A CASE REPORT ON PHENYTOIN INDUCED STEVENS-JOHNSON SYNDROME

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ABSTRACT

Adverse drug reactions are one of the leading causes of increase in mortality rate among hospitalized patients. These may vary from mild to severe reactions. Five to eight percent of hospitalized patients develop serious adverse drug reaction. However, these may often go undetected and unreported. Stevens-Johnson syndrome (SJS) is a life-threatening severe adverse mucocutaneous drug reaction that involves the skin and mucous membrane causing excessive necrosis and epidermis detachment. It is generally rare but considered as the medical emergency as it is fatal that is potentially life-threatening. SJS is a drug induced reaction, where the drugs that are believed to be inducing the SJS could be said as: as antiepileptic drugs, antipsychotic drugs, sulfonamide –antibiotics, cephalosporins, aminopenicillins, quinolones. Phenytoin, an antiepileptic drug commonly prescribed medication for seizures was found to be causative of SJS. We here report a case of phenytoin-induced SJS in a 56 years old female patient who developed SJS on the administration of phenytoin that prescribed for her post-operation craniotomy intracranial hemorrhage, because of immediate and early recognition of the SJS and starting the treatment, then the patient was stabilized and got recovered. Thus SJS that increases mortality rate should be considered in patients with SJS which is a result of phenytoin and keep monitoring the patient’s phenytoin serum levels which is crucial to assure the safety and efficacy of phenytoin therapy.

KEYWORDS: Phenytoin, stevens Johnson syndrome, toxic epidermal necrolysis, adverse drug reaction, serum level monitoring, medical emergency.
INTRODUCTION

Stevens Johnson syndrome (SJS)
Stevens Johnson syndrome (SJS) is a life threatening severe adverse mucocutaneous drug reaction that involve the skin and mucous membrane causing excessive necrosis and epidermis detachment. It is generally rare but considered as medical emergency as it is fatal that is potentially life threatening. SJS is a drug induced reaction.

Signs and symptoms
SJS signs and symptoms includes

- Fever
- Widespread skin pain.
- Skin rash that spreads (red or purple in color).
- Blisters on skin and the mucous membranes of eyes, mouth, nose and genitals.
- Peeling/shedding of skin within days.

Many days before the developing of rash on body, particular patient may experience:

- Fever
- Sore throat
- Fatigue
- Cough
- Burning eyes

Causes
Causatives of the SJS may not be exactly identified initially, but the condition basically gets triggered by medication or infection.

Reaction to a medication may start while the particular patient using it or up to two weeks after the drug intake was stopped.

- Medication causes
  - Allopurinol (Anti-gout drug)
  - Anticonvulsants
  - Antipsychotics
  - NSAID’S(Non steroidal anti inflammatory drugs)
  - Certain antibiotics.
• Infectious causes
  o herpes virus
  o pneumonia
  o HIV
  o Hepatitis A

SJS-TEN
SJS found to be in similarity with the Toxic epidermal necrolysis (TEN), in its clinical histopathologic findings, risk factors and drug causality.

These two, SJS-TEN considered severe variants of an identical process that differ in the extent of the final body surface exposed or involved.

SJS and TEN patients frequently experience burning pain of their skin at the starting. Ulcers and lesions begin later on their mucous membranes, in mouth and lips also in genital and anal regions. Those which occur in mouth are extremely painful and reduce the patient’s ability and acceptance to eat and drink.

![Figure: Image showing the patient Stevens Johnson Syndrome](image1.png)

Figure: Image showing the patient Stevens Johnson Syndrome

![Figure: Image showing the patient with Toxic Epidermal Necrolysis](image2.png)

Figure: Image showing the patient with Toxic Epidermal Necrolysis

PHENYTOIN
Phenytoin is an antiepileptic medication that commonly prescribed for seizures. It works by slowing down impulses in the brain that causes seizures. It is widely used, available in oral and parenteral forms. It is also among the drugs causing highest rate of cutaneous adverse drug reactions. Phenytoin is considered as the first line therapy for some types of seizures despite its inherited risk of dose-related toxicity attributed to its zero-order pharmacokinetics. Thus phenytoin serum level monitoring is important to assure the safety and efficacy of its therapy.

