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CaseReport:

Diffuse Large B-Cell Lymphoma Associated with Wiskott-Aldrich Syndrome: A Case Report

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Abstract

Context: Wiskott-Aldrich syndrome (WAS) is an X-linked primary immunodeficiency characterized by microthrombocytopenia, eczema, recurrent infections, and a significant predisposition to autoimmune diseases and malignancies, particularly B-cell lymphomas.

Case presentation: We report the case of a 14-year-old male with a confirmed diagnosis of WAS since infancy, who later developed Crohn's disease. He presented with vegetative lesions in the rectum and transverse colon, which were diagnosed as diffuse large B-cell lymphoma (DLBCL) based on immunohistochemistry and positive EBV-encoded small RNAs (EBER). The patient received 12 cycles of chemotherapy, including Rituximab and Etoposide, along with intravenous immunoglobulin (IVIG) support.

Conclusion: This is a rare case of EBV-associated DLBCL in a WAS patient from Iran. The case highlights the importance of early and routine malignancy screening in WAS patients, even in the absence of significant symptoms. Molecular and immunophenotypic assessments, including PCR and immunohistochemistry, are essential for accurate diagnosis and management.

Keywords: DLBCL, Wiskott-Aldrich syndrome

1. Context

Wiskott-Aldrich syndrome (WAS) is a rare X-linked disorder first described by Dr. Alfred Wiskott in 1937 and later by Dr. Robert Aldrich in 1954 [1]. Mutations in the WASP gene cause the disease, which is characterized by thrombocytopenia with small platelets, eczema, recurrent infections, autoimmune diseases, and malignancies [2]. Autoimmune disorders such as autoimmune hemolytic anemia, vasculitis, arthritis, and inflammatory bowel disease occur in approximately 40% of patients with WAS [3].

The risk of malignancy is a critical concern for WAS patients. The incidence of malignancy in patients with severe clinical manifestations ranges from 13% to 22%, with a mean onset age of 9.5 years [4]. Although malignancies are more common in adolescents and young adults, they may also occur in children. The most

frequently reported neoplasms are B-cell lymphomas, often associated with EBV infection [2].

Here, we report the case of an adolescent male with WAS and Crohn's disease who developed diffuse large B-cell lymphoma (DLBCL), diagnosed using immunohistochemical, flow cytometric, and molecular methods.

2. Case presentation

A 14-year-old boy, born to non-consanguineous parents with no significant past medical history or family history of genetic disorders, was diagnosed with WAS at 6 months of age and Crohn's disease at 7 years of age. At 13 years old, he presented with a mass lesion in the rectum and transverse colon. A biopsy confirmed diffuse large B-cell lymphoma.

The patient had hemorrhagic manifestations such as epistaxis and gum bleeding, as well as recurrent respiratory infections, warts, and frequent colds. Laboratory evaluation revealed microthrombocytopenia with platelet counts of 40,000/mm³.

Histopathology

Microscopic examination of the colonic biopsy revealed diffuse infiltration of large, atypical, pleomorphic lymphoid cells in the lamina propria, with glandular involvement and destruction.

Immunohistochemistry (IHC)

The atypical cells were positive for CD19, CD20, and BCL2, with focal CD23 expression. The Ki-67 proliferation index was approximately 40%. EBER in situ hybridization confirmed EBV positivity. CD10, CD21, CD30, and BCL6 were negative. CD3 highlighted numerous scattered small lymphocytes, while CD5 was positive in a few scattered lymphocytes.

FISH Analysis

Fluorescence in situ hybridization (FISH) testing was performed for BCL2, BCL6, and c-MYC gene rearrangements. Results showed BCL2 positivity, BCL6 negativity, and no c-MYC rearrangement, ruling out double-/triple-hit lymphoma.

Treatment

The patient received 12 cycles of chemotherapy, including Rituximab and Etoposide, as well as intravenous immunoglobulin (IVIG) for immune support.

Table 1. Summary of diagnostic findings

Category	Finding
Histopathology	- Diffuse infiltration of large, atypical pleomorphic lymphoid cells in lamina propria - Glandular destruction by tumor cells
Immunohistochemistry (IHC)	- Positive: CD19, CD20, BCL2, CD23 (focal), EBER (EBV+) - Negative: CD10, CD21, CD30, BCL6 - Proliferation index (Ki67): 40% - T-cell markers: CD3+ (scattered small lymphocytes), CD5+ (few scattered lymphocytes)
FISH Results	- BCL6: Negative - BCL2: Positive - C-MYC: Not rearranged (no double/triple-hit lymphoma)

3. Discussion

Wiskott-Aldrich syndrome is a primary immunodeficiency characterized by microthrombocytopenia, eczematous skin lesions, recurrent infections, and increased risk of lymphomas [5]. The WAS protein (WASP), encoded by the Xp11.22 gene, regulates actin cytoskeleton dynamics in hematopoietic cells [6, 7]. The average age of diagnosis is around 21 months, and bleeding manifestations are present in approximately 84% of patients [8].

Patients with primary immunodeficiencies, including

WAS, have an increased predisposition to lymphomas, often associated with EBV infection [9]. EBV infection of B-cells promotes immortalization and uncontrolled proliferation (10). Among WAS patients, approximately 75% of lymphomas are non-Hodgkin lymphomas (NHL), with DLBCL being the most common subtype [10, 11]. These typically present in extranodal sites such as the gastrointestinal tract, liver, brain, lungs, and skin.

Our case is consistent with previous reports, confirming the association between WAS and EBV-driven DLBCL.

4. Conclusion

This case underscores the strong association between Wiskott-Aldrich syndrome and EBV-associated diffuse large B-cell lymphoma. Given the high risk of malignancy in WAS patients, routine and comprehensive screening is essential, even in the absence of clear clinical symptoms. Early detection through clinical monitoring, imaging, and virological surveillance (e.g., EBV load) enables timely diagnosis and intervention, potentially improving outcomes in this high-risk population.

Ethical Considerations

Compliance with ethical guidelines

In order to release the information contained in the patient's medical record, written and informed consent was obtained from the parents.

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Author's contributions

The authors equally contributed to the preparation of this article.

Conflict of interest

The authors have no conflicts of interest to declare.

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