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NIMESULIDE INDUCED CONCURRENT LEUKOCYTOCLASTIC VASCULITIS AND HEPATITIS - CASE REPORT

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ABSTRACT

Nimesulide is a relatively cox-2 selective non-steroidal anti-inflammatory drug [NSAID] which has been already subjected to many controversies in the past. Many adverse drug reactions [ADR] have been attributed to this drug due to which it has already been banned in developed nations of world. Nimesulide is still easily available in developing countries including India. Although association of cutaneous vasculitis and hepatitis with nimesulide is well known separately. But there have been very few case reports in literature describing concurrent development of both hepatitis and cutaneous vasculitis with this drug. With this background we are reporting from tertiary care centre of north India a case of concurrent hepatitis and LCV with use of nimesulide. This case adds to the fact that, like developed nations, India and other third world countries should also ban use of nimesulide in all age groups.

KEYWORDS: Nimesulide, Vasculitis, Drug Reaction.

INTRODUCTION

Leukocytoclastic [LCV] is small vessel vasculitis which represents histopathological form of hypersensitivity vasculitis [HSV].[1] 50% cases of LCV are idiopathic followed by drugs,

malignancies and connective tissue disorders as other causes.[2] Although drugs, that too NSAIDS are the most common etiological factor associated with HSV, very few cases of nimesulide induced vasculitis has been reported in literature.[3] Commonly reported adverse events with nimesulide are peripheral edema, gastritis, stomatitis, necrotizing fascitis, Rey's syndrome, and coagulopathy with raised liver enzymes and acute hepatitis.

Nimesulide is a relatively cox-2 selective non steroidal anti inflammatory drug [NSAID] which has been already subjected to many controversies in the past. Many adverse drug reactions [ADR] has been attributed to this drug due to which it has already been banned in developed nations of world.[4] India has also banned nimesulide use in pediatric population since 2011.[5] Including India this drug is still in use in most of the developing world. Although association of cutaneous vasculitis and hepatitis with nimesulide is well known separately. But there has been very few case reports in literature describing concurrent development of both hepatitis and cutaneous vasculitis with this drug. With this background we are reporting from our tertiary care centre of north India a case of hepatitis and LCV with use of nimesulide. This case report will strongly support the fact that nimesulide should be banned completely in developing nations also.

CASE REPORT

34 year old male presented in medicine OPD with chief complaints of fever for 7 days, generalized body rash for 5 days, yellowish discoloration of eyes and urine for 5 days. For fever he took tablet nimesulide and paracetamol combination [100 mg Nimesulide + 325 mg Paracetamol], one tablet three times per day for 2 days following which he developed generalized body rash and yellowish discoloration of eyes and urine. Skin rash first developed over both upper limbs followed by both lower limbs and spread to all over body within 5 days. He had no history of oral or genital ulcerations, joint pain, cough, dyspnea, headache, pain abdomen, diarrhea, burning micturition. There was no history of intake of any other drug or herbal medicines. There was no history of taking nimesulide in past. There was no history of allergy to any other drug including paracetamol.

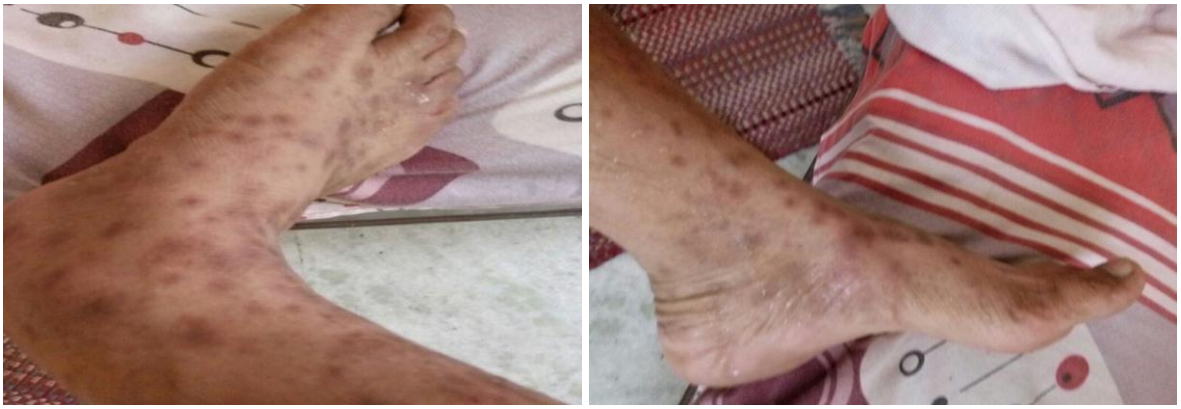

Figure. I and II- Multiple small maculopapular skin lesions.

