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Case Report

Severe anaphylactic reaction to diclofenac

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Introduction

Arachidonic acid metabolism takes place via the cyclo-oxygenase and the lipo-oxygenase pathway. Both the pathways produce potent mediators of a multitude of immune-induced and inflammatory reactions. Any blockade of cyclo-oxygenase pathway (COP) shunts the metabolism towards the lipo-oxygenase pathway (LOP) and can potentially increase the side-effects of that pathway by augmented production and release of cysteinyl-leukotriene.[1]

Diclofenac is a Non steroidal Anti inflammatory drug with specific inhibiting actions on cyclo-oxygenase-1 (COX-1) and cyclo-oxygenase-2 (COX-2) with relative equipotency. The drug has also been proven to be multimodal in action with extended spectrum of targets including thromboxane-prostanoid receptor, arachidonic acid release and uptake, lipoxygenase enzymes, and activate the nitric oxide-cGMP antinociceptive pathway.[2] As the drug has effects on both pathways (COP & LOP), it has been considered safer than other NSAIDs and is extensively used as an analgesic and antipyretic in both adults and children. We present a case of a young male who had a severe life threatening anaphylactic reaction to diclofenac.

Case report

A 35 years old male patient was brought to our hospital in a semi-comatose state by his peers after ingestion of 50 mg tablet of diclofenac sodium. He had developed a generalised rash and facial swelling within minutes of ingestion followed by difficulty in breathing and subsequent drowsiness.

The patient was drowsy and tachypnoeic (60/min) at presentation. He was hypotensive (60/40 mmHg) and had profound bradycardia (32/min) with significant desaturation (SpO_2 – 85%). He had urticaria, laboured breathing and generalised wheeze. The ECG showed bradycardia with normal sinus rhythm and no ST/T changes. The ABG analysis could not be done.

A CPR was initiated immediately and he was given IV adrenaline, pheniramine maleate and hydrocortisone along with fluids, oxygen and salbutamol nebulisation. The patient showed significant improvement almost immediately and the vitals had stabilised over the next 30 min. His progress over the next two days was uneventful. On recovering, he did give history of episodes of flushing, palpitation and urticaria off and on after consumption of diclofenac but did not give any other history of symptoms suggestive of atopy.

The haemogram (including ESR), metabolic and biochemical profile were normal. Troponin T was not done in the immediate anaphylaxis phase. The immunological profile revealed a raised IgE levels (854 IU/L), normal complement (C3,

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C4) levels and absence of auto-antibodies (ANA, Anti-dsDNA, ANCA). Stool was negative for ova/cysts of parasites on three occasions. The pulmonary function tests were normal. A skin prick test (SPT) for food and aeroallergens could not be done as they were not available in our centre. We did an SPT with syp diclofenac (1 ml of diclofenac sodium with 9 ml of normal saline) which was positive with recurrence of local erythema and induration immediately as compared to the control (injection of normal saline) on the other arm. As a urinary methylhistamine or serum tryptase level was not available a Naranjo probability scale was used to assess the causal relation.[3] A score of 8 was calculated indicating a probable reaction to the drug.

He was diagnosed as a case of acute anaphylactic reaction to diclofenac sodium and was advised not to consume diclofenac sodium in particular and take medical consult prior to taking any 'pain killers'. He continues to be on our follow-up and an oral provocation test with selective COX inhibitors is under consideration to determine drug/class specific sensitivity and safer analgesics or anti-pyretics.

Discussion

Our patient presented with hypotension, respiratory distress, bradycardia and cutaneous symptoms requiring immediate resuscitation at the emergency department. He also had a history of hypersensitivity reactions in the form of flushing and swelling over the lips after taking 'pain killers' in the past.

Hypersensitivity is a known feature of NSAIDs and is of predominantly two types.[4] The more common ones are the cross-reactive, COX-inhibitor–related syndromes which range from aspirin-exacerbated respiratory disease to urticaria and/or angioedema reactions. The less common group of reactions are drug-specific, probably immune mediated reaction which may range from delayed type hypersensitivity to immunoglobulin E–mediated anaphylaxis. Another group prone to such reactions are individuals with allergic respiratory disease.[5] Chronic urticaria may have exacerbations of symptoms after exposure to NSAIDs and cases have been reported where reactions to NSAIDs preceded the onset of chronic urticaria.[6]

Autoimmune disease may be an additional risk factor for such reactiveness to NSAIDs. Similar reactions have been documented with ibuprofen as the first manifestation of systemic lupus erythematosus.[7] Therefore, it should be important to evaluate the patient with such hypersensitivity to NSAIDs for an autoimmune inflammatory disease. Our patient was evaluated for the same and the auto-antibody panel was negative. As the patient is on our follow-up, it is planned to watch out for symptoms of any autoimmune disorder or urticaria that may develop in future.

Diclofenac by itself has been considered to be a safe drug and the experience in terms of patient-years is huge. The side effect profile is similar to other NSAIDs in terms of gastritis, peptic ulceration, and depression of renal function. The very rare adverse effects attributed to NSAIDs in general include erythema multiforme, hepatitis, anaphylaxis and urticaria which are more common when the drugs are given intravenous.[8] Our patient had been on tablets and there was no history of taking injections in the past.

A class specific hypersensitivity reaction to cyclooxygenase inhibition is possibly the reason for anaphylaxis in our patient, more so because our patient had been having similar episodes to a variety of NSAIDs although the patient was sure about the drug being diclofenac the last two times.

There possibly exists a subset of population that have a higher susceptibility to prostaglandin inhibition predisposing them to severe hypersensitivity to this class of drugs. While it is imperative to manage such emergencies effectively, it is also important to be able to suspect and evaluate such patients at an earlier stage of the hypersensitivity. Diagnostic oral testing and SPT may help in providing definite evidence of the sensitivity of the patient but they carry some risk.

Selective COX-2–specific medications may be an alternative for such patients as these agents would not inhibit COX-1 and may not divert the metabolism towards the lipooxygenase pathway.

Conclusions

NSAIDs hypersensitivity has a spectral manifestation varying from simple isolated urticaria to severe anaphylaxis which could be life threatening. These reactions are more common in patients with a known allergic reaction or autoimmune disorders which should be considered as the population at risk. It is therefore important that this thought be kept in mind while prescribing the 'commonly used NSAIDs' and any history of allergic reaction be evaluated in detail and the patient counselled for the nature of illness and subsequent precautions the patient has to follow.

Conflicts of interest

All authors have none to declare.

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