Stevens-Johnson Reaction: A Rare Case Report of Ibuprofen Induced Hypersensitivity Reaction in a Young Child

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Abstract
Ibuprofen is a commonly used over-the-counter drug for the treatment of fever, headache, joint pain, migraine, and other mild inflammatory conditions. It is available alone or in combination with various other drugs. Various drug reactions associated with non-steroidal anti-inflammatory drugs (NSAIDs) are rashes, gastrointestinal ulcers, hepatic toxicity, acute exacerbation of asthma, Stevens-Johnson syndrome, respiratory skin rashes and anaphylaxis. Though the hypersensitivity reactions to NSAIDs are not rare but remain unnoticed and undiagnosed, especially in children. This case report highlights the oral rehabilitation in a rare case of ibuprofen induced hypersensitivity reaction, which manifested as Stevens-Johnson reaction in a young female child.

Keywords: NSAIDs, dental management, hypersensitivity reaction, Ibuprofen, Stevens-Johnson reaction

Introduction
Ibuprofen is a phenyl propionic acid derivative, used as antipyretic and analgesic drug but has low anti-inflammatory action. It can be used as a single drug or in combination with other derivatives. When used with acetaminophen, antipyretic and analgesic effects are pronounced.

Ibuprofen, either alone or in combination with other medicine, is widely prescribed and purchased worldwide in developing countries.[1] Adverse drug reaction (ADR) is a major health problem with the use of drugs. Adverse drug reactions occur because of idiosyncrasy, overdose, and prolonged usage. Various drugs like diclofenac, ibuprofen, aspirin, indomethacin, naproxen, rofecoxib, and paracetamol have been associated with different adverse reactions. Depending on the type of NSAIDs used, the prevalence of ADR varies from 18-78%.[2] The most common ADR’s seen in children with these drugs are skin rashes, mild anaphylaxis, respiratory reactions, stevens Johnson reaction, generalized exanthemata, hepatic, gastrointestinal, and toxic epidermal necrolysis are uncommon.[3] In adults, incidence of ADR’s to NSAIDs are approximately 26%, and various hypersensitivity reactions range from skin rashes to acute bronchospasm, acute exacerbation of asthma, angioedema, and anaphylaxis are reported clinically.[4] This case report highlights the oral rehabilitation and clinical manifestations of ibuprofen-induced hypersensitivity reaction in a young female child.
Case Presentation

A 7-year-old girl reported with her father to the outpatient department with a chief complaint of decayed teeth. The medical history revealed that the child had an episode of allergic reaction to ibuprofen which manifested as a severe Stevens-Johnson reaction. The incident occurred one year ago when the child was given ibuprofen for the relief of pain. No other medications like antibiotics were given to the child. Extraoral examination revealed scar marks of healed rashes on the face, hands, abdomen, and legs. The child had dry eyes, corneal opacity, trichiasis, cicatricial entropion, symblepharon formation and visual impairment (Fig. 1a-c). The child also had malformed nails of the fingers and toes (Fig. 2a, b). The child had a good cognitive development and was able to understand the verbal commands. The child was managed with tender, love, care, and intraoral examination was done. Intraoral examination revealed multiple carious teeth with hypomineralized molars and mucosal adhesions in the buccal vestibule. The dorsum of the tongue was smooth without the papillae and whitish gray patches were present all over the tongue (Fig. 3a, b).

The parents were counseled about the importance of deciduous and permanent teeth, and the parents were agreed for the dental treatment. The child was anxious and was made cooperative with the presence of father in the operatory. All the permanent first molars and other deciduous teeth were restored with composite restoration (Filtek Z350 XT, 3M, ESPE, USA). Sodium fluoride varnish (Fluoritop SR, ICPA) application was done on the permanent first molars. Tooth preparation was done, and prefabricated stainless-steel crowns (3M, ESPE, USA) were placed in the deciduous maxillary and mandibular molars. Maxillary right central incisor was extracted as it was grade III mobile. (Fig. 4) The patient was advised to take good care of oral hygiene and consult a physician before taking any medication to relieve pain.

