Steven-Johnson Syndrome in Child

Steven-Johnson Syndrome (SSJ) is a rare, acute skin disorder that affects the skin and mucous membranes with severe damage to barrier function, massive water and electrolyte losses and evolution to exitus. In most cases, a direct link between the occurrence of symptomatology and the administration of a drug may be made.

SJ/NET is triggered by drugs in approximately 60-90% of children [1,2]. More than 100 drugs have been associated with this disease, including anticonvulsants, antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs) being the most common triggers [3,4]. Affected patients should be exposed to the suspected drug within 8 weeks before the rash occurs, and hence the importance of the history to identify the trigger agent.

Experimental part

Methods and materials

One-third of patients will experience nonspecific symptoms (fever, headache, dysphagia, cough) and/or eye pruritus followed by mucosal lesions of the eyes, mouth, genitals and urinary tract in 1 to 3 days and one third of patients will experience lesions of the mucous membranes [5,6].

Clinically there are cutaneous, extracutaneous and mucosal implications.

Classical cutaneous lesions look like red-purple macules that can form large vesicles or bubbles. Traumatized areas may break out and leave deep erosion.

Eye involvement is common and may involve severe conjunctivitis and blepharitis, along with visual disturbances and photophobia. Eyes may appear swollen, erythematous and inflamed. Involvement of the respiratory tract epithelium may occur and may subsequently lead to hypoxemia, hypcapnia and acidosis disorders [7,8].

The healing process is done by reepithelization due to the proliferation and migration of keratinocytes from the epidermis to the injured regions, often not requiring cutaneous grafts, but there is a risk of faulty healing with the appearance of sequelae. The differential diagnosis of Stevens-Johnson and NET syndrome includes multiform erythema, viral exanthema, toxic shock syndrome, exfoliative erythroderma, and thermal burns [9,10].

Steven-Johnson Syndrome is a well-known cutaneous reaction of type IV hypersensitivity, recognized as a disruption of cellular immunity, caused by the release of cytotoxic signals, including granulisin, perforin/granzyme B and Fas/Fas ligand that were activated by cytotoxic T lymphocytes and natural killer cells [11-13].

Anatomopathologically a massive, apoptotic keratinocyte destructive process was observed and the appearance of pathognomonic appearance of scalding skinned areas.

The finding of the causative agent and urgently disrupting contact with it is extremely important for survival, the risk of death being between 5 and 20%, increasing inversely in proportion to age and directly proportional to the duration of administration of the causative agent.

We live in a time of polypragmia, antipyretics, nonsteroidal antiinflammatory drugs and oral antibiotics, for example being administered without wisdom for years in children. Over the past 2-3 years, there has been a limitation on the release of antibiotics from the pharmacy, with the mandatory prescription. Obviously repercussions are extremely variable and important in case of antibiotic abuse, besides Stevens-Johnson Syndrome can occur: microbial alterations, severe diarrhea, colonization with Clostridium difficile, development of antibiotic resistance, severe candidiasis, etc.

The specificity of the child towards the adult is an additional wealth of the water content, which is 65-70%. The main function of the skin, considered to be the largest organ of the body, is the barrier to microbial attacks. The other functions are not to be neglected: plastic, organ and tissue support through tactile receptors participate in the exchanges between the body and environment, intervention in the excretion function by removing toxic compounds, participation in insipid perspiration through mucous membranes, participation in thermoregulation, etc.
Massive skin and mucous destructions can or cannot compensate for the functions described. Additionally, the child’s immature body presents a physiological deficiency of its own immune system, which increases the risk of severe prognosis.

The mechanism by which a pharmaceutical compound determines potentially life-threatening side effects is not very well demonstrated. It is unanimous to accept a theory centered on an immune response to the interaction of host cells with antigens resulting from active drug metabolites, associated with a genetic predisposition consisting in a decrease in the ability of organisms to dispose of toxic compounds.

