



Full Length Research Article

CLARITHROMYCIN ASSOCIATED RASH AND ARTHRALGIA IN A CHILD

***Dr. Manab Nandy, Partha Sarkar, Rabindranath Das, Suhrita Paul,
Pragnadyuti Mondal and Nirmal Polle**

95 Bidhan Nagar Road, HUDCO housing Estate, Block: 18, Flat 234, Kolkata -700 054, India

ARTICLE INFO

Article History:

Received 22nd September, 2015
Received in revised form
13th October, 2015
Accepted 18th November, 2015
Published online 30th December, 2015

Key Words:

Arthralgia,
Clarithromycin,
Rash.

ABSTRACT

Clarithromycin is an oral antimicrobial used increasingly in pediatric bacterial infections. We report a case of maculopapular rash and arthralgia following administration of Clarithromycin in for lower respiratory tract infection in a four-year-old female child. On discontinuation of the antibiotic, the child recovered full function of the knee joint within seven days. The causality of the event assessed as per the WHO-UMC system for standardized case causality assessment criteria can be considered as 'probable'. Analyzed by the Naranjo's ADR probability scale, the score was 7, which also makes it a 'probable' event.

Copyright © 2015 Dr. Manab Nandy et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Clarithromycin is a newer macrolide with a broader spectrum of activity against Gram-positive and few Gram-negative bacteria, and is acid stable. It is sensitive against atypical mycobacteria like *Mycobacterium avium* complex and some anaerobes except *Bacteroid fragilis*. Clarithromycin is indicated in the treatment of upper and lower respiratory tract infections, otitis media, whooping cough, atypical pneumonia, acute maxillary sinusitis, acute pharyngitis/tonsillitis, skin and soft tissue infections due to *Streptococcus pyogenes* and some staph aureus. It is of particular use in triple drug regimen to eradicate *H. pylori* infection (http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/050662s048,050698s029,050775s018lbl.pdf). Clarithromycin demonstrates adverse effects similar to erythromycin, which include oral indigestion, reversible hearing loss, pseudomembranous enterocolitis, hepatic dysfunction, rhabdomyolysis, hypersensitivity reactions, etc. (Westphal, 2000; Patel, 2013; Balaratnam, 2015; Pai *et al.*, 2000).

Case Report

A four-year-old girl (body weight 16 kg) presented with fever for three days.

**Corresponding author: Dr. Manab Nandy,
95 Bidhan Nagar Road, HUDCO housing Estate, Block: 18, Flat 234,
Kolkata -700 054, India.*

On examination, she showed fine crepitation over both lower lung fields (anterior and posterior). A plain X-ray of the chest on PA view demonstrated non-homogenous opacities in both lower lung zones. Blood examination report showed a normal hemoglobin and RBC count. Total WBC counts were 12,400/ μ l (N - 79%, L - 14%, E - 4%, M - 3%, B - 0). The diagnosis of lower respiratory tract infection was made and she was prescribed Clarithromycin 15mg/kg/day for 10 days and an ambroxol-salbutamol combination elixir. She was also advised paracetamol 15mg/kg/dose (250 mg thrice daily) for fever. Her fever subsided within the first two days of therapy after which paracetamol was discontinued. On the sixth day of therapy with Clarithromycin, she developed wide spread maculopapular rash (Figure 1). She also complained of pain over the right knee joint and refused to walk. There was no history of fall or injury to the knee. Local pain and tenderness were noted on flexion and extension of the right knee joint.

There was erythema but no appreciable swelling. X-ray showed no bony or joint space abnormality (Figure 2). Other joints like hips, elbows, and wrists were not involved. All medicines that the child was receiving including Clarithromycin were discontinued promptly. Paracetamol 15 mg/kg three times a day was prescribed again to provide relief from pain. The rash, local pain and tenderness resolved within three days. However, there was still some residual discomfort with joint mobility and difficulty in walking. She eventually recovered

full function of the knee joint and started walking without any discomfort on the seventh day following discontinuation of Clarithromycin.



