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Case Report

PHENYTOIN INDUCED TOXIC EPIDERMAL NECROLYSIS; A CASE REPORT

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ABSTRACT

Several drugs are at high risk of causing Toxic Epidermal Necrolysis (TEN) including Anti-convulsants such as phenytoin, carbamazepine and phenobarbital. Other drugs include antimicrobials like sulfonamides followed by Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and anti-gout drugs.[1]

We are presenting a case of 60 year old female patient with Phenytoin induced TEN. Who had a history of cranial surgery 3 weeks prior to admission and prescribed with discharge medications of phenytoin, diclofenac and dexamethasone. After 3 weeks of treatment, patient has developed oral and genital erosions with itchy vesicles and bullae all over the body and admitted to tertiary care hospital with complaints of burning sensation on chest and pedal edema and hematuria for 3 days. Phenytoin induced TEN was suspected and was admitted from causality. The patient was managed aggressively with steroids, higher antibiotics and creams (over the lesion), nutritional supplement was taken care of and palliative care was given. The patient expired due to septic shock and multiple organ dysfunctions with metabolic acidosis after 8 day of admission.

This case highlights the importance of Phenytoin possibly causing TEN. Government of India and Regulatory Authorities should create awareness among practitioners to report all the ADRs to concerned ADR Monitoring Centers.

Keywords: Phenytoin induced TEN, Septic shock, metabolic acidosis.

Introduction

Severe Cutaneous Adverse Reactions (SCAR) are life-threatening conditions associated with significant morbidity and mortality. In Toxic Epidermal Necrolysis (TEN) greater than 30% of the Body Surface Area (BSA) is involved. The incidence of TEN is estimated at 0.9 to 1.4 persons per million per year in the general population. [1]

Phenytoin is the most commonly prescribed antiepileptic drug in adults. In a case-control study of 73 patients taking anti-epileptic drugs 14 patients were reported with the Stevens - Johnson syndrome (SJS) associated with the phenytoin ingestion.[2]

CASE HISTORY

A 60 year old female patient was admitted with the complains of ulcer over lips, oral cavity, bilateral eyes and itchy blisters all over the body. She also had burning sensation of the chest, blood stained urine and swelling on the leg since 3 days. The patient had a history of left parietal craniotomy 3 weeks prior to admission and was put on tablet. Phenytoin table, dexamethasone and tablet diclofenac post which she developed above symptoms and was brought to the emergency department.

On the day of admission the patient was conscious, oriented and her blood pressure was 140/90 mmHg. Upon cutaneous examination, multiple flaccid bullae were seen all over the body including scalp. Oral and genital erosions with multiple bleeding points were present. Purulent eye discharge was present. The suspected drug phenytoin was advised to discontinue and kept under observation.

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Figure 1: Seventh day of admission

Table 1:

LABORATORY INVESTIGATIONS	NORMAL RANGE	DATE						
Blood Analysis		**1**	**2**	**3**	**4**	**5**	**6**	**7**
Hemoglobin	12-18mg/dl	10.8			9.4			**7.3**
WBC count	5000-11000cells/cumm	17,800	8600		9400			24919
Platelets	1.5-4.5lacs/cumm	5.3	3.4		1.86			1.1
ESR	0-20mm/hr	12	10		18			15
Urea & Creatinine Analysis								
Serum Urea	20-50mg/dl	43				68	130	149
Serum Creatinine	0.6-1.1mg/dl	0.7				0.9	1.8	2.3
Electrolytes								
Sodium	136-145meq/L	132		138			146	154
Potassium	3.5-4.5meq/L	6.7		4.1			4.1	4.4
Endocrine Test								
Random Blood Sugar	70-110mg/dl	50					116	96
Post-Prandial	110-140mg/dl	68		148				
Liver Function Analysis								
Total Bilirubin	0.3-1.2mg/dl	9.8		4.9		3.9	4.7	4.9
Direct Bilirubin	0-0.2mg/dl	4.8		3.0		2.0	2.9	1.8
Indirect Bilirubin	0.3-1.0mg/dl	5.0		1.9		1.7	1.8	1.2
SGOT	up to 31IU/L	82				74	31	52
SGPT	up to 34IU/L	96				43	17	13
ALP	42-98IU/L	173						143
Protein Analysis								
Total Protein	6.4-8.3mg/dl	5.6		4.5		4.4	4.4	3.4
Albumin	3.5-5.2mg/dl	2.0		1.7		1.3		1.0

Special diagnostic test revealed that the patient was anemic, Pus culture showed the presence of staphylococcus aureous.

