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Steven Johnson syndrome in patients with complications of elevated Alt and Ast levels: A Case Report

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ABSTRACT

Stevens-Johnson syndrome (SSJ) is an extremely rare, acute, and potentially life-threatening event; is an immune complex-mediated hypersensitivity reaction that is often associated with drug use. The aim of this study is to describe the Steven Johnson Syndrome experienced by patients with complications of increased ALT and AST levels. The patient is a 58-year-old male with complaints of red spots all over the body and fever before being admitted to the hospital. The skin rash increases in redness all over the body, there are loose and then burst bullae on the neck, chest, and back, it feels sore and burning, there are dry scars on the lips, nose, and ears, accompanied by complaints of red eyes, painful swallowing, and occasional coughing. The patient took dexamethasone, paracetamol, and allopurinol before symptoms appeared. The most common complications in SJS cases are respiratory problems including bronchopneumonia and moderate increases in transaminase enzyme levels that do not cause jaundice. Stopping previous drug consumption and prompt and appropriate treatment can reduce mortality rates.

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1. INTRODUCTION

Stevens Johnson's condition (SSJ) is a very exciting, intense, and possibly dangerous, safe, and often drug-related touch response (Pratama et al., 2023). Accompanied by acute mucocutaneous reactions characterized by necrolysis and extensive detachment of the epidermal layer. The rate of spread of SJS in Asian countries is higher than in Western countries (Brahmanti et al., 2018). The incidence rate of SJS is estimated at 2-3% per million population annually in America and European countries, while in Indonesia SJS cases occur around 12 cases each year (Djuanda A., 2013). SJS can occur at any stage in life, but is more normal in adulthood [4]. The mortality rate of SSJ in Europe reaches 34% in one year. It can also be according to the area of exfoliation, if the area of damage is <10% of the body surface area, the mortality rate is about 1-5% [5]. However, if the damaged area is>30% of the body surface area, the mortality rate is about 25-35% or can even reach 50% (Basak AK., 2013; Fitriany J., 2019). The etiology of SJS and NET is still not known with certainty. In the case of SJS, half of the cases relate to drug openness and more than 100 types of drugs have been considered potential causes [4]. Stevens-Johnson syndrome (SSJ) is a type IV extremely sensitive disease with an immune, complex intervention that is a serious articulation of erythema multiforme [6]. Hypersensitivity reactions in early lesions are caused by the reaction of *cell-mediated cytotoxic* to keratinocytes and fas ligands activated by cytotoxic T lymphocytes (CTLs) and *Natural Killer* (NK) cells causing massive apoptosis (Zhang et al., 2020). In addition, genetic factors of the HLA system are reported to also play a role (Wilson et al., 2022). Side effects of SSJ-NET appear within about two months after the start of treatment openness. In the intense stage before the onset of skin sores, prodromal or vague side effects may appear, then develop into a mucocutaneous appearance (Mockenhaupt M., 2019).

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (NET) these two diseases are similar in clinical side effects, histopathology, risk factors, causes, and pathogenesis so that both are currently divided into indistinguishable cycles, separated only due to the presentation of the surface

area of the body undergoing epidermal apoptosis. In SSJ, there *is epidermolysis* of < 10% of the body surface area (LPB), while in NET it is 30%. The involvement of 10%-30% LPB is referred to as SSJ-NET overlap (Pratama et al., 2023). Complications in SSJ cases were found 25% were respiratory problems such as increased breathing rate, and coughing, and 16% had *bronchopneumonia*. In addition, based on Zhang's research (2020), it was found that 40 out of 298 patients treated with SSJ experienced *drug-induced liver injury* (DILI) (Zhang et al., 2020; Mockenhaupt M., 2019). According to [8] SJ-NET is a rare disease, overall the number of SJ is 1-6 cases/million population/year, and the frequency of NET is 0.4-1.2 cases/million population/year. While according to [9] the number of SSJ cases is more common in men than women with a ratio of 3: 1.

2. METHOD

This study used the case report method with a descriptive quantitative observational design. Here are the case reports on this study: A 58-year-old male patient came to the emergency room of Mulya Hospital with complaints of reddish patches of pain throughout the body for 1 day and a fever felt since 2 days before entering the hospital. Skin rashes rise reddish all over the body, there are loose bullae then break on the neck, chest, and back feels sore and burning, there are dry scars on the lips, nose, and ears, accompanied by complaints of red eyes, canker sores, swallowing pain, and occasional coughing. Previously, patients went to the clinic with complaints of sore throat, red eyes, and sore feet and then took dexamethasone, paracetamol, and allopurinol drugs.

