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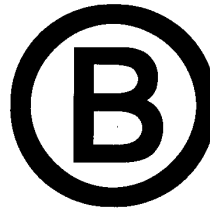
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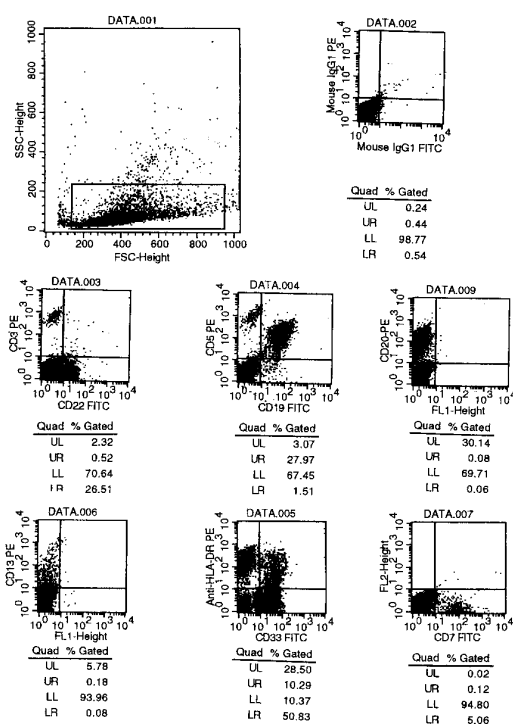


Figure 1. Light scatter properties of analyzed cells (top). The flow cytometric dot plots clearly show that virtually all CD19⁺ cells are positive for CD5 antigen and there are two cell populations with different HLA-DR antigen expression pattern. CD33 antigen is found to be the only antigen that expressed 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 than $10 \times 10^9/L$ 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.

Mustafa Nuri Yenerel,* Ibrahim Hatemi,° Hüseyin Keskin*

*Istanbul University, Istanbul Medical School, Department of Internal Medicine, Division of Hematology, Çapa, Istanbul; °Haseki State Hospital, Haseki, Istanbul, Turkey

Key words

CLL, AML, flow cytometry.

Correspondence

Mustafa Nuri Yenerel, MD, Istanbul University, Istanbul Medical School, Department of Internal Medicine, Division of Hematology, Çapa, Istanbul, Turkey. Fax: international +90.212.6311263.

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

Sir,

Vitamin B₁₂ (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 $9 \times 10^9/L$ was found. Hb was 99 g/L, mean corpuscular volume (MCV) 92 fL and leukocyte count was $7.06 \times 10^9/L$ with 84% of neutrophils with hypersegmentation. Reticulocyte count was $0.053 \times 10^{12}/L$ (1.66%). Vitamin B₁₂ 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 folic acid and vitamin B₁₂ 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 folic acid 12 mg iv in one single dose and folic acid 5 mg/day po for 14 days and parenteral vitamin B₁₂ 2 mg/day for 4 consecutive days. After 10 days of treatment the platelet count increased to 112×10⁹/L and reticulocyte count to 0.163×10¹²/L (5.41%). Vitamin B₁₂ 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 B₁₂ 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 B₁₂ 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 B₁₂ 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 B₁₂ deficiencies 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 B₁₂ or folic acid. The evaluation of serum HCY levels is an easy and non-invasive test for the diagnosis and follow-up of AM.

Marina Carrasco, Angel Remacha, Anna Sureda,
Pilar Sardà, Rodrigo Martino, Jorge Sierra

Department of Hematology, Hospital de la Santa Creu i Sant Pau,
Barcelona, Spain

Key words

Acute megaloblastosis, folic acid, cobalamin, homocysteine

Correspondence

Angel Remacha Sevilla, MD, Laboratorio de Hematología,
Hospital de la Santa Creu i Sant Pau, Antoni Maria i Claret,
167, 08025 Barcelona, Spain. Phone: international +34-93-2919290 – Fax: international +34-93-2919192 – E-mail: 2107@hsp.santpau.es

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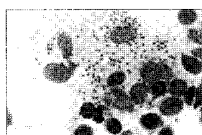
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Haematologica

is a Latin adjective, neuter and plural,
used in this context as a noun:
it means “hematological subjects”.
The appropriate English translation is therefore
Journal of Hematology.



On the cover. Bone marrow aspirate smear. *Leishmania sp* within reticulo-endothelial macrophages. Note the platelet clump to compare with the sharper and stronger staining of *Leishmania sp*. (see p. 750).

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