonstrates difficulties that arise at diagnosis of a rare entity with atypical presentation. In this particular patient clinical features, blood values and cytology indicated an acute leukemia with only a minor reservation due to cell morphology. At this time point, a limited diagnostic protocol would have mistakenly led to the diagnosis of acute lymphoblastic leukemia with subsequent improper management. Multiparameter flow cytometry, being a fast and informative diagnostic tool, in this case was of only suggestive value after certain exclusion of B-cell precursor phenotype, for CD5+, CD20++, IgM+ phenotype is typical, but not completely diagnostic for MCL, particularly facing the unusual presentation and cytomorphology. Immunohistochemistry for Cyclin D1 positivity or molecular genetics for t (11 : 14)/bcl-1 was necessary for final proof, the former was provided in this case, allowing to diagnose the extremely rare entity – blastoid mantle cell leukemia.