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Case report

Copper deficiency with increased hematogones mimicking refractory anemia with excess blasts

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Abstract

We describe a 19-year-old male patient with a previous diagnosis of familial Mediterranean fever (FMF), nephrotic syndrome and secondary amyloidosis, who presented with anemia and leukopenia. The bone marrow assessments showed dysplastic precursors including vacuolated myeloid and erythroid precursors and increased proportion of immature cells up to 19%. The patient received erythropoietin and G-CSF for myelodysplastic syndrome (MDS). No response was observed. During his evaluations copper deficiency was detected. One month after oral copper replacement, the peripheral blood counts and bone marrow findings became completely normalized. An evaluation to identify the cause of copper deficiency, revealed intestinal amyloidosis. Based on our experience we recommend serum copper determination in the diagnostic workup of MDS in patients with comorbidities.

Keywords: Copper deficiency; Amyloidosis; Nephrotic syndrome; Myelodysplastic syndrome; RAEB; Hematogones

1. Introduction

Copper is an essential element involved in growth, development and wound healing. Deficiency of copper is an uncommon condition since daily requirement is low and it is widely available in food. Acquired copper deficiency in adults occurs mostly after long-term parenteral nutrition or enteral feeding which does not include copper [1–4]. There are also rare reports of copper deficiency due to partial gastrectomy [5–8]. Copper deficiency usually presents with hematologic manifestations like anemia, neutropenia and less commonly thrombocytopenia in adults. It can also lead to striking neurologic signs like polyneuropathy and ataxia [8,9]. To our knowledge, this is the first report of a patient with copper deficiency due to malabsorbtion secondary to amyloidosis. A second interesting feature is the increase in the percentage of immature cells which could have lead to erroneous diagnosis of refractory anemia with excess blasts.

2. Case report

A 19-year-old medical student, followed with diagnosis of familial Mediterranean fever (FMF) and secondary amyloidosis who manifested with nephrotic syndrome was referred to our department because of severe anemia and febrile neutropenia. His hemoglobin was 5.6 g/dl, hematocrit 16.5%, MCV 85.2 fl, leukocyte count 2500 mm^{-3} and platelet count 469,000 mm^{-3}. He had long-standing history of FMF-related abdominal complaints. However, the diagnosis was newly established and he was taking colchicine for the last 4 months. The physical examination was unremarkable except for minimal hepatomegaly. Serum levels of vitamin B_{12} and folate were within normal limits. Serum iron was 40 μg/dl (59–158 μg/dl), total iron binding capacity 75 μg/dl (228–448 μg/dl) and ferritin 703 ng/dl (28–365 ng/dl). There

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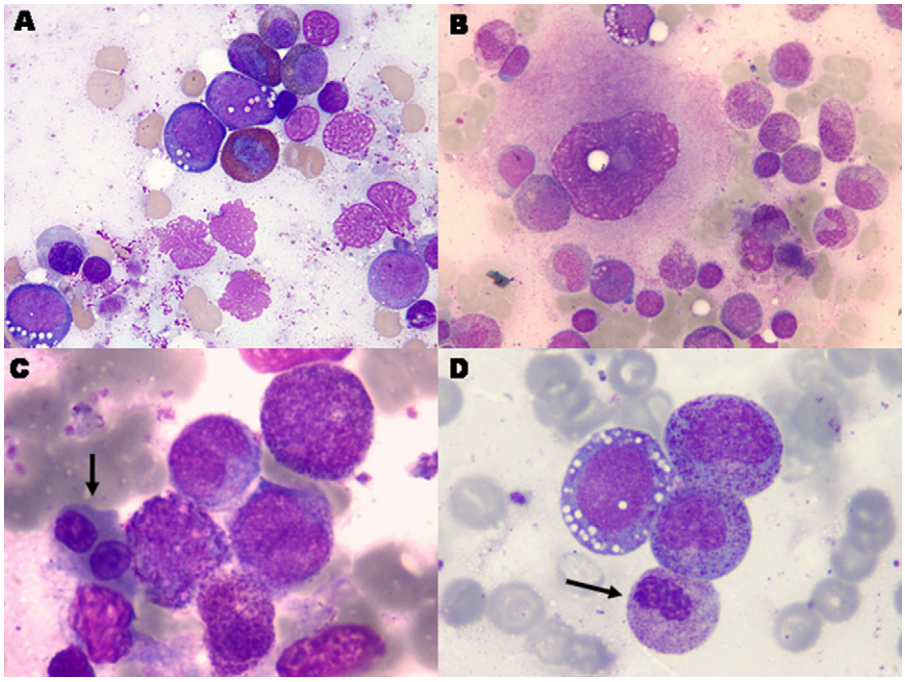