From first day to the sixth day the patient started with piperacilin and tazobactum combination, mupirocin, dexamethasone and nutritional supplements. Patient had fluid and electrolyte abnormalities. The fluid requirement during initial 24 hrs calculated using Parklands formula. She had purulent eye discharge which was taken care by eye drops. On seventh day the patient was shifted to MICU and started with higher antibiotics such as vancomycin and meropenem. She also had respiratory distress, which was treated with nebulisation of salbutamol and budesonide. On the eighth day she has developed multiple organ dysfunctions, metabolic acidosis, and sepsis, where multiple life saving medication had been administrated but the patient expired after 8 days of admission.

DISCUSSION

Both SJS &TEN are debatably included in the same spectrum as Erythema Multiforme (EM). In both the condition hemorrhagic erosions of mucous membrane including eye, lips, mouth, pharynx, trachea, bronchi, glans penis, urethra and anus are present in about 95% of the cases. Maculo–papular eruption which may also present with oral lesions and conjunctivitis must be considered as differential diagnosis in early stage of disease.[1.2.9]
Up to 60% of cases of SJS/TEN can demonstrate causality to a medication exposure, but other factors including infection (e.g., *Mycoplasma* pneumonia), genetic factors (HLA alleles) or graft versus host disease have been implicated in the development of this mucocutaneous condition, and up to 20% of cases remain idiopathic. The studies performed in Taiwan indicate a strong association between HLA-B*1502 allele and 15,16 phenytoin induced SJS/TEN and declared that the allele can be considered as a universal marker for phenytoin induced SJS/TEN, which is not supported by few studies. More than 200 medications have been identified as potential causative agents of SJS/TEN. Even though some drugs have been implicated in case reports, not all of these agents have demonstrated a strong association with the development of SJS/TEN.[3,4,6,7,8]

Early diagnosis with the prompt recognition and withdrawal of all potential causative drugs is essential for a favorable outcome. Removal of offending drug, its metabolites or cytokines by plasmepheresis or hemodialysis can also be considered. Various immunomodulatory treatments for SJS /TEN have been proposed, such as glucocorticosteroids, intravenous immunoglobulins (IVIG), and cyclosporine. The cost of these treatments is high; hence some patients may not be willing to buy. Patients will commonly have fluid and electrolyte abnormalities that require careful monitoring. Mouth care with disinfecting mouthwashes and mild ointments is essential in managing the mucosal lesions of the oral cavity and lips. In cases with eye involvement, ophthalmologic care is critical and specialized eye lid care should be provided daily in addition to anti-inflammatory eye drops. Treatment can include prophylatic ophthalmic antibiotics (e.g., bacitracin or a fluoroquinolone), preservative-free emollients, antiseptic eye drops, and/or vitamin. [2,3,4,6]

The Government of India and regulatory authorities should create awareness among practitioners to report all the ADRs to the Adverse Drug Reactions Reporting Centers, with special emphasis on the drugs banned outside India. There is a need for authorities to strengthen existing law regarding OTC drug to ensure their rational sales and use. [1,5]

CONCLUSION

If patient is affordable and willing, it is better to screen for HLA alleles before starting treatment with anticonvulsants. Hence, the medication of anticonvulsants could be individualized. If HLA screening for HLA alleles become common, phenytoin associated SJS/TEN incidence might be reduced.

As the adverse systemic reactions to antiepileptic drugs (AEDs) are rare and severe, physicians should counsel patients on the importance of notifying their physician if they develop any new or unusual symptoms and patient was provided with 'drug alert card' and was advised to carry it with her whenever she seeks medical attention.

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