Chemotherapy-Induced Rhesus Blood Group Switch in Pleomorphic Sarcoma Patient during Non-Rhabdomyosarcoma Soft Tissue Sarcoma (NRSTS) Chemotherapy Protocol, Cycle 5

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Introduction: Changes in Rhesus blood group during cancer treatment are very rare. The Rhesus blood group is a genetic characteristic that usually remains for a lifetime. In this case, a child experiences a Rhesus change during treatment of pleomorphic sarcoma using Non Rhabdomyosarcoma Soft Tissue Sarcoma (NRSTS) therapy, which includes surgery, chemotherapy, and radiotherapy. The side effects of chemotherapy on red blood cells may cause changes to the Rhesus antigen.

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Case: A 17-year-old boy underwent chemotherapy with a history of blood transfusion for 9 times using A Rhesus negative blood. However, the latest crossmatch examination showed his blood group was weak A Rhesus positive. The patient was then given a transfusion of A Rhesus positive blood which was considered compatible. Before transfusion, the patient was given a corticosteroid injection premedication and monitored for 2 weeks.

Conclusion: Pleomorphic sarcoma treatment, such as chemotherapy, has the potential to affect the expression of Rhesus antigen. Alkylating agents can replace hydrogen atoms with alkyl radicals, which can modify chemical groups and change the normal sequence of the polypeptide chain which can alter the expression of the Rhesus antigen.

Keywords: Rhesus blood group changes; Pleomorphic sarcoma; non rhabdomyosarcoma soft tissue sarcoma (NRSTS).

1. INTRODUCTION

Pleomorphic sarcoma also known as pleomorphic undifferentiated sarcoma or known as malignant fibrous histiocytoma (MFH), is a type of cancer that originates from soft tissues in the body, such as muscle, fat, blood vessels, nerves, tendons, and other connective tissues that support and connect various body structure organs. These tumors earn the name "pleomorphic" based on the variation in shape and size of cells found in the tumor. Pleomorphic sarcoma usually occurs in adults with an average age of 50-70 years, although it can appear at any age. These tumors usually grow in the extremities (arms and legs), but can also appear in the abdomen, chest or elsewhere in the body. The diagnosis of pleomorphic sarcoma is obtained through a series of physical examinations, medical imaging techniques such as MRI or CT scans, and tissue biopsies to examine cancer cells histopathologically [1,2].

In cases of pleomorphic sarcoma, chemotherapy is one of the chosen treatment methods for this disease. Chemotherapy is a therapy using cytotoxic agents aimed at killing or stopping the growth of cancer cells and is inseparable from various side effects.

Based on the observations emerging in this case are possible changes in the RBCs, including the potential for changes in antigen expression resulting in Rhesus changes in the patient [3].

Rhesus blood type changing during cancer treatment are not common case. Rhesus (Rh) blood type is determined by the presence or absence of specific antigens on the surface of red blood cells. Classified as Rhesus positive (Rh+) if the antigen is present, and Rhesus negative (Rh-) if the antigen is not present. The Rhesus blood type were inherited from parents and usually last a lifetime. In this case, a child experienced a Rhesus change while undergoing cancer treatment. The patient received chemotherapy therapy with the Rhabdomyosarcom Soft Tissue Sarcoma (NRSTS) which is well known of removing tumors, chemotherapy, and radiotherapy, depending on the stage and size of the tumor [2,4].

The chance of rhesus change is very small because it is part of blood type that influenced by genetic factor that usually did not change for life. Therefore, a change in the Rhesus blood type during cancer treatment is a very rare phenomenon. Observations from this case will hopefully add to our understanding of the complex dynamics between chemotherapy and physiological response to the therapy in patient [4,5].

2. CASE PRESENTATION

A 17-year-old boy patient named NA diagnosed with pleomorphic sarcoma in 20 July 2022. NA undergoing chemotherapy procedure (ifosfamide and mesna) for the first time on 27 July 2022. NA with blood type A negative Rhesus underwent a series of blood type and crossmatch tests to evaluate the compatibility of blood transfusions. Starting from 30 July 2022 to 19 November 2022, this test shows that the patient has a strong positive Anti-A response (4+), while Anti-B is negative (-), and is consistent with blood type A. The Rhesus test always shows a negative result, with major and minor crossmatches always showing compatibility. (Table 1)

NA came to the hospital complained that he wanted to continue the 5th cycle of chemotherapy, the patient complained that his an open post-biopsy wound from 4 months ago did not heal properly, the wound appeared to has
crossmatch was carried out with positive packed Rhesus +2 or weakly positive. Then a blood group examination that visually reads (4+/99). (Fig
the response to Cell B was strong positive Cell A1 shows a negative result (–/0). Meanwhile, the response to Cell B was still strongly positive (4+/99) (Fig. 3.). Then a blood group examination was carried out manually and visually it read weakly positive Rhesus. After crossmatching with positive Rhesus type A PRC blood, the results again showed a negative major crossmatch and positive auto controls. So that the blood is considered compatible and can be transfused into patients. Result from antibody screening examination showed that was negative (–/0). (Fig. 4.)

