Case Report:
SUCCESSFUL TREATMENT OF STEVENS JOHNSON SYNDROME -TOXIC EPIDERMAL NECROLYSIS WITH INTRAVENOUS IMMUNOGLOBULIN

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ABSTRACT

Steven Johnson Syndrome is a serious disease of the skin characterized by triad of erythema exudativum multiforme lesions affecting skin, orifices and eyes. Immunological basis of this disease is hypersensitivity type III and IV. The differential diagnosis are Staphylococcal Scalded Skin Syndrome and Toxic Epidermal Necrolysis. The mainstay of treatment is discontinuation of previously given drugs. Supportive treatment consisting fluid therapy, skincare, symptomatic and antibiotic for existing skin infection. Intravenous Immunoglobulins is used in severe skin involvement and severe complications including eyes. The prognosis is generally good, fatal outcome is usually due to delayed therapy and severe complication.

Keywords: Steven Johnson Syndrome, Toxic Epidermal Necrolysis, IVIG, prognosis

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INTRODUCTION

Stevens-Johnson syndrome (SJS) is a serious disorder of the skin and mucous membranes. It is thought to be an allergic reaction. SJS is an immune-complex–mediated hypersensitivity disorder that may be caused by many drugs, viral infections, and malignancies (Hurwitz 1993; Parillo 2006). Stevens-Johnson syndrome (SJS) may also present as a dermatologic emergency characterized by erythema exudativum multiforme and target lesions; full-thickness epidermal necrosis, although with lesser detachment of the cutaneous surface; and mucous membrane involvement (Parillo 2006, Smelik 2002).

The mainstay treatment of Steven Johnson syndrome-Toxic Epidermal Necrolysis is discontinuation of previously given drugs and supportive treatment. Given the importance of immune mechanisms in inflammatory drug reactions, IVIG has emerged as a potential immunomodulatory therapy for SJS/TEN. Although well-controlled trials have yet to be designed, results from a small number of patients treated thus far seem favorable. Through a series of in vitro experiments, it is evidenced that a drug trigger could activate keratinocyte production of an apoptotic ligand, known as the CD95 (fas) ligand. The binding of this ligand to a CD95 (fas) apoptotic receptor located on the keratinocyte cell surface led to programmed cell death. IVIG demonstrated the capacity to block the apoptotic ligand from binding to this receptor, thus preventing keratinocyte apoptosis and subsequent epidermal detachment (Metry 2003).

In this patient, treatment with corticosteroid has failed to improve the symptoms. Addition of Intra Venous Immunoglobulin has modified the course of the disease, all symptoms cleared within 3 days. These facts have led us to believe that in severe case, inflammation is not solely pathogenesis; apoptosis may play a role at least associated with existing inflammation. It is our plan in the future to conduct research e.g.: 1. factor predisposing which patient necessitate Intra venous Immunoglobulin, 2. whether combination of corticosteroid and Intra Venous Immunoglobulin is better than corticosteroid alone or Intra venous Immunoglobulin alone.

CASE REPORT

I, a seven-year-old girl was brought to Emergency Department Dr Soetomo Hospital, on February 9th 2005 with the assessment of Steven Johnson Syndrome. According to her mother, the main complaint was red spot on her whole body. The red spot began four days before admission. She suffered from fever, cough and rhinitis, and her mother gave her bodrexin as an antipyretic. One day after that, there was rash on her whole body, and her eyes swollen with some discharges. She was taken to a private midwife, and treated with
paracetamol, amoxicillin. The rash became more obvious, her whole body was covered with rash and blister formation, including her face and genital area. She suffered form soreness of the mouth and throat. She could not swell anything. The urination and defecation were normal. She was hospitalized for 3 days at Muhammadiyah Lamongan Hospital, and then referred to Dr Soetomo Hospital.

