

Chronic Lymphocytic Leukemia Presenting with Acquired Angioedema Kazanılmış Anjiödemle Prezente Olan Kronik Lenfositik Lösemi

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To the Editor,

Acquired angioedema (AAE) is a rare form of angioedema (AE) and its prevalence is unknown, it is thought to be one-tenth the prevalence of hereditary angioedema (HAE) (1). AAE is frequently associated with B-cell malignancies, MGUS, and less commonly autoimmune diseases, adenocarcinoma, and other malignancies (2-5). Clinical and diagnostic laboratory findings such as complement (C4), C1 esterase inhibitor protein (C1-INH), C1-INH function are similar to HAE (2,6). However, there are also differences from HAE. Acquired angioedema, unlike HAE, is observed in older ages and there is no family history. Patients may exhibit symptoms with underlying disease such as hematological or autoimmune diseases. In addition C1q is low 70% to 80% of the patients and anti C1-INH antibodies may be positive (1,6). The mechanism of AAE, increased consumption of C1-INH due to overactivation of the classical complement pathway and/or the presence of anti-C1-INH antibodies (1). As a result of excessive bradykinin production, vascular permeability increases and tissue edema occurs. Angioedema attacks regress with treatment of the primary disease, and in patients with persistent symptoms, bradykinin receptor antagonists and C1 esterase derivatives can be used, as in the treatment of acute HAE attacks (7). Androgens and TXA have both been reported to be effective treatments; agents that target B cell clones such as rituximab and cyclophosphamide have been reported with variable success (1,8). Here, we report a patient who presented with angioedema attacks and was diagnosed with chronic lymphocytic leukemia (CLL).

A 70-year-old patient who had a history of swelling of the tongue and lips, twice within two months, was admitted to our clinic. The patient's angioedema attacks were not accompanied by urticaria. While there was no trigger before the first angioedema attack, there was a history of dental procedure 24 hours before the second angioedema attack. She had no history of allergic diseases, urticaria or used angiotensin converting enzyme inhibitors or new medications and no family history of angioedema. The patient also had history of weakness and fatigue along with angioedema. She received allergy treatment in the emergency department and her angioedema resolved within 48 hours. Upon detection of hematological abnormalities in laboratory tests the patient was referred to the hematology clinic and diagnosed with CLL. Laboratory findings included a white blood cell count of 45,000/microliter, hemoglobin 9 g/dL, and platelets 92,000/microliter, consistent with CLL. PET CT revealed cervical, supraclavicular, axillary, mediastinal, abdominal, and inguinal lymphadenopathy. Fludarabine-cyclophosphamide-rituximab treatment (FCR) was planned for the patient. However, due to a history of angioedema, the patient was referred to our clinic before chemotherapy treatment. Normal C3 level, low C4 level (<0.03 g/L; normal 0.15-0.50 g/L), normal C1-INH quantitative level (0.32g/L; normal 0.21-0.39 g/L), low C1-INH function (<10 %, normal 70%-130%) were detected in complement tests. C1q level could not be available. Bradykinin receptor antagonist treatment was planned for the treatment of angioedema attack, the patient was diagnosed with CLL-related AAE. No angioedema was observed during the chemotherapy process and subsequent two years follow-up. Current laboratory results, after chemotherapy, revealed C4 level was slightly increased, C1-INH function was significantly increased, C1q level was low (Table 1). Shah et al. reported that lymphocyte proliferation can induce AAE (4). As in our patient's case, the improvement of attacks with chemotherapy also supports Shah's view. AAE can rarely develop in CLL patients and may resolve with chemotherapy.

References

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Table 1. Complement laboratory parameters before and after chemotherapy

	Before chemotherapy	After chemotherapy
C4, g/L (normal 0.15-0.50)	<0.03	0.04
C1-INH quantitative, g/L (normal 0.21-0.39)	0.32	0.27
C1-INH function, % (normal 70-130)	<10	92
C1q, ugEq/mL (normal 16-18)	-	<0.1