

Spontaneous remission (SR) of acute myeloid leukemia (AML) in adults is observed very rarely. To date, about 100 cases have been presented in the literature. To our best knowledge, we describe the first adult Polish patient suffering from acute myelomonocytic leukemia (48, XY, +13, +21/46, XY), in whom after supportive therapy, including non-irradiated, non-leukocyte depleted red cell transfusions and low-dose corticosteroid, we observed resolution of the disease without cytogenetic remission. We suggest a potential transfusion-associated graft versus-host-diseases (TA-GVHD) and graft-versus leukemia (GVL) reaction which might lead to spontaneous hematological remission. However, we did not observe clinical symptoms of such reactions apart from a short episode of non-infectious diarrhea. Additionally, steroids were administered but their role in inducing SR, in our opinion, seems less probable. This 77-year-old man remained in SR for 7 months, when repeated analysis showed AML recurrence. He died due to septic shock 2.5 months later. Additionally, we present a review of the literature.

**Key words:** acute myeloid leukemia, spontaneous remission, transfusion reaction, corticosteroids.

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# Spontaneous hematological remission of acute myeloid leukemia

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## Introduction

Spontaneous remission (SR) in the course of acute myeloid leukemia (AML) is observed very rarely. Till now, about 100 cases among adult patients have been reported in the literature, especially in the previous century. One of the explanations of this fact is that effective chemotherapeutic strategies have become widely available and are introduced just after establishing the diagnosis. Currently, only a small group of patients (advanced age, poor performance status, presence of severe comorbidities) disqualified from intensive, potentially curative treatment, or who refused such treatment, can present SR. The mechanisms of SR remain unclear but their association with preceding transfusions of blood components and severe systemic infections has been reported [1].

In this paper we report the first, to our best knowledge, case of a Polish adult patient with AML who had spontaneous remission.

## Case report

A 77-year-old man suffering from fatigue, dizziness and mild weight loss, which started in August, 2011, was admitted to hospital in September, 2011. Laboratory tests showed anemia (Hb 3.7 mmol/l), leukopenia with granulocytopenia (WBC 2.3 G/l, granulocyte count 0.26 G/l), and moderately elevated lactate dehydrogenase. Evaluation of peripheral blood (PB) and bone marrow (BM; 22 September, 2011) showed 16% blasts in PB and 82% in BM smear. Based on cytomorphology, cytochemistry and also on immunophenotyping, the diagnosis of acute myelomonocytic leukemia was established. Cytogenetic analysis showed the 48, XY, +13, +21/46, XY karyotype in 17/20 observed metaphases, which qualified the patient to the cytogenetic intermediate risk group. The patient did not receive intensive chemotherapy due to his performance status and presence of cardiological and neurological comorbidities, and was qualified only to the best supportive care. In this time he was treated with non-irradiated red cell transfusions (4 units) and low-dose corticosteroids (methylprednisolone 24 mg/d). During the whole hospitalization there was only one short episode of non-infectious diarrhea observed. In November, 2011 treatment in a clinical trial with 5-azacytidine was considered and, therefore, laboratory tests, PB and BM smear evaluation, flow cytometry of BM, and cytogenetics were repeated. Laboratory tests showed only moderate leukopenia (WBC 3.39 G/l). Cytogenetic analysis revealed the same aberrations as those present at the onset of the disease. Cytomorphologic and immunocytometric evaluation of PB and BM indicated improvement: 4% of blast cells in BM and presence of many cells in destruction were observed. The corticosteroids were stopped and 2 weeks later tests were repeated. The complete blood count became normal, with Hb 7.8 mmol/l, WBC 4.54 G/l, and platelet count of 165.0 G/l. Repeated cy-

tologic and immunocytometric evaluation of PB and BM showed complete hematological remission (25 November, 2011). Also histological evaluation of BM confirmed resolution of AML, showing fatty marrow with poor cellularity and few groups of immature cells (less than 5%). The patient was closely monitored during the following months and he remained in spontaneous hematological remission until May, 2012. Based on peripheral blood and bone marrow evaluation on 29 May, 2012 a relapse of AML was recognized. The patient and his family declined intensive treatment because of his bad performance status and palliative treatment consisting of hydroxyurea, 6-mercaptopurine and the best supportive care was provided. On 12 August, 2012 he was admitted to hospital with symptoms of septic shock. In spite of intensive treatment he died 6 hours after admission.