She was delivered spontaneously at term by a midwife with the birth weight 3100 grams and body length 50 cm. Her basic immunization was completed. The growth and development was normal. Nutritional status of the patient was moderate malnutrition (72% of Ideal body weight, and +1SD according to Z score). She neither had previous drug allergy nor food allergy. The history of allergy in her family was denied. Physical examination revealed a weak, aphatic girl with the body weight 20 kg and body height 115 cm. Blood pressure was 100/60 mmHg, pulse rate was 120 times per minute, respiratory rate was 28 times per minute and body temperature was 38.5°C. No anemia, cyanosis and dyspnea were noted. No nasal flare, no palpable edema, but swollen of both her conjunctiva palpebrae and blister on her eyelids were noted. Her lips were ulcerated, erythematous, swollen covered with grayish-white pseudomembrane and hemorrhagic crust. There were maculo-papular rash with vesiculae covered almost of her whole body. The chest moved symmetrically, retraction and wheezing were not found. Cardiovascular examination revealed normal. The abdomen examination revealed normal bowel sound and impalpable liver and spleen. The extremities were well perfused, edema, and cyanosis were not found.

Based on history and physical examination, working diagnosis on the first admission was Stevens - Johnson syndrome with differential diagnosis of Staphylococcal Scalded Skin Syndrome. All previously given drugs were discontinued, and supportive treatment with 5% Dextrose half saline 1500cc/24hour, cefotaxim 500mg three times daily, dexamethason 1/3 ampule three times daily, eurquinine 250mg three times daily, Borax glycerin and also wound care with normal saline solution. The Ophthalmology Department assessed Stevens-Johnson Syndrome-Toxic Epidermal Necrolysis and advised to give D51/2 S 1500cc/24hour, cefotaxim 500mg three times daily, dexamethason 1/3 ampule three times daily, eurquinine 250mg three times daily, Borax glycerin and also wound care with normal saline solution. The Ophthalmology Department assessed Ocular symblepharon and blepharoconjunctivitis due to Stevens - Johnson syndrome, and advised to treat the patient with chloramphenicol eye ointment three times daily, chloramphenicol eye drop three time’s daily, artificial tears three times a day, regularly cleanses of eye secrets. ENT department assessed pharyngitis due to Stevens - Johnson syndrome and advised oral hygiene care and gargarisma khan three times daily. Based on history, physical examination, laboratory the diagnosis was Stevens-Johnson Syndrome-Toxic Epidermal Necrolysis. The patient was treated with IVFD D5%/1/2Saline 700 cc/24 hours, cefotaxim 500 mg three times a day intravenously, dexamethason 1/3 ampoules three times daily intravenously, Ranitidine 15 mg twice a day intravenously, eurquinine 150 mg three times a day, wound dressing with normal saline solution, bronchial toilet, Borax glycerin for lips, and artificial tears eye drop.

On the 5th day of hospitalization, the patient still suffered from fever and cough. The chest moved symmetrically, retraction and wheezing were not found, coarse rales was positive. The lesions still looked inflamed but no new lesion formation. Vital sign showed blood pressure 100/70 mmHg, pulse rate 122 times per minute, respiratory rate 28 times per minute and body temperature 38.5°C. Laboratory examination revealed hemoglobin 13 g/dl, white blood cells count 6000 /mm³, platelets count 212000 /mm³. Renal function test showed blood urea nitrogen 9.9 mg/dl and serum creatinin 0.2 mg/dl. The liver function test showed AST 27 U/L, ALT 21 U/L, albumin 3.1 mg/dl. Serum electrolyte revealed sodium 132 mmol/L, potassium 4.2 mmol/L, calcium 8.9 mg/dl. ESR revealed 25mm/h. The stool and the urine examination revealed normal. Based on history, physical examination, laboratory examination we assessed that the patient suffered from Stevens Johnson syndrome-toxic epidermal necrolysis and suspicious septicemia. The therapy was IVFD D5%/1/2Saline 700 cc/24 hours, Cefotaxim 500 mg three times a day intravenously, Dexamethason three times daily intravenously, Ranitidine 15 mg twice a day intravenously, Equinine 150 mg three times daily orally. We planned to check blood culture.

