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Toxic epidermal necrolysis data from the CELESTE multinational registry. Part I: Epidemiology and general microbiological characteristics

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ABSTRACT

Introduction: Toxic epidermal necrolysis (TEN) is a rare, life-threatening autoimmune disease predominantly manifested in the skin and mucous membranes. Today, infectious complications have the dominant share in mortality of TEN patients. Due to the nature of the therapy and administration of immunosuppressive medications, a wide range of potentially pathogenic microorganisms, which cause infectious complications in different compartments in these patients, is not surprising.

Material and methodology: This is a multicentric study, which included all patients with TEN hospitalized between 2000–2015 in specialized centres in the Czech Republic and Slovakia. The total catchment area was over 12.5 million inhabitants.

The actual implementation of the project was carried out using data obtained from the registry CELESTE (Central European Lyell Syndrome: Therapeutic Evaluation), when specific

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parameters relating to epidemiological indicators and infectious complications in patients with TEN were evaluated in the form of a retrospective analysis.

Results: In total, 39 patients with TEN were included in the study (12 patients died, mortality was 31%), who were hospitalized in the monitored period. The median age of patients in the group was 63 years (the range was 4–83 years, the mean was 51 years), the median of the exfoliated area was 70% TBSA (total body surface area) (range 30–100%, mean 67%). SCORTEN was calculated for 38 patients on the day of admission. Its median in all patients was 3 (range 1–6; mean 3).

Any kind of infectious complication in the study group was recorded in 33 patients in total (85%). In total, 30 patients (77%) were infected with gram-positive cocci, 27 patients (69%) with gram-negative rods, and yeast cells or fibrous sponge were cultivated in 12 patients (31%). A total of 32 patients (82%) were found to have infectious complications in the exfoliated area, 15 patients (39%) had lower respiratory tract infections, 18 patients (46%) urinary tract infections and 15 patients (39%) an infection in the bloodstream.

The most common potentially pathogenic microorganism isolated in our study group was coagulase neg. *Staphylococcus*, which caused infectious complications in 24 patients. *Enterococcus faecalis/faecium* (19 patients), *Pseudomonas aeruginosa* (17 patients), *Staphylococcus aureus* (11 patients) and *Escherichia coli* (11 patients) were other most frequently isolated micro-organisms.

Conclusion: The published data were obtained from the unique registry of TEN patients in Central Europe. In the first part, we have succeeded in defining the basic epidemiological indicators in the group of patients anonymously included in this registry.

The study clearly confirms that infectious complications currently play an essential role in TEN patients, often limiting the chances of survival. The study also shows a high prevalence of these complications in the period after 15 days from the start of hospitalization, when most patients already have completely regenerated skin cover.

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1. Introduction

Toxic epidermal necrolysis (TEN) is a life-threatening autoimmune disease predominantly manifested in the skin and mucous membranes [1]. It is a toxic allergic reaction to the presence of a foreign antigen, most commonly a medication [2]. The pathophysiological basis of this disease is the induction of massive apoptosis in the area of dermo-epidermal junction by caspase and non-caspase mechanisms [3,4].

TEN, together with Stevens-Johnson syndrome (SJS), Drug reaction with eosinophilia and systemic symptoms (DRESS)/Drug induced hypersensitivity syndrome (DIHS) and Acute generalized exanthematous pustulosis (AGEP) belong to the group of SCARs (Severe Cutaneous Adverse Reactions). Diseases from this group are characteristic with their severity, very difficult predictability and frequent association with drug use [5].

It is a very rare disease, incidence of which is around 0.5–1.0 cases per million inhabitants per year according to a number of epidemiological studies [6,7]. Mortality is about 30–60% for TEN [8]. Women are more likely to be affected, but reasons for this have not been determined so far. Incidence also increases with patient age. Elderly patients take more drugs, so the likelihood of developing this syndrome is also increased for this age group. A higher incidence of this disease is also seen in HIV-positive patients or in bone marrow transplant patients [9].

Although more than 60 years have passed since the description of the first case of TEN, we still do not have a reliable therapeutic approach for these patients. The result is the unsatisfactorily high mortality of TEN patients, which has

not changed fundamentally during all this time. However, there have been changes in the causes of death. Previously, patients died from the progression of the underlying disease, nowadays they are dying particularly of complications resulting from the nature of TEN therapy.

Today, infectious complications have the dominant share in mortality of TEN patients [10]. Due to the nature of the therapy and administration of immunosuppressive medications, a wide range of potentially pathogenic microorganisms, which cause infectious complications in different compartments in these patients, is not surprising. Opportunistic pathogens are also used in the etiology of infectious complications.

2. Material and methodology

2.1. Setting

This is a multicentric study, which included all TEN patients hospitalized between 2000–2015 in burn centres and other workplaces in the Czech Republic and Slovakia. The total catchment area was over 12.5 million inhabitants. Clinical presentation and histological confirmation were primarily used for the diagnosis of TEN.

2.2. Data collection

The actual implementation of the project was carried out using data obtained from the CELESTE registry (Central European

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