On 13 December 2022, Du examination test was carried out at PMI to detect the D antigen variant and the results showed that the patient blood type was NA Rhesus D negative. Du Test test is performed on the blood sample to measure the level of Weak D Antigen in the blood. It confirms Rh Negativity and is also administered during and after Rh negativity treatment.

Examination of vital signs, obtained componens mentis awareness, pulse 102x/minute, respiratory rate 24x/minute, with a temperature of 36.7°C (axiller). Anthropometric data patient show the result 50 kilograms for weight and 170 centimeters for his height. Physical examination of the patient found palpebral conjunctiva to appear pale in both eyes. Examination of the right thigh revealed an open wound measuring 5x6 cm, muscle base, uneven tissue edges, pain (+), bleeding (-), seepage (+)

At the Anatomical Pathology biopsy examination on 20 July 2022, the results of a malignant tumor biopsy were obtained with a predominance of pleomorphic sarcoma.
Table 1. Result of blood type and crossmatch test

<table>
<thead>
<tr>
<th>Date</th>
<th>Grouping Cell</th>
<th>Rhesus</th>
<th>Blood Type</th>
<th>Crossmatch Mayor</th>
<th>Crossmatch Minor</th>
<th>Autocontrol</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 July 2022</td>
<td>Anti A 4+</td>
<td>Anti B -</td>
<td>Anti D -</td>
<td>A</td>
<td>Compatible</td>
<td>Compatible -</td>
</tr>
<tr>
<td>6 September 2022</td>
<td>Anti A 4+</td>
<td>Anti B -</td>
<td>Anti D -</td>
<td>A</td>
<td>Compatible</td>
<td>Compatible -</td>
</tr>
<tr>
<td>9 September 2022</td>
<td>Anti A 4+</td>
<td>Anti B -</td>
<td>Anti D -</td>
<td>A</td>
<td>Compatible</td>
<td>Compatible -</td>
</tr>
<tr>
<td>10 September 2022</td>
<td>Anti A 4+</td>
<td>Anti B -</td>
<td>Anti D -</td>
<td>A</td>
<td>Compatible</td>
<td>Compatible -</td>
</tr>
<tr>
<td>15 September 2022</td>
<td>Anti A 4+</td>
<td>Anti B -</td>
<td>Anti D -</td>
<td>A</td>
<td>Compatible</td>
<td>Compatible -</td>
</tr>
<tr>
<td>19 September 2022</td>
<td>Anti A 4+</td>
<td>Anti B -</td>
<td>Anti D -</td>
<td>A</td>
<td>Compatible</td>
<td>Compatible -</td>
</tr>
<tr>
<td>23 September 2022</td>
<td>Anti A 4+</td>
<td>Anti B -</td>
<td>Anti D -</td>
<td>A</td>
<td>Compatible</td>
<td>Compatible -</td>
</tr>
<tr>
<td>6 November 2022</td>
<td>Anti A 4+</td>
<td>Anti B -</td>
<td>Anti D -</td>
<td>A</td>
<td>Compatible</td>
<td>Compatible -</td>
</tr>
<tr>
<td>19 November 2022</td>
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<td>Anti D -</td>
<td>A</td>
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<td>Compatible -</td>
</tr>
<tr>
<td>6 December 2022</td>
<td>Anti A 4+</td>
<td>Anti B +</td>
<td>Anti D -</td>
<td>A</td>
<td>Compatible</td>
<td>Compatible +</td>
</tr>
<tr>
<td>9 December 2022</td>
<td>Anti A 4+</td>
<td>Anti B +</td>
<td>Anti D -</td>
<td>A</td>
<td>Compatible</td>
<td>Compatible +</td>
</tr>
<tr>
<td>10 December 2022</td>
<td>Anti A 4+</td>
<td>Anti B +</td>
<td>Anti D -</td>
<td>A</td>
<td>Compatible</td>
<td>Compatible +</td>
</tr>
<tr>
<td>11 December 2022</td>
<td>Anti A 4+</td>
<td>Anti B +</td>
<td>Anti D 50</td>
<td>A</td>
<td>Compatible</td>
<td>Compatible +</td>
</tr>
<tr>
<td>12 December 2022</td>
<td>Anti A 4+</td>
<td>Anti B 29</td>
<td>Anti D 50</td>
<td>A</td>
<td>Compatible</td>
<td>Compatible +</td>
</tr>
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</table>

Antibody Screening Test

<table>
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<tr>
<th>Date</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>11 December 2022</td>
<td>Negative (-/-)</td>
</tr>
<tr>
<td>12 December 2022</td>
<td>Negative (-/-)</td>
</tr>
</tbody>
</table>

Du Test

<table>
<thead>
<tr>
<th>Date</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>13 December 2022</td>
<td>Rhesus D (-)</td>
</tr>
</tbody>
</table>

Fig. 1. ABO-D group Rhesus 11 December 2022

Fig. 2. Anti body screening 11 December 2022

Fig. 3. ABO-D group Rhesus 12 December 2022
3. DISCUSSION

Rhesus blood type is the second most important after the ABO blood type in the field of transfusion medicine. The Rhesus antigen system consists of several antigens, including the D, C, c, E, and e antigens. Rhesus D antigen is the most important and immunogenic among these five antigens [6]. Variations in expression of Rhesus antigens on red blood cells occur due to differences in the structure and amount of antigen present on the surface of red blood cells.

