The use of plasmapheresis in a 4-year-old boy with toxic epidermal necrosis

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Abstract

**Background:** Toxic epidermal necrosis (TEN) is a severe and life-threatening syndrome manifesting as extensive necrosis of the epidermis and mucous membranes accompanied by systemic symptoms. The causative factor is exposure to drugs, such as sulphonamides and antiepileptic preparations, non-steroidal anti-inflammatory drugs and paracetamol. The mechanism leading to the development of lesions is unknown and there is no uniform strategy of management.

**Case report:** A 4-year-old boy was admitted with late-stage TEN; he was additionally affected by partial atrophy of the corpus callosum, mental retardation and drug-resistant epilepsy. Three weeks before the first symptoms developed, antiepileptic treatment was widened with lamotrigine, which seems to be the causative factor of TEN. Since general and topical pharmacological therapy failed, plasmapheresis was applied and already after 2 cycles, the progression of lesions was inhibited and circulation was gradually stabilized.

**Conclusions:** The use of plasmapheresis in a child with TEN can result in substantial improvement of the general and local condition. The case presented clearly indicates that standards of management of children with suspected or developed TEN should be urgently instituted.

**Key words:** intensive therapy, children, toxic epidermal necrosis
ment of Paediatrics, where the diagnosis of Stevens-Johnson syndrome (SJS) was suspected. Lamotrigine, considered the most likely causative factor, was withdrawn. The supply of anticonvulsants was continued. The following were instituted: steroid therapy (hydrocortisone in a dose of 18 mg kg\(^{-1}\) day\(^{-1}\)), broad-spectrum antimicrobial treatment (cefotaxime, metronidazole, fluconazole, acyclovir), diuretics (furosemide), anti-ulcer prophylaxis, parenteral nutrition and the infusion of albumins. Mometasone furoate was applied topically. On day 6, therapy with immunoglobulins was initiated (0.5 g kg\(^{-1}\) day\(^{-1}\)). Skin lesions progressed and evolved — scaly blisters developed, and the extent of lesions increased to 70% of the body surface. Additionally, laboratory results demonstrated substantial dyselectrolytaemia, hypalbuminaemia, thrombocytopenia, normalised CRP levels and persistent rejuvenation of the blood picture. Due to the deteriorating condition of the patient, he was transferred to PICU on hospitalization day 8. On admission, his condition was severe — hyporeflexia, oliguria and extensive necrolysis of the epidermis and mucous membrane were observed. The supply of IVIGs (1 g kg\(^{-1}\) was continued for the next 3 days. Considering the deterioration of renal and circulatory functions (at this stage supported with dobutamine), it was decided to pursue plasmapheresis on day 10. Three procedures were performed: on day 10 with albumins and on days 11 and 13 with plasma. After the first two procedures, progression of skin lesions was inhibited and the cardiovascular system stabilized. After the plasma procedures, dobutamine was withdrawn. On day 14, the child ran a fever, and the concentration of CRP increased to 123 mg L\(^{-1}\). Linezolid was started. The urine culture was found positive for *Enterococcus faecium*. Although the dose of furosemide was increased in a continuous infusion (8 mg kg\(^{-1}\) day\(^{-1}\)), oliguria with increasing features of overhydration developed. The decision was made to perform 24-hour haemofiltration. After the completion of renal replacement therapy, diuretic infusion was continued. On day 22, new papuleoerythematous lesions, fever and hepatomegaly were observed; additional tests demonstrated Epstein-Barr virus infection with an increased IgM titre. During the next days, the child's condition improved, and on day 24, the endotracheal tube was removed. The circulation was efficient. Due to improved renal functions, the dose of furosemide was reduced. The skin lesions started to heal (Fig. 1D); topical treatment with corticosteroids and greasing preparations was continued. On day 29, the child was re-transferred to the Department of Paediatrics, where he went through catheter-associated sepsis complicated by renal failure. Finally, on day 48 after the onset of disease, the boy was transferred to the Department of Paediatric Nephrology for further treatment. At this stage, the patient's skin lesions had healed to a considerable degree, and he maintained proper respiratory and circulatory functions, yet, his renal function was deteriorating.

![Figure 1. A–C — Day 10 of disease — epidermal slippage and blisters involving about 70% of body surface; D — day 23 — healing skin lesions](image-url)
DISCUSSION

The available data in the literature are insufficient to establish the exact prevalence and mortality in children with TEN. Reports regarding TEN management and prognosis in this population are also scarce. The TEN studies are generally retrospective and involve small groups of patients. Additionally, the majority of publications do not include basic clinical details; therefore, consensus recommendations for management and treatment of TEN cannot be formulated.

Authors agree only as to the strategy of management in the early stages of TEN. The strategy involves early diagnosis, elimination of a causative factor, immediate institution of treatment and transfer of a patient to a specialist department. All the measures mentioned above have been demonstrated to affect the disease course and reduce mortality rates. Moreover, prevention of remote complications is crucial. To achieve the best treatment outcomes, multidisciplinary cooperation is recommended. The team should include a plastic surgeon, a specialist in anaesthesiology and intensive care, an ophthalmologist and a dermatologist [4]. Protective antibiotic therapy still provokes much controversy. At present, the majority of authors recommend the inclusion of antibiotic therapy only when an infection has been confirmed. Plastic surgeons are of a different opinion, believing that prevention of infections is of fundamental importance, reducing mortality rates and increasing the chances of recovery [15].

Our case clearly indicates that standards of management in children with suspected or developed TEN are urgently needed. We believe that the clinical picture and severe course of treatment in our patient can be attributed to the lack of established guidelines regarding diagnosis and therapeutic management. Analysis of the diagnostic-therapeutic process clearly indicates that in our case, the diagnosis of toxic epidermal necrolysis was established too late, and it seems justifiable to suppose that late diagnosis affected the efficacy of treatment. The deteriorating condition of our patient and the onset of multiple organ failure observed on PICU admission required modifications and intensification of therapy. According to the literature reports, there were only two less commonly used options of systemic treatment, i.e., cyclosporines and plasmapheresis. Because the patient showed clinical features of renal failure after admission to the PICU, the institution of therapy with cyclosporines was contraindicated due to its potential nephrotoxicity. Based on the reports demonstrating effective use of plasmapheresis [14, 17] in SJS, the decision was made to apply this therapy, despite the late stage of disease. After only two days, remarkable improvement of local and general condition was achieved.

Furthermore, it should be stressed that antibiotic therapy was used throughout the PICU stay. Antibiotics were initially applied as a continuation of earlier prophylaxis for infections, despite the lack of recommendations for such management [8, 16]. Our decision resulted from the fact that antibiotics were already administered for several days prior to admission. Once urine and rectum cultures were found to be positive, targeted antibiotic therapy was instituted.

Del Pozzo-Magana and colleagues [2] have demonstrated decreased numbers of complications in the group of children treated systemically, as compared to the group treated supportively. The methods of systemic treatment, however, require further studies to evaluate their efficacy. Considering the rarity of the syndrome, planning of randomised controlled studies is practically impossible. Many authors think that national and international registers of cases are required. Cases should be notified according to uniform criteria to formulate diagnostic and therapeutic guidelines for children. We believe that a centre conducting the registry of cases should also be designated in Poland. Additionally, such a centre should coordinate the transport of patients to specialist centres and provide consultative assistance for departments undertaking treatment of this rare and severe syndrome.

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