



PIC QUESTION OF THE WEEK: 6/18/07

Q: What is the recommended dose of intravenous IgG for treating toxic epidermal necrolysis?

A. Toxic epidermal necrolysis (TEN), also known as Lyell's syndrome, is a severe dermatologic reaction most often associated with drugs such as anticonvulsants, nonsteroidal anti-inflammatory agents, and several antimicrobials including the sulfonamides, penicillins, and fluoroquinolones. It is a rare disorder with an estimated incidence of 0.4 - 1.2 cases per million per year. Mortality rates may be as high as 20% to 40%. The condition usually presents with a myriad of signs and symptoms including fever, dusky macular eruptions, bullae, confluent erythema, and a positive Nikolsky's sign (the detachment of apparently normal epidermis when pressure is applied with a lateral motion). Mucosal membrane involvement and detachment of >30% of the patient's body surface area (BSA) are required for a diagnosis of TEN. In many respects, it is a more severe variant of Stevens-Johnson syndrome (SJS). The widespread detachment of skin is caused by apoptosis of keratinocytes secondary to up-regulation of the Fas ligand (CD95L) present on the membrane of keratinocytes. This ligand binds with Fas (CD95), the "death receptor," also located on the keratinocyte membrane resulting in apoptosis and epidermal cell necrosis. Several treatment options have been explored in patients with TEN including corticosteroids and immunosuppressants such as cyclosporine and cyclophosphamide. Intravenous immunoglobulin (IVIG) has also been proposed as a therapeutic measure for patients with TEN. IVIG is made from purified, pooled human plasma and is comprised mostly of IgG with trace amounts of IgA, IgM, and other markers of the immune system. With IVIG administration, the IgG antibody blocks the binding of Fas with the Fas ligand, thereby halting further keratinocyte apoptosis and permitting re-epidermalization. Dosage appears to be a key element when using IVIG for patients with TEN as only high dose regimens are efficacious. Doses have ranged from 0.2 – 2 g/kg/day for 3-5 days. The minimum *total* dose of IVIG that is considered to be necessary is 2 g/kg. The use of IVIG within 48 hours of diagnosis may also contribute to better patient outcomes. Although IVIG holds some promise for the treatment of TEN and SJS, additional clinical trials are necessary to define its role in the management of these severe cutaneous drug reactions.

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