On the 12th day of hospitalization the patient still suffered from fever and cough. The lesions still looked inflamed but no new lesion formation. Vital sign
revealed blood pressure 110/70 mmHg, pulse rate 124 times per minute, respiratory rate 30 times per minute, and body temperature 38.5°C. Blood culture showed Pseudomonas aeruginosa. Based on history, physical examination, and laboratory we diagnosed with Stevens Johnson syndrome-toxic epidermal Necrolysis and septicemia. The therapy was IVFD D5%1/2Saline 500 cc/24 hours. The antibiotic was continued with amikacin 250 mg once daily intravenously. The dexamethason intravenously was stopped and changed with tablet three times daily orally, equinine 150 mg three times daily orally. Because skin blistering continued to spread, Immunoglobulin 7.5 g drip/ 6 hours was initiated. Physical medical department advised proper positioning, breathing exercise, and ROM exercise.

On the 13th day of hospitalization, the patient still suffered from fever and cough. There was no new lesion formation. Vital sign revealed blood pressure 100/60 mmHg, pulse rate 120 times per minute, respiration rate 28 times per minute, body temperature 38.6°C.

On the 15th day of hospitalization, the symblepharon improved, the patient could open her eyes. Hemorrhagic crust covered her lips started to detach and the sign of inflammation ceased. The patient was still feverish and cough persisted. The patient’s condition became better with vital sign revealed blood pressure 100/60 mmHg, pulse rate 120 times per minute, respiration rate 32 times per minute, body temperature 39.2°C. The therapy was IVFD D5%1/2Saline 500 cc/24 hours. The antibiotic was continued with amikacin 250mg once daily intravenously. The dexamethason twice a day half tablet orally, equinine 150 mg three times daily orally, Immunoglobulin 7.5 g / 6 hours intravenously.

On the 17th day of hospitalization, patient still suffered from fever and cough. The lesions covered almost her whole body or the lesion around her genital began to recover. The patient’s condition became better with vital sign revealed blood pressure 100/60 mmHg, pulse rate 120 times per minute, respiration rate 28 times per minute, body temperature 38.6°C. The therapy was IVFD D5%1/2Saline 500 cc/24 hours. The antibiotic was continued with amikacin 250mg once daily intravenously. The dexamethason ½ tablet orally. Immunoglobulin 7.5 g/6 hours intravenously, equinine 150 mg three times daily orally.

On the 18th day of hospitalization, the patient had no difficulty in taking oral diet anymore. Patient still suffered from fever and cough. The patient’s condition became better with vital sign revealed blood pressure 100/60 mmHg, pulse rate 120 times per minute, respiration rate 28 times per minute, body temperature 38.8°C. IVFD of D5%1/2Saline 500 cc/24 hours was stopped. The antibiotic was combined cefoperazone 500 mg twice a day with amikacin 250 mg once daily intravenously. The dexamethason and immunoglobulin were stopped. On the 20th day of hospitalization, patient still suffered from fever and cough. Either lesions covered almost her whole body began to recover. The patient’s condition became better with vital sign revealed blood pressure 100/60 mmHg, pulse rate 118 times per minute, respiration rate 26 times per minute, body temperature 37.9°C. The antibiotic was combined cefoperazone 500 mg twice a day with amikacin 250mg once daily intravenously, equinine 150 mg three times daily orally.

On the 22nd day of hospitalization, patient was sub febrile and coughs. The patient’s condition became better with vital sign revealed blood pressure 100/60 mmHg, pulse rate 110 times per minute, respiration rate 26 times per minute, body temperature 37.6°C. The antibiotic was combined Cefoperazone 500 mg twice a day with amikacin 250mg once daily intravenously. We planned to check blood culture, C-reactive protein and chest roentgenogram.