**Prophylactic control of seizures during neurosurgery**
Phenytoin adult dose: 100-200mg I.V at intervals of about 4 hours during perioperative and postoperative periods.

**Case Report**
A 56 years old female patient came with the complaints of oral ulcers with pain, rash over the body.

History of administration of EPTOIN-100mg, prescribed for her post operation Craniotomy intracranial hemorrhage (ICH).

**Surgery History**
Patient came with complaints of reeling sensation and vomiting and admitted in he hospital, where she was diagnosed with a clot in brain considering the CT-SCAN reports, but no signs of seizures were reported or seen in the patient.

**CT SCAN BRAIN-REPORT**
- Craniotomy defect in the left temporal bone
- Subacute hemorrhage in the left temporoparietal lobe with surrounding edema causing mass effect on the adjacent sulci.

The Patient was then suggested – surgery.

**Treatment Advised on discharge – post operation craniotomy ICH**
Patient was prescribed with EPTOIN-100mg twice daily, to prevent the occurrence of seizures in patient along with other medications after 1 week of surgery and discharged and was asked review after 10 days.
During the course of the treatment, patient had not developed any signs of seizures, or rashes on body and got back to hospital for review. Where she was there then asked to continue the usage of **EPTOIN (phenytoin)-100mg thrice daily.**

where she suddenly presented with onset of painful mouth ulcers and rashes (fluid filled ) on the surface of body within 2 days of the administration of drug. But it was misunderstood and considered as chicken pox by the patient family members and no measures was taken to consult a doctor, meanwhile the administration of the phenytoin 100mg thrice daily was continued as usual by the patient.

On the 3rd day following the onset, patient’s mouth ulcers and rashes got severe and were not able to take food and water, then she was brought to our hospital.

On evaluation of the patient condition and medical history, Case seen by Neurologist and Neurosurgeon, advised relevant investigations.

She was conscious and following commands.

**Her Vitals on admission**

BP – 130/80 mmHg, P.R - 94/min
CVS- S1+S2+, R.S - B/LAE +
RR- 20/min, temperature –normal
Dermatology opinion was sought.

**Provisional diagnosis**

SJS was made.

*Figure: Image showing ulcers on lips and rashes near eye.*
INVESTIGATIONS

pathology

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<thead>
<tr>
<th>Observations</th>
<th>Observed value</th>
<th>Normal value</th>
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</thead>
<tbody>
<tr>
<td>AEC</td>
<td>882 cells/cumm</td>
<td>40-440</td>
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</tbody>
</table>

(AEC – Absolute eosinophil count)

Serum electrolytes

<table>
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<tr>
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<th>Observed value</th>
<th>Normal value</th>
</tr>
</thead>
<tbody>
<tr>
<td>K+</td>
<td>4.5 mmol/L</td>
<td>3.40-4.50</td>
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<tr>
<td>Na+</td>
<td>150 mmol/L</td>
<td>134-146</td>
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</tbody>
</table>

Complete blood picture

<table>
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<tr>
<th>Observations</th>
<th>Observed value</th>
<th>Normal value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>10.6 g/dl</td>
<td>11.5-16.5</td>
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<tr>
<td>RBC</td>
<td>3.6 millions/cumm</td>
<td>3.8-6</td>
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<tr>
<td>WBC</td>
<td>10190 cells/cumm</td>
<td>4000-11000</td>
</tr>
<tr>
<td>DLC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutrophils</td>
<td>70%</td>
<td>40-70</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>18%</td>
<td>20-45</td>
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<tr>
<td>Eosinophils</td>
<td>09%</td>
<td>1-6</td>
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<tr>
<td>Monocytes</td>
<td>04%</td>
<td>1-4</td>
</tr>
<tr>
<td>MCH</td>
<td>29.4 millions/cumm</td>
<td>28-32</td>
</tr>
<tr>
<td>MCHC</td>
<td>33.3%</td>
<td>3.3-36</td>
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<tr>
<td>MCV</td>
<td>88.3 cubic microns</td>
<td>80-94</td>
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<tr>
<td>ESR</td>
<td>60 mm/hr</td>
<td>1-20</td>
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<tr>
<td>Platelets</td>
<td>3.99 lacks/cumm</td>
<td>1.5-4.5</td>
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<tr>
<td>PCV</td>
<td>31.8%</td>
<td>42-52</td>
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</table>

