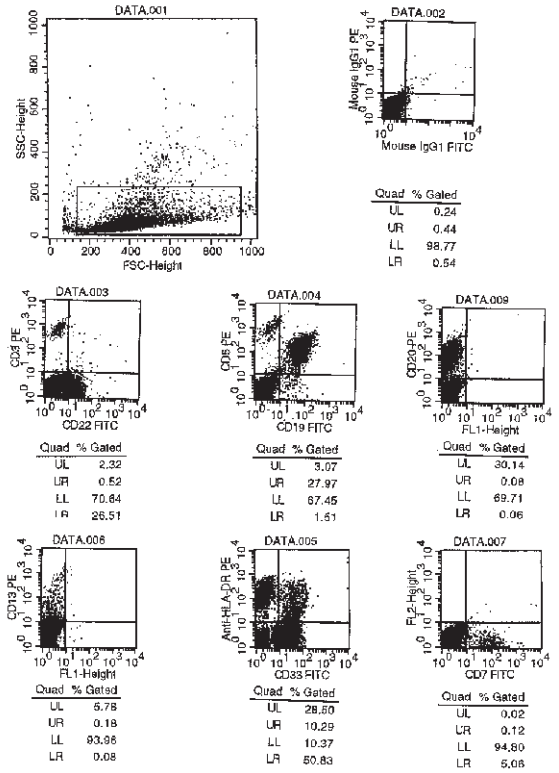

Figure 1. Light scatter properties of analyzed cells (top). The flow cytometric dot plots clearly show that virtually all CD19+ cells are positive for CD5 antigen and there are two cell populations with different HLA-DR antigen expression pattern. CD33 antigen is found to be the only antigen that expressed more than 50% of the cells and most of them are negative for HLA-DR antigen.

nosis but we do not have any doubts about the diagnosis because more then 10×10^9/L cells expressed CD5, CD19, CD20 and CD22 (Figure 1).

The concomitant presentation of AML and CLL is extremely rare and the use of two-color flow cytometry to differentiate the cell populations demonstrates the utility of this technology in the diagnosis of unusual hematologic malignancies.

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Acute megaloblastic anemia: homocysteine levels are useful for diagnosis and follow-up

Sir,

Vitamin B_{12} (cobalamin) and folic acid deficiencies lead to megaloblastic anemia (MA), and induce accumulation of methylmalonic acid (MMA) and homocysteine (HCY).[1] The most common presentation of MA is classical macrocytic anemia. Other presentations are acute megaloblastosis (AM) and masked megaloblastosis.[2,3] In this report, we present a case of AM diagnosed and followed up by evaluation of HCY levels.

A 45-year old male was diagnosed as having Philadelphia-positive chronic myelogenous leukemia. Three years after diagnosis the patient developed a lymphoid blast crisis and was started on a chemotherapy protocol. The first consolidation treatment consisted of 6-mercaptopurine, methotrexate (MTX), VM-26 and cytarabine. MTX rescue with folinic acid was performed following standard guidelines. On day +14 a platelet count of 9×10^9/L was found. Hb was 99 g/L, mean corpuscular volume (MCV) 92 fL and leukocyte count was 7.06×10^9/L with 84% of neutrophils with hypersegmentation. Reticulocyte count was 0.053×10^{12}/L (1.66%). Vitamin B_{12} levels and red cell folate were 322 pmol /L (normal 150-1200) and 938 nmol/L (normal 441-1285), respectively. A BM aspirate revealed 30% of erythroid precursors with megaloblastic features and a 55% of myeloid precursors with increased size and no blast cells. Serum HCY levels were 38 µmol/L (normal < 16). The

Table 1. Evolution of analytical parameters during folinic acid and vitamin B_{12} treatment.

	Pre-treatment Day –9	*Onset Day 0*	*Post-treatment Day +9*
Platelets ($x10^9$/L)	134	9	112
Leukocytes ($x10^9$/L)	6.76	7.06	5.72
Hemoglobin (g/L)	91	99	95
MCV (fL)	93	92	95.3
Reticulocytes ($x10^{12}$/L)	0.037	0.053	0.163
Homocysteine (µmol/L)	–	38	9

AM, acute megaloblastosis; MCV, mean corpuscular volume.

patient was diagnosed as having AM and began treatment with folinic acid 12 mg iv in one single dose and folic acid 5 mg/day po for 14 days and parenteral vitamin B_{12} 2 mg/day for 4 consecutive days. After 10 days of treatment the platelet count increased to 112×10^9/L and reticulocyte count to 0.163×10^{12}/L (5.41%). Vitamin B_{12} level was 716 pmol/L, red cell folate level 1,506 nmol/L and serum HCY level decreased to normal value (9 µmol/L) (Table 1).

Four different clinical forms of megaloblastosis have been described.[3,4] The classical form has an insidious onset with frequent neurologic symptoms and macrocytic anemia. Vitamin B_{12} and/or red cell folate levels are decreased. The second form is the subtle MA anemia with ill-defined clinical symptoms and decreased or borderline vitamin B_{12} and folic acid levels with other abnormalities (dUST, HCY, MMA).[2] Masked megaloblastosis coexists with other deficiencies; MCV is normal or decreased.[5,6] MA of acute onset is the rarest form.[3] There are two clinical presentations; the masked undiagnosed classical MA with cytopenias of abrupt onset and the so-called AM.[3-7] In AM severe thrombocytopenia develops in 1 to 3 weeks, MCV is normal or only moderately increased. This presentation is more frequent in patients with risk factors: parenteral nutrition, infection, dialysis or treatment with some antifolate drugs. Mortality is high.[3] The reticulocyte count is low. Vitamin B_{12} and red cell folate levels are normal. BM aspirate shows megaloblastic changes. Classically, dUST is used as a diagnostic test. Nevertheless, HCY serum assays provide a sensitive test for the diagnosis of AM, especially in its early stages.[8] In vitamin B_{12} deficiences both HCY and MMA levels are high. In folate deficiencies only HCY concentration is increased.[9,10] HCY levels are also useful for AM follow-up of AM; levels return to normal after starting treatment with vitamin B_{12} or folic acid. The evaluation of serum HCY levels is an easy and non-invasive test for the diagnosis and follow-up of AM.

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