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Case Report

Leukapheresis in management hyperleucocytosis induced complications in two pediatric patients with chronic myelogenous leukemia

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ABSTRACT

Complications caused by elevated white blood cell count in pediatric patients with CML could be a presenting feature of the disease. Here, we present two adolescents, aged 16 and 17 years, who were admitted for investigation of extremely elevated leukocytes and complications of leucostasis. Initial manifestations were priapism and blurred vision, respectively. Diagnosis of chronic phase of chronic myeloid leukemia is established, and conventional measures for leucoreduction began. However, since there were no improvements, a leukapheresis procedure was initiated. After undergoing 3 daily procedures the leukocyte count declined for each patient, with resolution of pripaism and ophtalmological disturbances. Leukapheresis is safe and effective therapeutic option for patients with complications of hyperleucocytosis. If started in a timely manner, permanent organ damage or death could be avoided.

1. Introduction

Chronic myelogenous leukemia (CML) is a rare disease in children, accounting for 2–3% of all leukemias in children and adolescents [1].

Experience with pediatric CML patients is limited due to its rarity. There are several studies on a small number of patients during the past decades. The largest reported series of patients is published in 2006, with 39 pediatric cases [1]. In the majority of cases, the diagnosis was made in chronic phase, and most of the patients were older than 10. Pediatric patients with CML were more common than adults with some symptoms due to leucostasis such as headache, dizziness, priapism, hearing and visual disturbances [2,3] Molecular pathophysiology in all age groups was identical, as well as the diagnostic approach [1].

Complications due to hyperviscosity and leucostasis were found in approximately 60% children with hyperleucocytosis in chronic phase CML [3]. Pulmonary leucostasis leading to acute respiratory distress syndrome and leucostasis in brain could contribute to early mortality in these patients, even before specific therapy was initiated. Permanent organ damage is also a concern in these patients [4–6].

In this manuscript we present two pediatric patients with hyperleucocytosis induced complications of CML in chronic phase of the disease that were successfully treated with leukapheresis.

2. Case reports

2.1. Case 1

A 16 years old boy was referred to our service from the Urology Department for having extremely elevated white

Abbreviations: CML, chronic myelogenous leukemia; M, male; F, female; Hgb, hemoglobin; RBC, red blood cells; WBC, white blood cells; Plt, platelet; RT PCR, real-time polymerase chain reaction; LMWH, low molecular weight heparin; NSAID, nonsterod antiinflammatory drug; HES, hydroxyethyl starch; PMN, polymorphonuclear cells.

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blood cells (WBC) count and priapism. A day before his admission to the hospital he suffered a painful, continuous erection. Urologist estimated that surgical interventions was not indicated, and the boy was transferred to our haematooncology department. He is the first of two children from healthy unrelated parents, with uneventful personal and family history.

On admission he was in good general condition, with a sustained and painful erection and abnormal blood tests. Spleen was palpable for 4 cm bellow costal margin. Complete blood count (CBC) was as follows: Hemoglobin (Hgb) 110 g/L, Red Blood Cells (RBC) 3.1×10^{12}/L, White Blood Cells (WBC) 320×10^{9}/L, Platelet (Plt) 417×10^{9}/L. Serum biochemistry was normal with exception of elevated lactate dehydrogenase (LDH) activity of 2235 IU/L. Bone marrow biopsy revealed extreme hypercelularity, with normal hematopoietic lineages, granulocyte hyperplasia and around 3% of myeloblasts cells. BM karyotype showed *t*(9; 22) (q34; q11); molecular analysis confirmed bcr/abl fusion protein p^{210}.

He was diagnosed as CML in a chronic phase of disease (Table 1). He has received anticoagulant therapy, cytoreductive chemotherapy and drugs for pain control (Table 2). Hyperleucocytosis persisted despite cytoreductive chemotherapy, and we decided to start with leukapheresis. Improvement of his medical state began after the first cycle of leukapheresis and priapism resolved completely within 13 d. Histocompatibility testing with family members was performed and no compatible donor for allogenic bone marrow transplantation was found. Treatment with imatinib (Gleevec, Novartis Pharmaceuticals, USA) had a good response. Unfortunately, we had no follow up because he was lost.