Fig. 1. Initial bone marrow smear showing vacuoles and dysplastic features in three lineages. Note the hypergranularity in myeloid cells, mononuclear megakaryocyte (B), binuclear erythroid precursor (C) and pseudo-Pelger-Huët abnormality (D) (Wright).

were no findings of hemolysis or bleeding. There was trilineage dysplasia including prominent cytoplasmic vacuolization (Fig. 1), with an increase in mature lymphoid cells (27%) in bone marrow aspiration. Erythroid precursors, especially late normoblasts, were strikingly decreased with maturation block at proerythroblast stage. Increased storage iron and occasional ring sideroblasts were observed (Fig. 2). Atypical mononuclear cells with deeply basophilic cytoplasm, high nuclear/cytoplasmic ratio and relatively immature chromatin pattern resembling lymphoblasts were observed (Fig. 3). Bone marrow flow cytometric analysis showed increased proportion of mononuclear cells positive for CD10, CD19, CD22, CD34, TdT and negative for CD20. The cytogenetic analysis was normal. Viral markers for hepatitis and parvovirus PCR were negative. Colchicine was discontinued.

The patient required frequent RBC transfusions. He was given G-CSF 48 MU/week and erythropoietin 10,000 U/day with a probable diagnosis of myelodysplastic syndrome (MDS). No improvement was observed. Repeated bone marrow assessments were done in monthly intervals for subsequent 4 months. The proportion of cells which were then interpreted as blasts reached up to 19%. The patient had full-matched sibling allogeneic donor and sequential

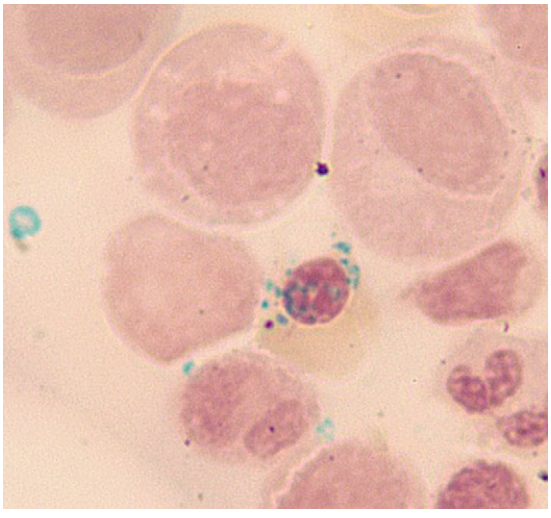

Fig. 2. Ringed sideroblast (Prussian blue).

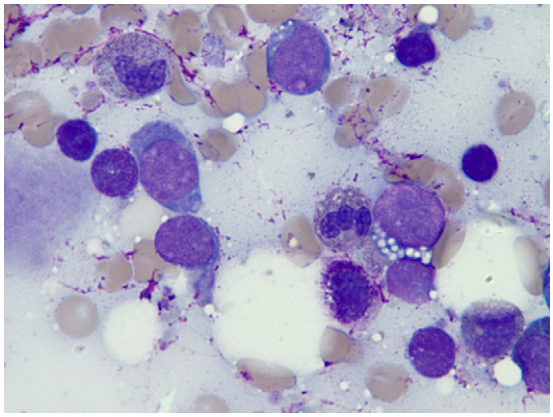

Fig. 3. Bone marrow smear showing mononuclear cells with immature chromatin pattern resembling lymphoblasts (Wright, ×1000).