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ANGIOEDEMA DUE TO ACQUIRED C1-INHIBITOR DEFICIENCY- A CASE STUDY

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ABSTRACT Angioedema is a self-limited, localized swelling that involves subcutaneous tissue or mucosa of the face and other areas. It affects males and females equally, usually during the 3rd and 4th decades of life. We present a patient with angioedema of the head, neck, upper trunk and both upper limb with a typical clinical picture of an acquired type and with a low level of C1-INH. Initially the patient was treated with a combination of drugs for allergy. However, the swelling did not respond to the therapy and patient had a history of recurrent admission in our hospital with the complaint swelling over face and shortness of breath. After the 3rd day, the edema began reducing progressively.

KEYWORDS : C1-INH, angioedema, allergy

INTRODUCTION

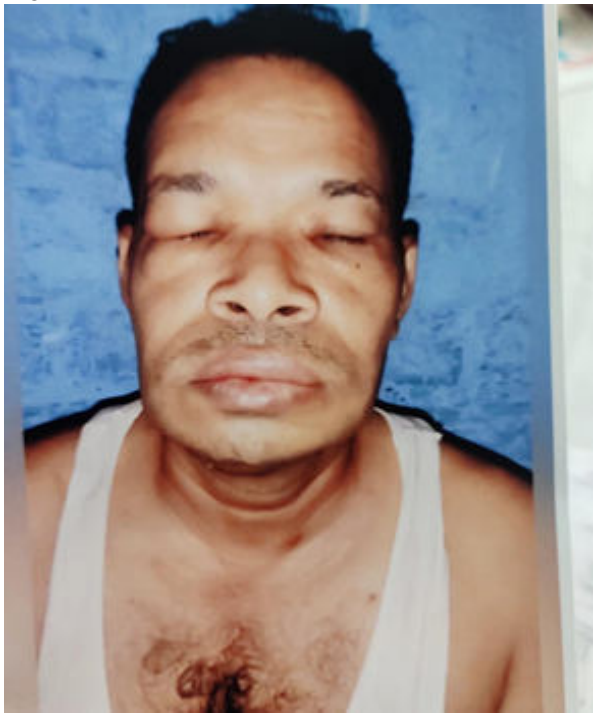
Angioedema is a self-limited, localized swelling that involves subcutaneous tissues or mucosa of the face and other areas. Skin color is usually unchanged. [1] The main reason for the angioedema is the loss of vascular integrity allowing fluid to escape into soft tissues. Exposure of the vasculature to inflammatory mediators causes dilatation and increased the permeability of capillaries and venules. [2-4] Angioedema without urticarial flares (hives) is poorly understood. Its causes are diverse, and little is known about its pathogenic mechanisms. [5] Angioedema occurs without urticaria and does not respond to drugs against allergies. Depending on the underlying mechanism, Hallak et al. (2012) subdivided angioedema into three types: mast cell mediated, bradykinin mediated, and unknown etiology. [6] Lack of response to therapies including antihistamines, steroids, and epinephrine suggested the possibility of angioedema related to a deficiency in the C1-inhibitor protein. The first case of the acquired form of angioedema (AAE) related to a deficiency in C1-inhibitor was published in 1972 by Caldwell et al. [7] The angioedema related to a hereditary or acquired deficiency in protein C1-inhibitor has bradykinin as a mediator. We present a patient with angioedema of the head and neck with a typical clinical picture of an acquired deficiency in the protein C1-inhibitor activity but with a low level of C1-INH.

CASE STUDY

A 45yr old male resident of Indore, Muslim by religion, Vegetables, and fruits vendor by occupation, presented with the Chief complaints of Recurrent On and off Swelling over face and hand - for 3 months.

As per the history given by the patient, he was apparently alright 3 months back after which he developed an episode of swelling over face which was sudden in onset, more in morning after awakening, reduces slowly by day, involving face, hands and scalp which was sudden onset, asymmetric, skin colored, painless a/w hoarseness of voice and difficulty in deglutition, non-itchy, with no particular triggering factor and resolved in 2-3 days with medication. . Routine laboratory blood and urine tests were normal. Immune status (C1, C3, ANA, ANCA, SS-A, /SS-B) was also normal. Serum Protein electrophoresis was normal.

Fig. 1. Showing 45 yr. old male with periorbital, upper /lower lip swelling with mild swelling of tongue and difficulty in deglutition.



No history of allergy to drugs, food material, clothing materials, dust, other fomites, insect bite, prominent pain, pruritis, burning of skin and peeling of skin, skin erythema and warmth over swelling. hyperpigmentation after episodes of swelling, travel, Itching around anal area, passes of worm in stool, fever, allergic rhinitis , bronchial asthma in the past, lower limb swelling (u/l or b/l) ,abdominal distension or generalized oedema over the body, shortness of breath on exertion, exertional dyspnoea in the past, rashes over body, finger discolouration on exposure to cold, joint pain and swelling, contrast dye used in past.