History of previous drug allergic reactions (-), HT (-), DM (-), and Asthma (-). History of allergies to drugs (-), food (-), temperature (-). No patient's family has the same complaints as the patient. Physical examination: obtained awareness of GCS E4V5M6 compos mentis, blood pressure 130/80mmHg, pulse 98x/m, regularly strong, respiratory frequency 20x/m, regular, temperature 38.5c, oxygen saturation 98% with free air, weight 75kg, height 165cm. Dermatological Status: Multiple blackish-red crusts, and irregular boundaries of the labial, nasal, and auricular regions. Squama smooth on buccal. Maculopapulmonary lesions, blackish erythema plaque throughout the body, sagging wall bullae that have broken into epidermal eruption (epidermal *necrolysis*) multiple erythema base in the colli region, thorax, and buttocks.

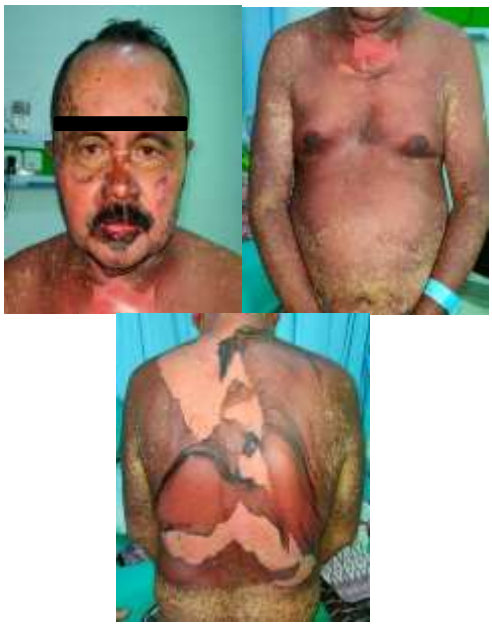

Figure 1. There are hemorrhagic crust lesions, plaque erythema, loose bullae that have ruptured Clinical photo after 15 days of treatment:

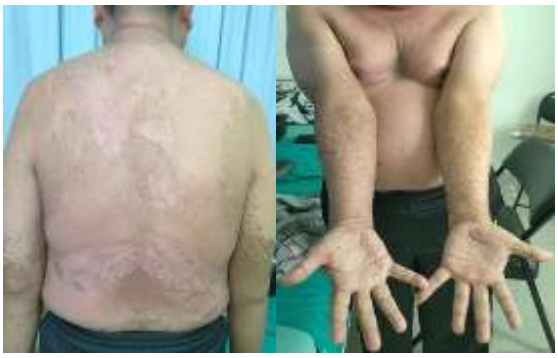

Figure 2. Epidermal, maculopapular and plaque erythematous eruption lesions appear

Laboratory tests: Hemoglobin (Hb): 12.1g/dL, leukocytes (WBC): 7.08 x103/uL, hematocrit (Ht): 36.2%, platelets (Plt): 152 x103/uL, erythrocytes: 3.83 x106/uL, stem neutrophils/segments: 0/65%, lymphocytes: 29%, eosinophils: 2%, monocytes: 4%, basophils: 0%, SGOT: 140 U/L, SGPT: 508 U/L, cream: 36 mg/dL, creatinine: 1.19 mg/dL, current blood glucose (GDS): 169 mg/dL. Thorax X-ray: bronchopneumonia.

Therapy given during treatment is to stop all previous drug consumption, maintain room temperature, and oral nutrition in the form of a 6x150cc liquid diet per day. Intravenous therapy in the form of 0.9% Nacl liquid 500cc / 8 hours, methylprednisolone 125mg / 12 hours, stronger neo-mitophagy C (SNMC) 20ml / 24 hours for 2 days. Oral therapy cetirizine 2x10mg. Topical therapy compresses Nacl 0.9% on the crust of the lips followed by gentian violet 1% 3 times a day 3 drops and on dry skin followed by giving mupirocin 2% cream 2 times a day. From the eye part, therapeutic ointment chloramphenicol 1% is applied 3 times a day, and secretions are cleaned with 0.9% Nacl liquid [10].

3. RESULTS AND DISCUSSION

SJS is interesting but dangerous and often caused by drugs (Pratama et al., 2023). SSJ occurs in all age groups and the risk increases in adulthood. In the case of a 58-year-old male. The exact cause of SSJ is unknown. Medications are the biggest cause of SSJ (50%-80% of cases). Research on the risk of SSJ due to drug use reports that the highest-risk drug classes are allopurinol, lamotrigine, cotrimoxazole, carbamazepine, NSAIDs, phenobarbital, phenytoin, and valproic acid. Medium-risk groups such as cephalosporine, macrolide, quinolone, and tetracycline. Low-risk groups of beta-blockers, ACE inhibitors, CCBs, thiazides, antidiabetic sulfonylureas, and NSAIDs (ibuprofen) (Mockenhaupt M., 2019).

Clinical manifestations appear within 8 weeks (usually 4-28 days) after the first exposure to the drug (Zhang et al., 2020). Non-specific symptoms acquired fever, headache, rhinitis, cough, sore throat, or malaise are found 1-3 days before skin manifestations appear (Mockenhaupt M., 2019). Non-specific symptoms in the above cases such as fever appear 2 days followed by skin lesions on 4 after taking allopurinol [11].