## Discussion

Among adults, spontaneous remission has been observed in various hematological malignancies. Spontaneous remission has been reported for adult T-cell leukemia/lymphoma, chronic lymphocytic leukemia, chronic myelogenous leukemia, myelodysplastic syndrome, acute lymphoblastic leukemia and also acute myeloid leukemia [2–6]. The first description of spontaneous remission was published in 1878 by Eisenlohr [7]. Approximately 100 patients with SR of AML have been reported, mainly before 1954 [8]. After that time only a few case reports of SR were published. Between 1979 and 2008 about thirty patients were described manifesting SR of AML. The median duration of remission was generally short (the mean was about 6 months); however, even long-term and complete cytogenetic remissions were documented [9, 10].

The mechanisms of SR still remain unclear but it is often triggered by severe, especially bacterial, but also viral or fungal infections. In particular, severe systemic infections appear to precede SR [11–14]. The explanation of this phenomenon is that infections could lead to exuberant activation of the immune system and could exert an anti-leukemic effect causing containment of the leukemia. In severe infections a profound increase in levels of cytokines such as tumor necrosis factor  $\alpha$  (TNF- $\gamma$ ), interleukin 2 (IL-2) and interferon  $\gamma$  (IFN- $\gamma$ ) as well as increased antibody-mediated cytotoxicity of NK and activity of cytotoxic T cells and macrophages were observed [13, 15, 16]. It was also reported that cytomegalovirus (CMV) reactivation, in some conditions, could elicit  $\gamma\delta$  T cells which were able to cross-recognize both CMV-infected cells and primary leukemic blasts [17]. Some authors suggested that CMV could have an antileukemic effect by infecting CD33-positive hematopoietic progenitors [18]. However, this hypothesis was not supported by other authors [19]. Additionally, infections are frequently accompanied by hypergammaglobulinemia [11, 20].

An adverse transfusion reaction might have also played some role in the occurrence of spontaneous remission. The association between transfusions of blood components and SR was reported. Transfusion-associated graft versus-host-diseases (TA-GVHD) and graft-versus leukemia

(GVL) reaction were observed after transfusion [21]. Such anti-leukemic effects might stimulate remission of AML, especially in patients treated with non-irradiated blood products. However, at present, nearly all AML patients receive leukocyte-depleted transfusions, which highly reduce probability of the above-mentioned reactions.

Infections and/or blood transfusions are postulated as the main causes of SR but there were also patients with SR reported who had neither infections nor transfusions [10].

Other factors which might play a role in SR of AML are corticosteroids or colony-stimulating factors (CSF) [9]. Although in some cases of SR the administration of corticosteroids was described, a review of the literature shows that there is no evidence that steroid treatment is able to induce remission in AML [22, 23]. It is well known that in biphenotypic leukemia, which is partially responsive to steroid treatment, remission might be misinterpreted as a case of SR [9]. Maturation of leukemic cells was reported to be induced *in vitro* by colony-stimulating factors [24, 25]. Some authors even speculated that severe infections might cause an augmented release of hematopoietic growth factors (granulocyte or granulocyte-macrophage CSF and/or other) that results in transient overgrowth of leukemic cells, leading to further maturation and differentiation [26].

In this paper we present a patient with acute myelomonocytic leukemia. Acute myeloid leukemia with myelomonocytic/monocytic differentiation represents the largest group of reported cases [9, 10]. During hospitalization the patient did not present symptoms of infection. Because of deep anemia he was treated with non-irradiated, non-leukocyte depleted transfusions (in a local hospital). Therefore, a potential TA-GVHD/GVL might lead to spontaneous hematological remission. However, we did not observe clinical symptoms of such reactions apart from a short episode of non-infectious diarrhea. Additionally, steroids were administered but their role in inducing SR, in our opinion, seems less probable.

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*Authors declare no conflict of interest.*

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