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RESEARCH ARTICLE

STEVENS-JOHNSON SYNDROME (SJS) AND TOXIC EPIDERMAL NECROLYSIS (TEN) ASSOCIATED WITH ANTI-TUBERCULAR DRUGS: A CASE REPORT

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Abstract

Introduction: Steven-Johnson syndrome (SJS) is an acute reaction that typically involves the skin and mucous membranes which are characterized by damage and flaking of the skin, accompanied by pain, and can cause death. Toxic epidermal necrolysis (TEN) is a rare, life-threatening skin reaction usually caused by medication,which is characterized by widespread erythema, necrosis, and bullous detachment of the epidermis and mucous membranes, resulting in exfoliation and possible sepsis and/or death.SJS and TEN are some of the rare side-effects from Drugs used in Anti-Tubercular Treatment.we report here a caseofSJS and TEN, due to side effects of 1st line Anti-Tubercular Drugs.

Case description: A 50-year-old man presented at emergency room with chief complaints ofmultiple blisters on the trunk and erosions on the mouth and genitals for the past 4 days.He also had shortness of breath for the past 10 days, fever and cough for the past 3 days. He was apparently normal 11days back.Symptoms started appearing after initiation of Anti-Tubercular Treatment.

Conclusion: As soon as the diagnosis of Anti-Tubercular Drugs induced SJS and TEN was confirmed, Patient was taken offfrom ATD and administeredwith intravenous systemic steroids as immunosuppressive therapy, antifungals, and antibiotics. After 10 days of treatment, lesions healed and started desquamating.

Introduction:-

Stevens Johnson Syndrome is a serious mucocutaneous illness with systemic symptoms and signs with significant mortality, characterized by the presence of flat atypical target lesions or purpuric macules with blisters that are distributed mainly on the trunk or widespread and the epidermal detachment being less than ten percent of body surface area (BSA). Toxic Epidermal Necrolysis is a life-threatening illness characterized by high fever and confluent erythema followed by necrolysis. The epidermal detachment is more than 30 per cent of BSA. In the overlap category (SJS/TEN) the area of epidermal detachment, which is often much less than the area of erythema, is between 10 and 30% of the BSA.[1] The incidence of SJS has been reported to be between 2.9 and 6.1 cases per 1 million persons per year, while the incidence of TEN is much lower, at <1 case per 1 million persons per year.[2] SJS was first discovered in 1922 by a paediatrician after diagnosing a child with a disorder caused by a drug reaction.

SJS usually starts within 8 days after drug administration (range 4-30 days).[3]

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Tuberculosis (TB) is a chronic granulomatous infection principally caused by **Mycobacterium TB** and less frequently by ingestion of **Mycobacterium bovis** infected unpasteurized cow's milk or by other atypical mycobacteria. [4] The frequency of TB in underdeveloped nations is snowballing, and this is believed to coexist with poor hygiene environments and increased occurrence of acquired immunodeficiency syndrome.[5]

Depending on the organ system involved, tuberculosis is classified clinically as pulmonary and extra-pulmonary. Pulmonary tuberculosis remains the most common form of the disease. Extra-pulmonary involvement in tuberculosis is uncommon, accounting for approximately 10% to 15% of all the patients. TB mainly affects the lungs but also affects intestine, meninges, bones, joints, lymph glands, skin and other tissues of the body.[6]

Case Description

A 50-year-old man was admitted to our hospital with complaints of multiple blisters on the trunk and erosions on the mouth and genitals for the past 4 days. He also had shortness of breath for the past 10 days, fever and cough for the past 3 days. He was diagnosed with TB lymphadenitis and started anti-tuberculosis treatment 15 days ago consisting of isoniazid, rifampicin, pyrazinamide, and ethambutol. He was also diagnosed with HIV positive 10 days before but not on antiretroviral therapy. He had no history of diabetes mellitus, hypertension, and coronary artery disease. He was neither alcoholic nor a smoker. On the day of admission, maculopapular rashes with pruritis were observed in more than 90% body surface area including the skin of the posterior trunk, upper limbs, lower limbs, neck, face, genitals (Figure). Erosions appeared in the oral mucosa and conjunctiva. The blood pressure was 130/80 mmHg, pulse 84 beats/minute, respiratory rate 22 breaths per minute and temperature 98.4° F. Complete blood count shows leukocytes 6.4 with 74% of neutrophils and 20% lymphocytes. Initially, the patient was diagnosed as Steven Johnson Syndrome as less than 30 percent body surface was involved and gradually progressed to Steven Johnson

Syndrome and combination and Toxic Epidermal Necrolysis combination, later progressed to Toxic Epidermal Necrolysis as body surface involved more than 90 percent. After admission, all the anti-TB drugs were stopped, intravenous dexamethasone and pheniramine malate, fusidic acid cream were given to control the skin reaction. Antibiotics and antifungal medications were given. chlorhexidine mouth wash and benzocaine mouth gel were given to treat lesion in the oral mucosa. Ciprofloxacin eye drops and methylcellulose eye drops were also given. After 7 days of continuous treatment, erosions & skin lesions were getting healed and by the 10th day of treatment, healed lesions were desquamating.

