



## NSAID INDUCED RASH AND FEVER IN SYSTEMIC ONSET JUVENILE IDIOPATHIC ARTHRITIS; A DIAGNOSTIC DILEMMA

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### ABSTRACT

We describe a case of 6 year male child with diagnosis of s-JIA used to develop rash following administration of naproxen. It was associated with febrile episodes for few occasions because of delayed hypersensitivity reaction to naproxen. It continued to manifest for five days, which is extremely uncommon and not reported till date.

**KEYWORDS:** Systemic onset juvenile idiopathic arthritis, Naproxen, rash, fever.

### INTRODUCTION

Systemic onset juvenile idiopathic arthritis (s-JIA) also called still's disease, is an auto inflammatory condition of the childhood. Though, it constitutes around 10% of all forms of juvenile idiopathic arthritis, it is associated with high mortality.<sup>[1]</sup> The distinctive features are fever, evanescent rash, generalised lymphadenopathy and serositis. Naproxen is one of the commonest nonsteroidal anti-inflammatory drug used at the outset for this clinical condition. However, naproxen may complicate with rash accompanying fever on rare occasion.

### CASE

A 6 year male child resident of Madhubani, Bihar, India, presented with history of, off and on fever and swelling of joints for two and half years. Fever was mild to moderate grade, was not associated with chills or rigor. He was afebrile and vitals were stable at admission. General physical examination revealed moderate pallor. On systemic examination, there was swelling of bilateral ankle joints and neck movement was restricted. Investigation revealed, Haemoglobin 8.3gm%, Total leucocyte count, 22,000/mm<sup>3</sup>, Platelets 8 lacs, Erythrocyte sedimentation rate 40, C reactive protein 1.8mg/dl, Antinuclear antibody and Rheumatoid factor was negative, blood culture and urine culture did not reveal any growth. Chest x- ray was within normal limit and mantoux test was negative. Radiological examination of the neck showed ankylosis of cervical vertebrae. Liver function test was within normal limit. On ophthalmological examination, there was no evidence of uveitis. He started on naproxen considering the diagnosis of systemic onset juvenile idiopathic arthritis. After three days of hospitalisation, he developed rash which used to follow the administration of the naproxen.

The rash was pruritic, maculopapular and mainly on the trunk. There was no involvement of palm and soles. He continued to have similar nature of rash for five days and antihistamine was used for the treatment purpose. The rash was also associated with febrile episodes for two occasions. He used to have high grade fever documented up to 102<sup>0</sup> F mostly during morning hours. He was not ill looking during the defervescence period. Naproxen was discontinued, and there was no recurrence of the same event. Subsequently, systemic steroid was started and he improved. During follow up, after 15 days in pediatric rheumatology clinic his condition was normal.

### DISCUSSION

Systemic onset juvenile idiopathic arthritis (s-JIA) is one of the most baffling clinical conditions of the childhood. The rash is one of the unique manifestations of this condition and around 81% of children of s-JIA present with rash.<sup>[2]</sup> It is evanescent in nature and bright salmon pink in color, often with central clearing, tends to be migratory and widespread.<sup>[3, 4]</sup> It is initially noticed on the limbs and trunk and less commonly on the face, neck, palm and sole. The rash is fleeting and it correlates with acute febrile episodes. The rash in s-JIA is most often nonpruritic but in less than 5% case may be pruritic in nature.<sup>[5]</sup>

Although, quotidian fever is one of the ILAR criteria for diagnosis of s-JIA, different pattern of fever may be seen.<sup>[2]</sup> The classic pattern only seen in 37% cases, morning fever in 12%, bidaily fever 15%, intermittent fever 27%, unremitting fever 5%, as well as not reaching to 39<sup>0</sup> C. The index case used to having fever often during morning hours. A typical pattern of fever may be observed following initiation of NSAID in this clinical condition.<sup>[6]</sup> In our case, the child had maculopapular rash

associated with pruritus, on trunk, accompanied by febrile episode for two occasions always within an hour of administration and after 72 hours of initiation of naproxen suggestive of delayed hypersensitivity reaction to naproxen, one would come across rarely.

NSAID groups of drugs are potentially associated with varied groups of skin reactions. It may cause acute reaction or delayed hypersensitivity reaction. The features of delayed hypersensitivity reaction are cutaneous symptoms, systemic symptoms and fever.<sup>[7]</sup> Onset is from 24 hours to days or weeks after initiation of therapy. The most common cutaneous manifestation is maculopapular exanthema, observed commonly with ibuprofen, pyrazolone, flurbiprofen, diclofenac and celecoxib. The other reaction includes, fixed drug eruption, delayed urticaria, less commonly Steven Johnson syndrome and toxic epidermolysis necrosa.

The delayed hypersensitive reactions involve many more distinct mechanisms which related to the discrete functions of drug reactive T-cells.<sup>[8]</sup> Drug-specific T cells orchestrate inflammatory skin reactions through the release of various cytokines and chemokines. The activation of T-cell is explained by the hapten concept which suggests small molecule become antigenic when binds to the high molecular protein. However, why only minority patient develop clinically symptomatic immune reaction is unclear.<sup>[8]</sup>

There are various tests available to confirm the diagnosis of drug reaction. Patch tests may be done with reading at 48, 72 and 96 hours if history indicates delayed reaction. The other methods are lymphocyte transformation test and drug provocation test. However, patch tests and lymphocyte transformation tests are available in few centres. Though, all investigations are required for further confirmation of diagnosis, the cornerstone of diagnosing delayed hypersensitivity reaction to NSAID depends upon the history and timing, and the use of the NSAID belong to the same chemical family should be avoided.

## CONCLUSION

Therefore, to reiterate s-JIA most commonly present with fever, arthritis and rash. NSAID like naproxen, which most often used for this clinical entity in the beginning, can complicate with rash which is a rare phenomenon, and pediatricians should be aware of this perplexity.

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