On the 29th day of hospitalization, the patient was in a good condition. Her lesions were getting better. The patient’s condition became better with vital sign revealed blood pressure 100/60 mmHg, pulse rate 100 times per minute, respiration rate 24 times per minute, body temperature 37.0°C. From laboratory examination revealed hemoglobin 12.1 g/dl, white blood cells count 9100 /mm², platelets count sufficient, Blood culture and C-reactive protein were. Chest roentgenogram showed normal. The antibiotic was continued with Cefoperazone 500 mg twice a day and Amikacin 250 mg was stopped.

On the 30th day of hospitalization, the lesions over her face and her body showed hypopigmented macula without sign of inflammation. The vital sign showed blood pressure 100/60 mmHg, pulse rate 88 times per minute, respiratory rate 24 times per minute and body temperature 36.9°C. She discharged in good condition and advised routinely to visit to pediatric, dermatology and ophthalmology outpatient clinic. The lesions were getting better and she discharged without any complication.

**DISCUSSION**

The patient came to the hospital with the main complaint of rash and blister formation on her whole body including her face and genital area. She also suffered from fever and cough since four days before hospitalization, after ingestion of bodrexin, paracetamol,
and amoxicillin. Days afterwards, some vesicles contain liquid developed over her face and chest. Her lips were ulcerated, erythematous, swollen covered with grayish-white pseudo-membrane and hemorrhagic crust. There were maculo-papular rash with vesiculae covered almost of her whole body. Based on the data, the diagnosis of Stevens - Johnson syndrome was established. Diagnosis was based primarily on clinical appearance. This disorder lasted as long as 6 weeks and was characterized by sudden onset, a prodromal period of 1 to 14 days, which could include fever, malaise, headache, cough, coryza, sore throat, vomiting, diarrhea, myalgia and aethralgias. It was known as a serious systemic disorder with the potential for severe morbidity and even death (Hurwitz 1993; Pushker 2000). Prodromal symptoms, such as fever, malaise, myalgias, arthralgias, headache, sore throat, and cough are sometimes reported as a feature, and they usually occur one to 14 days prior to full-blown presentation (Kawasaki 2000; Lobereze, 2000). In this case she suffered from fever, cough and rhinitis since four days before admission. There was rash on her whole body, and her eyes were swollen with discharge. The rash and blister formation emerged, including on her face and genital area. Mucocutaneous lesions developed abruptly. Inflammatory vesiculobullous lesions, often with hemorrhage and necrosis, were typical. Characteristically, an erythematous macula evolved into papules, which enlarged to form small plaques. The central necrosis resulted in a white-gray area surrounded by erythema. If fluid accumulates, blister formation occurs. Mucous membranes are strongly affected, most commonly mouth, lips, bulbar conjunctivae, and less often, anogenital mucosa. The mouth lesions are said to be diagnostic, with redness and swelling of the lips followed by hemorrhagic crusting. Vesiculation is followed in 24-28 hours by formation of a gray pseudo-membrane that, when removed, leaves a raw, bleeding surface (Inambar 2000; Kawasaki 2000., ). Clinical features of our case were symblepharon, swollen at both of her conjunctiva palpebrae and blister on her eyelids. Her lips were ulcerated, erythematous, swollen covered with grayish-white pseudo-membrane and hemorrhagic crust. There were maculo-papular rash with vesiculae covered almost of her whole body.

SJS is an immune-complex–mediated hypersensitivity disorder. Stevens-Johnson syndrome (SJS) also called Erythema multiforme (EM) "major" type. Steven Johnson Syndrome is a complex of symptoms characterized by triad lesions of skin, orifices and eyes. People with Stevens Johnson Syndrome may have purplish or red lesions that may be flat or small and raised. The lesions may turn into fluid-filled blisters. Stevens Johnson syndrome can also cause blisters or bleeding in the mucous membranes of the lips, mouth, eyes, nasal passages, and genitals (Kawasaki 2000). In the United States the incidence rates of SJS were 7.1 cases per million populations per year. A study in Europe reported the incidence of SJS to be 1.1 cases per million populations per year. SJS occurs most often in children and young adults. The male-to-female ratio is 2:1. Most patients are in the second to fourth decade of their lives; however, cases have been reported in children as young as 3 months (Hurwitz 1993; Smelik 2002).

