CASE REPORT

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Subtle angioedema presented systemic lupus erythematosus: A case report

Shera Irfan Ali, Yousuf Qayser, Rasool Roohi

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).

Shera Irfan Ali¹, Yousuf Qayser², Rasool Roohi³
Affiliations: ¹MD, Senior Resident, Department of Immunology & Molecular Medicine, Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, Jammu & Kashmir, India; ²MSc, Research Fellow, Department of Advanced Centre for Human Genetics, Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, Jammu & Kashmir, India; ³MD, Associate Professor, Department of Immunology & Molecular Medicine, Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, Jammu & Kashmir, India.

Corresponding Author: Dr. Roohi Rasool, Associate Professor, Department of Immunology and Molecular Medicine, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, Kashmir, India- 190011; Phone: PABX +91-194-2401013, Ext: 2262; Fax: +91-194-19077662; Email: roohi_wani@yahoo.com

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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 $2.88 \times 10^3/\mu\text{L}$ (normal range 3.30×10^3 – 9.66×10^3), an absolute lymphocyte count of $0.9 \times 10^3/\mu\text{L}$ (normal range 1.04×10^3 – $2.86 \times 10^3/\mu\text{L}$) and a platelet count of $46 \times 10^3/\mu\text{L}$ (normal range 150×10^3 – $450 \times 10^3/\mu\text{L}$). 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.

Figure 1: Allergic angioneurotic edema in a young adult female.

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), her C3 complement levels were 82 mg/dL (normal range 90–180 mg/dL) and her C4 complement was 8.2 mg/dL (normal range 10–50 mg/dL) indicating the provisional diagnosis of acquired angioneurotic edema with underlying allergic disorder. Acquired angioedema in lupus has been found associated with classical pathway mediated hypocomplementemia (low C3 and C4) and transient low C1-INH antigenic and functional levels. Further, AAE in lupus has also been found associated with absence of lymphoproliferative disease and absence of clinical SLE activity during acute angioedema [6]. As our patient presented with the acute angioedema, our focus was more on any underlying allergic disorder rather than on SLE. In order to establish the diagnosis, additional investigations for lymphoproliferative and autoimmune disease were carried out including complete

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 pathogenetic 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 gammopathy 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.

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, Analysis and interpretation of data, 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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