NSAID (Non-Steriodal Anti-Inflammatory Drugs) Induced Rash: A Case Report

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***Abstract*- Frequent use of non-sterodial anti-inflammatory drugs(NSAIDS) has been paralleled by increasing occurrence of Adverse reactions which may vary from mild Local skin rashes to gastric irritation to, generalized symptoms even life-threatening anaphylaxis. NSAIDS are among the most commonly used drugs and are the first or second to the antibiotics based on the patient requirements. NSAID induced Hypersensitivity reactions are character by a wide pattern of symptoms which involve both Immunological and non-immunological mechanisms. Drug induced hypersensitivity reactions cannot be achieved without understanding the underlying mechanism and that history alone cannot be sufficient to accurate diagnosis and management.**

Index terms- Anti-inflammatory drugs, Aspirin, Allergy, Adverse drug reactions, Hypersensitivity reactions, management

I. INTRODUCTION

Pharmacology textbooks define NSAIDs as compounds that antagonize inflammation through the inhibition of a group of enzymes known as cyclooxygenase (CoXs). Some drugs, notably pyrazolones and acetaminophen, were previously not classified into this group because they did not inhibit COX enzymes. In recent years, new COX isoenzymes have been described, such as COX-2b and COX-3, that can be selectively antagonized by these drugs, and therefore they would fit into the NSAID category(1). Frequently use of non-sterodial anti-inflammatory drugs (NSAIDs) has been paralleled by increasing occurrence adverse reactions, which vary from mild local skin rashes or gastric irritation to severe, generalized symptoms and even life-threatening anaphylaxis. NSAID-induced hypersensitivity reactions may involve both immunological and non-immunological mechanisms and should be differentiated from type A adverse reactions (2). Cutaneous drug eruptions are one of the most common types of adverse reaction to drug therapy, with an overall incidence rate of 2-3% in hospitalised patients. 1-3 Almost any medicine can induce skin reactions, and certain drug classes, such as non-sterodial anti-inflammatory drugs (NSAIDs), antibiotics and antiepileptics, have drug eruption rates approaching 1-5%. 4 Although most drug-related skin eruptions are not serious, some are severe and potentially life-threatening. Serious reactions include angio-oedema, erythroderma, Stevens-Johnson syndrome toxic epidermal necrolysis. Drug eruptiobs can also occur as part of a spectrum of multiorgan involvement, for example in drug-induced systemic lupus erythematosus(3). Individuals who develop drug Hypersensitivity reactions (DHRs) to chemically unrelated non-sterodial anti-inflammatory drugs (NSAIDS) are considered cross hypersensitive. The hallmark for this classification is that the patient presents a reaction after intake of challenge with acetylsalicylic acid (ASA). Whether patient reacts to two or more NSAIDS while tolerating ASA remains to be studied (Selective reactions, SRs)(4). Several adverse events have been reported, including skin eruptions mostly caused by non-immunological rather than allergic mechanisms. NSAIDS exert their analgesic, antipyretic, anti-inflammatory and antithrombin effects by inhibiting both COX-1, and COX-2 activities. However, the primary responsibility for the synthesis of prostanoids involved in acute and chronic inflammatory states has been credited to COX-2, whereas the gastrointestinal adverse effects have been attributed to COX-1 activity. The consequent hypothesis that specific inhibition of this enzyme could have therapeutic effects similar to those of other NSAIDS but without causing gastrointestinal side effects led to the development of COX-2 selective antagonists(5). A common confounding factor in many studies

concerning Hypersensitivity to NSAIDS is that investigators have included a mixed population of subjects with various clinical manifestations such as respiratory(Dyspnea, wheezing, nasal congestion, rhinorrhea, sinusitis), cutaneous (Urticaria, angioedema, different types of Skin rashes), patients with a mixed picture of respiratory and Skin symptoms, or individuals who exhibit systemic manifestations resembling anaphylaxis. Other Hypersensitivity reactions such as cutaneous(fixed eruptions, exfoliative dermatitis, toxic epidermal necrolysis, Stevens Johnson syndrome, erythema multiforme, erythema nodosum, morbiliform and maculopapular eruptions, allergic and photallergic contact dermatitis, purpura, vasculitis), neurological (aseptic meningitis), pulmonary(interstitial pneumonitis) or renal (interstitial nephritis)(6).

