Myelodysplastic syndrome with pseudoreticulocytosis

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ABSTRACT

A patient with myelodysplastic syndrome (MDS) with refractory anemia who had marked reticulocytosis in the absence of hemolytic anemia and/or blood loss is reported. Erythrocyte survival test showed that more than 50% of the patient's reticulocytes were still present on day seven. This should be due to the prolongation of reticulocyte maturation in MDS, and is known as pseudoreticulocytosis. This phenomenon which mimicks hemolytic anemia is an unusual presentation of myelodysplastic syndrome, with only 7 patients with pseudoreticulocytosis being reported previously.

Key Words: Myelodysplastic syndrome, Pseudoreticulocytosis.

ÖZET

Psödoretikülositoz görülen bir miyelodisplastik sendromu olgusu

Bu olgu sunumunda hemoliz ve kanama olmaksızın belirgin retikülositoz görülen refrakter anemi ile seyreden bir miyelodisplastik sendromu olgusu sunulmuştur. Olguda yapılan eritrosit yaşam süresi değerlendirmesinde olgunun retikülosit sayısının yedinci gün sonunda halen başlangıç değerinin %50'sinin üstünde olduğu saptanmıştır. Bu durum MDS'li hastalarda eritroid matürasyonunun kesintiye uğramasına bağlı olabilmekte ve psödoretikülositozis olarak adlandırılmaktadır. Son derece nadir görülen bu fenomen hemolitik anemiyi taklit edebilmektedir. Literatürde daha önce yedi olgu bildirimi mevcuttur.

Anahtar Kelimeler: Miyelodisplastik sendrom, Psödoretikülositoz.

INTRODUCTION

Myelodysplastic syndrome (MDS) is a clonal disorder which is usually characterized by peripheral reticulocytopenia, leukopenia, and/or thrombocytopenia due to inadequate and dysmorphic hematopoiesis[1]. Reticulocytosis is a rare manifestation of MDS, and when present, it is usually attributed to bleeding or immune hemolysis. Anemia with reticulocytosis in the absence of hemolysis or blood loss may arise in MDS as a consequence of delayed maturation. This phenomenon mimicks hemolytic anemia and is called pseudoreticulocytosis. Pseudoreticulocytosis in MDS patients is extremely rare and only a few reports have been published so far[2-8]. In this case presentation, we report an MDS refractory anemia (MDS-RA) with pseudoreticulocytosis.

A CASE REPORT

A 74-years-old female patient was referred to our University Hospital because of progressive weakness due to anemia. Her hemoglobin levels ranged between 7-9 g/dL. Her medical history included mild thrombocytopenia which was revealed 7 years ago. Then she had refused bone marrow aspiration and biopsy, and has not been followed up further. The patient had been noted to have reccurrent abscesses in the area of left labium majus of vagina, refractory to antibiotherapy. No spesific causes could be identified, such as tuberculosis, deep fungal infection or granuloma inguinale, but chronic inflamation was documented by biopsy and *Staphylococcus aureus* was cultured from the lesion. During the following period, *Proteus mirabilis* was also documented. On physical examination, she looked pale. No lympadenopathy or hepatosplenomegaly was found. Suppurative and oedematous abcess formation with enduration at the area of left labium majus of vagina was observed. At presentation, the leukocyte count was 4.9 x 10^9/L, hemoglobin 7.8 g/dL, mean corpuscular volume 107.5 fl and platelet count 50.0 x 10^9/L. Lactic dehidrogenase level was 924 mg/dL, two-fold higher than the normal range. Vitamin B12, folic acid, AST, ALT, BUN, creatinin, AP, GGT and albumin levels were normal. Examination of peripheral blood smear showed marked anisocytosis, poikilocytosis, macrocytosis, polychromatophilia, basophilic stipling and fragmentation of erythrocytes, and white blood cell morphology was normal with neutrophil prevalence. No blastic cell was seen. The reticulocyte percentage was 27% with the standart supravital staining technique and the reticulocyte count was persistently high, ranging between 25-32%. Bone marrow revealed normocellularity with dysplastic features. Erythroid lineage showed nuclear budding and irregularities. Megakaryocytes displayed nuclear fragmentation. Myeloblasts made up to 1.6% of marrow elements. The diagnosis of the patient was confirmed as MDS with refractory anemia (MDS-RA). The Coombs test was negative, the chest radiogram and computerised tomography of the abdomen were normal. The haptoglobulin level was slightly decreased and indirect hyperbiluribinemia was documented. Pyruvate kinase and glucose 6 phosphatase dehidrogenase levels were normal. The osmotic fragility of the erythrocytes were normal and the membrane inhibitor of reactive lysis (MIRL) and decay accelerating factor (DAF) antigens were expressed on the surface of erythrocytes. During the hospitalization period, blood loss was ruled out and the vaginal abcess was treated with surgical drainage and appropriate antibiotics. The patient was on steroid therapy during the follow up, yet the hemoglobin level did not drop and reticulocytosis persisted. To evaluate the etiology of reticulocytosis, red cell survival test was performed. Venous blood sample was collected from the patient and incubated at 37°C. Reticulocyte count was performed every other day by using standart supravital staining on day 0 to day 7. A patient with Coombs positive hemolytic anemia was used as control. The value obtained on day 0 was expressed as 100%[6]. In the control blood sample, more than 50% of the reticulocytes disappeared

on day 1, while more than 50% of the patient's reticulocytes were still present on day 7. This finding demonstrated the delayed maturation of erythroid cells in our patient (Figure 1).