Figure: Image showing rashes over hands.
Diagnosis
Phenytoin induced Stevens-Johnson syndrome

Therapy
Phenytoin administration was stopped and patient treated with steroids, antibiotics, antacids, antiepileptics (levetiracetam-500mg), antiallergics, Moxiflox eye drops, neuroprotective drugs, multivitamins and other supportive care given. On dermatologist opinion, added kenacort (for oral ulcers), emoderm cream (over body), Dermocal lotion, Momate cream, Candid mouth paint given.

As patient condition got stabilized and showed improvement in clinical and biochemical parameters during the treatment, and no other severe conditions, patient was advised to discharge with follow-up medication.

Conditions at time of discharge
Patient conscious, following commands (+), pupils: NSRL, afebrile, CVS: S1+S2+, Bp: 130/80 mmHg, Lungs: B/L AE, PR: 80/min, RR: 22/min,

Discharge therapy
antibiotics, antacids, antiepileptics (levetiracetam-500mg), antiallergics, Moxiflox eye drops, neuroprotective drugs, multivitamins and other supportive care given. On dermatologist opinion, added kenacort (for oral ulcers), emoderm cream (over body), Dermocal lotion, Momate cream, Candid mouth paint.

Patients was asked to review after 10 days, to check for any reactions occurs and stop them.

DISCUSSION
SJS is one of the enervating adverse drug reactions that were noticed. It is generally rare but considered as medical emergency as it is fatal that is potentially life threatening. SJS is a drug induced reaction. SJS found to be in similarity with the Toxic epidermal necorlysis (TEN), in its clinical histopathologic findings, risk factors and drug causality. These two, SJS-TEN considered severe variants of an identical process that differ in the extent of the final body surface exposed or involved. In this case, Patient was prescribed with EPTOIN-100mg twice daily, to prevent the occurrence of seizures. During the course of the treatment, patient had
not developed any signs of seizures, or rashes on body and got back to hospital for review. Where she was there then asked to continue the usage of EPTOIN (phenytoin)-100mg thrice daily. She suddenly presented with onset of painful mouth ulcers and rashes (fluid filled) on the surface of body, it was misunderstood and considered as chicken pox by the patient family members and no measures were taken to consult a doctor, mean while the administration of the phenytoin 100mg thrice daily was continued as usual by the patient.

On the 3rd day following the onset, patient’s mouth ulcers and rashes got severe and was not able to take food and water, then she was brought to our hospital. On clear examination of the patient and the treatment she undergoing and cross checking the drugs, we understood and believed that the Usage of phenytoin 100mg trice daily, was the reason behind the occurrence of the rashes and it was diagnosed as SJS by dermatologist and under the supervision of the neurologist and neurosurgeons the phenytoin was withdrawn and the treatment was started. from the third day of her treatment and withdrawal of phenytoin, patient condition got stabilized and showed improvement in clinical and biochemical parameters during the treatment, and no other severe conditions, patient was advised to discharge.

CONCLUSION
SJS, which is a drug induced adverse reaction, usually caused by antiepileptics, antipsychotics, antibiotics, being seen and reported from many parts of the world. Phenytoin, the first line drug for the treatment of a variety of seizures, and is given as Prophylactic control of seizures during neurosurgery. It is also among the drugs causing highest rate of cutaneous adverse reactions. Hypersensitivity to phenytoin is not unexpected. Serum level monitoring is important to assure the safety and efficacy of its therapy further early recognition and treating with corticosteroids might improve the outcome and the patient counseling about the drugs that he prescribed with and about the adverse events, allows patient to recognize the symptoms immediately and rush to the doctor for the treatment, this minimizes the severity and mortality rates.

Disclosure
No conflicts of interest in this work.
REFERENCES