The complexity of the Rhesus blood group antigen starts with the highly polymorphic gene that encodes it. Significance of the Rhesus blood group is related to the fact that the Rhesus antigen is highly immunogenic. In the case of the D antigen, individuals who do not produce the D antigen will produce anti-D if they encounter the D antigen on an RBC transfusion (causing a hemolytic transfusion reaction). Therefore, Rhesus status is routinely determined in blood donors and transfusion recipients [6].

It is important to always perform an accurate serological examination and consider the various factors that can influence the expression of the Rhesus antigen before carrying out a blood transfusion [4].

Sometimes there is a change in the Rhesus blood group from negative to positive. Previous study in 1998 which was carried out in Denmark show that a female patient had an altered Rh phenotype shifted from RhD-positive to RhD-negative over 3 years period (1991–94), during which time he was treated mastectomy (1992) and local irradiation for low levels breast cancer recurred, and was later diagnosed as CML 1994 where he received chemotherapy (hydroxyurea and tamoxifen). These findings suggest a somatic mutation which most probably occurred in a stem cell common to the myeloid lineage because there is no modification of other blood group antigens could be detected [7]. Meher and Khan from Pakistan in 2020 also report that that there are a female patient whose blood group changed from A, Rh positive to A, Rh negative, over the period of 10 years (1999-2009). She was diagnosed with breast carcinoma and a lumpectomy was performed, followed by chemotherapy (with anthracycline and docetaxel) along with local irradiation. Possible reason may be Rh mosaicism and a mutation in the Rh gene, resulting in the alteration of Rh antigen expression. The reason causing this mutation is unclear. However, in some cases changes in blood groups are related to patient chemotherapy treatment and their remission status [8].

In this study, rhesus change probably due to variations in the expression of the Rhesus antigen on the patient's red blood cells. Variations in the expression of the Rhesus antigen on red blood cells which can lead to inconsistent Rhesus test results. In this case, the examination results showed that the patient had a weakly positive Rhesus. Weak positive rhesus is a condition in which the expression of rhesus antigen in red blood cells is lower than normal, and this can cause false or variable results on serological tests [9,10].

This patient underwent ankylating agent chemotherapy. Alkylating agents can bind to the surface of red blood cells, potentially disrupting the cell surface. Alkylating agents can replace hydrogen atoms with alkyl radicals, cross-chain DNA and protein strands, and cause mutations and chromosomal aberrations so that the possibility of Rhesus changes occurs [11].

Blood transfusion administration protocol for patient NA in accordance with the regulations of the Indonesian Minister of Health based that published in 2015. Patients with positive Rhesus blood group (D+) do not require a re-examination of Rhesus (D) on donor blood. However, in patients with negative Rhesus (D-) blood group, a re-examination of Rhesus (D) and weak D on donor blood should be performed. Only Rhesus
negative (D-) blood with weak D negative can be given to patients with Rhesus negative (D-) blood group. Patients with weak D positive should be given Rhesus negative (D-) blood. In an emergency situation, the patient can be given a transfusion with positive Rhesus blood type (D+) for the first blood bag, however, it is better to be transfused with negative Rhesus (D-). So that in this patient with the last positive rhesus (D+) it is recommended to give a blood type transfusion with negative Rhesus (D-) [12].

In cases of emergency blood transfusions, positive Rhesus can be given and before the transfusion procedure, premedication is given in the form of corticosteroid injections with monitoring. This patient received 62.5 mg/8 hours of methylprednisone (1 mg/kg/8 hours) before a positive Rhesus transfusion with 2 weeks of monitoring [6].

4. CONCLUSIONS AND SUGGESTIONS

Rhesus blood type is important in blood transfusions and variations can be caused by several factors. Pleomorphic sarcoma patients undergoing chemotherapy with ankylosing agents may experience Rhesus changes because these agents can damage red blood cells and induce mutations and chromosomal aberrations that can cause Rhesus changes.

Our suggestion is before performing any transfusion procedure, make sure for always double checking and doing an accurate Rhesus serological examination of the patient. Ensure post-transfusion monitoring to prevent adverse reactions from transfusions.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES


12. Regulation of the Minister of Health of the Republic of Indonesia No. 91/2015 about Blood Transfusion Procedure Standards.

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