In Stevens-Johnson syndrome, epidermal detachment involves less than 10% of total body skin area, transitional Stevens-Johnson Syndrome-Toxic Epidermal Necrolysis is defined by an epidermal detachment between 10% and 30%; Toxic Epidermal Necrolysis is defined by detachment greater than 30% (Cheriyon 1995; Inambar 2000). In this case, the skin lesions contained erythematous macula, vesicle, and some blisters formation which firstly affected her face and upper trunk, and suddenly spread almost her whole body. Three mucosal membrane surfaces involved, including ocular, oral, and external genital, showed erythematous maculae, edema, painful erosion and hemorrhagic crusts. Oral involvement was severe enough to result in difficulty in eating and drinking. Epidermal detachment more than 10% was mainly in her upper trunk.

Many potential triggers have been implicated as possible causes of Stevens - Johnson syndrome. Medications appear to be the most common cause of Stevens - Johnson syndrome and have been implicated in as many as 60% of cases studied. The most common cause of SJS-TEN are Sulfonamide, beta-lactam, imidazol and NSAID’s, second most common cause are quinolon, anticonvulsant aromatic and haloperidol. Many other causes of SJS are: infection (herpes simplex virus, and Mycoplasma pneumoniae), food (chocolate), and vaccine. A subsequent report suggested that penicillin was the drug most associated with Stevens-Johnson syndrome. Penicillin had taken by 50%, short acting sulfonamides by 29%, and long acting sulfonamides by 11% (Inambar 2000; Tripathi 2000). In this case, the etiology was strongly suggested drug exposure, which may caused by Bodrexin, paracetamol, amoxicillin. One day after that, there was rash on her whole body, and her eyes was swollen with discharge. These medications were discontinued a day after administration due to the skin eruption and mucosal involvement. The average time from first drug administration to the onset of reaction is 1-45 days (mean 2 weeks).

No specific laboratory tests are indicated. In severe cases, laboratory testing should be guided by clinical
Complications, such as pulmonary involvement, may occur as an extension from the oropharynx and tracheobronchial tree or may be due to pneumonia associated with viral infection or secondary infection. If the central nervous system is affected, there may be drowsiness, confusion, delirium, convulsions, and coma. Encephalitis has also been described. Renal involvement may result in hematuria, nephritis, acute tubular necrosis leading to renal failure. The patient with genitourinary involvement may complain of dysuria, or an inability to void. Gut lesions may present as red spots in the intestine, mucosal hemorrhage and diarrhea. Epithelial loss results in vulnerability to bacterial and fungal infections, lead to septicemia and severe fluid (Lobreze 2000, Gruchalla 2006). In this case pulmonary involvement was not found, since the chest examination and thorax roentgenogram showed normal. The liver and renal involvement was absent; with the normal result of both liver and renal function tests. Central nervous system was not affected, because the patient was alert, without altered consciousness, but the patient suffered from septicemia and treated with antibiotics based on sensitivity test.

The differential diagnoses of Stevens-Johnson syndrome are including Toxic Epidermal Necrolysis and Staphylococcal Scalded Skin Syndrome. When the diagnosis is indeterminate, this disease can be differentiated from histopathological examination. In staphylococcal disorder, the disruption showed cleavage in the epidermis, while in Toxic Epidermal Necrolysis, separation is seen in the upper dermis below the basement membrane similar to the cleavage seen in Stevens-Johnson syndrome (Huwitz 1993). Toxic epidermal Necrolysis is established by the presence of bullous on more than 30% of the total body surface area. In this case the histopathological examination was not done because her parent refused and clinical appearance and history were enough to establish the diagnosis of Stevens-Johnson Syndrome-Toxic Epidermal Necrolysis (Freiman 2005; Tripathi 2000).