Figure 1:- Maculo-papular rashes and erosions on face, trunk and genitals on the day of admission.

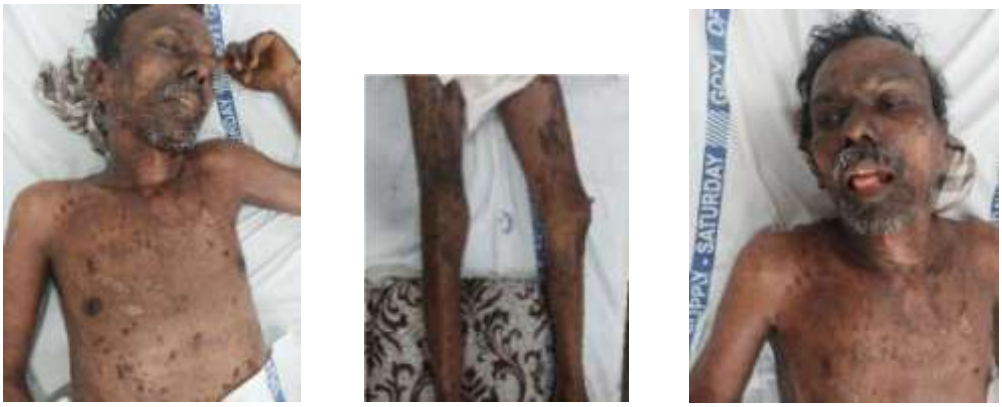

Figure 2:- Healed lesions on the day of discharge.

Discussion:-

Non-immediate hypersensitivity reactions (Hypersensitivity type-4) are much more common than the immediate reaction to anti-TB drugs. These include maculopapular eruption, lichenoid drug eruptions, haematological reactions, hepatitis, SJS and TEN.[6] The duration between drug intake and first onset of symptom in SJS/TEN ranges between a few hours and 45 days.[7] As this case, our patient starts the symptoms around 11 days after drug consumption.

In this case we have observed maculopapular rashes involving more than 30 percent of body surface area, diagnosed as SJS initially and later on progressed to combination of SJS and TEN and finally Toxic Epidermal Necrolysis as more than 90 percent body surface involved. Initially lesions started 10 days after initiation of anti-tubercular drugs. We have suspected anti-tubercular drugs would be a prime reason for lesions and started discontinuing one by one and stopped all the drugs within a week and treated with antibiotics and antifungals both local and systemically. Oral mucosa was taken care.

Patient have no lesions before the start of anti-tuberculosis drugs. Lesions were started immediately after initiation of anti-tuberculosis drugs and slowly disappeared with discontinuation of medication. This clearly indicates the prime reason for the lesions was anti-tubercular drugs.

According to causality assessment of World Health Organisation, the relation between mucocutaneous lesions and anti-tubercular drugs can be categorised under CERTAIN.

Rechallenging not done.

WHO-UMC causality assessment categories: [8]

Causality term	Assessment criteria (all points should be reasonably complied)
Certain	• Event or laboratory test abnormality, with plausible time relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically) • Event definitive pharmacologically or phenomenologically (ie, an objective and specific medical disorder or a recognized pharmacologic phenomenon) • Rechallenge satisfactory, if necessary
Probable/likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable • Rechallenge not required

Possible	Event or laboratory test abnormality, with reasonable time relationship to drug intake Could also be explained by disease or other drugs Information on drug withdrawal may be lacking or unclear
Unlikely	Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) Disease or other drugs provide plausible explanation
Conditional/unclassified	Event or laboratory test abnormality More data for proper assessment needed, or Additional data under examination
Unassessable/unclassifiable	Report suggesting an adverse reaction Cannot be judged because information is insufficient or contradictory Data cannot be supplemented or verified

Conclusion:-

Severe hypersensitive reactions are more common with anti-tubercular drugs especially with Rifampicin and Isoniazid which can be life threatening sometimes. Before prescribing these drugs, patients should be well counselled about the adverse events and drug interactions which can be associated with these drugs.

Conflict Of Interest:

The author declares there is no conflict of interest regarding the publication of current report.

Ethical Aspect:

Theinformed consentfrom patient obtainedfor the publication of their respective photographs in journal article.

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