2.2. Case 2

Patient was admitted for evaluation of pain in the knees, elevated WBC and blurred vision. Intermittent pain in knees are noticed two months before admission. A few days before admission to our hospital she suffered blurred vision. She is the second child from healthy unrelated parents, with uneventful personal and family history.

On admission she was 17 years old girl, ambulatory, in a good general condition. Spleen was palpable for 4 cm bellow costal margin. Other physical findings were normal. CBC were as follows: WBC 435×10^{9}/L, Hgb 110 g/L, RBC 2.8×10^{12}/L, Plt 295×10^{9}/L. Biochemistry of serum was normal, except elevated activity of LDH of 2018 IJ/L. Fundoscopic examination revealed papilledema and peripapillary hemorrhages on the right eye. Nuclear Magnetic Resonance (NMR) of the cranium revealed normal optic nerve morphology, as well as absence of morphological signs of elevated intracranial pressure; a small pineal cyst was incidental finding. Bone marrow biopsy revealed extreme hypercellularity, with normal hematopietic lineages. Granulocyte hyperplasia and around 2% of myeloblasts (CD34+/CD117+ cells) were found. BM karyotype showed *t*(9; 22) (q34; q11); molecular analysis confirmed bcr/abl fusion protein p^{210}.

She was diagnosed CML in a chronic phase. The girl received cytoreduction therapy, antibiotics, and hydration. After five days we began with leukapheresis due to an increase in WBC count despite chemotherapy. After the leukapheresis WBC count in the peripheral blood decrease gradually and visual acuity improved after 14 d. Patient's characteristics are shown in Table 1, and therapeutic approach in Table 2, respectively.

In both patients the leukapheresis was conducted by using a continuous flow blood cell separator (Cobe Spectra Apheresis System; Gambro BcT, Inc., Lakewood, CO, USA) and by selecting regular program for polymorphonuclear cells collection. All procedures were performed via peripheral veins with a slow flow rate of 35 mL/min. Around one patients' blood volume was processed per session during 1.5–2 h, and 1/3 of total leukocytes in circulation was approximately removed. Acidum citricum–dextrosa (ACD–A) (Haemonetics Corp. Brantree, USA) was used for anticoagulation in a ratio 1:12. Collection rate varied from 3 to 5 mL/min. Three leukapheresis procedures were performed on each patient in consecutive days. WBC counts before leukapheresis for both of the patients are presented in Fig. 1, and bags with removed granulocytes for the first patient in Picture 1. In both patients leukapheresis was efficient and successful, resulting in drop circulating granulocytes and resolution sings of leucostasis. There were no

Table 1
Summary of patient data.

Patient	Age (years)	Sex	Hgb g/L	RBC $\times 10^{12}$/L	WBC $\times 10^{9}$/L	Plt $\times 10^{9}$/L	Symptom	Karyotype	Molecular pattern RT PCR
1.	16	M	110	3.17	320	427	Priapism	46, xy, *t*(9; 22) (q34; q11)	p^{210}
2.	17	F	110	2.86	435	298	Blurred vision	46, xy, *t*(9; 22) (q34; q11)	p^{210}

M–male; F–female; Hgb–hemoglobin; RBC–red blood cells; WBC–white blood cells; Plt–platelet; RT PCR–real-time polymerase chain reaction.

Table 2
Management of hyperleucocytosis induced complications in pediatric patients with CML.

Patient	Chemotherapy	Leukapheresis	Anticoagulant therapy	Analgetics	Complete resolution of symptoms (d)
1.	Hydroxiurea ARA-C	One session per day for 3 d	LMWH	NSAID	13
2.	Hydroxiurea ARA -C	One session per day for 3 d	No	No	14

LMWH–low molecular weight heparin; NSAID–nonsterod antiinflammatory drug.