The higher the half-life of a drug, the higher the risk of Steven-Johnson Syndrome. The pathogen process involves cytokines: TNF-α, IL-6, IL-18, IFN-α and Fas ligand. In keratinocytes, there is expression of the Fas ligand-receptor ligand (CD95) Fas ligand (CD95L). Fas ligand has increased expression in Steven-Johnson syndrome and cytolitic activity, justifying the use in monoclonal antibodies in medical practice [14-16].

Results and discussions

The clinical cases described were at 4 months interval, and affected different ages: infant (5 months) and child (3.4 years). The cases were initiated by oral antibiotic treatment, the antibiotics incriminated being Amoxicillin, respectively, Ampicillin in the young child. In infant, the clinical manifestations occurred on the 3rd day of treatment and at the child on the 6th day of treatment. It is important to note was the lack of prior antibiotherapy in the infant and the presence of polypragmazia in the case of the young child.

Clinically, the prodrome, quite specific to rhinorrhea, dysphagia, conjunctivitis, subfebrilitis, has been found in the 3.4 year old child and has been unnoticed in the baby.

The specific skin manifestations were noted in both age groups and were quite characteristic, with the evolution from the erythematous macula to the bubbles and the extensive tegumental take-off, being unequivocal in the infant, where the extension of the necrosis process was superior to the 3 year old child. Mucosal damage was noted in both children, aggravating oral supportive treatment (Fig. 1-4).

The treatment was performed in an ATI section and was complex: antiseptic solutions, local antibiotics, nonadherent silicone dressings, daily wound dressing with the utmost attention to patient mobilization due to increased skin friability and risk of expanded skin surfaces. The region of the face, eyes, mouth, nose, ears or anogenital was inspected daily and kept in perfect hygienic condition. In addition, parenteral nutrition, hydroelectrolytic and parenteral reequilibration, systemic corticosteroids, anti-inflammatory, high-dose intravenous immunoglobulins (for the therapeutic block of Fas-FasL interaction) were applied for 4 and 3 consecutive days, respectively.

Laboratory revealed anemia (Hb = 10.9 g/dl in the 3 year child and 10.6 g/dl in the infant), leukocytosis (L = 11200 and L = 14300/mmc respectively) with neutrophil left shift and neutrophilia (61 and 64% granulocytes). Transaminases were elevated in both cases, and both children had mild eosinophilia of 6 and 8%, respectively. The rest of the biological parameters were within normal limits.

Both cases had a satisfactory evolution under treatment, complete cure being achieved after about 6 weeks.

Conclusions

Steven-Johnson syndrome, considered a rare pathological entity, is likely to occur more frequently in the child than in the adult because of the higher exposure to various inadequate therapies and due to the higher frequency of various illnesses.

In the cases presented, the tegumental detachment of 45% of the body area in the case of the infant is considered to be a process of toxic epidermal necrolysis (NET, a superior variant of Steven-Johnson syndrome, both being considered different manifestations of the same disease). The direct relationship of skin destruction with antibiotic administration and its immediate discontinuation and the establishment of appropriate therapy increased the chances of survival.

Skin sensitization and fragility make the body susceptible to an identical reaction and in the event of possible subsequent therapies that influence long-term prognosis. Impairment of multiple skin functions requires complex, prolonged therapy under strict conditions of asepsis and antisepsis.

Polipragmazia in recent years has created an iceberg phenomenon with regard to the affections of the Steven-Johnson and NET syndrome.

Recently, it has been found that IL-15 is useful in predicting severity and prognostic monitoring.

If IL-15 is indeed the major cytokine involved in SSJ/NET, new therapeutic modalities promise efficacy in a disease that requires a treatment option. Tofacitinib and ruxolitinib are new JAK-STAT (Janus kinase-Signal Transducer and Activator of Transcription proteins) inhibitors, inhibiting JAK 1 and 2, respectively.

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