Case Report :

Supersensitivity psychosis: A case report

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ABSTRACT:

A 30 yrs old male patient diagnosed as a case of paranoid schizophrenia was treated initially, with various antipsychotics, both typical and atypical, for a long period, without any significant improvement and having marked extrapyramidal symptoms. Subsequently clozapine was administered and patient had shown significant improvement to that but afterward patient had worsened again with appearance of involuntary dyskinetic movements. Clozapine was substituted with quetiapine with which patient responded but relapsed again after sometime. Sodium valproate was added and patient had sustained improvement after that. The concept of supersensitivity psychosis alongwith its treatment implications was reviewed from the relevant literature.

Key words: *supersensitivity psychosis, antipsychotics, clozapine*

Introduction

Since the introduction of neuroleptics in psychiatry, the behavioural toxicity of these drugs has been increasingly recognized. Over 30 years ago, Chouinard and colleagues described worsening of psychotic symptoms in association with long-term neuroleptic therapy (Chouinard et al, 1978). It had been observed that psychotic relapse in a number of patients on neuroleptics did not follow the usual course of schizophrenic illness. For example, certain patients relapsed immediately upon a reduction in dosage and showed new schizophrenic symptoms or worsening of previous psychopathology. Prior to these observations, Ungerstedt and Ljungberg (1977) had predicted limbic dopaminergic supersensitivity on the basis of animal experiments. The clinical syndrome, termed supersensitivity psychosis (SSP), is hypothesized to result from post-synaptic dopamine (DA) receptor supersensitivity in mesolimbic pathways in the same way that tardive dyskinesia (TD) is thought to develop in the neostriatum (Chouinard & Jones, 1980).

The phenomenon of SSP is still under investigation - at least three psychiatric presentations during the past twenty years have dealt with its documentation (Borison, 1987; Sramek et al, 1989; Green et al, 1989). Specific diagnostic criteria have been developed to distinguish SSP from pre-existing psychopathology (Table 1).

Table 1

Chouinard's Diagnostic Criteria for Supersensitivity Psychosis

(A) The patient must have a 3 month history of receiving antipsychotics.

(B) At least one of the following major criteria must be present:

1) Reappearance of psychotic symptoms upon decrease or discontinuation of medication during the last 5 years - within 6 weeks for oral medication, 3 months for I.M. depot medication.

2) Greater frequency of relapse (acute psychotic exacerbation) during continuous treatment with neuroleptics.

3) Tolerance to the anti-psychotic effect of the neuroleptic (overall increase in dose by 20% or more).

4) Extreme tolerance: worsening of psychosis whenever dosages are increased without presence of significant parkinsonian symptoms.

5) Psychotic symptoms upon decrease of medication are new schizophrenic symptoms (not previously seen) OR are of greater severity.

6) Psychotic relapse occurs upon sudden decrease (20%) of medication but not if same decrease is gradual.

7) Presence of drug tolerance in the past but presently treated with high doses of neuroleptics on at least a bid regimen.

(C) At least one of the following minor criteria must be present if only one major criterion is present:

1) Tardive dyskinesia.

2) Rapid improvement in psychotic symptoms when the neuroleptic dose is increased after a decrease or discontinuation.

3) Clear exacerbation of psychotic symptoms by stress.

4) Appearance of psychotic symptoms at the end of the injection interval (for patients on long-acting intramuscular medication).

5) High levels of prolactin or neuroleptic activity (twice normal).

(D) Exclusion criteria:

1) Patients in the first acute phase of illness.

2) Patients with continuous severe psychosis unresponsive to neuroleptics.

(E) Subtypes:

Stage I: Withdrawal type: reversible when only major criteria #1 and/or #6 are present.

Stage II: Tardive type:

IIA - masked and mostly reversible when major criterion #3 is present.

IIB - masked and mostly irreversible when major criterion #7 is present.

IIC - overt and mostly irreversible when major criterion #1 is present with any other major criteria (other than #6).

Stage III: Severe type: when major criterion #4 is present.

Case Report

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Discussion

The considerable improvement witnessed in the patient suggests that anticonvulsants may have a role in the treatment of SSP. The dose used in the patient was low and serum level was below the conventional therapeutic range.

Antiepileptic drugs are not known to be effective in previously untreated psychosis, although their use is well recognized in bipolar affective disorder. A report has appeared documenting the successful use of these drugs in three patients treated with neuroleptics (Wassef et al, 1989). Our rationale for prescribing antiepileptics in SSP is based on the hypothesis that neuroleptics facilitate a kindling-like effect in the limbic system, thereby aggravating psychotic symptoms. Limbic kindling in animals has been studied as a model for human psychopathology (Stevens & Livermore, 1978).

