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STEVENS-JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS (LYELL'S SYNDROME) ARE SEVERE BULLOUS DERMATOSES.

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Annotation : This article focuses on Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN, Lyell's syndrome)—severe, life-threatening acute hypersensitivity reactions affecting the skin and mucous membranes. It explores the concept of a single pathological spectrum, where SJS and TEN represent different degrees of severity of a single process, distinguished by the area of epidermal detachment. The epidemiology, key etiologic factors (primarily drugs), pathophysiological mechanisms (massive keratinocyte apoptosis), and clinical presentation are described in detail. Particular attention is paid to diagnostic stages, including the SCORTEN prognostic scale, and modern treatment principles based on rapid discontinuation of the causative drug, multidisciplinary supportive care, and specific immunotherapy (intravenous immunoglobulin, cyclosporine, or tumor necrosis factor inhibitors). The need for immediate hospitalization in a specialized hospital and the inadmissibility of self-medication are emphasized.

Keywords: Stevens-Johnson syndrome, toxic epidermal necrolysis, Lyell's syndrome, drug reaction, severe cutaneous adverse reactions, SCORTEN, keratinocyte apoptosis, erythema multiforme, epidermal detachment, immunosuppressive therapy.

Introduction

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN, Lyell's syndrome) are acute, life-threatening illnesses that represent severe forms of drug allergy with systemic manifestations. They are characterized by extensive necrosis (death) and sloughing of the epidermis and mucous membranes. Currently, they are considered a single continuum (spectrum) of disease, differing only in the severity of the lesions:

Stevens-Johnson syndrome: Skin involvement < 10% of the body surface area (BSA) with extensive mucosal involvement.

TEN with mucosal lesions (transitional form): Skin lesions 10-30% of the total area.

Toxic epidermal necrolysis (Lyell's syndrome): Skin lesions > 30% BSA.

These conditions require emergency medical care and treatment in a burn or intensive care unit.

Epidemiology and etiology

Incidence: Rare conditions. The incidence of SSc is 1.6 cases per million people per year, TEN is 0.4-1.5 per million.

Mortality: High, especially with TEN: from 10% (SSD) to 30-50% (TEN) depending on the extent of the lesion and complications.

The main cause (in 75-95% of cases): Taking medications. The most commonly associated:

Antibiotics: Sulfonamides, penicillins, cephalosporins, quinolones.

Anticonvulsants: Carbamazepine, phenytoin, lamotrigine.

Allopurinol (gout treatment).

Nonsteroidal anti-inflammatory drugs (NSAIDs), especially oxicams.

Other causes: In rare cases, infections (mycoplasma pneumonia, herpes), malignant neoplasms, and vaccinations can occur. In some cases, the cause remains unknown.

Pathogenesis

The underlying cause is massive apoptosis (programmed cell death) of keratinocytes, the main cells of the epidermis. This occurs due to impaired immune tolerance to the drug or its metabolites. The key factors are:

1. Genetic predisposition: Association with certain HLA alleles (eg, HLA B 1502 in Asians in response to carbamazepine).

2. Immune-mediated response: The drug hapten activates cytotoxic T lymphocytes and natural killer (NK) cells.

3. Release of cytotoxic mediators: Activated cells release perforin/granzyme and, most importantly, bind to the death receptor Fas (CD95) on keratinocytes. This triggers a caspase cascade leading to apoptosis.

4. Role of soluble Fas ligand (sFasL): Its level in serum and vesicular fluid correlates with the severity of the disease.

Clinical picture

Prodromal period (1-3 days): Fever (≥38.5°C), flu-like symptoms (malaise, sore throat), cough, eye pain. Then a more complete picture develops:

Skin lesion: Sudden appearance of painful erythematous or purplish spots, often with target-shaped elements, which quickly coalesce. Flaccid blisters form in their centers, easily rupturing to form large, bright red, oozing erosions. A positive Nikolsky sign is when the epidermis peels off easily with gentle pressure or stretching. The lesion is painful, similar to a second-degree burn.

Mucosal involvement (95-100% of cases): Always severe and painful.

Oral cavity: Stomatitis, cheilitis, painful erosions that interfere with the intake of food and water.

Eyes: Conjunctivitis, ulceration, risk of developing dry eye syndrome, symblepharon, blindness.

Urogenital tract: Urethritis, vulvar/vaginal erosions, phimosis, strictures.

Damage to internal organs: Pneumonitis, myocarditis, hepatitis, nephritis, gastrointestinal tract damage.

Diagnostics

1. Clinical: Based on the anamnesis (taking the drug 1-8 weeks before the start) and the typical clinical picture.

2. Laboratory: Nonspecific. Leukocytosis/leukopenia, increased ESR, CRP, and signs of multiple organ dysfunction are noted.

3. SCORTEN prognostic scale: Used in the first 24 hours of hospitalization to assess severity and predict mortality. It takes into account seven parameters (age >40, heart rate >120, history of cancer, lesion >10% of BSA, urea, bicarbonate, and glucose levels).

4. Skin histology: The gold standard. Reveals complete epidermal necrosis with detachment from the dermis and minimal inflammatory infiltration.

5. Differential diagnosis: Erythema multiforme exudative (EME), staphylococcal scalded skin syndrome (SSSS), generalized pemphigus, acute generalized exanthematous pustulosis (AGEP).

Treatment

Principle 1: Immediate admission to an ICU/burn center and discontinuation of all potentially causative drugs.

A. Supportive care (the basis of treatment, similar to that for burns):

Sterile care: The patient is placed on an anti-decubitus mattress under aseptic conditions.

Correction of losses: Infusion therapy to replenish fluid and electrolyte losses (formulas as for burns), parenteral nutrition.

Skin care: Careful cleaning of erosions, application of non-adhesive atraumatic dressings, use of antiseptics.

Mucosal care: Consult an ophthalmologist (to prevent symblepharon), dentist, and urologist/gynecologist. Rinse your mouth with antiseptics.

B. Specific therapy (aimed at stopping the immune cascade):

Intravenous immunoglobulin (IVIG): High doses (1.2 g/kg for 2.5 days) can block Fas receptors and apoptosis. Most effective when administered early.

Systemic glucocorticoids: Controversial. A short course of pulse therapy is possible in the early stages, but their use is associated with a risk of sepsis.

Cyclosporine: Suppresses T-lymphocyte activity. Proven effective in reducing mortality.

TNF-α inhibitors (Etanercept): Shown high efficacy in controlled studies.

Plasmapheresis: To remove cytotoxic mediators and antibodies.

Antibiotics are prescribed only for proven bacterial infection.

Prognosis and complications

The prognosis depends on the extent of the lesion, the patient's age, and the prompt initiation of therapy. Possible complications:

Acute: Sepsis, multiple organ failure, TEN-associated lung disease (ALI/ARDS).

Remote: Cicatricial changes in the skin, post-traumatic alopecia, pigmentation disorders.

From the eyes: Dry keratoconjunctivitis, symblepharon, entropion, blindness.

From the gastrointestinal tract and genitourinary system: Strictures of the esophagus, urethra, phimosis.

Conclusion

SJS/TEN is a dermatological and therapeutic catastrophe that requires the utmost vigilance from physicians of all specialties and patient awareness of the risks of taking new medications. Treatment success is determined by speed: rapid discontinuation of the offending drug, immediate initiation of intensive supportive care, and, if possible, specific immunomodulatory therapy. Surviving patients require long-term multidisciplinary monitoring to address late sequelae.

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