Megaloblastic Anemia Presenting with Massive Reversible Splenomegaly

Vineet Behera · Makarand Randive ·
Praveen Sharma · Velu Nair

Received: 22 August 2014 / Accepted: 29 September 2014 / Published online: 14 October 2014
© Indian Society of Haematology & Transfusion Medicine 2014

Abstract Megaloblastic anemia (MA) is a common disorder with varied manifestations. It generally results in mild to moderate splenomegaly which is due to sequestration of macrocytic erythrocytes in spleen. Massive splenomegaly is generally seen in infections, myeloproliferative diseases, neoplasms, storage disorders or hematological conditions; but is not heard of and has rarely been reported in MA. We discuss a case of massive splenomegaly who presented with symptomatic anemia and was found to have MA. He was extensively evaluated for all other causes of massive splenomegaly which was normal. Further, after a therapeutic trial of MA he showed a regression in spleen size confirming that the massive splenomegaly was attributable to MA.

Keywords Megaloblastic anemia · Splenomegaly · Massive splenomegaly

Introduction

Megaloblastic anemia (MA) is a common disorder with varied manifestations. It is characterized by ineffective erythropoiesis leading to macrocytes which are sequestered in the spleen leading to mild to moderate splenomegaly. But, MA can have massive splenomegaly; with only a few anecdotal reports cited in literature. We present an interesting case of MA causing massive splenomegaly which regressed with treatment of MA; and discuss the various aspects linked to the case.

Case Report

A 32 years old male presented with dyspnea on exertion, easy fatigability with dyspeptic symptoms of 4 months duration. He also developed dragging sensation left upper side of abdomen and early satiety for 1 month. There was no history of any bleeding per rectum, melena, diarrhoea, weight loss or any blood transfusions. He was a lacto-vegetarian. Clinically he was hemodynamically stable with heart rate of 86/min and blood pressure of 122/76 mm of Hg. He had pallor, pigmentation of knuckles with no icterus or pedal edema. Spleen was palpable 13 cm below left costal margin which was firm, non-tender with the anterior notch palpable (Fig. 1). Liver was palpable 3 cm below right costal margin which was firm, non-tender with span being 15 cm. Ejection systolic murmur was present in pulmonary area. Other systemic examination was within normal limits.

On evaluation his hemoglobin was 5.2 gm/dL with MCV-112fL (leucocyte count—3,500/cu mm³, platelets—80,000/cu mm³, MCH-34 pg, MCHC-30 g/dL, RDW-40 %). Peripheral smear showed macrocytes, macroovalocytes with hypersegmented polymorphs as shown in Fig. 2. His serum bilirubin was 1.9 mg/dL, AST—24 IU/L, ALT—32 IU/L, LDH—1017 IU/L and other biochemistry was normal. Ultrasonography (USG) of abdomen showed hepatosplenomegaly with no ascites and his chest X-ray was normal. CECT abdomen showed enlarged spleen (21 cm) and liver (19 cm) with no lymph nodes or any other abnormality (Fig. 3). Vitamin B₁₂ levels were reduced (40 pg/mL) (normal 183–803 pg/mL) with normal folic acid levels.

In view of massive splenomegaly and anemia he was further evaluated with bone marrow aspiration and biopsy which showed megaloblastoid erythroid hyperplasia with

V. Behera (✉) · M. Randive · P. Sharma · V. Nair
Department of Internal Medicine, Armed Forces Medical
College, Pune 411040, India
e-mail: beheravineet@gmail.com

Fig. 1 Liver palpable 3 cm below *right costal margins* and spleen palpable 13 cm below *left costal margin* with anterior notch palpable

Fig. 2 Peripheral blood smear showing macrocytosis and hypersegmented polymorphs

no atypical cells; no granuloma, Leishman Donovan bodies, amyloid or any glycogen deposits, or any evidence of malignancy. His peripheral smear for malarial parasite, paracheck, IgM malarial antibody titres, K 39 antigen, hemoglobin electrophoresis, abdominal fat pad biopsy for amyloid and serum protein electrophoresis and doppler of abdomen vessels were normal or negative. He was further evaluated for etiology of MA and his upper gastrointestinal endoscopy, stool for occult blood, stool for fat globules, tests of malabsorption, anti-parietal cell antibody were normal.

He was diagnosed as MA, probably nutritional in etiology. He was treated with parenteral vitamin B₁₂ 1,000 µg twice a week intra-muscularly, folic acid 5 mg daily and

other hematinics. He was followed up after 1, 3 and 6 months which showed dramatic improvement in his condition, sense of well being and rise in hemoglobin to 7, 10 and 13 gm/dL respectively. Serial USGs showed gradual decrease in splenic size which regressed to 11 cm after 6 months. MCV and LDH decreased to 94fL and 422 IU/L respectively.

