Attention to TEN

Dear Editor,

The authors of the article "Toxic Epidermal Necrolysis Managed with Immunoglobulin" MJAFI 2008; 64: 272-3 deserves kudos for their success. But my heart felt compliments are reserved for the patient who survived not only the potentially fatal disease but also the frightening therapeutic exercise.

The role of antibiotics in treating a patient of TEN is circumspect when 'multiple blood, urine and fluid from blister cultures were sterile' as reported. Antibiotic therapy is recommended only when signs of sepsis occur; and if commenced prophylactically or empirically, can lead to emergence of resistant strains and increased mortality [1].

The choice of antibiotic also deserves attention. The authors have surmised that cefixime, a third generation cephalosporin and a beta-lactam drug, may have caused TEN. Yet, piperacillin - another beta-lactam drug was exhibited, which has issues of cross-sensitisation with cephalosporin. Though some workers report less cross-reactivity between penicillins and the newer generation cephalosporins [2], it is well known that cross-sensitisation can cause TEN within different classes of beta-lactams like penicillins and cephalosporins [3]. Recently, allergic reaction to piperacillin has been reported in a case of ceftioxone (another third generation cephalosporin) – induced TEN, suggesting an undelineated mechanism of cross sensitivity and hypersensitivity between β -lactams [4].

With the clinical and biochemical data available, the basis of arriving at SCORTEN value of three is not clear. Histopathology, if performed, could have corroborated by demonstration of necrotic epidermal cells and quantification of dermal mononuclear cell infiltrate, the density of which correlates with the severity of TEN and is almost as accurate as SCORTEN in predicting outcome [5].

It was also too enthusiastic to propound IVIg as a panacea for

TEN. While literature abounds with successes with IVIg, there are many well planned studies which do not echo the same view [6].

The most crucial management in a case of TEN is discontinuation of the offending drug and intensive supportive care [6]. Sadly, both of these seem to have somehow missed the focus here.

References

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Toxic Epidermal Necrolysis Managed with Immunoglobulin

Reply

We thank the reader for critical appraisal of our report and kind remarks. The reply to queries raised by him is as follows;

Our patient had presented with fever and was receiving antibiotics at the time of presentation which was the reason of negative cultures. Sepsis is the most debilitating complication in TEN and is one of the leading causes of mortality [1]. Patient had onset of TEN following therapy for fever, cough and sore throat and was continuing antibiotics till consultation in the emergency at our centre. In presence of >80% body surface area involvement with purulent mucositis of the oral and urethra and urinalysis full of pus cells, infection was very much evident which prompted us to continue with changed antibiotics despite culture reports being negative. Lastly, offering antibiotic therapy after obtaining culture positive reports and or signs of septic shock seems purely academic and sometimes dangerous in day to day practice.

IgE mediated hypersensitivities are well known to be cross reactive between cephalosporins and penicillins, however, non IgE mediated hypersensitivities usually are not cross reactive. Patients with a prior immediate hypersensitivity reaction to penicillin should generally not be treated with cephalosporin unless: Penicillin or cephalosporin skin testing, if available, is negative or a graded challenge with the cephalosporin can be given under careful observation by an allergist. A history of a rash or unclear reaction to penicillin does not necessarily preclude administration of cephalosporins [2]. Moreover, there is not a single report of TEN attributable to piperacillin till date on medline search. Only single case report putatively linking cephalosporin hypersensitivity to Meropenem induced TEN has been reported [3]. This does not preclude the use of other beta lactam antibiotics, it just merits caution. Compared to sulfonamides antibiotics, other sulfonamides

like sulfonylurea, thiazides etc do not show cross sensitivity just because of the structural similarities. It may be other metabolites of the drugs that can induce TEN or individuals with metabolic defects or polymorphisms in cytochrome metabolizing enzymes are predisposed to TEN. It will be too hasty to generalize and blame beta lactam structure as the cause of TEN. Our patient did not have immediate hypersensitivity reaction to cephalosporins hence Tazobactam Piperacillin was continued under supervision. Regarding IgE mediated allergic reaction to piperacillin in a case of ceftriaxone induced TEN, the reason is evident in the case report itself, if the reader would have cared to read the paper carefully. This patient had received piperacillin before ceftriaxone administration that could have sensitized him and led to IgE mediated Type I hypersensitivity reaction, subsequently. Moreover TEN is mediated by T cells and macrophages/monocytes, and is unrelated to B cell mediated effects. Lastly, the SCORTEN score of 3 was arrived at based on following criteria, age >40 years, tachycardia (>120) and BSA >80% involvement. Regarding the biopsy confirmation of the diagnosis, the clinical presentation was so characteristic and therefore it was needless to subject already critical patient to an invasive procedure which would have been purely academic without any additional advantage. On the basis of experience in one case, we are not advocating IVIg as panacea for all the cases of TEN, rather since there are not many reports of similar experience from our country we thought it prudent to share our experience with medical fraternity to increase the awareness. Moreover, after the index case, we have treated three more cases of TEN with IVIg and one patient died. This patient had presented with severe neutropenia (absolute neutrophil count <200/ μ l) and respiratory tract infection. We encourage other centers from our country to share their experience with therapy of TEN. As far as the rationale of IVIg is concerned, there is ample evidence both in vitro [4] and clinical to recommend its use in such a life threatening condition [1, 5]. The numbers of studies that question the efficacy of IVIg are small with small patient population as compared to numbers of studies that report benefit with large number of patients.

Since randomized placebo controlled trial is virtually impossible for such a rare and sporadic adverse event, it's up to readers to decide which school of thought to follow. Regarding the discontinuation of the offending agent and intensive supportive therapy, it cannot be over emphasized and we agree with the reader but since the aim of our case report was to highlight the beneficial effect of IVIg in addition to these measures, we discussed more about IVIg. However, we never intend to sideline the significance of these measures.

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Events Calendar

June 27-28, 2009

CME on Stroke

Theme: Emerging Trends in Management of Stroke

Venue: AFMC & Command Hospital (SC), Pune

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