The Egyptian Journal of Hospital Medicine (January 2018) Vol. 70 (7), Page 1121-1122

Acquired Angioedema in a Patient with Chronic Lymphocytic Leukaemia

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ABSTRACT

Acquired angioedema (AAE) is defined by acquired deficiency of C1 esterase inhibitor. It is a rare disorder characterized by recurrent angioedema without urticiaria, which may be associated with lymphoproliferative disorders (LPD). We are reporting a case of 71 years old female, known case of Chronic Lymphocytic Leukaemia (CLL) who presented to the emergency room (ER) with generalized body swelling during her disease course. Investigations were ordered to confirm that the symptoms were due to acquired angioedema, and the patient was managed for this diagnosis.

Knowing the association between acquired angioedema and lymphoproliferative disorder is crucial, because AAE can be treated medically and responds within hours but delayed diagnosis can lead to unnecessary invasive procedures or asphyxiation and death due to laryngeal oedema.

Finally, treating the underlying cause as CLL in our case could prevent further recurrence of angioedema.

Keywords: Acquired Angioedema, Chronic Lymphocytic Leukaemia, Lymphoproliferative Disorders.

INTRODUCTION

Acquired angioedema (AAE) is defined by acquired deficiency of C1 esterase inhibitor. It is a rare disorder characterized by recurrent angioedema without urticiaria, which may be associated with lymphoproliferative disorders (LPD). It can cause severe abdominal pain mimicking an acute surgical abdomen. Angioedema affects the skin, tongue, larynx, extremities and mucosal tissue of respiratory and gastrointestinal tracts, which leads to self-limited swelling of these tissues although laryngeal oedema can be fatal. AAE is similar to hereditary angioedema (HAE) clinically but usually occur in older age and associated with disorders like lymphoproliferative neoplasms, autoimmune disorders, and infections especially H.Pylori infection [1,2,3,4,5] . We are reporting a case of 71 years old female, known case of Chronic Lymphocytic Leukaemia (CLL) who presented to the emergency room (ER) with generalized body swelling during her disease course.

The study was done after approval of ethical board of KFSH&RC.

CASE PRESENTATION

A 71 years old woman, known case of CLL, presented to the ER with mild swelling of both upper limbs and eyelids after taking Diclofenac. The patient labeled to have a probable allergy toward Diclofenac and she received IV Hydrocortisone and IV Benadryl (Diphenhydramine) and discharged home with oral Cetirizine and Hydroxyzine. Her regular medications included calcium carbonate, vitamin D and baby aspirin.

One month later, the patient presented with history of generalized non-erythematous body swelling mainly in both upper limbs and in the left upper eyelid that started four days prior to the patient presentation to the ER.

The patient denied allergy to food or any medication, any history of shortness of breath, wheezing, changes in her voice, newly medication introduced, herbal use, and family history of the same condition.

Physical examination in the ER revealed blood pressure 134/53 mmHg, pulse 98 beats per minute, respiratory rate 18 cycles per minute, pulse oximetry of 96% on room air, and temperature 99.7 °F (37.6 °C). The patient was alert and oriented to person, place, and time, not in pain or distress. Cardiopulmonary examination was unremarkable. Abdomen was soft and lax, not tender. Skin examination showed non-erythematous swelling of the upper and lower limbs, lips and the lower lids of both eyes. The patient had no pitting edema. Throat examination showed patent airway with no evidence of tongue or throat swelling. The patient had palpable cervical and supraclavicular lymph nodes.

The patient was started on IV Benadryl and Methylprednisolone. Four hours later, the patient suddenly developed shortness of breath and her oxygen saturation dropped from 96% to 84% with respiratory rate of 26 per minute, blood pressure was 124/69 mmHg and heart rate was 108 beats per minute. The patient was alert and oriented to person, place, and time and she was talking in clear sentences. Chest examination showed no wheezing with equal air entry bilaterally. Cardiovascular

Received: 25/10/2017 DOI: 10.12816/0044329
Accepted: 05/11/2017

examination was unremarkable. Oxygen was given for her via a simple facemask. The patient's labs showed: white blood cell count of 100.8×10^9/L, absolute lymphocyte of 92.77×10^9/L, neutrophil count of 6.05×10^9/L, monocyte of 2.05×10^9/L. The patient's hemoglobin was normal and D-dimer was 6,850. Cardiac enzymes were negative. Electrocardiogram (ECG) was unremarkable. Chest x-ray did not show anything that justify the patient's shortness of breath. Oxygen saturation improved to 94% but because there was no explanation for the patient's tachypnea and tachycardia, ER physician proceeded with computed tomography Pulmonary Embolus Study that was negative for pulmonary embolism (PE). Based on the above findings, sepsis, PE and pneumonia were excluded. Moreover, because of the associated non-erythematous swelling and the background of previous history of transient swelling in the upper limbs and eyelids, the possibility of acquired angioedema was entertained. Complement (C3 & C4) were normal, C1 esterase inhibitor was low, and C1q was low. Based on those results a diagnosis of AAE was made.

The patient was treated with Chlorambucil for few years then her disease progressed and she was changed to Bendamustine and Rituximab, which she could not tolerate after one cycle. Then the patient was treated with Ibrutinib, achieved complete hematological remission, and continued to be in hematological remission until the writing of this report. Since treatment was started, angioedema has never recurred.

DISCUSSION

AAE is defined by acquired deficiency of C1 esterase inhibitor. It is a rare disorder characterized by recurrent angioedema without urticiaria, which may be associated with LPD. It can cause severe abdominal pain mimicking an acute surgical abdomen. [1,2,3,4,5] .

Angioedema affects the skin, tongue, larynx, extremities and mucosal tissue of respiratory and gastrointestinal tracts, which leads to self-limited swelling of these tissues although laryngeal oedema can be fatal [1,2] .

AAE is similar to HAE clinically but usually occur in older age and associated with disorders like lymphoproliferative neoplasms, autoimmune disorders, and infections especially H.Pylori infection [2,3] .Test results for AAE type one and two are low C1 inhibitor level and low C1q level. AAE is differentiated from HAE by C1q level, which is normal in HAE but reduced in AAE [1].

Association between AAE and LPD, such as CLL, lymphoma, monoclonal gammopathy of unknown significance (MGUS) and multiple myeloma (MM) is will established [2,3] .

In previous study of 32 patients diagnosed with AAE, Castelli found that 13 patients (40%) had MGUS and 9 of them (28%) had LPD [2] .

Twenty five percent of CLL patients suffer from autoimmune complications. Autoimmune haemolytic anaemia is the commonest. However, non-haematological autoimmunity as angioedema is very rare with around 150 cases reported [2,4] .

For this reason, patients presenting with AAE need further investigations to rule out an underlying LPD. Angioedema could be the presenting symptom of LPD or it could occur along the course of LPD [3,4].

AAE is a medical emergency that typically respond to treatment within hours. However, delayed diagnosis can lead to asphyxiation and death due to laryngeal oedema [2]. Treating the underlying cause as CLL in our case could prevent further recurrence of angioedema [1,4].

CONCLUSION

All cases of acquired angioedema need further investigations to rule out underlying causes like LPD.

Knowing the association between acquired angioedema and lymphoproliferative disorder is crucial, because AAE can be treated medically and responds within hours but delayed diagnosis can lead to unnecessary invasive procedures or asphyxiation and death due to laryngeal oedema.

Finally, treating the underlying cause like CLL in our case could prevent further recurrence of angioedema.

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