

BRIEF REPORT

Leukocytosis in patients with favism and association with blood transfusion

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Abstract

Introduction: Leukocytosis is a condition marked by abnormal increase in leukocyte count due to an inflammatory response as a defense against most of the infections, or bone tumors; including leukemia. The aim of this study is to analyze the effect of blood transfusion in leukocytosis patients with favism as compared to patients treated with antibiotics or combination of both.

Methods: A total of 97 patients with favism who were referred to the University hospital in 2016-2017 were studied.

Key findings: These patients experienced acute hemolysis following beans meal. These patients were either treated with blood transfusion, antibiotics or combination of both.

Conclusions: This study shows that blood transfusion is an effective therapeutic option for the treatment of leukocytosis. Antibiotics are not deemed necessary for the treatment and blood transfusion alone, can decrease leukocytes to the normal level.

KEYWORDS

blood transfusion, favism, leukocytosis

1 | INTRODUCTION

Elevation in the levels of leukocytes above the normal range, leukocytosis, is considered to have several malignant and non-malignant origins, thereby requires accurate diagnosis. Depending on the levels of elevated leukocytes, it can be due to infections (50 000-100 000 cells per mm³) or hematological disorder such as leukemia (≥ 10 000 cells per mm³). Diagnosis of leukocytes is initiated by the presence of clinical symptoms such as fever, night sweats, weight loss, and abnormal bleeding. However, history of previous disease, smoking, and infection is also significant in this case. Laboratory findings such as complete blood count (CBC) are then to reveal abnormal elevation in white blood cells count.¹

Favism, a hereditary disorder, involves an allergic-like reaction against fava bean (*Vicia faba*). Patient is likely to present blood

disorder (hemolytic anemia) after eating the beans, or even by walking over the plant fields.² The common spread of the disease is confined to people of Mediterranean origins (Italians, Spaniards, Armenians, Greeks, and Jews). Moreover, it is inherited as a sex-linked trait and is closely related to glucose-6-phosphate dehydrogenase deficiency (G6PD).³ G6PD is one of the enzymes expressed in all tissues that is involved in glucose metabolism.⁴ This enzyme catalyzes the first reaction of the pentose phosphate pathway (PPP) converting hexose sugar (glucose) to pentose.⁵ Furthermore, nicotinamide adenine dinucleotide phosphate (NADPH) is also produced in this pathway.⁶ One of the functions of NADPH is the reduction of glutathione, that is greatly involved in oxidants neutralization and detoxification.⁷

Phagocytosis and respiratory burst reactions are the major mechanisms of defense against microorganisms, by neutrophils

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and other white blood cells (WBCs). Studies have shown the role of G6PD deficiency in sepsis⁸; however, most of them focus on the hemolysis of erythrocytes due to treatments of microorganisms in patients.⁹ In this study, the effect of blood transfusion is analyzed in leukocytosis patients with favism, as compared to patients treated with antibiotics or combination of both.

2 | METHODS

A total of 97 patients with favism who were referred to the University hospital in 2016-2017 were studied. These patients experienced acute hemolysis due to beans. The treatment group was divided into three: In the first group, only blood transfusion was performed; in the second group, only antibiotics were used; and in the third group, combination of both blood transfusion and antibiotic was used for the treatment. Leukocytosis was defined by white blood cell count of patients greater than the normal value between 10 000 and 11 000. These patients were mostly referred with urine discoloration and icterus, but there were other symptoms such as vomiting, fever, or abdominal pain. On the day of admission, following clinical tests were performed: CBC-DFF, G6PD, Retic, BUN-Cr, and U/A. In patients with hemoglobin <8, packed RBC was injected. In CBC, many of them had leukocytosis (white blood cell count greater than 11 000); however, the number of white blood cells (WBCs) declined the day after injection of packed cell without any antibiotics, and patients with good general condition were discharged within 2-3 days, and they did not have a clinical or laboratory abnormality in follow-up.

Patients records included: gender, age, place of living (city or village), blood group and Rh factor, WBC count before and after blood transfusion, polymorphonuclear neutrophils (PMN) % before and after transfusion, CRP, ESR and platelet of the first day (before transfusion), coombs, Retic, G6PD the first day (before transfusion), have a fever or not (in the same hospital), have taken an antibiotic or not (in the same room), given transfusion (in this context).

Given that the number of white blood cells during acute hemolysis in favism was in some cases markedly increased, but one day after injection, the packed cell was reduced to approximately normal levels (without antibiotics). It is recommended that the administration of antibiotics to these patients should not be promptly decided if clinical signs and symptoms are not in the interest of the infection. Meanwhile, these patients reappear a week after the recovery.

SPSS v.16 software was used for the statistical analysis. The box and whiskers (Boxplots) were used to determine the relationship between dependent and independent variable. $P < 0.05$ was considered statistically significant.

3 | RESULTS

In this self-reported clinical study, 97 patients with favism were referred to the hospital. These patients experienced acute hemolysis

What is known on this topic?

Leukocytosis is a condition where the leukocyte count is above the normal range. This condition is often an indication of an inflammatory response, such as infection, but it may also occur after parasitic infections or bone tumors as well as leukemia.

