Simultaneous occurrence of toxic epidermal necrolysis and neuroleptic malignant syndrome

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ABSTRACT

Toxic epidermal necrolysis (TEN) is an acute life-threatening blistering disease characterized by involvement of the skin, multiple mucous membranes and internal organs. It is most commonly precipitated by the administration of medications like anticonvulsants. Neuroleptic malignant syndrome (NMS) is a rare complication of neuroleptic therapy characterized by catatonic behavior, generalized muscular rigidity, hyperthermia and autonomic dysfunction. An 18-year-old girl presenting with simultaneous appearance of TEN and NMS following anti-psychotic drugs given for bipolar mood disorder, is reported for the rare association and her complete recovery.

Key Words: Toxic epidermal necrolysis, Neuroleptic malignant syndrome

INTRODUCTION

Toxic epidermal necrolysis (TEN) also known as Lyell’s syndrome, is an uncommon but acute life-threatening idiosyncratic syndrome involving the skin and multiple mucous membranes. It is characterized by fever, systemic toxicity, skin tenderness, erythema and widespread epidermal detachment. Although Ruskin described this condition in 1948, it was Lyell in 1956, who reported four cases and proposed the name TEN.[1] TEN is often fatal; mortality ranges from 20-30%.[2] Death usually occurs due to septicemia or other systemic complications. Many etiological factors have been proposed. Although TEN is often idiopathic, it mostly represents an idiosyncratic drug-induced dose-independent reaction in about 77% cases.[3] Frequently implicated are antiepileptic drugs (carbamazepine, phenytoin), sulfonamides and NSAIDs. TEN is known to affect women more than men. The incidence is high in HIV patients.

Neuroleptic malignant syndrome (NMS) is characterized by catatonic behavior, generalized muscular rigidity, hyperthermia and autonomic dysfunction. It can suddenly arise in patients treated with neuroleptic drugs and causes a high mortality rate even today. It was first described by Delay et al in 1960. The incidence is 0.02% to 3.23%.[3] Virtually all classes of \( \text{D}_2 \) dopamine receptor antagonists such as haloperidol and chlorpromazine have been associated with NMS. NMS is not the result of overdosage. Concomitant treatment with lithium or carbamazepine potentiates the risk. It usually occurs within 30 days of neuroleptic treatment and the reported mortality rate is 10-20%. Death results from cardiac or respiratory arrest.[3]

The combination of these two severe complications of drug therapy in a patient and her complete recovery from these two is reported here. To the best of our knowledge, such an association has not been previously reported.
CASE REPORT

An 18-year-old girl was brought to our casualty in a comatose state with high-grade fever and generalized charred appearance with peeling of skin in sheets. There were a few bullous and target lesions. She had incontinence of urine, sialorrhea and diaphoresis. All these developed following administration of carbamazepine (100 mg tid) and chlorpromazine (100 mg bid) for her bipolar mood disorder, for two weeks. About 95% of her body was involved with denudation, including her scalp. Nikolsky sign was demonstrable. Oral, conjunctival and genital mucosae were involved with erosions. She had muscular rigidity of the lead pipe type. Her blood pressure was 150/100 mm of Hg. Her respiratory system and cardiovascular systems were normal except for tachypnea and tachycardia.

Baseline investigations showed leukocytosis with eosinophilia and hyperglycemia (fasting blood sugar 250 mg/dl). She was polyuric with glycosuria and no albuminuria. The serum creatinine phosphokinase (CPK) level was raised (294 units/L). Blood cultures were negative for organisms on repeated testing. Pus culture from cutaneous lesions showed growth of Staphylococcus aureus sensitive to ceftazidine and the patient was started on this drug.

As a burn care center was not available, we managed the patient in our intensive care unit (ICU). She was on parenteral nutrition and fluids with monitoring of all vital parameters. She was given systemic steroids starting from 8 mg/day of intravenous betamethasone, which was gradually tapered off over 3 weeks. Her skin lesions dried up and started epithelializing after a week. She started recovering from coma after 3 days of admission. She was discharged after 3 weeks on thioridazine after a psychiatry consultation for her mood disorder.

DISCUSSION

Our patient had all the classical features of TEN and satisfied the criteria for the diagnosis of NMS as proposed by Caroff and Mann in 1991. Chlorpromazine is a neuroleptic drug and it might have produced NMS. The simultaneous ingestion of carbamazepine might have potentiated the NMS. It is a form of drug-induced hyperthermia. All neuroleptics implicated in NMS share the property of central D₂ dopamine receptor antagonism, particularly in nigro-striatal and hypothalamic pathways. Generalized rigidity (lead pipe type) is reported in 97% of cases. CPK from skeletal muscle is raised in 95% cases and myoglobinuria is seen in 67% of cases. Increased levels of serum and blister fluid CPK are reported in TEN patients also.

Both carbamazepine and chlorpromazine can induce TEN. But, in our experience, among these, the most probable cause is carbamazepine. The pathogenesis of TEN remains largely unknown. The cytotoxic lymphocyte-mediated immune reaction aimed at destruction of the keratinocytes expressing foreign (drug-related) antigens is proposed as the primary cause for the development of TEN. Histologically, TEN is characterized by extensive keratinocyte apoptosis, which is induced by a suicidal interaction between ‘Fas’ and ‘Fas ligand’ (Fas L), which are both expressed by keratinocytes.

TEN has been reported to be associated with a few other life-threatening conditions, most commonly adult respiratory distress syndrome (ARDS) and other pulmonary complications. Fulminant hepatitis has been noted with TEN due to nevirapine in AIDS patients and due to moxifloxacin. Recently, a novel manifestation of lupus with TEN has been reported. To the best of our knowledge, the co-occurrence of two life-threatening reactions, NMS and TEN has not been documented.
We treated the patient in our ICU, with a moderately high dose of systemic steroids under cover of antibiotics, even though the usefulness of corticosteroids is controversial. Her miraculous escape from both these rare life-threatening conditions is interesting.

REFERENCES