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ABSTRACT N. PO30

ACQUIRED ANGIOEDEMA ASSOCIATED WITH B-NON HODGKING LYMPHOMA: A CASE REPORT.

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Background

Acquired angioedema (AAE) is a rare and likely underdiagnosed condition. It presents with angioedema of the skin, gastrointestinal tract, or upper airways, typically beginning around age 60 without a family history. AAE is characterized by reduced activity of C1 inhibitor (C1-INH), often due to its consumption or neutralization by autoantibodies. An underlying disorder, most commonly hematological malignancies, is found at diagnosis or develops later in about 80% of cases. Treatment includes on-demand therapies targeting the kallikrein-kinin system, long-term prophylaxis, and management of the associated disease. However, most therapies are off-label, and optimal treatment strategies remain undefined.

Case Report

In October 2022, a 60-year-old woman was referred for lymphocytosis and recurrent angioedema. Since November 2021, she had experienced multiple severe angioedema episodes involving the upper airways, requiring ICU observation. She had no significant comorbidities, allergies, or family history of angioedema. Previously documented transient lymphocytosis (5,000/µL) and monocytosis (1,400/µL) were noted. Initial work-up revealed relative lymphocytosis, hypogammaglobulinemia (IgG 533 mg/dL), elevated β2-microglobulin (3.98 mg/dL), and type I cryoglobulinemia. C1-INH level (0.08 mg/dL) and activity (22%) were reduced, and C4 was depleted (<15.4 mg/dL). Flow cytometry of peripheral blood showed clonal CD10−/CD5− B-cell expansion. Imaging ruled out organomegalies and significant lymphadenopathy. HIV, HBV, and HCV serologies were negative. Bone marrow biopsy was consistent with marginal zone lymphoma. After multidisciplinary evaluation, IV rituximab was administered in two cycles (8 doses total) between April and July 2023. Treatment was well tolerated, resulting in both clinical and flow-cytometric remission, along with increased C1-INH and C4 levels. Prophylaxis with tranexamic acid was initiated. During follow-up, no severe recurrences occurred. C1-INH levels remained stable, and flow cytometry remained negative. However, two mild relapses occurred when prophylaxis was interrupted. In both instances, C4 levels normalized about a month after resolution. Notably, the last recurrence was preceded by a C4 decrease two weeks prior. C1-INH levels during these episodes were unavailable. From August 2023, the patient underwent radical mastectomy, axillary dissection, and hormonal therapy for invasive ductal carcinoma. She remains in follow-up with no new angioedema episodes and stable hematological and oncological status.

Conclusions

In this case, the suspicion of an associated condition arose from the known link between AAE and non-Hodgkin lymphomas, underscoring the need for high clinical suspicion to enable timely diagnosis and treatment of associated diseases. Reduced C1-INH and C4 levels supported the diagnosis, while increased levels post-rituximab suggest therapeutic benefit. However, clinical and biochemical responses to rituximab are not universal and may reflect heterogeneity in underlying pathophysiology. The recurrence-associated C4 depletion observed in this patient suggests C4 could serve as a potential biomarker for relapse prediction. While the patient responded well to rituximab, clinical trials are needed to define optimal treatment. The emergence of breast cancer post-rituximab raises concerns about potential immune effects, though causality is unproven. Recurrences also raise questions about the durability of remission and highlight the need for ongoing monitoring and individualized management strategies.

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