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Case Report
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Warm Autoimmune Hemolytic Anemia (wAIHA) in Patient with Diffuse Large B-Cell Lymphoma (DLBCL): A Case Report

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Abstract

Warm Autoimmune Hemolytic Anemia (wAIHA) can be primary or secondary. In this case, we found DLBCL as the underlying disease of wAIHA. We report a 50-year-old female presented with fatigue, fever, and dyspnea when activity for 3 months before admission. Physical examination showed both of the conjunctiva were pale and multiple lymphadenopathy at Regio colli, axilla, and inguinal bilateral. Coombs test revealed IgG and C3d. The result of histopathology and immunohistochemistry of excisional biopsy was DLBCL. We administered blood transfusion and steroid for wAIHA and treated the underlying disease DLBCL with R-CHOP, we found complete remission of both wAIHA and DLBCL.

Keywords: wAIHA; DLBCL; Blood transfusion; Steroid; R-CHOP

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Introduction

AIHA is a decompensated acquired hemolysis caused by hyperfunctioning B lymphocytes, which produce large amounts of autoantibodies and/or complement against Red Blood Cells (RBCs), resulting in their lysis [1,2]. DLBCL is the most common subtype of Non-Hodgkin Lymphoma (NHL) in adults worldwide, accounts for 30% to 40% cases [3]. Non-Hodgkin Lymphoma can co-exist with AIHA, known as AIHA-associated Non-Hodgkin Lymphoma. Approximately 1 from 5 AIHA patients develop lymphoma, while 7% to 10% of lymphoma patients have co-existing AIHA [2]. AIHA is diagnosed by detection of autoantibodies with the direct antiglobulin test (DAT/direct Coombs). In warm AIHA, IgG is almost present and C3 (C3b and C3d) may be present as well. In cold AIHA, C3 is present while IgG is mostly absent [4].

Case Presentation

A 50-year-old female patient consulted due to ovarian cyst and anemia pro evaluation. She complained fever, fatigue, and dyspnea when activity for 3 months before admission. There was no night sweat and weight lost. She also presented with palpable lymphadenopathy in the colli, axilla, and inguinal. The physical examination we found that she had a pale conjunctiva and multiple lymphadenopathy at Regio colli, axilla, and inguinal. Laboratory test showed: Hemoglobin (Hb) 8.5 g/dL (normal range: 12 g/dL to 14 g/dL), white blood cell 7200/uL (normal range: 5000/uL to 10000/uL), platelet count 400/uL × 10^3/uL (150–400 × 10^3/uL), reticulocyte 14%, bilirubin total 3.46, bilirubin direct 1.2, bilirubin indirect 2.26, Lactate Dehydrogenase (LDH) 648 (normal range: 240 U/L to 480 U/L), Coombs test blood type O rhesus + IgG and C3d were positive. MSCT (Multislice Computed Tomography) of whole abdomen revealed there were multiple lymphadenopathies at Regio para-aorta, para-iliac, and inguinal dextra et sinistra. After one week, patient underwent ovarian cystectomy and excision suspicious lymph node biopsy with the microscopic result was malignant diffuse non-Hodgkin lymphoma, large cell type. The immunohistochemistry result was CD20, CD10, bcl-2: Positive with nodular and diffuse pattern; CD-3: Negative; MUM-1: Positive in some cells; Ki-67: Positive (80% cells). The conclusion was DLBCL (Figure 1).

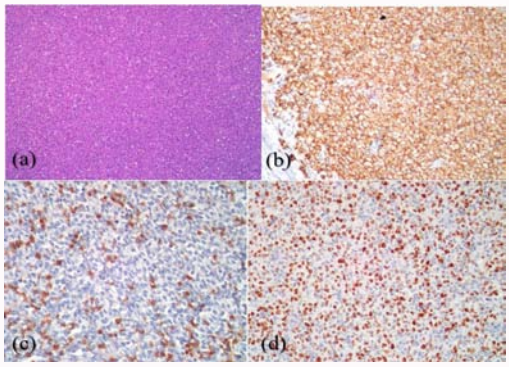

Figure 1: A) Diffuse proliferation of lymphoid cells (Hematoxylin Eosin/HE 100x), B) CD20+ (Immunohistochemistry 400x), C) CD3- (Immunohistochemistry 400x), D) High Ki67 proliferation index (400x).

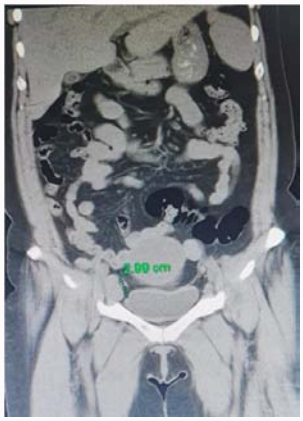

Figure 2: MSCT whole abdomen revealed inguinal lymphadenopathy.