Management

Management of this disease consists of early management, symptomatic management, and specific management. Most cases of SJS are drug induced. Treatment of SJS is primarily discontinuation of previously given drugs, supportive and symptomatic. Some have advocated immunomodulating agents such as cyclophosphamid, cyclosporine, and immunoglobulin, but none of those should be considered standard at this time. Mortality is usually related with severe complication or delayed treatment (Hurwitz, 1993, Ghislain 2003).

Early management

The management of patients must be prompt; early diagnosis with early recognition and withdrawal of all potential causative drugs is essential to a favorable outcome. We observe that death rate is lower when causative drugs with short elimination half-lives were withdrawn no later than the day when blisters or erosions first occurred. No difference is seen for drugs with long half-lives. Second, intravenous fluid replacement must be initiated using macromolecules or saline solutions. Third, the patient must be transferred to an intensive care unit or a burn center. Prompt referral reduces risk of infection, mortality rate and length of hospitalization (Ghislain 2003; Huwitz 1993; Scheuerman 2006; Tripathi 2000).

Symptomatic treatment

The main types of symptomatic treatment are the same as for burns, and the experience of burn units is helpful for the treatment of TEN. Environmental temperature control, careful and aseptic handling, sterile field creation, avoidance of any adhesive material, maintenance of venous peripheral access distant from affected areas (no central line when possible), initiation of oral nutrition by nasogastric tube, anticoagulation, prevention of stress ulcer, and medication administration for pain and anxiety control are all essential. However, TEN and burned patients are not identical, i.e.: burns happen in a very short time period (a few seconds) and do not spread thereafter; the TEN-SJS progress occurs during several days, including after hospital admittance. Therefore the fluid requirements of TEN patients are habitually two-thirds to three-fourths of those of patients with burns covering the same area. Since the lesions are restricted to the epidermis and usually spare the hair follicles, the re-growth of epidermis is quick in patients with SJS-TEN. This
supports a different approach of topical treatment. Ophthalmology consultation is mandatory for those with ocular involvement (Lobreze 2000; Scheuerman 2006; Smelik 2002). In this case the patient was given IVFD Dextrose 5%1/2 Saline and blepharo-conjunctivitis due to SJS was diagnosed and treated with chloramphenicol eye ointment and cleans the eye’s secretion.

Systemic management

Pulmonary care includes aerosols, bronchial aspiration and physical therapy. If the trachea and bronchi are involved, intubations and mechanical ventilation are nearly always necessary. Early and continuous enteral nutrition decreases the risk of stress ulcer, reduces bacterial translocation and enterogenic infection, and allows earlier discontinuation of venous lines. Phosphorus levels must be measured and corrected, if necessary. Most authors do not use prophylactic antibiotics. Bacterial sampling of the skin lesions is performed the first day and every 48 hours. Indications for antibiotic treatment include an increased number of bacteria cultured from the skin with selection of a single strain. Antacids reduce the incidence of gastric bleeding. Emotional and psychiatric support must not be forgotten. Euquinine was given to decrease pain and fever (Huwitz 2000; Tripathi 2000). In this case antibiotics use was based on positive blood culture. Ranitidine was added to reduce gastric bleeding.