DISCUSSION

Myelodysplastic syndrome (MDS) is a clonal disorder that is usually characterized by peripheral reticulocytopenia, anemia, thrombocytopenia and leukopenia due to ineffective hematopoiesis, despite increased bone marrow cellularity[1]. Erythroid activity in the bone marrow of MDS patients can vary widely from hypoplasia to hyperplasia with dysplastic changes and ineffective erythropoiesis. Although reticulocyte counts are normal or low in MDS, many qualitative abnormalities of erythrocytes have been described, in some instances leading to hemolytic anemia with reticulocytosis. Clinically significant hemolysis and reticulocytosis have been reported in association with a reduction in pyruvate kinase or an increase in adenosine deaminase activities and particularly with Coombs positivity[1,9-12]. Reticulocytosis is extremely rare in MDS patients in the absence of hemolysis and blood loss. When present, it may be due to prolongation of reticulocyte maturation and is known as pseudoreticulocytosis[2-8]. Pseudoreticulocytosis, mimicking hemolytic anemia, is an unusual presentation of myelodysplastic syndrome. Only 7 patients with pseudoreticulocytosis have been reported in the literaure previously[2-8]. Our patient has presented with erythroid fragmentation in the peripheral smear, a high LDH level, indirect hyperbiluribinemia, marked reticulocytosis and a slightly low haptoglobulin level, thus mimicking hemolytic anemia. Despite these findings, erythroid cellularity in the bone marrow was normal, Coombs tests were negative, the hemoglobin level was stable and no cause for hemolysis could be found. The diagnosis of MDS-RA with pseudoreticulocytosis was reached by the help of the erythrocyte survival test and the bone marrow biopsy. The cytogenetic profile of the patient was unavailable, therefore it could not be determined whether the cytogenetic profile also contributed to pseudoreticulocytosis.

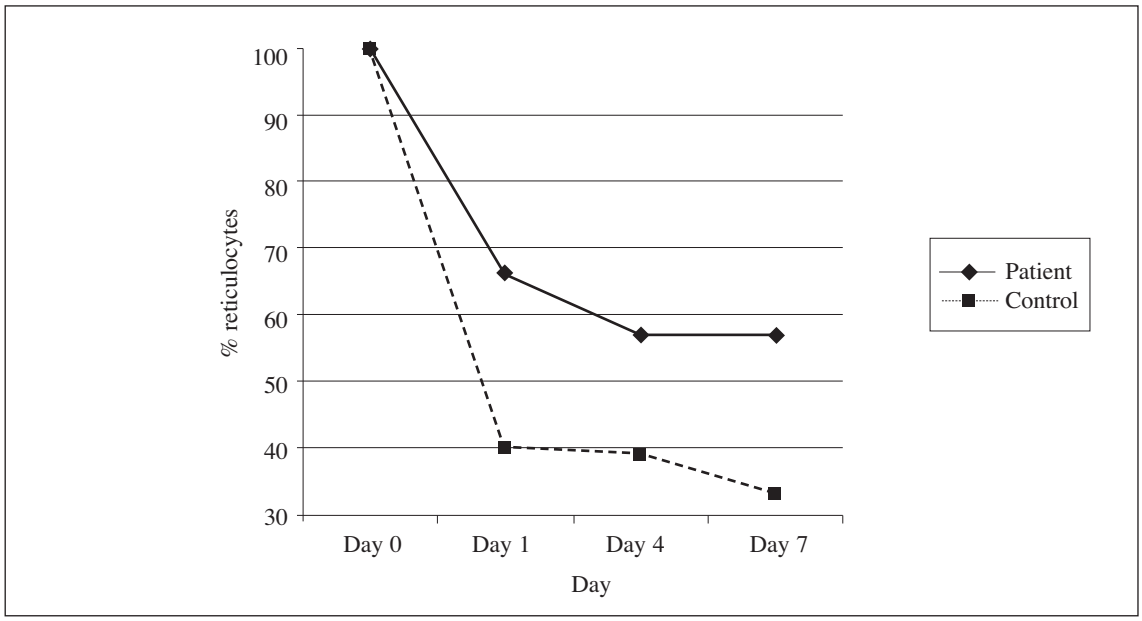

Figure 1. In vitro reticulocyte survival test result.

In conclusion, although pseudoreticulocytosis is a rare phenomenon, this diagnosis should be kept in mind in MDS patients who present with an unknown etiology of reticulocytosis.

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