

THE NEUROLEPTIC MALIGNANT SYNDROME : REPORT OF THREE CASES

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ABSTRACT

Three patients, one male and two females who developed neuroleptic malignant syndrome following exposure to depot and oral neuroleptic are presented. The patients satisfied Levenson's criteria for diagnosis. Bromocriptine and Electro Convulsive Therapy were found effective whereas trihexyphenidyl proved unsatisfactory in the treatment. All the patients recovered completely without complications.

KEY-WORDS: *Neuroleptic Malignant Syndrome; Creatinine Phosphokinase; Electro Convulsive Therapy; Extra Pyramidal Symptoms; Trihexyphenidyl; Bromocriptine.*

INTRODUCTION

The neuroleptic malignant syndrome was first described by Delay and Deniker in 1968. Initially thought to be rare, Neuroleptic Malignant Syndrome (NMS) is now more frequently reported in patients treated with butyrophenones and phenothiazines (Singh, 1981; Levenson, 1985; Kurien et al, 1993). Besides neuroleptics, non-neuroleptic pharmacotherapy has also been known to produce NMS (Kurlan et al, 1984; Guze and Baxter, 1985). The diagnostic criteria proposed by Levenson in 1985 have been used in selecting cases and use of anti-cholinergics, dopamine-agonist and Electro Convulsive Therapy (ECT) in the treatment of NMS is described.

CASE REPORTS

The socio- demographic data, primary diagnosis and treatment information of the three cases is given in Table-1. All the three patients had fever, rigidity, altered consciousness- one patient had fluctuating blood pressure and unexplained sweating, suggesting autonomic imbalance.

The clinical details are given in Table 2. One patient in addition also had tubercular pleural effusion. All the patients were discharged without complications. The treatment was directed at withdrawal of offending drug and precipitating

causes like dehydration. Specific therapy for the condition was initiated at the earliest and continued till the muscle rigidity completely subsided.

DISCUSSION :

The incidence of NMS has varied in literature from 0.02 per cent to 3.23 per cent (Lazarus et al, 1989). Fever, rigidity and raised Creatinine Phosphokinase (CPK)*have been labelled major criteria and tachycardia, tachypnoea altered mental state, abnormal B.P., diaphoresis and leucocytosis as minor criteria (Levenson 1985). For diagnosis, the presence of all the 3 major criteria or 2 major with all the minor criteria has been suggested.

In the first case where NMS developed after flupenthixol injections, after initial improvement with trihexyphenidyl (THP) and promethazine, the symptoms worsened. Promethazine, resolved all the symptoms markedly though it took nearly 6 weeks for complete recovery. Similar delay in recovery has been described in patients receiving depot neuroleptics (Greenberg and Gujavarty, 1985; Deng et al, 1990) Symptoms like strong desire to cry, restlessness and insomnia after a few days of therapy of bromocriptine are consistent with its dopamine agonistic activity in limbic path ways.

TABLE-I

AGE, SEX, PRIMARY DIAGNOSIS, NEUROLEPTICS, DURATION OF NEUROLEPTIC TREATMENT, SPECIFIC TREATMENT, RESPONSE, HOSPITAL STAY, COMPLICATION AND OUTCOME.

Case No.	Age (In Years)	Sex	Primary Diagnosis	Neuroleptics	Duration of Neuroleptic	Specific treatment	Other treatment	Response	Hospital stay	Complications	Outcome
1	55	F	Unipolar depression	Plupenthrol depot 20 mg 1/M Injection	7 days	Trihexyphenidyl 6 mg/day Promethazine HCL 150 mg/day Bromocriptine 12.5 mg/day	Supportive	Inadequate Inadequate Marked	15 days	Sacral sore	Complete recovery
2	18	F	Mania	Haloperidol 15-30mg/day	7 days	Trihexyphenidyl 6mg/day Promethazine HCL 150 mg/day Diazepam 10mg/day Electro convulsive Therapy (Total-6)	Supportive	Inadequate Inadequate Marked	20 days	NIL	Complete recovery
3	40	M	Schizo- phrenia with Tubercular Pleural effusion	Trifluoperazine 15 mg/day	9 days	Trihexyphenidyl 6-8 mg/day	Supportive * and ATT	Significant	30 days	NIL	Complete recovery

TABLE-II

DIAGNOSTIC FEATURES IN THREE CASES

Case No.	Maximum temperature	Muscle rigidity	Mental state	Pulse rate	Respiration rate per min	BP	Dysphoria	Tremors	Incontinence	TLC	CPK	Criteria*
1	101°F	Profound	Stuporous	120/mr	24	160/100 mm Hg	+++	+++	+	12000/cmm	150 IU/l	MJ-3 MN-5
2	101°F	Severe	Drowsy	124/mr	20	140/80 mm Hg	++	++	+	11,400/cmm	123 IU/l	MJ-3 MN-4
3	100°F	Severe	Drowsy	100/mr	22	100/70 mm Hg	+++	++	-	12,500/cmm	200 IU/l	MJ-3 MN-4

*MJ- Major and MN-Minor criteria full filled.

In the second case, ECT proved very useful in treating NMS. However due to poor response to THP in the first two cases and prolonged recovery time in this case, the possibility of natural recovery cannot be excluded. Spontaneous recovery and variable treatment response to THP in NMS has been described (Weinberger and Kelly, 1977 Henderson and Wosten, 1981).

Pre-disposing factors which have been implicated in the syndrome include discontinuation of dopamine agonists, anti-parkinsonian drugs (Friendman et al, 1985), use of dopamine depleting drugs (Henderson and Wosten, 1981), rapid upward titration of neuroleptics (Sandy and Lacono, 1986), physical exhaustion, dehydration and underlying organic brain disorders. (Guze and Baxter, 1985)

The exact pathogenesis of NMS is not clear but there is evidence in favour of the hypothesis that NMS develops as a result of functional dopaminergic deficit in striatal and hypothalamic areas (Lazarus et al 1989; Mann et al. 1991). Bromocriptine, a dopamine agonist and ECT which increase catecholamine levels including dopamine gives support to the above hypothesis (Greenberg and Gujavarty, 1985). However there are other theories which have been put forward to explain the pathophysiology of NMS such a hypermetabolic state in muscles (May et al 1983) and sympathoadrenomedullary hyperactivity (Fiebel and Schiffer, 1981). Also, it has been documented that treatment modalities which increase dopamine levels at post synaptic sites are not always effective (Greenberg and Gujavarty, 1985). It could be argued therefore that there may be more than one etiological explanation for the development of NMS.

No complications were seen in either of the present cases except for a sacral bed sore in the first case. A favourable outcome and decline in mortality due to cardio-respiratory or acute renal failure and have also been reported in recent studies (Shalev et al., 1989; et al 1990; Keck et al., 1991).

The present work underlines the need to

minimise the risk factors, identify the syndrome early, stop the offending neuroleptic and institute intensive medical care and specific treatment with bromocriptine and/ or ECT to prevent the lethal complications.

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