Vitals, General and systemic examination was unremarkable, blood investigation revealed Serum IgE- 95.14 (Ref <100 Iu/ml), low C4- 0.27 gm/dl (0.1- 0.4 gm/dl), normal C3 level , low C1-INH 0.184 (0.21-0.39gm/dl), normal C1q level .

Table 1.

Parameter	Value
Total Cholesterol	97 Mg/Dl
TG	170 Mg/Dl
HDL	50 Mg/Dl
LDL	92 Mg/Dl
HIV	Non-Reactive
HBSAG	Negative
HCV	Negative
ECG	Within normal limit
ANA	Negative
C-Xray	No abnormality detected
Haemoglobin	10.4%
Wbc Count	7300/Cumm
Platelet Count	1.3 Lakh
Total Bilirubin	1.02 Mg/Dl
Direct Bilirubin	0.2 Mg/Dl
SGOT	16 U/L
SGPT	22 U/L
ALP	90 U/L
Total Protein	7.1 G/Dl
S. Albumin	5.0 G/Dl
Creatinine	0.66 Mg/Dl
Urea	24 Mg/Dl
Na+/K+	136/4.2 Meq/L

There is a same episode of swelling over face, lips, tongue and hand during the hospital stay, associated with abdominal pain in epigastric and left hypochondrium region, sudden onset, colicky in nature with no radiation, moderate in intensity, increased after taking meals and relieved by medication. Examination during this event

General examination- Oedema + (over face, lips, tongue and hands, for which he was given antihistaminic , I/M epinephrine but there was no response after that he was treated with FFP which was the only emergency medication available in our setup, patient responded well and swelling reduced 2nd day. Now the patient is on follow up therapy with attenuated androgens. After allergological, hematological and gastroenterological consultations, the possibility of a lymphoproliferative syndrome and gastrointestinal carcinoma were rejected.

Fig. 2. Edema subsided patient recovered.

Angioedema is a rare disease that affects males and females equally, usually during the 3rd and 4th decades of life. Our patient, aged 45, presented with recurrent cutaneous and mucosal angioedema without urticaria, without an evident triggering factor, and without a family history of angioedema. The clinical picture of angioedema showed an absence of allergy.

Prada et al. (1998) describe the primary biologic roles of C1 inhibitor (C1-INH) in the regulation of activation of the classical complement pathway and of contact system of kinin formation. [8] We identified our patient to have Acquired form of angioedema having low level of C1-INH. [9, 10] Hereditary angioedema (HAE) is based on deficiency or dysfunction of C1-INH. Hallak et al. defined two subtypes of HAE and three subtypes of AAE. Type II HAE resulted from the presence of a dysfunctional C1-INH, which is present in normal or elevated amounts and Type II AAE due to inactivation of C1-INH by autoantibodies. [6] The results of complete physical exam, laboratory testing for complete blood cell count with differential, serum protein electrophoresis, chest X ray and abdominal ultrasound assessing lymphoid tissue are normal. The recommended standard testing for lymphoproliferative and autoimmune disease [12] in our patient was negative When laryngeal edema presents angioedema can progress to asphyxiation and death. Initially we suggested a possible diagnosis of anaphylaxis and infection, and treatment involved antihistamine, steroids, epinephrine, and antibiotics therapy. However, patient again complained of facial, lip and hand swelling. The literature suggests that application of C1-INH concentrate is highly and rapidly effective in the treatment of acute attack of HAE and AAE. [13] The laboratory test for C1-INH was low, but we performed replacement therapy with fresh frozen plasma, also contains C1 inhibitor, in reverting acute attack. We applied 3000 U of FFP. The same approach has been useful for HAE. This treatment lasted for 3 days with good results. The success of this treatment approach with FFP in our patient confirms findings of other studies, although this effect is not examined given the nature of disease [12]. There are no studies evaluating its effectiveness, but multiple case reports appear to support its use in acute attacks. [13-19] Despite the risk of blood borne infection, worsening the severity of the attack because of the inclusion of other biologically active molecules [20], FFP can be used as an alternative where C1 inhibitor concentrate is not available. Preventing attacks with long term prevention with antifibrinolytics or androgens, or by curing the associated disease [21, 22] is an effective way to prevent new swelling. Patient has been on follow up and no recurrence noted after treatment with attenuated androgens.

Drugs like ICATIBANT, ECALLANTIDE can be useful for prophylaxis but was not available in our clinical setting.

CONCLUSION

Angioedema is a potentially life-threatening condition, and it is the result of a variety of pathophysiological processes. Diagnosis is based on specific clinical criteria, and in addition, analysis of immunoglobulin levels and various mediators should be carried out. For successful therapy the differentiation of bradykinin induced angioedema to allergic is crucial. In our case, angioedema occurred without urticaria and did not respond to anti-allergy, steroids, and epinephrine dugs. Then the choice of treatment remained FFP.

Abbreviation list:

FFP - fresh frozen plasma
C1-INH - C1 inhibitor
AAE - acquired form of angioedema
HAE - Hereditary angioedema

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