Beta-lactam-induced pyrexia

Martha Belete and Colin Bigham

To the Editor:

Many thanks to Walter and Carraretto for their interesting article on drug-induced pyrexia.¹ This led us to consider pyrexia associated with antimicrobials, specifically beta-lactams. “Beta-lactam fever” results in clinical ambiguity due to difficulty differentiating drug reaction from resistant primary or secondary infections, or even a non-infective fever. It has been suggested that antimicrobials, particularly beta lactams, are the culprit of drug-induced fevers in up to a third of cases.² A well-recognized clinical conundrum is the persistent fever during the beta-lactam treatment of infective endocarditis.³

One of the first noted beta lactam “drug reactions” was in the penicillin treatment of syphilis. This was termed the Jarisch–Herxheimer reaction, and had in fact been noted with mercury, arsenic and bismuth before penicillin was discovered.⁴ It is thought to be related to toxin release by the dying spirochetes.³ Similar reactions are seen with Lyme disease, brucellosis and typhoid.

More classical drug fever is noted with a number of therapeutic agents, although antimicrobials (notably beta lactams, minocycline, nitrofurantoin and sulphonamides), anticonvulsants and allopurinol are the commoner agents associated with these conditions. The mechanism behind beta-lactam-induced fevers is poorly understood, although drug hypersensitivity is the most common label applied. This can be an antibody response resulting in antigen–antibody complex formation, or excitation of T cells to the drug (or metabolite) resulting in a cytokine response.⁵

The clinical features can take days to develop, often arising around the cessation of the intended course of antibiotics. Clues that this might be a drug fever would be the development of a rash, an alteration in liver function tests or an eosinophilia. These are all seen in the concerning DRESS syndrome. However, many or all of these clinical signs are usually absent. The pattern of the fever is also not a reliable method of diagnosis. Median time to onset is eight days, with low grade to high swinging fevers being seen.² The fever will often recur early on rechallenge.⁵

Beta-lactam fever is a diagnosis of exclusion, and as such is associated with further investigations and treatments looking for alternative causes. It should, however, be considered under the appropriate clinical circumstances.

References

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Intensive Care Department, Derriford Hospital, Plymouth, UK

Corresponding author:

Martha Belete, Intensive Care Department, Derriford Hospital, Plymouth, PL6 8DH, UK.

Email: marthabelete@nhs.net