Published in final edited form as:

Dermatitis. 2014 ; 25(5): 284–285. doi:10.1097/DER.0000000000000074.

Hepatitis Due to Mycophenolate Mofetil Used to Treat Atopic Dermatitis and Allergic Contact Dermatitis

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To the Editor:

Mycophenolate mofetil (MMF) was started as a corticosteroid-sparing agent for a 48 year old woman with severe atopic dermatitis and allergic contact dermatitis, at a dose of 500 mg three times daily. After a month, her dermatitis improved significantly, but she was noted to develop a biochemical hepatitis, with blood alanine aminotransferase (ALT) rising from 22 IU/L before starting MMF to 418 IU/L and aspartate aminotransferase (AST) from 20 IU/L at baseline to 139 IU/L. We reduced the MMF dose to 500 mg twice daily, but after 2 weeks, both ALT and AST rose to 821 and 203 IU/L, respectively. Throughout this time, she denied abdominal pain, malaise, yellowing of skin, dark urine or light stools. Past medical history was unremarkable and she denied use of alcohol or herbal products; her only other medication was hydroxyzine, which she only took intermittently. CBC and serologic tests for hepatitis A, B, and C were negative, but ANA was positive for a speckled pattern at 1:160. We discontinued MMF and requested a consult from our hepatology clinic, which agreed with our impression of MMF-induced hepatitis. Repeat blood tests one month after stopping MMF revealed normal ALT and AST levels.

While gastrointestinal symptoms such as nausea, vomiting, and diarrhea are commonly associated with MMF treatment, elevated blood hepatic aminotransferases are extremely rare.^{1–4} In our case, there was a strong temporal relationship between starting MMF and development of the biochemical hepatitis. Buttressing the causal relationship were negative serologies for the most common hepatic viral infections, exclusion of other drugs or hepatotoxic agents, and rapid resolution of the hepatitis after stopping MMF.

The very rare reports of MMF-induced elevations in hepatic transaminases include a study by Balal et al. of 79 organ transplant patients treated with MMF, 11 of whom had modest elevations in liver enzymes. The median time of increase in transaminases was 28 days (range of 4 to 70). In their study, liver enzymes returned to normal values 16 days (range of 4–210) following either complete withdrawal of the drug or in some patients a reduction in MMF dose to 50%.² Hantash reported two patients with severe atopic dermatitis on MMF

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Conflicts of Interest For the remaining author none were declared.

who developed elevated liver enzymes in a range similar to our case.³ Toxic hepatitis with AST and ALT up to 750 IU/L occurred in a patient with ANCA-positive vasculitis treated with MMF.⁴ Lastly, another case presented by Loupy et al, highlighted mycophenolate sodium-induced hepatotoxicity in a renal transplant patient. Similarly, elevated liver enzymes returned to normal after withdrawal of mycophenolate.⁵

We conclude that MMF is a relatively safe immunosuppressive drug and a good steroid-sparing agent. However, we must not be lulled into a completely benign perspective. Especially because of its increasing use, including for refractory atopic and allergic contact dermatitis, we must continue to monitor adverse effects and consider the rare possibility of hepatitis due to drug hypersensitivity.

Acknowledgments

Source of Funding: Dr. Cruz has received honoraria from Mary Kay, RCTS, and Galderma. He is currently receiving a grant from the National Institutes of Health and from the Department of Veterans Affairs.

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