Acute encephalitis syndrome following scrub typhus infection

Sir,

We read the article titled "Acute encephalitis syndrome following scrub typhus infection" by Kar *et al.* with great interest.[1] The author reported six cases of acute encephalitis syndrome (AES) secondary to scrub typhus infection. We want to highlight certain issues regarding the management of these patients.

According to the author, once the diagnosis of scrub typhus was established, patients were continued only on doxycycline 100 mg twice daily for a period of 7–10 days. For patients who showed inadequate response to doxycycline alone, azithromycin was "added." We also agree that doxycycline is the first drug of choice for scrub typhus and, for doxycycline-resistant cases, azithromycin is a safe "alternative."[2] But, we could not find any literature in which the combination of doxycycline and azithromycin was used for the treatment of poorly responsive scrub typhus.

The Cochrane review 2010 found no difference between azithromycin and doxycycline for the treatment of scrub typhus.[3] A recent meta-analysis found macrolide antibiotics such as azithromycin to be highly effective against scrub typhus and concluded that they are appropriate "alternatives" in areas where doxycycline-resistant scrub typhus is prevalent.[4] The only study that evaluated combination therapy for scrub typhus used doxycycline and rifampicin.[5] But, unfortunately, this combination therapy was found to be ineffective against O. tsutsugamus*hi* and rifampicin monotherapy was found to be more effective than doxycycline in the resistant strain.

Therefore, we think that addition of azithromycin to doxycycline for patients who showed inadequate response to doxycycline alone was irrational. The author should have replaced doxycycline with azithromycin in those cases.

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