Fig. 1. Maculopapular rash on extensor surface



Fig. 2. X-ray of right knee joint

Causality assessment

The child was suspected to have suffered an episode of rash and arthralgia with Clarithromycin treatment. None of the concomitant medications, e.g., ambroxol, salbutamol, and paracetamol is known to cause arthropathic symptoms or joint damage. An exanthematous febrile illness of viral origin, albeit rarely, is known to usually affect older teens and adults. Known as the *fifth disease* as the maculopapular rash appears on the fifth day of the fever, it is also characterized by swelling and pain of joints (Pai *et al.*, 2009). The clinical presentation in this patient excludes the diagnosis of fifth disease. In this case there was reasonable temporal relationship between the adverse event and drug exposure. Also, pain disappeared and functional joint disability was resolved on dechallenge. Rechallenge did not occur. Further, no alternative cause, including any disease, was likely to have caused the adverse event. As per the WHO and Uppsala Monitoring Center standardized case causality assessment criteria, (<http://who-umc.org/Graphics/24734.pdf>, 2011) this event can be considered as a “probable” reaction to due to Clarithromycin. The Naranjo’s ADR probability score, (Naranjo *et al.*, 1981) 7, also confirmed this causality as “probable”.

DISCUSSION

Arthralgia and arthropathy are known side effects with many antimicrobials including macrolides. Recently Adverse Drug Reactions Advisory Committee (ADRAC), received many reports of arthritis or arthralgia associated with the use of the newer generation macrolide, Clarithromycin.

The majority of the reports concerned pediatric patients under 16 years of age (Ohnishi, 2004). Since Clarithromycin has been an effective and safe drug in pediatric bacterial infections (Gandhi *et al.*, 2013), clinicians are increasingly using this antimicrobial agent. Although post-marketing experience has shown that it can cause rare cases of rash, arthralgia, hepatitis with cholestatic jaundice, pseudo membranous enterocolitis and rhabdomyolysis (Patel *et al.*, 2013). An extensive literature search could not reveal any report of rash and arthropathy associated with use of Clarithromycin in children in India. The presence of joint pain or frank arthritis in children treated with Clarithromycin is of clinical importance, and may be overlooked or misinterpreted. It is important for prescribers to be aware of a possibility of Clarithromycin-induced rash and arthralgia and consider withdrawing this drug if such an adverse event occurs.

REFERENCES

- Dighe, N., Pattan, S., Bhawar, S., Dighe, S., Kale, S., Hole, M., *et al.* 2009. Fifth disease: A review. *J. Pharm. Sci. Res.*, 1:15-25.
- Gandhi, S., Jamie, L., Bailey, D.G. *et al.* 2013. Calcium-Channel Blocker–Clarithromycin Drug Interactions and Acute Kidney Injury. *JAMA*. 310(23):2544-2553.
- Naranjo, C.A., Busto, U., Sellers, E.M., Sandor, P., Ruiz, I., Roberts, E.A., *et al.* 1981. A method for estimating the probability of adverse drug reactions. *Clin. Pharmacol Ther.*, 30:239-45.
- Ohnishi, H., Abe, M., Yokoyama, A. *et al.* 2004. Clarithromycin-induced eosinophilic pneumonia. *Intern. Med.*, 43:231-235.
- Pai, M.P., Graci, D.M., Amsden, G.W. 2000. Macrolide drug interactions: an update. *Ann Pharmacother.* 34(4):495-513.
- Patel, A.M., Shariff, S., Bailey, D.G., *et al.* 2013. Statin toxicity from macrolide antibiotic coprescription: a population-based cohort study. *Ann. Intern. Med.*, 158 (12): 869-876.
- Balaratnam, J, N. Irreversible sensorineural hearing loss due to clarithromycin. <http://pmj.bmj.com/content/81/951/58>. Viewed on 26.11.2015
- The use of the WHO-UMC system for standardized case causality assessment [monograph on the Internet]. Uppsala: The Uppsala Monitoring Centre; 2005. Available from: <http://who-umc.org/Graphics/24734.pdf>. [Last Accessed on 2011 May 6].
- US Food and Drug Administration. BIAXIN Filmtab (clarithromycin tablets, USP) BIAXIN XL Filmtab (clarithromycin extended-release tablets) BIAXIN Granules (clarithromycin for oral suspension, USP). http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/050662s048,050698s029,050775s0181bl.pdf. Accessed November 25, 2015.
- Westphal, J.F. 2000. Macrolide-induced clinically relevant drug interactions with cytochrome P-450A (CYP) 3A4: an update focused on clarithromycin, azithromycin and dirithromycin. *Br. J. Clin. Pharmacol.*, 50(4):285-295.
