LUPUS PRESENTING AS ANGIOEDEMA- A CASE REPORT

Anusuya Meganathan\(^1\), S. Anu\(^2\)

\(^1\)Professor, Department of General Medicine, Government Stanley Medical College, Chennai.  
\(^2\)Junior Resident, Department of General Medicine, Government Stanley Medical College, Chennai.

**ABSTRACT**

**BACKGROUND**

A 40-year-old hypertensive female presented with history suggestive of recurrent attacks of intestinal angioedema. She had mild anaemia, raised ESR, low serum C3, C4. Serum C1 inhibitor level was normal with reduced function and ANA was positive. Hence, a diagnosis of acquired angioedema was made. She also had acute nephritic syndrome, renal biopsy showed lupus nephritis. Linking both she had acquired angioedema secondary to SLE. Lupus presenting as angioedema is rare and the acquired type even rarer.

**KEYWORDS**

Angioedema, Intestinal Oedema, Complements, Acute Nephritis, SLE, Acquired C1 Inhibitor Functional Deficiency.


**BACKGROUND**

Angioedema secondary to C1 inhibitor deficiency has been rarely reported to be associated with systemic lupus erythematosus. A genetic defect of C1 inhibitor produces hereditary angioedema, which is usually presented with cutaneous painless oedema, but oedema of the genital area, gastrointestinal and laryngeal tracts have also been reported. In lupus patients, angioedema may be the result of an acquired type of C1 inhibitor deficiency, most probably due to antibody formation directed against the C1 inhibitor molecule.

A 40-year-old female, a known case of systemic hypertension for past 10 years presented with 2 days complaints of abdominal pain, loose stools and vomiting. She has underlying history of recurrent attacks of swelling of face, hands, lips associated with itching following ingestion of non-vegetarian food items, especially seafood for past 3 years.

She has recurrent similar complaints of vomiting, abdominal pain and loose stools in the past 5 months and her last admission in a private hospital shows diagnosis of acute gastroenteritis, prerenal AKI with creatinine 1.6. General examination- patient conscious, oriented, afebrile, b/l pitting pedal oedema++; -no pallor/icterus/cyanosis/clubbing/raised jugular venous pressure.

Vital signs-Blood pressure-140/80 mmHg, Pulse rate 78/min., Respiratory rate 16/min., arterial oxygen saturation 100%.

Systemic Examination: Cardiovascular- heart sounds normal, no murmurs, Respiratory- air entry reduced bilateral basal areas, no adventitious sounds, Per abdomen- abdominal distension+, free fluid+; no renal bruit. Neurological- No focal deficit.

Her investigations showed-

- Hb 8 g/dL, ESR 90 mm/hr.
- RBS-90 mg/dL
- RFT-b.urea-39 mg/dL, s. creatinine-1.7 mg/dL
- LFT: TB/CB- 0.6/0.3 mg/dL, SGOT/PT- 20/35 IU/L, SAP- 48 IU/L, T.prot/alb-5.8/3.6 g/dL, glob 3.2 g/dL
- Serum sodium-134 mEq/L, potassium-3.6 mEq/L

URE- Pro 3+, rbc 3+. USG abdomen, KUB (29/8/16)- bilateral normal-sized kidneys, bilateral minimal pleural effusion, minimal free fluid noted in abdomen, diffuse abdominal wall and bowel wall oedema seen.

Her 12-lead ECG: normal sinus rhythm, no ST-T changes, CXR- PA-bilateral costophrenic angles obliterated-suggestive of bilateral minimal pleural effusion. Urine protein/creatinine<2.5 with 24-hour urine protein-2.65 g (40-150 mg/24 hrs.). Arterial and venous Doppler both lower limbs-normal, no evidence of DVT/arterial occlusion.

Viral markers-ictc, HbsAg, Anti HCV were negative.

Serum C3 complement-36.9 mg/dL (90-180). Serum C4 complement-4.0 mg/dL (10-40); S. C1 esterase inhibitor-Normal, with reduced function.

ANA was positive in 1:100, Anti-double stranded DNA-negative.