Specific treatment

Corticosteroid infiltrations are among the most accepted, most frequently administered, and most successful treatments used by rheumatologists, orthopedic surgeons, and primary care physicians. They stand in sharp contrast to systemic (oral or parenteral) corticosteroids, which are rightfully used with caution because of their myriad cumulative side effects. Corticosteroid use is highly debated. Many studies showed beneficial effects of using steroid agents in adults and in children. One study suggested that mild to moderate disease can be managed with corticosteroid agents on an out patient basis. Renfro et al suggested that the immunosuppressive and anti-inflammatory properties of corticosteroids could decrease the severity of the disease if they were administered early in the course of illness, thereby shortening convalescence time and preventing development of serious complications. Atherton reported two cases where administration of intravenous methylprednisolone arrests progression of acute attacks and recurrence of the disease with no sequels. Tapering the dosage is over a period of 1 to 3 weeks during the healing phase of the illness (Huwitz 2000).

Corticosteroids reduce inflammatory response by maintaining vascular integrity, promoting synthesis of lipocortins and decreasing the expression of leukocytes adhesion molecules. Corticosteroid also has immunomodulatory effect by down-regulating cytokine gene expression. Dexamethasone is a synthetic member of the glucocorticoid class of hormones. It acts as an anti-inflammatory and immunosuppressant. Unbound dexamethasone crosses cell membranes and binds with high affinity to specific cytoplasmic receptors. This results in a modification of transcription and, hence, protein synthesis in order to achieve inhibition of leukocyte infiltration at the site of inflammation, interference in the function of mediators of inflammatory response, suppression of humoral immune responses, and reduction in edema or scar tissue. The anti-inflammatory actions of corticosteroids are thought to involve phospholipase A2 inhibitory proteins, lipocortins, which control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes. The use of this drug has to avoid more than 1.5 mg daily, because serious side effects are more frequently encountered with higher doses. Others series claimed also excellent results but the diagnosis of SJS-TEN was debatable for most of the cases. On the other hand some investigators consider systemic corticosteroids provoke prolonged wound healing, increased risk of infection, and masking of early sign of sepsis, severe gastrointestinal bleeding and increase mortality (Ghislain 2003). If there is no response to this form of therapy within 3-5 days, the corticosteroids should be abruptly discontinued in an effort to avoid the risk of associated complications and morbidity. A study administering early and short course of corticosteroids favorably influences the course of erythema multiforme major in children (Ghislain 2003; Inambar 2000). These drugs are a mainstay in some units, but other investigators consider systemic corticosteroids to provoke prolonged wound healing, increased risk of infection, masking of early signs of sepsis, severe gastrointestinal bleeding and increased mortality. This review of literatures shows only patients series and no randomized clinical trials. In two retrospective studies, no difference in mortality rates or infectious complications was noted in patients who received steroids before or after referral. By contrast, other studies claimed that corticosteroid use was detrimental. Thirty patients with SJS or TEN were included in an uncontrolled prospective study. The first 15 patients received corticosteroids and the mortality rate was 66%. Therefore, the next 15 patients were treated without corticoids and the mortality rate was 33%. Both groups were similar in other described aspects. However, 11 of the 15 patients "without corticosteroids" had received corticosteroids prior to referral. Thus no conclusion may be made about exclusive early administration of
corticosteroids. In a retrospective study, a multivariate analysis of prognostic factors showed that corticosteroid therapy was an independent factor for increased mortality. Other series provided the same conclusion. Other studies suggest no benefits with steroid use and that others suggest that systemic steroid use might be associated with delayed recovery and clinically significant side effects (Smalik 2002). Moreover, many TEN cases have occurred during treatment with high doses of corticosteroids for preexistent disease.

Immunomodulating agents

Cyclophosphamide in a retrospective comparative study with cyclosporine was safe and was associated with a more rapid re-epithelialization rate and a lower mortality rate than treatment with cyclophosphamide and corticosteroids. Cyclosporine has also received attention as a useful drug for treatment of TEN; however, further investigations are needed to evaluate the real value of cyclosporine (Parillo 2006, Cheriyon 1995).