Discussion

Anti-inflammatory and analgesic drugs are widely used as over-the-counter drugs for fever, pain, and inflammation. After the beta-lactam antibiotics, anti-inflammatory drugs are most commonly used, thus the reason for the various adverse drug reactions.[5] The prevalence of

Figure 1. Extraoral examination of the child showing dry eyes, corneal opacity, visual impairment, scar marks on the face (a), abdomen (b) and hand (c)
hypersensitivity reactions to NSAIDs has been found to be around 0.5 to 1.9%, and 21 to 25% of the adverse drug reactions in the general population are due to these drugs.[6] NSAIDs are among the leading causes of allergic reactions and anaphylaxis. The various risk factors like young adulthood, female gender, patients with atopy, and use of intermittent NSAIDs for the relief of acute pain are responsible for NSAIDs hypersensitivity.[7] In the present case, the hypersensitivity reaction to Ibuprofen was manifested in a young female child.

Anaphylaxis is defined as a response to an allergen with symptoms involving two organ systems or hypotension development. Pathophysiological mechanisms like mast cell degranulation and basophil activation play an active role in the pathogenesis of anaphylaxis. The cell mediators released during these reactions caused vasodilatation, increased mucosal secretions, fluid extravasation and smooth muscle contraction. Hypersensitivity reactions to Ibuprofen can be associated with both IgE mediated and non-IgE mediated.

![Figure 2. Photograph showing malformed nails of the finger of hand (a) and toes of the feet (b)](image)

![Figure 3. Intraoral photograph of the child showing smooth surface tongue (a) and preoperative intraoral image of the child (b) showing multiple carious teeth)](image)

![Figure 4. Post-operative intraoral photograph after complete oral rehabilitation)](image)
Hypersensitivity reactions can be classified as immediate or acute and delayed types based on the time of onset and the clinical manifestations. Acute or immediate reactions start immediately or within a few hours, but delayed reactions begin 24 hours after drug administration.[8] There are various hypersensitivity reactions which clinically manifested as either organ-specific or multi-systemic disease (Table 1).[7-11]

Drug-specific IgE antibodies mediate acute hypersensitivity reactions. The measurement of specific IgE antibodies can identify this either through skin tests or in vitro tests. Delayed reactions are type IV hypersensitivity reactions mediated by drug-specific cytotoxic T cells.[9] There are various effector cells like neutrophils, monocytes, eosinophils, CD4, and CD8 lymphocytes, which cause IVa, IVb, IVc, and IVd subtypes of reactions depending on the effector cells involved.[10] Various clinical manifestations like urticaria, angioedema, and anaphylaxis induced by a NSAID are more frequently triggered by pyrazolones. The increased frequencies of these reactions are observed in patients with food or drug allergy and patients with the previous history of atopic disease. These clinical manifestations are also reported for aspirin, paracetamol, ibuprofen, diclofenac, and naproxen and constitute about 30% of adverse reactions to NSAIDs. A review of literature on adverse reactions to NSAIDs in children revealed that the most common clinical presentation is angioedema with or without hives and these hypersensitivity reactions were non-IgE mediated. In a prospective study, 55785 children who were given 5 or 10 mg/kg of ibuprofen with acute febrile illness did not observe a single case of anaphylaxis, which suggested that anaphylaxis is very rare in children exposed to ibuprofen.[11,12]

Diagnosis of Ibuprofen hypersensitivity reaction is considerably difficult as there is a wide clinical variety of reactions. There are no reliable in vitro confirmatory tests for the hypersensitivity reaction. The provocative challenge test is the only effective way to establish the diagnosis.

The use of cyclooxygenase inhibitor drugs such as COX-2 inhibitors drugs (celecoxib) should be considered as an alternative drug or first-line option in cases where the risk of both IgE and non-IgE mediated hypersensitivity reactions to NSAIDs is high.[13,14] Regardless of the mechanisms involved leading to NSAIDs hypersensitivity, the best management strategy is drug avoidance or preventing re-exposure of the same drug.

**Conclusion**

Ibuprofen is a type of NSAIDs which causes various hypersensitivity reactions which might be immediate or delayed type with different clinical presentations. Patient management includes using alternative NSAIDs, i.e., cox-2 inhibitors, or preventing re-exposure in patients with atopy or any past episode of hypersensitivity reaction with these drugs. Dental management using behavior management techniques and parents presence might help in completing the oral rehabilitation in these cases.

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**References**


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**Table 1. Type of hypersensitivity reaction and their clinical manifestations**

<table>
<thead>
<tr>
<th>Hypersensitivity type</th>
<th>Clinical manifestations</th>
</tr>
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<tbody>
<tr>
<td>Immediate</td>
<td>Urticaria, Angioedema, Laryngeal edema, Anaphylaxis, Generalized pruritus, Rhinitis or bronchospasm[7]</td>
</tr>
</tbody>
</table>
3. Kidney: Nephritis  
4. Central nervous system: Aseptic meningitis |