**Figure 1**

CT abdomen showing normal-sized kidneys with preserved CMD, abdominal wall and bowel wall oedema.

In view of acute nephritic syndrome, we proceeded with renal biopsy.
Renal Biopsy -
1. Light microscopy- increase in mesangial and endocapillary cellularity, wire loop lesions in 7 glomeruli, double contours on GBM.

Figure 2

2. Immunofluorescence microscopy- IgG, M, A, C3, C1q are positive over capillary walls and mesangium. IgG, C3 and C1q present over tubular basement membrane.

Figure 3

Suggestive of ISN/BPS lupus nephritis stage IV (G) and V.

Hence, this patient was started on IV steroid and cyclophosphamide therapy for lupus nephritis, now better and on routine followup.

This case is unique in the sense that lupus presenting as angioedema is rare and also the acquired type of angioedema still rarer.

DISCUSSION
Angioedema is the swelling of deep dermis, subcutaneous, or submucosal tissue due to vascular leakage. Acute episodes often involve the lip, eyes, and face; however, angioedema may affect other parts of body, including respiratory and gastrointestinal (GI) mucosa. Laryngeal swelling can be life-threatening.

Pathophysiology
Angioedema is a result of the fast onset of an increase in local vascular permeability in subcutaneous or submucosal tissue. Histamine and bradykinin are the most recognised vasoactive mediators known to be critical in the pathologic process of angioedema; most cases of angioedema are primarily mediated by one of these two mediators, though some investigators indicate the possibility that both may be involved in certain cases.[2]

C1-INH is a serine protease that is involved in the regulation of bradykinin, a potent vasoactive substance. Low levels of this protease (either hereditary or acquired) results in unchecked activation of the kallikrein-kinin system, which leads to the overproduction of bradykinin (see the image below).[3]

Epidemiology
The World Allergy Organization (WAO) notes that urticaria and angioedema affects up to 20% of the population.[4] It is estimated that approximately 10-20% of population may experience at least 1 episode of angioedema during their lifetime.[5]

The prevalence of acquired angioedema is very low; until 2006, only about 136 cases have been reported in the literature.[6]

Types of Angioedema
1. Hereditary.
2. Acquired.
3. Others-Angiotensin converting enzyme inhibitor induced, pseudoallergic.

Acquired (Now preferred to be named as C1-Inhibitor-Acquired angioedema) is classified as either type 1 or type 2.

C1-INH (AAE Type 1) is associated with B-cell proliferative disorders and is characterised by hypercatabolism of C1-Inhibitor. Immune complexes are formed between antibodies and abnormal immunoglobulins on the cell surface of B cells. The complement cascade hyper-reacts, producing large amounts of C1. C1-inhibitor is then consumed in attempts to prevent the activation of the continuously activated C1. As a result, levels of serum C1q are decreased in patients with C1-inhibitor-acquired angioedema, but not in those with C1-INH-hereditary type angioedema.

The relative deficiency of C1-inhibitor causes increased activation of the kallikrein-kinin system. Enzymatic cleavage by kallikrein is increased with consumption of kininogen, and subsequently, the production of bradykinin increases. The end result of this intricate molecular cascade is vasodilation mediated by the interaction of kinins with the endothelial cell receptors B1R and B2R.

Type 2 Acquired angioedema is associated with autoantibodies (IgG, and less often IgM) directed against the C1-Inhibitor molecule.[7] Depletion of C1-inhibitor results in the production of large amounts of bradykinin and other vasoactive substances, which causes the signs and symptoms of angioedema.

Treatment of acquired type angioedema relies on treatment of underlying cause.
Approach to Angioedema

CONCLUSION
Angioedema as the initial presenting feature is rare in SLE. Here we have presented a case of intestinal angioedema as per the history and imaging finding of bowel wall oedema. There was no similar family history. Her serum complements C3, C4, C1 INH function were all reduced. The same patient had acute nephritic syndrome and renal biopsy was consistent with lupus nephritis, hence diagnosed as SLE as per SLICC criteria.

Hence, we came to a conclusion that the angioedema was acquired type most probably secondary to the autoimmune disease SLE.

REFERENCES