Author’s response to reviews

Title: Agranulocytosis and hepatic toxicity associated with ticlopidine therapy: a case report

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Author’s response to reviews: see over
Dear Sirs,

we wish to thank the two reviewers for their useful and precious comments which allowed us to revise and improve our work.

Please find below the detailed answers to the comments suggested.

Reviewer 1

I. “Is the case report authentic?

No; the authors state at the outset in the introduction that this adverse reaction to TICLID, namely hepatitis and blood dyscrasia has already been reported a few authors. Furthermore, the heading of "cholestatic hepatitis" is erroneous for the toxic liver injury generated by Ticlid in this case. The enzyme pattern reflects a mixed hepatocellular (AST 551, ALT 560) and cholestatic (ALP 821, GGT 449) hepatocyte injury without overt cholestasis as bilirubin was normal!”

We changed “cholestatic hepatitis” with a more generic term “hepatic toxicity”, in order to indicate a mixed pattern of cholestasis and hepatocellular injury.

II. “Is the case report ethical?

Yes; although rechallenge with Ticlid would have been solid proof of causality between the drug and bone marrow/liver toxicity, a fatal toxicity could have evolved, and the authors wisely did not subject the patient to rechallenge.”

We agree with the reviewer.

III. “Is there any missing information that you think must be added before publication?

Yes; liver biopsy (obtained via transjugular route would have been safe) would have added much information as to causality between Drug and adverse reaction. Furthermore, in vitro lymphocyte testing may have added some information relating Ticlid to the adverse reactions.”
We didn't perform liver biopsy because of her simultaneous serious hematologic dyscrasia and because of the self-limiting nature of the hepatitis. The liver biopsy, as in other cases of drug-induced hepatotoxicity, can suggest but not establish the diagnosis of ticlopidine-induced hepatic injury, and is directed mainly to exclude other diagnoses.

We didn't perform any lymphocyte test in vitro.

Reviewer 2
No comment.

We look forward to hearing from you.

Best regards

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