Discussion

Megaloblastic anemia is a common illness known to have protean manifestations. It is quite prevalent in the population but most of the cases have subclinical deficiency or have a well compensated anemia which may not come to attention. [1] MA is known to cause splenomegaly which generally occurs due to reticuloendothelial hyperplasia, secondary to removal and sequestration of large number of defective macrocytic red cells occurring in MA. [2] The incidence of splenomegaly in MA varies from 3 to 45 % and is generally mild to moderate with a size ranging from 3 to 14 cm below left costal margin. [3].

Massive splenomegaly is defined as palpable spleen greater than 8 cm or spleen weighing more than 1,000 gm². The common causes of massive splenomegaly include infections like hyper-reactive malarial splenomegaly, kala azar; chronic myeloproliferative diseases and neoplasms like chronic myeloid leukemia, hairy cell leukemia, chronic lymphocytic leukemia, lymphomas; storage disorders like Gauchers disease, amyloidosis and Niemann Pick disease and hematological conditions like thalassemia.

Massive splenomegaly is very rare in MA with only a few reports. Pruthi et al. describe a 46 year old male with anemia who had a palpable spleen of 8 cm, laboratory findings of MA and in whom the spleen regressed on treatment of MA. [4] Enokohara et al. [5] also describe a similar case of MA with a spleen size of 14 cm, in a 48 year old lady. In a study of 2,505 cases of splenomegaly from California, MA was found to be the incriminating factor in 31 cases (3 % of all cases) and amongst which, one patient had massive splenomegaly. [6] In another study done by Bigg et al. in past, incidence of massive splenomegaly in MA has also been reported to be 3 %. [7].

The exact underlying mechanism of massive splenomegaly in MA is not clear. In MA there is hyperplasia of reticuloendothelial system to remove the defective erythrocytes; as seen in hemoglobinopathies, erythrocyte membrane defects. This may go unchecked in some cases to cause grossly enlarged spleen. Secondly, MA being a thrombotic state can cause splenic and portal vein thrombosis leading to enlarged spleens due to abnormal blood flow. [8, 9] MA can predispose to or can have coexisting viral and bacterial infections which can also contribute to

Fig. 3 CECT abdomen—axial view (a) and coronal view (b) showing massive splenomegaly (21 cm) and hepatomegaly (19 cm)

splenomegaly. [10] It is possible that an immune mediated mechanism linked to disordered immune regulation in MA (especially pernicious anemia which is also immune mediated) may also contribute to massive splenomegaly but there is no data to support this fact. In our case, the first cause is the most likely as there was no evidence to support the other mechanisms.

In all cases of massive splenomegaly, all efforts need to be done to exclude the various causes by a targeted and intelligent work up and evaluation. In our case, the patient setting, clinical profile, hematological profile, a negative work up for other causes of splenomegaly, and a regression of splenomegaly with improvement of MA after treatment with B₁₂ injection and hematinics; all support a diagnosis of MA being the underlying cause of splenomegaly.

MA is a relatively benign condition which can rarely present with massive splenomegaly, which can also have sinister etiologies. Once encountered with massive splenomegaly in MA, all efforts must be done to exclude other causes and a therapeutic trial of vitamin B₁₂ must be given. Early identification and prompt therapy of this easily treatable disorder is very essential to prevent anxiety of patient and to prevent unnecessary investigations and therapies of this easily treatable condition.

References

1. Greer JP, Forester J, Rodgers GM, Paraskevas F et al (eds) (2009) Wintrobe's clinical hematology, 12th edn. Lippincott Williams & Wilkins, Philadelphia, pp 1143–1172
2. Longo D, Fauci A, Kasper D (2012) Harrison's principles of internal medicine, 18th edn. The McGraw-Hill Companies Inc, New York, pp 862–871
3. MacCarty WC (1928) Chronic splenomegaly. Arch Intern Med 41:536–548
4. Pruthi RK (1993) Reversible marked splenomegaly in pernicious anemia. Ann Intern Med 119:1053
5. Enokihara H, Saito K, Hazama S, Hirose K, Komatsu H, Furusawa S et al (1978) A case of pernicious anemia with giant splenomegaly. Jap J clin hematol 19(12):1684–1689
6. O'Reilly RA (1998) Splenomegaly in 2,505 patients at a large university medical centre. West J Med 169:78–87
7. Bigg E (1940) Spleen size in pernicious anemia. Ann Intern Med 14:277–280
8. Limal N, Scheuermaier K, Tazi Z, Sene D, Piette JC, Cacoub P (2006) Hyperhomocysteinaemia, thrombosis and pernicious anaemia. Thromb Haemost 96(2):233–235
9. Fernández-Ruiz M, Alonso-Navas F, Muro E, Pérez-Carreras M (2011) Portal and mesenteric vein thrombosis associated with hyperhomocysteinemia and pernicious anemia in a patient heterozygous for the MTHFR C677T mutation. Med Clin (Barc) 136(5):225–226
10. Erkurt MA, Aydogdu I, Dikilitaş M, Kuku I, Kaya E, Bayraktar N et al (2008) Effects of cyanocobalamin on immunity in patients with pernicious anemia. Med Princ Pract 17(2):131–135