Kindling represents a model of epilepsy and neuronal plasticity in animals. The term "kindling effect" was coined by Goddard in his classic paper off the subject (Goddard et al, 1969). Intermittent application of an initially subconvulsive electrical stimulus leads to progressive intensification of seizure activity culminating in the production of a generalized motor convulsion from the same stimulus. Seizures in the early stages resemble the manifestations of human complex partial epilepsy (McNamara, 1986). Important parameters in the induction of kindling include the nature of the stimulus and its ability to induce an after discharge. The interval between successive stimuli is particularly important - continuous stimulation does not lead to development of kindling. Once kindled, the animal remains susceptible to seizure provocation upon reintroduction of the stimulus at a later date. In other words, the effect is long-lasting, if not permanent. If spaced repetition of the stimulus is continued after completion of kindling, the animal will eventually develop spontaneous seizures. Thus, the kindling phenomenon is one of several experimental models of epilepsy.

Kindling can be elicited from many sites in the brain where a hierarchy of susceptibility exists. The limbic system, particularly the amygdala, is generally held to be the most susceptible. Kindling has been described in many

species and may contribute to human epileptogenesis as suggested by several lines of indirect evidence (McNamara, 1986). Diverse modes of stimulation can elicit kindling. For example, systemically administered metrazol, lidocaine, or cocaine can induce pharmacological kindling (Majkowski, 1986).

Neuroleptic drugs are known to lower the seizure threshold to varying extents. Clinically, this effect is quite minimal and seizures are infrequently observed in patients taking neuroleptics, even those with a past history of epilepsy. However, if the concept of a repeated, subthreshold, seizurogenic chemical stimulus is applied to neuroleptic therapy it is easy to see how kindling may be possible. Continuous treatment invariably involves a fluctuation in blood levels from peak values to trough levels. In contrast, erratic or discontinuous drug exposure may alter the "inter-stimulus" interval sufficiently to ensure that the changes necessary for kindling never take place.

Neuroleptic drugs exert powerful antidopaminergic effects in the brain, which are felt to be the basis of their antipsychotic action. Although the effects of DA on kindling are far from clear, an intact dopaminergic system appears to protect against the progress of amygdala-kindled seizures to generalized convulsions (Sato et al, 1979). In the study haloperidol was found to decrease the latency for appearance of kindling in rats. Furthermore, there is evidence of a link between aberrant limbic electrical activity and a subsequent increase in DA sensitivity (Csernansky et al, 1985; Csernansky et al, 1988). Thus, limbic kindling as a result of repeated administration of a seizure threshold-lowering drug with antidopaminergic properties could be expected to result in increased psychotic symptomatology. At the same time, though, the treatment for such a condition would be neuroleptic drugs. This fits with clinical observations of SSP in which worsening psychosis follows prolonged treatment, and is masked in the early stages by increasing the dose of the offending agent. The model predicts that DA depletion states predispose patients to SSP whereas functional DA overactivity protects against the development of SSP. Once SSP is established, however, dopaminergic supersensitivity will worsen psychotic symptoms. In severe cases of SSP increasing the dose of neuroleptic leads to a worsening of symptoms, as though reintroduction of the causative stimulus were triggering the psychosis.

One might expect antipsychotic drugs with more potent effects on the seizure threshold to be more associated with the development of SSP. Clinically, such a correlation has not been reported so far. This is understandable since these drugs have a variety of effects on other neurotransmitter systems. Any correlation is further confounded by the concomitant use of anticholinergic medication. Kindling is retarded by muscarinic blockers and facilitated by a decrease in noradrenaline, serotonin, or DA (Majkowski, 1986). Although other drugs such as tricyclic antidepressants also lower the seizure threshold, they tend to enhance the noradrenergic system which inhibits kindling (McIntyre & Edson, 1982). Nonetheless, tricyclic antidepressant drugs have been reported to induce rapid-cycling illness in some bipolar patients (Wehr & Goodwin, 1987).

Earlier reports of SSP found a relationship between this condition and the presence of TD in affected patients (Chouinard et al, 1978). However, later studies in different patient populations have not replicated this finding (Chouinard et al, 1986; Csernansky et al, 1986), supporting the idea that different susceptibilities exist among patients. Clinically, "poor prognosis" schizophrenia is associated with a tendency to develop TD, whereas "good prognosis" patients are more likely to develop SSP (Chouinard et al, 1986). The correlation of TD and SSP in a population of patients was reported with poor prognosis schizophrenia. Subsequent studies included both good and poor prognosis patients. Thus, any study looking at the relationship between TD and SSP should examine patients according to their prognosis.

There are important implications for continuing to escalate the dose of neuroleptic in the face of SSP. TD, originally thought to be its homologue in a different neuronal pathway, appears to reach a plateau of severity beyond which it does not worsen. For this reason, neuroleptics are prescribed in treatment-resistant cases to mask the movement disorder. In SSP, however, there should be no limit to the expected severity of the condition if kindling is indeed contributing to its pathogenesis.

Conclusion

The authors have presented evidence that antiepileptic therapy is beneficial in some drug-resistant schizophrenics who have SSP. Further understanding of the pathophysiology of SSP would enable clinicians to take prophylactic measures when prescribing neuroleptics, and to administer specific treatments for the condition once it developed.

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