Skin lesions are symmetrically distributed on the face, trunk, and upper and lower limbs. Skin lesions can be macular erythema, papules, and bullae which then break down into confluent necrotic lesions giving rise to widespread and diffuse erythema. Nikolsky's sign is positive and found around the lesion. Abnormalities in the mucous membrane can be found in the oral cavity, lips, eyes, nose, and genitals, sometimes affecting the mucous lining of the trachea and bronchi. As many as 80% of cases experience conjunctivitis with symptoms of pain, watery eyes, redness, and secret. Lesions in the oral cavity and lips can be in the form of hemorrhagic erosion, and crusting (Mockenhaupt M., 2019). Lesions in some cases are found in erosion, hemorrhagic crusts on the lips, nose, and ears, macular lesions to blackish erythema plaque throughout the body, and epidermal eruptions in the Colli region, trunk, and extremities. Accompanied by itchy red eyes and secretions. SSJ and NET have similar symptoms and lesions so they are distinguished based on the area of epidermolysis of the body surface, cases obtained with epidermolysis area >10 it becomes a case of SSJ with the possibility of overlapping NET [12].

The most common complication of SSJ is the respiratory and digestive systems. The above case experienced complaints of cough with a picture of bronchopneumonia in the rotgen thorax. The most frequent complications of the digestive system are decreased liver function to DILLI with an increase of >5x normal values in alanine aminotransferase (ALT / SGPT), aspartate aminotransferase (AST / SGOT), >2x normal values of bilirubin, >2x normal values of alkaline phosphate, and other liver markers. In SSJ/NET the elevated levels of transaminase enzymes are moderate and do not cause jaundice. To determine the drug that causes DILLI, an evaluation is carried out with the Causality Assessment Method (RUCAM) and the Algorithm for Drug Causality for Epidermal Necrolysis (ALDEN) score (Zhang., 2020; LiverTox., 2012).

The results of research conducted by Zhang (2020) show that there are three classes of drugs that can cause an increase in transaminase enzymes including xanthine oxidase inhibitors (allopurinol), anti-convulsants (carbamazepine, phenytoin, phenobarbital), and traditional medicines. The cause of acquired DILI in SSJ / NET patients is a drug reaction due to hypersensitivity reactions or immune-mediated adverse drug reactions. Leukocyte antigens also play an important role in cases of SSJ and elevated levels of liver enzymes among them HLA B*58:01 (LiverTox., 2012). Cases obtained consume allopurinol so that complications may occur increased SGOT levels: 140 U / L and SGPT: 508 U/L [13].

With prompt and precise treatment, SSJ's guess is excellent. In writing, mortality rates range from 5-15% [14]. In the skin and genitals of Cipto Mangunkusumo Hospital, the mortality rate is around 3.5%. Death usually occurs as a secondary result of infection (Wilson et al., 2022). The prognosis can be predicted using the SCORTEN score. In this case, the SCORTEN score is 2 which is a mortality rate of 12%.

Prognostic factors	Points
Age > 40 years	1
Tachycardia > 120 bpm	1
Neoplasia	1
Initial detachment > 10%	1
Serum urea > 10 mmol/L	1
Serum bicarbonate < 20mmol/L	1
Blood glucose > 14 mmol/L	1
SCORTEN	**Mortality (%)**
0-1	3
2	12
3	35
4	58
≥ 5	90

Figure 3. SHORTEN: Score Calculation System for Determining Prognosis

The main therapeutic principle is self-recognition and discontinuation of suspected drugs and the provision of supportive therapy (Perdoski., 2017).

Non medicated

1. Fluid therapy should be given as early as possible and the volume measured.
2. Room temperature should be 28c - 30c
3. Nutritional therapy.
4. Systemic antibiotics are given if there is an indication of infection.
5. Eye care.

Medication.

1. Topical
   - Oily moisturizers such as 50% petroleum gel with 50% paraffin liquid.
   - Eye involvement should be treated with an ophthalmologist.
2. Systemic
   - Systemic corticosteroids: intravenous dexamethasone with equivalent doses of prednisone SSJ : 1-4 mg/kgbb/day

SSJ-NET : 3-4 mg/kgbb/day
NET : 4-6 mg/kgbb/day

- Analgesics may be given. If mild pain can be given paracetamol Other options:
- High-dose intravenous immunoglobulin (IVIg) can be given as soon as the patient is diagnosed with NET at a dose of 1g/kg/day for 3 days.
- Cyclosporine may be given.
- The combination of IVIg with systemic corticosteroids can shorten healing time but does not decrease mortality

4. CONCLUSION

Stevens-Johnson syndrome (SSJ) is a very rare, acute, and potentially life-threatening occurrence, which is a complex immune-mediated hypersensitivity reaction often associated with drugs. The most common complications in cases of SSJ are breathing problems to bronchopneumonia and elevated levels of transaminase enzymes moderate and do not cause icteric/jaundice. With prompt and appropriate treatment, the prognosis of SSJ is very good, thus reducing mortality.

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