Spontaneous remission in acute myeloid leukemia: A Case Report

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Abstract

Spontaneous remission of Acute Myeloid leukaemia (AML) is an uncommon event, temporary and its mechanism is yet to be determined.

We report here a case of spontaneous remission of AML in a 35 years old male who was diagnosed with AML (M4) in Jan 2011. He presented very ill with fever, bleeding tendency and oral candidacies. He received supportive care only and chemotherapy was withheld. His general condition improved and fever subsided. White blood cell (WBC) count started to drop spontaneously and gradually until he became leukopenic and developed febrile neutropenia. After the second recovery, his full blood count (FBC) and bone marrow examination showed haematological remission. He was followed up for six weeks after which relapse occurred. Chemotherapy was started immediately, but unfortunately was not continued because of sepsis. The patient died four weeks after relapse.

Other reports on the spontaneous remission of AML showed a similar temporary period of remission with different duration, and then followed by relapse. Possible mechanisms of spontaneous remission in AML are discussed with a review of the literature.

Keywords:

Acute myeloid leukemia, spontaneous remission

Introduction

Sir W. Osler (1901) noted that spontaneous remission of cancer metastases is among the most remarkable events we witness in the practice of medicine [4]. Spontaneous remission in patients with AML is not common and only temporary, with a mean of 7.7 months [1]. About 100 AML patients with spontaneous remission were reported between 1878 and 1955, while only four adult were reported between 1955 and 1985. There were less than 10 additional reports of spontaneous remission after 1985 [2] and a report of 33 patients with spontaneous remission in the course of acute myeloblastic leukemia published from 1980 to 2004 [3]. The events leading to these occurrences have yet to be determined, although literature suggests that there may be some correlation to infection and blood transfusion [1].

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Case report

A 35-years old male presented in Jan 2011 with fever, oral thrush and bleeding gums; his previous medical record was insignificant. On admission he was very ill, pale, temperature was 38.1°C with subcojuctival haemorrhage, bleeding gums and oral candidacies. He had generalized lymphadenopathy and hepatosplenomegaly. FBC showed features of AML with WBC count at $98.8x10^9$/L, blasts $90.8x10^9$/L, neutrophils $1.0x10^9$/L, lymphocytes $2.0x10^9$/L, monocytes $5.0x10^9$/L. Haemoglobin 7.7 g/dl, platelet count at $33x10^9$/L. RFT, LFT and chest X -ray were normal. Ultrasound examination of the abdomen revealed enlarged spleen 15cm and liver 14cm with no focal lesions. Bone marrow examination confirmed the diagnosis of AML (M4) according to French, American and British classification. The bone marrow was extremely hypercellular and replaced by myeloblasts, there were eosinophils with abnormal granulations; the other haematopoietic precursors were scanty.

As a result of infection and the patient's poor performance status, chemotherapy was withheld