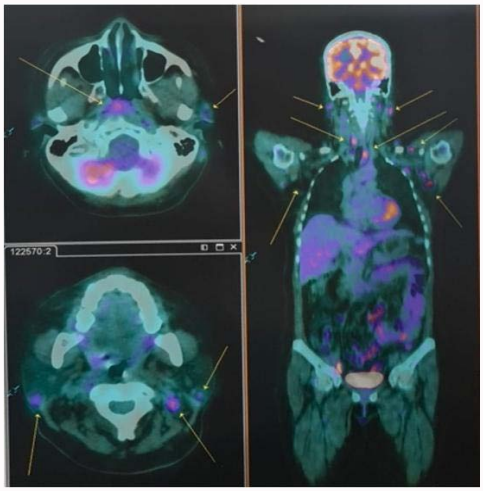

Figure 3A: Initial PET-CT.

We made working diagnosis wAIHA, DLBCL stage III post ovarian cystectomy. We administer RBC transfusion and steroid methyl prednisolone 62.5 mg once daily. After established DLBCL, we administer chemoimmunotherapy R-CHOP every 3 weeks for 6 cycles. After one cycle of R-CHOP, the patient developed febrile neutropenia, however the patient tolerated well to the rest of R-CHOP. A PET-CT (Positron Emission Tomography-Computed Tomography) after 6 cycles revealed complete remission (Figures 2, 3A, 3B).

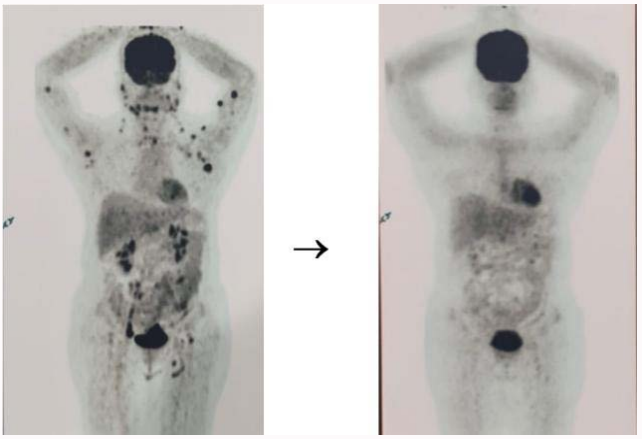

Figure 3B: Comparison of pet scan after 6 cycles of RCHOP was good based on Deauville score 1.

Discussion

We diagnosed wAIHA based on anemia, signs of hemolytic such as: elevated reticulocyte count, high level indirect bilirubin, and positive DAT IgG and C3d. wAIHA is the most prevalent form AIHA, accounts for 60% to 70% cases, caused destruction of RBC by Immunoglobulin G (IgG) autoantibody. wAIHA can be primary or secondary associated with other conditions such as autoimmune and lymphoproliferative disorder, viral infection, immunodeficiency, and drugs [5,6]. In this case, the etiology of wAIHA was DLBCL.

The mechanism AIHA caused by NHL still unclear [2]. In NHL there are hyperproliferative B-cell lymphocytes, T-cell lymphocytes, and Natural Killer (NK) cell lymphocytes which are caused by accumulation of lesions affecting proto-oncogenes or tumor suppressor genes, resulting in cell immortalization [7]. Autoantibody are produced by both tissue and circulating self-reactive B lymphocytes, whereas T-cell recognize antigen presented by other cell [8]. This autoantibody could make RBC lysis with or without complement activation optimally at 37°C. Red blood cell coated by warm-reacting IgG are bound and phagocytosis or part of their membrane removed by spleen macrophages. When high concentration or high affinity IgG bound to RBC, complement C1q gets activated toward C3b then RBC opsonized by C3b are phagocytosis by liver macrophages. CD8+ T cells and NK cells are also contributing to RBC destruction at extravascular hemolysis *via* Antibody-Dependent Cellular Cytotoxicity (ADCC) [9]. IgG is the most common caused antigen against RBC, which produce by B-cell that mainly determine extravascular hemolysis (reticuloendothelial system: spleen and liver). The antigen against RBC can be detected by DAT, and C3 can be present too [10].

First line treatment of warm type AIHA is corticosteroid which are given 2 to 3 weeks until the Hb levels >10 g/dL. After stabilization, corticosteroid can be gradually tapered off. Warm type AIHA patient should continue with low dose corticosteroid for minimum three or four months [10]. In addition, blood transfusion can be given for severe patients and in life-threatening condition [4]. In this patient, we administered RBC due to operation until target Hb >10 g/dL and methylprednisolone 62.5 mg once daily, after patient reached Hb >10 g/dL, the patient underwent cystectomy and excisional biopsy of lymph node. When the patient discharged, we change into

methylprednisolone orally 16 mg tid.

Since the underlying disease warm type AIHA in this case was DLBCL, we stopped methylprednisolone and administered R-CHOP at the one-day care clinic. The patient experienced febrile neutropenia at the first cycle of R-CHOP otherwise she was able to tolerate the chemoimmunotherapy R-CHOP well until 6 cycles and the response of treatment both AIHA and DLBCL were complete remission.

Conclusion

We should consider DLBCL as the cause of AIHA. The response of treatment of DLBCL to RCHOP was good.

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