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# Challenges of transfusion therapy in multiply alloimmunized patients: A case report

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## Abstract

Alloimmunization to erythrocyte antigens after transfusion is one of the most important late complications of transfusion therapy, which can lead to major difficulties in providing compatible blood units for patients who frequently receive multiple red blood cell transfusions.

In this paper, we present the case of a female patient with colon cancer who, in addition to her primary oncological disease, also had autoimmune conditions including Hashimoto's thyroiditis and ulcerative colitis. Over years of treatment for her underlying diseases, the patient underwent intensive transfusion therapy, receiving dozens of units of red blood cell concentrates, which ultimately resulted in alloimmunization in the form of four clinically significant antierythrocyte antibodies: anti-C, anti-e, anti-K, and anti-Fya.

Timely introduction of preventive extended phenotyping of erythrocyte concentrates and the use of antigen-matched blood before the first transfusion is the key to preventing alloimmunization, preserving blood supplies, and ensuring effective and safe therapy for transfusion-dependent patients.

**Keywords:** Alloimmunization, colorectal cancer, anemia, prevention

## Introduction

Alloimmunization to erythrocyte antigens is a very common complication of transfusion treatment, especially in patients who are chronically dependent on transfusions [1]. Despite decades of efforts to improve laboratory diagnostic methods for detecting erythrocyte antibodies and to standardize the use of preventive measures, alloimmunization after transfusion still represents a major problem in transfusion medicine [2]. Repeated exposure to foreign antigens outside the ABO system can stimulate the development of clinically significant antibodies, which makes it harder to find compatible blood and increases the risk of hemolytic transfusion reactions [3].

In oncology patients, chronic blood loss from the digestive system, extensive surgical procedures, and myelosuppressive chemotherapy often create a need for long-term and intensive blood support, which progressively increases the risk of alloimmunization. The presence of multiple antibodies drastically reduces the pool of compatible donors in the general population and creates exceptional logistical challenges [4]. This case report demonstrates the complex challenge of managing a patient with colorectal cancer who was found to have the simultaneous presence of four clinically significant antierythrocyte antibodies, which required advanced immunohematological evaluation and a highly individualized approach in the selection and preparation of safe transfusion support.

## Case report

A 50-year-old woman was admitted to the hospital for receiving a maintenance cycle of chemotherapy for the treatment of relapsed colorectal adenocarcinoma. The current illness appeared two years ago with accompanying symptoms of weakness, fatigue during moderate exertion, continuous and massive gastrointestinal bleeding, as well as signs of severe anemia. The diagnosis of invasive colorectal adenocarcinoma was made, after which she underwent a total of 6 chemotherapy cycles, surgical removal of the tumor, and postoperative radiotherapy.

Ten years before the current illness, she was treated with medication for Hashimoto's thyroiditis including levothyroxine replacement therapy, and five years ago she was also diagnosed with ulcerative colitis, for which corticosteroids and salicylates were included in her treatment.

Due to chronic anemia and the use of cytostatic therapy over a 2-year period, she received multiple blood transfusions, receiving about 30 doses of red blood cell concentrates. The patient was blood type “O RhD+” with the ccDEE phenotype. After multiple transfusions, she developed multiple alloimmunizations with antierythrocyte antibodies anti-C, anti-e, anti-K, and anti-Fya. The previously transfused doses belonged to blood types “O RhD+/-“with different erythrocyte antigen phenotypes in the Rh-system, as not all Rh-antigens are routinely phenotyped in our laboratory. Kell and Duffy blood group system antigens were also unknown since they are not subject to standard phenotyping.

During the ongoing transfusion treatment, the doses of red blood cell concentrates had to be strictly phenotyped in all three mentioned blood group systems. Due to the very rare erythrocyte phenotype of the patient and the presence of antierythrocyte antibodies, it was extremely difficult to find a compatible blood dose. Considering the severe degree of anemia, it was often necessary to transfuse multiple doses of blood at once, which posed a big transfusion challenge since the mentioned erythrocyte phenotype is very rare in the local donor population. Therefore, it was necessary to use all available resources, including targeted and family blood donation, to find compatible blood donors.

## Discussion

In everyday clinical practice, securing compatible blood for chronically dependent oncology and hematology patients represents a significant technical and organizational challenge for the transfusion service, as well as a serious therapeutic obstacle [4]. The immunohematological profile of our patient required a demanding and extensive blood dose screening, because the likelihood of finding compatible blood that was simultaneously negative for C, e, K, and Fya antigens in the general population is extremely low. Every time trans-

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fusion support was needed, the service had to carry out expanded phenotyping of large batches of blood, often having to test up to 50 doses at once, just to isolate a single dose of antigenically compatible blood.

Unfortunately, in cases of advanced anemia caused by colon cancer and autoimmune diseases of the thyroid and colon, a single dose of blood was often not enough to raise the extremely low red blood cell parameters through transfusion and stabilize the patient. The long-standing autoimmune diseases of the thyroid and colon have been shown in all studies as factors that stimulate and accelerate the development of alloimmunization, and combined with the transfusion burden, this represented a key factor in the development of multiple alloimmunization [5,6]. This case clearly demonstrates a kind of vicious circle that occurs in high-risk patients with multiple alloimmunizations and the problems that transfusion services face in trying to provide compatible blood for the patient.

Therefore, the main focus of this discussion is the justification for timely implementation of systemic measures to prevent alloimmunization, primarily including expanded patient phenotyping and the use of compatible blood right from the start of treatment, especially for chronically transfusion-dependent patients such as oncology and hematology patients [7]. The preventive strategy of 'prophylactic antigen matching' is not only medically justified for patient safety but also represents an economically sustainable model that reduces the pressure on blood transfusion center resources, particularly in settings with limited supplies of specific blood types [8,9].

## Conclusion

The presented case of a patient with multiple sensitizations to red blood cell antigens and the presence of even four clinically very significant antibodies clearly points to serious logistical and therapeutic challenges in transfusion medicine. The increasing number of autoimmune and oncological diseases in the population also creates a medical need for implementing measures to prevent alloimmunization caused by transfusion burden in transfusion-dependent patients.

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