



Happy Thanksgiving!

PIC QUESTION OF THE WEEK: 11/22/10

Q: Are TNF-inhibitors used in the treatment of toxic epidermal necrolysis?

A: Toxic epidermal necrolysis (TEN), also known as Lyell's syndrome, is a severe drug-induced dermatologic reaction first described in the 1950s. It bears considerable resemblance to Stevens-Johnson syndrome (SJS), but involves a greater area of body surface and is associated with a much higher mortality rate. Nearly 80% of the episodes of TEN are related to pharmaceuticals. Extensive skin loss ($\geq 30\%$ body surface area) and mucous membrane (eyes, oral mucosa, and genital tract) involvement characterize TEN. Early signs consist of macular or erythema multiforme-type lesions and fever. Complications include infection, fluid and electrolyte loss, possible pulmonary involvement, and renal failure. The drugs most frequently implicated as causes of TEN are the antimicrobial sulfonamides, anticonvulsants, non-steroidal anti-inflammatory drugs (NSAIDs), penicillins, and allopurinol. A large number of other drugs including some anti-tubercular agents and fluoroquinolones have also been reported to cause TEN. Recognition of the possible association between drug administration and this severe dermatologic reaction is crucial. Treatment consists of appropriate antimicrobials, maintenance of fluid and electrolyte balance, and management of oral and ophthalmic lesions. Although no specific therapy is curative, TEN has been treated (with variable results) with corticosteroids, intravenous immune globulin (IVIG), cyclosporine, and plasmapheresis. Tumor necrosis factor (TNF)- α , various cytokines and oxidative stress play a significant role in the tissue destruction related to TEN. In this cell-mediated, delayed hypersensitivity (Type IV) drug reaction, keratinocytes are injured and depleted due to the apoptotic and necrotic effects of these destructive factors. TNF- α inhibitors have been beneficial in the treatment of a small number of patients with TEN. In one study, six patients were treated with infliximab (3-5 mg/kg as a two hour infusion) and, in a separate report, another patient received etanercept (25 mg sub-q on days four and eight after admission). In both instances, response was noted within a few days of drug administration. There were no adverse reactions in any of the treated individuals. Another case described a woman with TEN and treated with a single dose of infliximab (5 mg/kg). Her response was rapid and additional skin loss was no longer evident at 24 hours. Re-epithelialization occurred approximately five days after institution of therapy. TEN is one of the most severe of dermatologic conditions attributed to drug administration. Few therapies provide consistent response; however, TNF- α inhibitors offer a new approach to the management of a potentially fatal condition.

References

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