Intravenous immunoglobulin (IVIG)

IVIG is an immunomodulating agent that has multiple activities. It was based on in vitro demonstration that intravenous immunoglobulin can inhibit Fas-Fas ligand mediated apoptosis. IVIG contains cytokines, antibodies of unclear clinical significance, perhaps neutralizing; interestingly, antibodies against granulocyte macrophage colony-stimulating factor, interferon, interleukin 1, and interleukin 6 in immune globulin have biologic activity in vivo. IVIG contains natural antibodies, accounting for some of its effects. Intravenous Immunoglobulin has a number immunomodulatory effects, including blockade of reticuloendothelial Fc receptors, inhibition of complement-mediated damage, modulation of cytokines, and neutralization of circulating auto antibodies or antigens. Precisely which of these effects are primarily operative during intravenous immunoglobulin therapy for SJS is unclear. IVIG is used to treat a variety of autoimmune, infectious, and idiopathic diseases. IVIG has both agonistic and blocking antibodies against Fas (CD95), the receptor for the Fas ligand, which triggers apoptotic signals into cells. This is what underlies its efficacy for treating toxic epidermal necrolysis (Gunwitch 1998; Scheinfeld 2006). The immunomodulatory effects of IVIG are complex, involving modulation of the expression and function of reticuloendothelial Fc receptors; interference with the activation of complement and cytokine networks; provision of anti-idiotype antibodies; and effects on the activation, differentiation, and effector functions of T and B cells. Therefore, in addition to its ability to block keratinocyte-mediated apoptosis, IVIG may have additional effects that contribute to its overall therapeutic benefit in patients with severe cutaneous drug reactions. For example, patients with severe cutaneous drug reactions are prone to infectious complications that IVIG may limit through its anti-infectious properties. Furthermore, IVIG restores protein and fluid, which may help to limit the extent of fluid loss that occurs through the denuded skin. Ten consecutive patients with TEN of moderate severity were treated with different doses of IVIG (0.5 to 1 g/kg of body weight per day for four consecutive days); all survived. Duration of therapy of 3 days does not seem to be as effective as 3 or 4 consecutive day. However, no randomized clinical trial is published on this, and other authors have not obtained the same results. Rational evaluation of the benefit of this treatment cannot currently be done. Duration of fever was shortened in patients treated with IVIG, although statistical significance was marginal. The hospital stay was slightly shortened in patients treated with IVIG; however, statistical significance was not reached (Metry 2003; Scheinfeld 2006). In this case IVIG was administered for four times at day first, second, fourth, and six. The result of this management showed good and reduced length of hospital stay.

SJS-TEN is an acute, self-limited disease, with high morbidity, that is potentially life-threatening. Mortality rates are 5% with SJS, 30-35% with TEN and 10-15% with transitional forms. Epidermal detachment may be extensive, to the entire skin surface. As in severe burns, fluid losses are massive, producing electrolyte imbalance. Super-infection, thermoregulation impairment, excessive energy expenditure, alteration of immunologic functions and hematological abnormalities are usual systemic complications. Mucous membrane involvement (oropharynx, eyes, genitalia and anus) require attentive nursing care. The tracheobronchial epithelium and less often gastrointestinal epithelium can be involved and cause high morbidity. Age, percentage of denuded skin, neutropenia, serum urea nitrogen level, and visceral involvement are prognostic factors. After healing, altered pigmentation and corneal lesions are the main long-term complications. Morbidity and mortality increase if the culprit drug is withdrawn late (Inambar 2000; Scheuerman 2006). In this case prognosis showed good and the patient discharged with good condition.

CONCLUSION

The diagnosis of Stevens - Johnson syndrome and Toxic Epidermal Necrolysis in a seven-year-old girl was established on the basis of clinical signs confirmed by the history of drug ingestion (bodrexin), clinical
appearance after drug ingestion and laboratory finding. The management of this disease includes supportive and symptomatic therapy. Intravenous immunoglobulin was administered due to large area of blister in the skin. In this case skin lesions improved in thirteen days and the disease recovered uneventfully. The prognosis of this patient was good, based on her clinical response to therapy and absent of complication.

REFERENCES