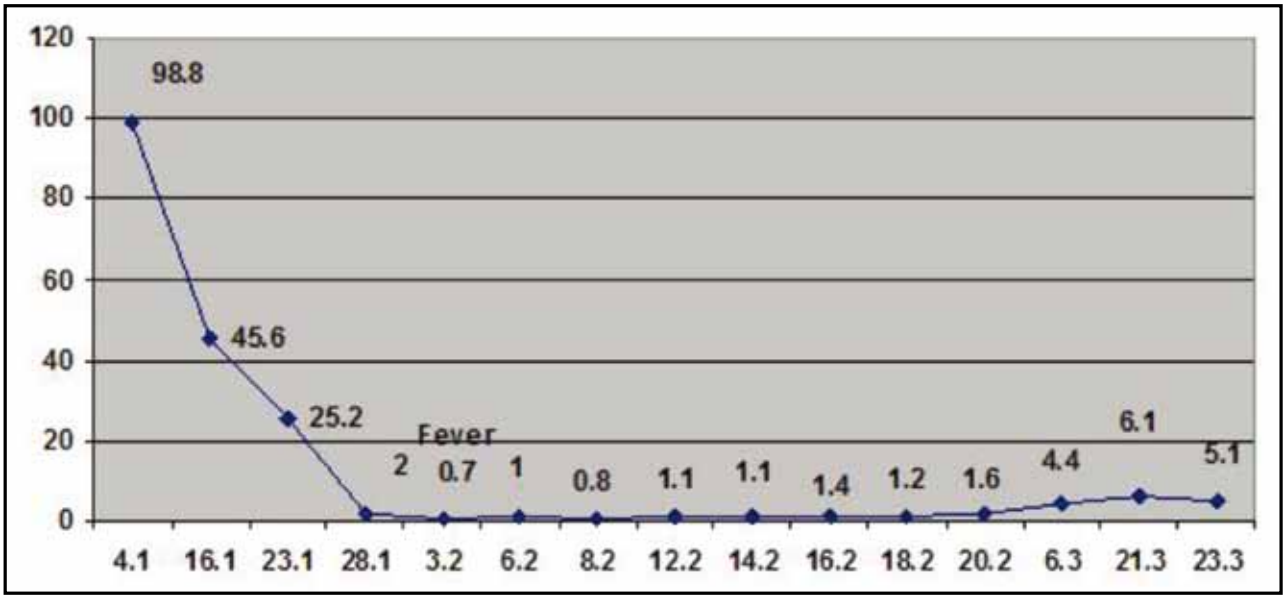

Fig. 1: Follow up of WBC count WBC **from presentation until remission**

and supportive care was initiated. He received blood and platelet transfusion, broad spectrum antibiotics and antifungal treatment. His general condition improved and fever subsided. WBC count started to drop gradually, it was $25.2x10^9$/L three weeks after diagnosis, then sharply reduced to $2.0x10^9$/L five days later. Subsequently the patient developed febrile neutropoenia and received the management of febrile neutropoenia including granulocyte colony stimulating factor (G-CSF) . The WBC count recovered after 5 weeks (Fig 1).

Bone marrow examination showed haematological remission, granulopoiesis was active with orderly maturation, erythroid was normoblastic, megakaryocytes were adequate and blasts were 2-3%.

The patient was discharged in a good condition; the plan was to follow up with FBC. 6 weeks later the patient presented with relapse with WBC count at $50.3x10^9$/L, haemoglobin at 12.8g/dl and platelet count at $29x10^9$/L. He was admitted and chemotherapy was started immediately (Daunorubicin 45mg/m^2 and cytarabine 100mg/m^2). Two days later he developed fever, vomiting and severe chest pain. WBC count was at $6.9x10^9$/L, neutrophils at $0.14x10^9$/L, lymphocytes at $0.78x10^9$/L, monocytes at $0.64x10^9$/L, blasts at $5.4x10^9$/L (76%) and NRBCs at 2%. Haemoglobin was at 13.9 g/dl, and platelets at $20x10^9$/L. Chemotherapy was stopped. The patient died with septic shock about four weeks after the second admission.

Discussion

The duration of spontaneous remission in the present case was about six weeks. Previous reports of spontaneous remission of leukemia showed short lived remission periods ranging from 4 weeks to 36 months [4]. The remission is usually followed by relapse of disease and subsequent progression. One patient was reported to have two remissions [4].

The exact mechanism of spontaneous remission in AML is not known, although literature suggests that there may be some correlation to infection and blood transfusion[1]. The effect of infection through cellular and humoral factors, or the effect of graft versus host disease by transfused lymphocytes were considered to be the pathogenetic mechanism for the eradication of leukemic cells [5].

Professor Busch in 1868 introduced the infection of cancer patients by purpose as a novel strategy to treat cancer. He achieved a dramatic regression with his first patient using live Streptococcus pyogenes bacteria. This strategy was exploited by Coley in 1891, who systematically applied Streptococcus pyogenes extracts to cancer patients and achieved a remarkable rate of regressions [6].

He described spontaneous remission of a large lymphosarcoma of the head and neck following streptococcal infection[4]. Infection may produce a cross-activated immunity that may control the leukemic clone. The production of cytokines: interleukin (IL)-1, IL-6 and tumor necrosis factor- α (TNF-α) were suggested as a possible mechanism [7]. Infection stimulates the production of granulocyte colony stimulating factor (G-CSF). Thus, G-CSF may suppress the leukemic cell clone by inducing apoptosis and suppressing the renewal of leukemic cells or the potential increase in effector cytotoxic cells[8]. There are reported cases of G-CSF induced remission in AML without chemotherapy [8-10]. Fever stimulates the proliferation but not the cytotoxic activity of cytotoxic T lymphocytes[5]. In vitro studies showed that Dendritic cells (DC) treated with fever-like heat (41°C, 6 h) was significantly superior compared to non-heat-treated DC in stimulating T-cells both in the presence and without antigen. Perhaps fever can generate a missing co-stimulatory signal via DC needed by resting tumor-specific T-cells for full activation, followed by partial or complete 'spontaneous' regression in an established tumor. Moreover tumor cells are more vulnerable to heat than normal cells and undergo necrosis to a larger extent [6].

However, some of the patients who underwent spontaneous remission had neither infection nor did they require transfusions, which imply that these circumstances are not important for achieving spontaneous remission [2]. It is obvious that most patients with AML are immune deficient and cytopoenic, requiring antibiotics and transfusions. In this regard, one may want to consider this concurrent result merely coincidental versus causative [3].

Further investigations are needed to determine the mechanism responsible for this spontaneous remission, which may lead to novel therapies of leukaemias.

As many other reported cases, spontaneous remission in our patient followed infection, the obvious cause was candidacies, but blood culture was not available to exclude bacterial infection, also he received blood and platelets transfusion which were not irradiated or leucocytes depleted as this is not available in Sudan.

In this case, spontaneous remission of AML was preceded by a five-week period of leucopoenia, which was not reported before according to our knowledge.

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