March 2018

Cold agglutinins in peripheral blood with atypical cells with an owl-eye appearance in bone trephine

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Available at: https://ecommons.aku.edu/pakistan_fhs_mc_pathol_microbiol/705
INTRODUCTION

Autoimmune hemolytic anemia (AIHA) is an acquired clinical condition which is characterised by the presence of autoantibodies that bind to the surface of circulating red blood cells, leading to hemolysis and shortened red blood cells survival. AIHA is very rarely reported in patient with Hodgkin's lymphoma, with an approximate incidence of around 0.2-4.2%.1,2 Case reports and reviews have shown that AIHA occurs mostly at stages III and IV of Hodgkin's Lymphoma.3 Most of the cases reported show an association of Hodgkin's lymphoma with either warm or mixed type of AIHA.4 Here, we report an unusual case of cold type AIHA in association with classic Hodgkin's lymphoma.

CASE REPORT

A 20-year female presented with a history of fever, weakness and weight loss for the last 2 months. General physical examination revealed pallor and cervical lymphadenopathy. Baseline complete blood counts showed hemoglobin: 102 g/L, HCT: 5.1%, mean corpuscular volume (MCV): 91.1 fl, mean corpuscular hemoglobin (MCH): 182.1 pg, white blood cells (WBC): 4.5 x 10^9/L, and platelets: 452 x 10^9/L. Peripheral blood film showed numerous red cell agglutinates (Figures 1A and 1B). White blood cells and platelets were normal on film. Considering the red cell indices and presence of agglutinates on peripheral blood film, the blood sample was incubated at 37°C water bath for about half hour. Post-incubation sample was re-run and peripheral blood film reviewed. Red cell agglutinates disappeared after incubation (Figure 1C) and red cell indices were corrected as hemoglobin: 100 g/L [Reference range: 113-145 g/L], HCT: 29.3% [Reference range: 35.4-42.0%], MCV: 89.9 fl [Reference range: 76-96 fl], MCH: 31.6 pg [Reference range: 26-32 pg], WBC: 4.6 x 10^9/L [Reference range: 4-10 x 10^9/L] and platelets: 396 x 10^9/L [Reference range: 150-400 x 10^9/L]. Direct antiglobulin test [DAT] was positive (3+). Monospecific DAT was positive for C3d.

Figure 1: Peripheral blood film showing numerous red cell agglutinates [A and B]. Peripheral blood film after incubation at 37°C showing disappearance of agglutinates [C]. Bone trephine showing few granulomas with multinucleated giant cells [D]. Bone trephine with large mononuclear cells exhibiting owl's eye appearance [E]. CD 30 positive in large atypical mononuclear cells [F].
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(3+) and negative for IgG. Cold agglutinin titre was not done in this patient. Other laboratory findings favouring hemolytic anemia included reticulocyte count of 0.04 proportion of red blood cells [Reference range: 0.003-0.01], lactate dehydrogense (LDH) of 7.51 µKat/L [Reference range: 3.47-6.31 µKat/L], and indirect bilirubin of 25.6 µmol/L [Reference range: 1.71-13.68 µmol/L].

Bone marrow examination was done for workup of cold agglutinin disease. Bone marrow was dry tap. Bone trephine biopsy was a good length specimen showing effaced architecture. Cellular areas showed pleomorphic background comprising of mainly inflammatory cells including lymphocytes, plasma cells and eosinophils. Few granulomas were seen comprising of multi-nucleated giant cells (Figure 1D). Several interspersed large mononuclear cells were also noted exhibiting owl's eye appearance (Figure 1E). Few areas showed intense fibrosis. These large atypical mononuclear cells stained positive for CD 30 (Figure 1F) and negative for CD 20 and CD 3 on immunohistochemical stains. Findings were suggestive of bone marrow involvement with Hodgkin's lymphoma. For further confirmation, lymph node biopsy was advised. Cervical lymph node biopsy was consistent with the Classical Hodgkin's lymphoma. The patient was given 6 cycles of ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) and responded to the treatment. DAT was performed after 6 months of treatment and was found to be negative.

DISCUSSION

The exact mechanism of AIHA in Hodgkin's lymphoma is not clear. It is hypothesised that the autoantibodies are produced against the neoplastic lesion and erythrocytes as a paraneoplastic phenomenon. In addition, Hodgkin's lymphoma patients are known to have an impaired cell-mediated immunity. This is due to a qualitative defect in T lymphocytes function and decreased number of cytotoxic T cells. Reduction in cytotoxic T cells may cause hyperactivation of B cells leading to increase autoantibody production.5,6

This case highlights the importance of diagnosing cold agglutinin disease. Cold agglutinin disease is not indolent, therefore, early diagnosis and identification of underlying cause is very important. While evaluating a case of hemolytic anemia, either warm or cold type, Hodgkin's lymphoma must be kept in mind.

REFERENCES