What this paper adds?

Blood transfusion could improve leukocytosis in patients without additional treatment with antibiotics therapy.

due to the intake of bean. To assess the therapeutic effect of interventions (including blood transfusion, antibiotic therapy) in regard to the reduction in the level of WBC, the correlation between WBC before and after the treatment was 0.69 and 0.64, respectively, from analysis using Adjusted Measurement of Change.¹⁰ This analysis specifies statistical variation in the levels of WBCs after the administration of packed cell. Data analysis was performed using R software (Figures 1 and 2).

Primarily, the independent t test confirmed that the WBC level reached the desired level ($\leq 11\ 000$) after the interventions (one side P -value = 0.1259). The variables such as blood group, antibiotic therapy, and the number of days after consumption of bean did not have a significant relationship with changes in WBC before and after the intervention (Figure 3).

Also, the results showed that the reduction in WBC before and after the intervention in the group that received the packed cell transfusion was significantly higher than the other groups (P -value = 0.014). Figure 4 shows that injections in people with low Hb levels can successfully reduce WBC.

4 | CONCLUSION

The G6PD is a main enzyme in the glucose metabolism.¹¹ The susceptibility to acquire hemolytic anemia and leukocytosis following the ingestion of fava beans has been extensively studied in the Mediterranean population; however, this condition has

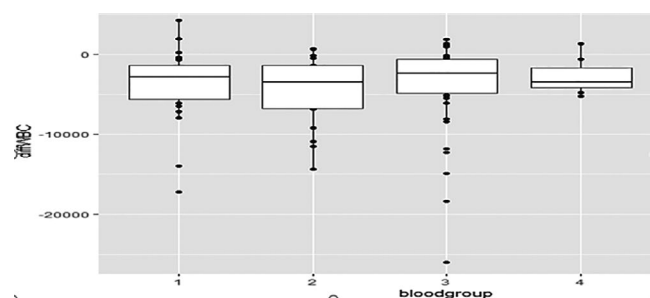


FIGURE 1 The level of WBC in the variable blood group

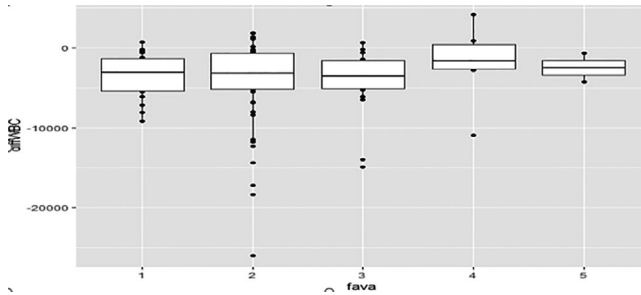


FIGURE 2 Level of WBC in patients with favism

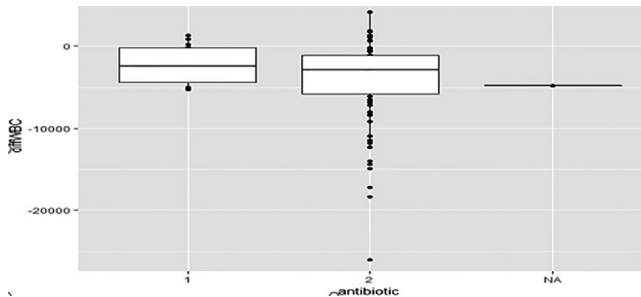


FIGURE 3 Antibiotic intervention in patient with higher WBC level

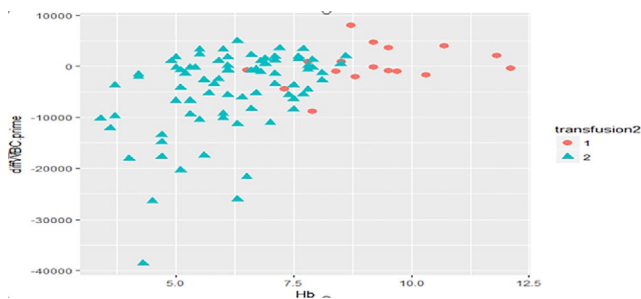


FIGURE 4 Transfusion of packed cells in patient with higher WBC level

also been noticed in other countries.¹² It is mediated by G6PD, upon the intake of fava beans; however, mechanism of action is yet to be fully elucidated. It has been shown that besides sex-linked deficiency, an autosomal locus is also involved in favism, since not all G6PD deficient develops favism during exposure.¹³ Blood transfusion is a usual answer to hemolysis of RBC in this condition.¹⁴

By the end of the study, we hypothesized that cytokines produced by leukocytes are triggered by the beans and might play role in the onset of leukocytosis. This condition can be seen similar to sepsis, that is characterized by a state of “cytokine storm,” in which numerous anti-inflammatory and inflammatory mediators are released such as IL-6 and IL-8.⁸

This study presents blood transfusion, as an effective therapeutic option to treat leukocytosis in favism, rather than treatment of antibiotics.

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CONFLICT OF INTEREST

The authors deny any conflict of interest in any terms or by any means during the study. All the fees provided by research center fund and deployed accordingly.

ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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