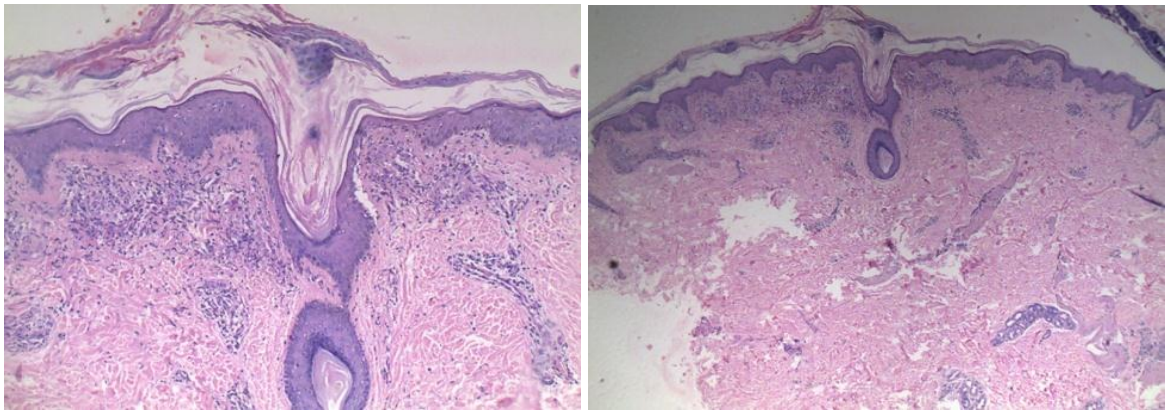

Figure. III and IV- Biopsy shows moderately dense superficial and deep perivascular wedge shape infiltrate of lymphocytes and neutrophils. The epidermis is slightly hyperplastic and the dermoepidermal junction shows focal infiltration by lymphocytes. The mid and lower dermis shows extensive collagen degeneration and pyknosis of inflammatory cells with leucocytoclasia. Several small vessels in mid and lower dermis show abundant fibrin deposits. Overlying epidermis shows extensive necrosis.

On examination our patient was afebrile with pulse rate of 80 per minute, blood pressure of 120/70 mm of Hg, respiratory rate of 16 per minute. He was icteric. He had multiple small maculopapular skin lesions all over body including bilateral upper limbs, bilateral lower limbs, trunk and back [Fig I,II] Examination of oral cavity and genitals was within normal limit. Systemic examination revealed no other abnormality.

On investigation following was recorded- hemoglobin of 11.8 gm/dl, total leucocyte count - 8400[N70, L8, E8], platelet count - 3.5 lac/cmm, total bilirubin-10.46 mg/dl, direct bilirubin-7.86 mg/dl, alkaline phosphatase- 1877 U/L, gamma GT- 701 U/L, SGOT- 367 IU/L, SGPT-300 IU/L, total protein 7.18 gm/dl, serum albumin- 2.97 gm/dl. His serum electrolytes and

renal function tests were within normal limit. Serology for acute hepatitis A and E was negative. Viral markers for HIV, hepatitis B and C were non reactive. Antinuclear antibody and rheumatoid factor were negative. Biopsy from skin lesions of lower limb was done which had features suggestive of leukocytoclastic vasculitis[FIG III,IV].

Development of cholestatic hepatitis and LCV in our patient was clearly preceded by nimesulide intake. Most importantly there was no evidence of any infective or autoimmune cause or any other alleged drug intake. According to Narango's adverse drug reaction algorithm our patient's score was 9 which is suggestive of definite adverse drug reaction and the culprit was clearly nimesulide. We treated him conservatively with systemic corticosteroids [methylpresdnisolone 1gm/day for 3 days followed by oral prednisolone in tapering dose] along with other supportive measures. Following this his skin lesions started disappearing within 5 to 7 days, along with normalization of liver function tests by day 15 after which he was discharged.

DISCUSSION

According to American College of Rheumatology [ACR], classification of drug induced HSV requires presence of three or more of following five criteria- age greater than 16 years, history of taking a drug at onset that may have been a precipitating factor, the presence of palpable purpura, the presence of maculopapular rash, and a biopsy demonstrating granulocytes around an arteriole or venule.[6] Our case satisfied all these five criteria for LCV along with both clinical and biochemical evidence of acute cholestatic hepatitis. All this developed within 2 days of exposure to offending drug. In our case Naranjo score for ADR is nine which strongly supports definite ADR.[7] According to previous case reports, two thirds of patients start liver toxicity 15 to 90 d after 100 mg nimesulide intake.[8] Our patient was taking 300 mg daily, which may be responsible for development of both hepatotoxicity and LCV within 2 to 3 days of intake. Prognosis of drug induced LCV is usually good and management involves withdrawl of the offending drug, glucocorticoids and supportive management. Concomitant development of nimesulide induced hepatotoxicity and LCV is not only rare but also caused marked morbidity and prolonged hospital stay in our patient. Nimesulide is still easily available in developing nations including India. This case adds to the fact that, like many developed nations India and other third world countries should also ban use of nimesulide in all age groups.

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