DICLOFENAC INDUCED ANGIOEDEMA-A CASE REPORT

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ABSTRACT

Diclofenac is one of the most commonly prescribed non steroidal anti-inflammatory drugs (NSAID). Diclofenac has been linked with hypersensitivity reactions including angioedema. Angioedema is the abrupt swelling of the skin, mucous membranes of the face, lips, mouth, throat, larynx, extremities and genetilia. Angioedema caused by NSAID may be due to increase in the production of leukotriene due to block in cyclo-oxygenase pathway. Early recognition and discontinuation of the drug should be done. Treatment with anti-histamines and corticosteroids is useful in the management of angioedema. The author reports a case of angioedema in association with the use of diclofenac.

KEYWORDS: Diclofenac, NSAID, Angioedema.

INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the most commonly prescribed groups of drugs for variety of indications ranging from acute pain to chronic conditions for their analgesic and anti-inflammatory effects. However, they are associated with many potential adverse drug reactions.[1] NSAIDs are the most frequent drugs involved in hypersensitivity drug reactions. Such reactions are due to both immunological and non immunological mechanisms. Five major clinical entities are currently accepted in the classification of hypersensitivity reactions to NSAIDs. These include angioedema/urticaria, exacerbated cutaneous disease, exacerbated respiratory disease, delayed hypersensitivity reactions, and single-NSAID-induced urticaria/angioedema or anaphylaxis.[2] The prevalence of NSAIDs induced angioedema is 50% followed by antibiotics that have 20%. Angioedema
is an abrupt localized swelling of the skin and mucous membranes of the face, lips, mouth, throat, larynx, extremities and genitalia. Angioedema due to NSAIDs use may be caused due to increase in production of leukotriene due block in cyclooxygenase pathway. Sometimes angioedema may prove fatal if not treated promptly.[1] The commonest NSAID inducing angioedema are ibuprofen and diclofenac.[3] Herewith we report a case of diclofenac induced angioedema which was treated with antihistamines and corticosteroids.

**Case report:** A 16-year old girl presented with chief complaints of fever (100 degree F), with myalgia and generalized weakness of two days duration. She did not reveal any history of painful micturition, her bowel was normal. She was on Tab Dolo 650mg(paracetamol), TID, from past 2 days. On examination, she was mildly febrile; her pulse rate was 92/min, regular. Her general physical examination revealed no abnormality. She was treated with injection Diclofenac Sodium 50mg intramuscularly in view of severe myalgia. Half an hour after the administration of injection diclofenac sodium, she complained of severe itching over the chest and forehead which was the first symptom. This was followed by severe redness, rashes, urticaria over the face and swelling of the peri-orbital area as shown in Fig 1. She also developed dry cough. She did not give any history of allergic disorder or allergy to medication and no history of similar complaints in the past. She was not on any other medication other than Paracetamol at the time of presentation. Physical examination was normal except for swelling of the peri-orbital region, rashes over the face. The patient was treated with anti-histamines (Tab cetrizine 10mg, Inj Chlorpheneramine Maleate IV) and corticosteroids (Inj hydrocortisone 100mg IV stat). She showed good response to treatment and swelling decreased within 8hours as shown in Fig 2. She was followed up for a week. Her laboratory investigations including CBC were normal. The chest X-ray posteroanterior view did not reveal any abnormality.

![Figure 1: Diclofenac induced angioedema at onset](image)
DISCUSSION

Angioedema is known side effect of drugs commonly used in day to day practice. It is the end result of deep dermal, subcutaneous and/or submucosal swelling.\cite{4} It is typically non pitting, skin coloured or erythematous and occurs at areas where the skin is lax. It is generally self limiting but may sometimes result in respiratory tract obstruction, which can prove fatal.\cite{1} Drug induced angioedema without urticaria has a prevalence of 2.3% among patients with adverse drug reactions.

Various studies have shown that NSAIDs and antibiotics are most commonly implicated in angioedema.\cite{1} Studies have shown that most common NSAIDs causing angioedema are non-specific cyclo-oxygenase (COX) inhibitors such as ibuprofen, aspirin, and diclofenac.\cite{3} The concurrent administration of drugs known to cause angioedema, for example, angiotensin converting enzyme inhibitors should be avoided.

In a case report published by Tiwari AK et al., in 2013, patient developed chest pain and pruritis over the lip with redness and wheal over the site of injection after diclofenac sodium 50mg intramuscularly. Electrocardiography (ECG) showed ST-segment elevation in leads II, III and avF. An ST-segment elevation myocardial infarction of inferior wall was diagnosed. This is referred to as Kounis syndrome. In this syndrome, there is coincidental occurrence of chest pain and allergic reactions. This can be substantiated by clinical and laboratory findings of classic angina pectoris including release of inflammatory mediators.\cite{5}

In another case report by Sanuki T et al., in 2010; a 45-year-old male patient developed anaphylactic reaction to oral diclofenac (25 mg). The patient was scheduled for dental implant under sedation. After 30 minutes of uneventful surgery, oral diclofenac (25 mg) was

Figure 2: Diclofenac induced angioedema after 8 hours
administered. Within 15 minutes of the oral drug, the patient developed urticaria on the face, both arms, and legs, that spread later to the entire body suggesting an allergic onset.\textsuperscript{[6]}

In another case report by Hedar A et al., in 2010; a 39 year old woman who received a diclofenac suppository for analgesia 6-hours after cesarean section developed angioedema and profound hemodynamic shock after 10 minutes.\textsuperscript{[7]}

Diclofenac sodium is considered to be safe with a World-wide administration to 7.6 million patients per year.\textsuperscript{[6]} It is one of the most commonly used analgesic in emergency department. The common adverse effects are gastritis, peptic ulceration and depression of renal function. Diclofenac has been linked with some cases of angioedema. It is usually self limiting but sometimes can be fatal. The condition should be recognized early and the drug should be discontinued. The condition should be treated with corticosteroids, norepinephrine and anti-histamines..Severe cases may require tracheostomy or intubation. Patient should be well informed regarding offending agent and physicians should keep in mind the possibility of this adverse drug reaction while using this drug.

REFERENCES
5. Tiwari AK, Tomar GS, Kapoor MC. Kounis syndrome resulting from anaphylaxis to diclofenac. Indian J Anaesth., 2013; 57(3): 282-84