CASE:

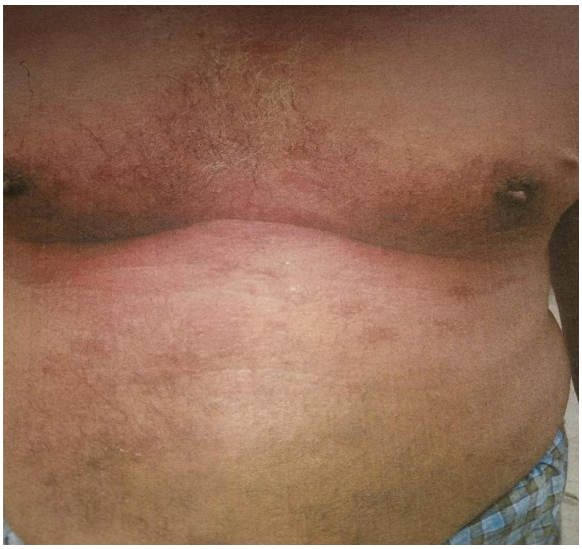
A 59years ole male patient came with chief complaints of rash over neck, and, upper limbs since 1 week. History of itching and burning sensation over lower lips since 1 day. No history of fever, and burning micturition. On examination the patient was afebrile, pulse rate -76/min, Blood pressure-120/70mmhg, Heart/Lungs-NAD, Cutaneous examination show Diffuse, blanchable, Maculopapular rash over the neck, abdomen, upper limbs are observed. Eczematous, Erythematous plaque are present over neck, abdomen. Groin-MP rash+. Laboratory findings are RBS-116%, Blood urea-28mg%, Sr. Creatinine- 0.8mg%, Sr.Bilirubin: Total Serum Bilirubin-0.7mg%, SGPT-26 IU/L, ALP-67 IU/L, Sr.Electrolytes: Na-136mEq/L, K-3.8mEq/L, Cl-110mEq/L. Past medication history: Tab. Cefotaxime 200mg BD, Tab. Covering 75mg BD, Tab. Ramya 150mg BD.

Description of Suspected ADR:

The patient has a history of 2×2 swelling on lateral aspect of left Knee joint and surgery was done. He was on NSAIDS for 1 week then he developed rash over neck, abdomen, itching and burning sensation over lower lips since 1 day.

Management of the ADR:

The suspected drug was stopped. Antihistamines, topical emollients were helpful for skin



reactions. And an alternative. Like opioid analgesic (Tramadol) was administered.

DISCUSSION:

The definitive mechanism of NSAID Hypersensitivity has not been conclusively elucidated as yet, but it is likely that NSAID-INDUCED COX blockade results in excessive prostaglandin E2, production in affected individuals(7). The availability of these medications over the counter , combined with their often first line use in most types of pain and fever, make them one of the most popular classes of medications used worldwide(8). Diagnosis of Hypersensitivity to a NSAID includes understanding of the underlying mechanism and is necessary for prevention and management. A stepwise approach to the diagnosis of Hypersensitivity to NSAIDS is proposed, including clinical history , in vitro testing and provocation test with a culprit or alternative drug depending on the type of the reaction(9). In suspetible individuals, NSAIDS may induce Hypersensitivity reactions varying in timing (immediate/delayed), organ involvement (Skin, airways, or other organs), and severity (from mild Dyspnea, rhinorrhea, exanthema, or urticaria to anaphylaxis and death). Since aspirin (Acetylsalicylic ;ASA), the first synthetic compound with antipyretic analgesic and anti-inflammatory activity, dozens of compounds with similar activity have been developed and commercialized and almost all of them management of the ADR:ere reported to induce Hypersensitivity reactions in susceptible subject(10). Hypersensitivity to acetylsalicylic acid is

characterized by the co-occurrence of symptoms so called aspirin triad, which include bronchial asthma, chronic rhinitis and sinusitis and the nasal mucosa polyps. Hypersensitivity to aspirin is a difficult diagnostic problem, so the increased knowledge on this subject is a very important for the physicians of many specialties(11). A large proportion of the population is exposed to nonsteroidal antiinflammatory drugs worldwide from either medical prescription or self-educated. It is then not surprising that these drugs constitute the second major cause of Hypersensitivity reactions to drugs after beta-lactamic antibiotics. The measures that are recommended for patients with AERD: avoidance of all classic COX-1 inhibitors. Pharmacological treatment with topical and systemic corticosteroids, leukotriene receptor antagonists, and 5-Lipoxygenase inhibitors, antibacterials, and antifungals(12). Mild and moderate AERD responds well to topical and systemic corticosteroids and leukotriene modifiers, however the severe forms of the disease should be desensitized to ASA and treated with this drug on a long term basis. In the future , new drugs that prevent eosinophil activation and chemotaxis or enhance eosinophil apoptosis are likely to be useful(13). Subjects who have chronic urticaria or angioedema exacerbated by ASA and NSAID are believed to be sensitive to inhibition of the COX enzyme. Subjects who have urticaria or angioedema after ingestion of one, but not other, inhibitors belonging to the ASA and NSAID family and who do nit have chronic urticaria are suggested to have drug-specific IgE antibodies as the underlying mechanism(14). The ingestion of NSAIDS can give rise to several allergic and pseudoallergy reactions, which develop within minutes to hours of administration. Allergic reactions are abnormal immunologic reactions to NSAIDS, while pseudoallergy reactions are non-immunological reactions(15).

CONCLUSION

Hypersensitivity to NSAIDS is based on understanding of the complexity of Clinical presentations and diversity of immunological/ non immunological mechanisms of reactions. If the type of NSAID Hypersensitivity is confirmed, recommendations based on the current classification for drug avoidance, use of alternative NSAIDS, and other management modalities, including aspirin desensitization can be implemented.

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