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Reply to letter by Efe et al.

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Reply to letter by Efe et al.

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3 We thank Dr Efe and colleagues¹ for their interest in our review article regarding the
4 modern management of autoimmune hepatitis (AIH).² Tumour necrosis factor (TNF)-
5 alpha, clearly plays a major role in promulgating autoimmune processes and, indeed,
6 has been implicated in the pathogenesis of AIH.³ In addition, an association has been
7 identified between genetic polymorphisms in the TNF promoter region and type I
8 AIH which, significantly, was also associated with higher rates of cirrhosis and poorer
9 responses to corticosteroids.^{4,5} However, in respect of the management of AIH, we
10 feel it is important to proceed with caution in respect of agents that block TNF-alpha
11 for the following reasons.
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25 Firstly, the evidence for their use comes from very few, single case reports,^{6,7}
26 with therapy in one report instituted for non AIH indications.⁵ Secondly, these agents
27 appear to be potentially hepatotoxic, which is clearly undesirable in a hepatic disease
28 process such as AIH.⁸ Indeed, AIH has actually been shown to be precipitated by
29 TNF-alpha therapy.⁹ Finally, there remains the concern surrounding the risk of
30 opportunistic infection. Indeed, in the case report cited by Dr Efe and colleagues⁶, the
31 patient suffered 2 infection related complications necessitating withdrawal of therapy.
32 Interestingly this patient was not managed with either tacrolimus or cyclosporine.
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44 Consequently we believe the vast majority of AIH patients non responsive to
45 standard therapy can be successfully managed through better implementation of
46 longer established, non-hepatotoxic immunosuppressive therapies (MMF, tacrolimus,
47 ciclosporin) whose side effect profile is well understood. Whilst it is accepted that,
48 conceptually at least, TNF-alpha therapies may be novel agents in difficult to treat
49 AIH, their use is little studied in this context with particular concerns existing over
50 their safety. For these reasons their utility was not expanded upon in this review and
51 their future use should be limited to clinical trials.
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