ABSTRACT

Introduction: Acquired allergic angioneurotic edema secondary to systemic lupus erythematosus (SLE) is rare so herein we present angioedema as the initial presentation that led to the diagnosis of SLE in a young adult female. Case Report: A diagnosis of angioneurotic edema with underlying allergic disorder was made in a young adult female patient presenting with the swelling of dorsum of hands, lips and right periorbital region of the recent origin. The associated clinical and laboratory features finally led to a diagnosis of SLE. Conclusion: The uniqueness of this case suggests that the subtle presentation of angioedema as a secondary cause to various life-threatening medical disorders should not be underestimated.

Keywords: Angioedema, Acquired angioedema (AAE), Systemic lupus erythematosus (SLE), C1-esterase inhibitor protein (C1-INH).

INTRODUCTION

Angioedema/angioneurotic edema is a well-demarcated localized edema involving deeper layers of the skin, including the subcutaneous tissue [1]. Unlike urticaria, where skin eruptions are distinctly pruritic and can involve any area of body from scalp to the soles of feet, in angioedema the most common sites of involvement are the periorbital tissue and lips [2, 3]. Angioedema may either be acquired due to variety of causes or may be hereditary in nature [4]. Acquired angioedema (AAE) is characterized by acquired deficiency of C1 inhibitor (C1-INH), hyper activation of the classical pathway of human complement and angioedema symptoms mediated by bradykinin released by inappropriate activation of the contact-kinin system [5]. Reports on acquired allergic angioneurotic edema secondary to systemic lupus erythematosus (SLE) have been rare so herein we present angioedema as the initial presentation that led to the diagnosis of SLE in a young adult female.

CASE REPORT

A 32-year-old Kashmiri female was presented with swelling of dorsum of hands, lips and right periorbital region of recent origin. She had a previous history of primary hypothyroidism for last six months. She was taking 75 μg of levothyroxine per day. She denied any recent exposures to drugs, food, insect venom stings and physical factors prior to the onset of facial and hands swelling. She had no previous history of similar attacks,
and no family history of angioedema. Her past medical history was otherwise unremarkable.

On general physical examination, she was tall, thin built and afebrile. She had erythematous swelling of dorsum of hands involving all fingers without tenderness and induration. This was associated with unilateral periorbital swelling and erythema (Figure 1), for which provisional diagnosis of angioneurotic edema with underlying allergic disorder was entertained. There was no pedal or sacral edema, no lymphadenopathy or hepatosplenomegaly on clinical examination. She had no features of vasculitis on physical examination. Laboratory investigation showed bicytopenia with hemoglobin of 11.4 g/dL (normal range 10.7–14.9), a white blood cell count of 2.88x10³/μL (normal range 3.30x10³–9.66x10³), an absolute lymphocyte count of 0.9x10³/μL (normal range 1.04x10³–2.86x10³/μL) and a platelet count of 46x10³/μL (normal range 150x10³–450x10³/μL). Her ESR measured 30 mm/h (normal range 0–20 mm/h). She was further investigated by estimating levels of C1-esterase inhibitor protein (C1-INH), found low 180 mg/L (normal range 210–390 mg/L). Bone marrow examination and plasma electrophoresis was normal. Imaging techniques namely, ultrasonography, magnetic resonance imaging (MRI) and computed tomography (CT) scans of various parts of body were normal.

The possibility of acquired angioedema with underlying immune-complex disease was made by demonstrating a positive antinuclear antibody and hypocomplementemia. Her C2 complement was 1.3 mg/dL (normal range 1.6–3.5 mg/dL), C4 complement 8.2 mg/dL (normal range 10–50 mg/dL) and C3 complement level 82 mg/dL (normal range 90–180 mg/dL).

In view of bicytopenia with lymphopenia, ANA positive and hypocomplementemia, diagnosis of systemic lupus erythematosus was suspected. This was confirmed when further investigations revealed antibodies to double stranded DNA (dsDNA) 189 IU/L (normal <25 IU/L) and asymptomatic lupus nephritis (24-hour urinary protein of 0.54 g/day). She was asked to undergo kidney biopsy but denied against it. She had raised anti-thyroid peroxidase (TPO) antibodies measuring 71.07 IU/mL (normal <35 IU/mL), further depicted association with autoimmune disorder.

In the outpatient setting, she had received moderate-dose of 0.5 mg/kg oral corticosteroids for six weeks followed by maintenance dose of 0.07 mg/kg per day. She is currently well; with no proteinuria, normal full blood counts and improved outlook. Angioneurotic edema subsided at sixth day of her treatment. Her C1-INH levels and C4 complement had normalized on the first follow-up visit to 224 mg/L and 13 mg/dL, respectively. These further increased subsequently to 310 mg/L and 48 mg/dL at last follow-up. Her latest anti-TPO antibody levels have considerably decreased to the normal limits. She was regularly following our allergy/immunology clinics till date.

DISCUSSION

Acquired angioedema is first suspected in patients aged 40 or above who presented with recurrent cutaneous and/or mucosal angioedema without urticaria, without an evident triggering factor, and without family history of angioedema. The measurement of C1-INH and C4 antigen in such patients is the first step [4]. In our case, the levels of C1-esterase inhibitor protein (C1-INH) was found low 180 mg/L (normal range 210–390 mg/L). Bone marrow examination and plasma electrophoresis was normal. Imaging techniques namely, ultrasonography, magnetic resonance imaging (MRI) and computed tomography (CT) scans of various parts of body were normal.

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Figure 1: Allergic angioneurotic edema in a young adult female.
blood count (CBC), erythrocyte sedimentation rate (ESR), antinuclear antibodies, anti-thyroid peroxidase (TPO) antibodies, 24-hour urinary protein, bone marrow examination and whole body scan. There was least possibility of orbital cellulites and pseudotumor as patient was afebrile and had normal MRI of orbits. The patient did not show any lymphoproliferative diseases like non-Hodgkin lymphoma of orbit and hairy cell leukemia that was ruled out by the imaging techniques and bone marrow examination. Although lymphoproliferative diseases represent the main group encountered in AAE and a direct pathogenic relationship between the two conditions cannot be questioned, SLE, different neoplasia and infections have also been described in association with AAE [7-17]. Benign forms of lymphoproliferation disorders like monoclonal gammapathy of uncertain significance (MUGS) have been reported with high frequency in association with AAE [5]. The patient’s angioneurotic edema subsided at sixth day of oral corticosteroid treatment. Resolution of angioedema with immunosuppressive therapy is associated with normalization of C3, C4 and C1-INH levels [18].

CONCLUSION

Allergic angioneurotic edema secondary to systemic lupus erythematosus occurs due to the acquired deficiency of C1-esterase inhibitor protein (C1-INH), positive antinuclear antibody and hypocomplementemia. The uniqueness of this case suggests that one should not underestimate the subtle presentation of angioedema as a secondary cause to various life-threatening medical disorders.

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Author Contributions
Shera Irfan Ali – Conception and design, Acquisition of data, Drafting the article, Critical revision of the article, Final approval of the version to be published
Yousuf Qayser – Acquisition of data, Drafting the article, Analysis and interpretation of data, Critical revision of the article, Final approval of the version to be published
Rasool Roohi – Acquisition of data, Drafting the article, Critical revision of the article, Final approval of the version to be published
Yousuf Qayser – Acquisition of data, Drafting the article, Critical revision of the article, Final approval of the version to be published

Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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