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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/10685

DOI URL: <http://dx.doi.org/10.21474/IJAR01/10685>



RESEARCH ARTICLE

A CASE REPORT ON AMOXICILLIN INDUCED TOXIC EPIDERMAL NECROLYSIS

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Manuscript Info

Manuscript History

Received: 17 January 2020

Final Accepted: 20 February 2020

Published: March 2020

Key words:-

Toxic Epidermal Necrolysis,
Amoxicillin, Adverse Drug Reactions

Abstract

Adverse drug reactions are unintended hazardous effects of drug that can occur with any class of medication; however studies have shown a high incidence with antibiotics. Amoxicillin is a broad spectrum beta lactam antibiotic, commonly used in treating infections, is known to cause cutaneous skin eruptions. Toxic epidermal necrolysis (TEN) is a rare but severe life threatening dermatological reaction most often triggered by medications. Here we describe a case of TEN in a 69 year old male following Amoxicillin therapy presenting with mucocutaneous lesions with super added multidrug resistant bacterial infection requiring 20 days of rigorous hospital care.

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Introduction:-

Toxic Epidermal Necrolysis (TEN) is a severe immune-system mediated mucocutaneous condition characterized by extensive necrosis and detachment of the epidermis.^[1] It is probably caused by drugs or their metabolites^[2]. Both TEN and Stevens - Johnson syndrome (SJS) have similar pathological process but can be differentiated by the degree of body surface area involved, below 10% in SJS whereas greater than 30% in TEN.

Worldwide, the annual incidence of TEN is 0.4 to 1.2 per million cases and most commonly affected groups being women, elderly and retroviral disease patients.^[1] TEN associated mortality rate varies broadly in different reports from 10-70% depending on the extent of mucocutaneous involvement; the primary cause of death being septicemia and multisystem organ failure^[3]. Life-long sequelae are common, including internal-organ damage and visual impairment.

In 1956, Alan Lyell described about his patients with an eruption resembling scalding of skin which he called TEN. Most frequent triggers are drugs such as antiepileptics, barbiturates, pyrazolones and sulphonamides^[4]. Often it may result from drugs with long half-lives and/or circulating active metabolites. No specific laboratory test is available to confirm the aetiological agent, a causal link is suggested when it occurs in first few weeks of medication therapy, usually between 1 to 3 weeks^[3,5].

Case Report:

A 69 years gentleman presented with skin eruptions and fever of 3 days duration. He had taken oral Amoxicillin since 5 days for throat infection following which he developed blisters over trunk, limbs, genital region that had rapidly progressed with skin peeling over the next few days. He had no other systemic symptoms. On examination, he was febrile, tachypnoeic, tachycardic, maintaining normal saturation on room air. Skin examination revealed flaccid vesicles over the thigh, groin, genital, perianal region, abdomen, elbows, arms and forearms with areas of

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blackish discolouration, necrosis and skin peeling (Figure 1,2); Nikolsky sign was positive. Multiple ulcers with whitish exudate were noticed in the oral cavity. Eye examination was normal. Rest of the systemic examination was normal. He was managed in the intensive care unit; after securing central venous access, intravenous normal saline and stat dose of injections Hydrocortisone, Pheniramine, Paracetamol were administered. Samples were collected for culture and antibiotics Meropenem, Clindamycin were commenced.

His blood tests showed haemoglobin 13g/dl, total leucocyte count 5000/cumm, platelet count 150000/cumm, sodium 134mEq/l, potassium of 4mEq/l, elevated creatinine 3.73mg/dl and C reactive protein 320.70mg/dl, Total protein 5.70g/dl, Albumin 3 g/dl, normal liver enzymes. The renal parameters normalised with treatment. After multispeciality discussion, thrice daily immunosuppressant cyclosporine 100mg and intravenous steroid betamethasone 4mg were added. Multidrug resistant *Acinetobacter baumannii* was isolated from the blood, urine and skin lesion swab cultures; antibiotic therapy was revised to a combination of Colistin, Meropenem and Ticoplanin. Additionally, strict contact precautions, skin care with liquid Paraffin and fucidin ointment, hydroxypropylmethylcellulose eye gel for dry eyes, chlorhexidine gargle for oral hygiene, local antifungal mouth pain, nasogastric feeds and deep vein thrombosis prophylaxis were provided.

Repeat Cultures after 2 weeks were sterile thus antibiotics were stopped. Patient responded to treatment and successfully discharged home after 20 days of rigorous treatment. Steroid was discontinued but Cyclosporine was continued for two more weeks. The skin and mucosal lesions slowly healed.

Discussion:-

TEN, also known as Lyell's syndrome is a life-threatening mucocutaneous reaction with high mortality rate^[6,7]. It is commonly characterized by widespread scattered lesions with dark-red centre and lighter red macules with central blistering that can coalesce followed by sloughing of skin. In about 85-95% cases haemorrhagic mucositis of the mouth, genitals, eyes and respiratory tract is observed^[7]. Systemic symptoms like fever, malaise, with possible internal organ involvement can worsen the condition^[8]. Majority of deaths occur due to secondary infections, sepsis and multi organ system failure^[6]; hypovolemic shock, bronchopneumonia, pulmonary oedema, Pulmonary embolism, acute tubular necrosis, membranous glomerulonephritis, gastrointestinal haemorrhage and disseminated intravascular coagulation are other major complications^[7].



Figure 1, 2:- Skin peeling with areas of necrosis noted in the thorax, groin, hips, arm, forearm and elbow.

Drugs can activate the immune system by binding directly or reversibly to immune receptors.^[6] The prevalence of antibiotics triggered TEN ranges from 29%-42%.^[9] Beta lactams and sulphonamide are most commonly associated with TEN, symptoms usually manifesting within the first week of antibiotic therapy^[6]. Slow progression and gradual recovery over a period of 14-28 days with frequent relapses may occur. The mortality rate rises with age, more than 50% mortality occurring in the elderly.^[7]

We made a diagnosis of TEN in our case based on history of drug exposure with typical clinical manifestation of mucosal involvement, skin eruptions with peeling (Nikolsky positive) over the thorax, groins, genital region, arms forearms, elbows, posterior and lateral aspect of thigh involving more than 30% of BSA supported by histological evidence.

If TEN is suspected, important aspects of care include early diagnosis, analysing disease severity, and withdraw the possible culprit drug. Management is mainly supportive in the intensive care or burns unit with a multidisciplinary team approach^[1].

The management of SJS/TEN including treatment with intravenous immunoglobulin (IVIG) are able to prevent Fas-mediated cell death. Cyclosporine, a calcineurin inhibitor has newly been used in successful treatment of SJS/TEN. Thalidomide has an Anti-Tumour Necrosis factor alpha (TNF-alpha) activity and should theoretically improve TEN. Though systemic corticosteroid has been used for long in the treatment of SJS/TEN, it remains a matter of debate due to the contradictory outcomes in terms of lowering the mortality rate and duration of hospitalisation in different group of patients. Other techniques includes plasmapheresis and haemodialysis that aim to eradicate the causative agent, its metabolites and proinflammatory cytokines from the circulation in an effort to terminate progression of the disease.^[7,8]

Zacharia T G et al reported TEN following Amoxicillin in a 12 year old male successfully treated with antibiotics, immunosuppressant and other supportive measures^[10]. Patel JB et al describe a case of TEN rigorously managed with systemic corticosteroid and IVIG reporting improvement^[8]. Our patient, a case of Amoxicillin induced TEN was successfully treated with cyclosporine, systemic steroid along with appropriate antibiotics to tackle the secondary infection along with adequate cutaneous care.

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