Case Conference

Bipolar Affective Disorder- Diagnostic issues

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Abstract : *Acute and transient psychotic disorder [ATPD] as diagnosed by ICD is a heterogeneous disorder with ill-defined course. When ATPD is encountered in patients with history of depressive episode, it would require careful scrutiny and long-term observations to delineate the episode from mania/ mixed episode and to make a comprehensive diagnosis. Further presence of Schneiderian first rank symptoms at any stage may complicate the whole picture. In this interesting case, apart from diagnostic issues we had to be selective in our management strategy due to treatment related complications like Neuroleptic Malignant Syndrome (NMS) and ECT induced mania.*

Keyword : Bipolar affective disorder, acute and transient psychotic disorder, catatonia, neuroleptic malignant syndrome, ECT induced mania

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INTRODUCTION

Ever since Emil Kraepelin crystallized dementia praecox and manic-depressive insanity from the heterogeneous group of madness, the dichotomy has prevailed and is evident in current classificatory systems.[1] Many authors did not believe this dichotomy to be mutually exclusive and complete.[2] Psychiatrist from different parts of the world, identified disorders like cycloid disorders (the Germans), bouffe´e de´lirante (the French), reactive psychoses (the Scandinavians), emotional psychoses (the Swiss), good-prognosis schizophrenia (the Americans) and atypical psychoses (the Japanese) that drew attention to the possible overlaps and islands between these dichotomous categories.[3] These disorders are currently subsumed under 'Acute and Transient Psychotic disorders' [F23] in ICD-10[4] and 'Acute psychosis' in DSM-IV TR.[5] Although little is known about the family history, pre-morbid functioning and course of ATPD, researchers point out that ATPD as defined by ICD-10 may be a group of heterogeneous disorders with favourable outcome.

Schneider proposed symptoms of first rank (FRS), the presence of which was considered as characteristic of schizophrenia. These symptoms are currently incorporated in the ICD-10 general criteria (a) to (d) for schizophrenia, the presence of only one of these symptoms for more than 1 month in absence of substance use or an organic bases, is diagnostic of schizophrenia (ICD-10).[4] The ICD-10 further maintains that the same symptoms may be present in schizoaffective disorder [F25] and acute polymorphic psychotic disorder with symptoms of schizophrenia [F23.1] although the duration of these symptoms may vary. However, in a startling contrast to the Kraepelinian dichotomy, these 'characteristic symptoms of schizophrenia' have been shown to have prevalence in the range of 22-29% in affective disorders.[7-9]

Here, the authors present a case of a young woman with episodic illness. From the time of her current presentation and almost 3 weeks beyond, her psychopathology continued to change. Additionally the antecedent history available was equally favoring psychotic [F20-

F29] and affective illness. It was only later that a diagnosis of consensus be reached.

CASE

Mrs K, 24 year old hindu, married female of middle-class family, admitted in emergency medicine OPD (on 20th June 2010) with chief complaints of mutism, altered sensorium, fever and rigidity in body for 1day.

Total duration of illness was 1.5 yrs, episodic course and current episode was acute in onset, three months in durations, and possibly precipitated by post partum state. The episode started in end of March 2010, two weeks after birth of her 2nd child when family member noticed that she started remaining aloof for most part of the day. She did not speak with anyone in the family and lost interest and enjoyment in activity which made her happy. She did not do any household work. She occasionally expressed a feeling of how she would take care of her newborn child and she felt life was a burden to her. Her sleep wake cycle was disturbed with difficulty in initiating and maintaining sleep. She however remained on bed for most part of the day. Family member also noticed decreased appetite, poor care for self and her newly born child. As her condition worsened, family members brought her to Psychiatry OPD, GMCH, Chandigarh, after 3 weeks of illness. She was started on tab Escitalopram 10mg per day. However she did not come for follow up in OPD and stopped taking medicine as it did not give her complete relief.

In first week of May, she fell down from stairs and hence was taken to emergency of a hospital with complaint of jerky movement followed by loss of consciousness. She was discharged after ruling out the possibility of seizure, as per information given by family member. After that she was referred to psychiatry OPD of same hospital where she was put on tab Olanzapine 5 mg per day dose of which was increased up to 10mg within a week. Olanzapine was replaced by tab Valproate 1000mg and tab Escitalopram 10mg on next visit and within 10 days she showed improvement in her symptoms. She left this treatment on her own around mid-May. In end of May, she had complaint of gastro-enteritis and was treated by various private doctors. She remained on treatment given by private practitioner (non-psychiatrist) till mid-June and no psycho-tropics were received from mid-May to mid-June. In June she was referred to private psychiatrist and though she was symptom free but because of her past psychiatry illness, she was started on tab Risperidone 3 mg per day with tab Quetiapine 50mg per day. Unfortunately she relapsed to symptoms in the same evening in form of irritability, suspiciousness and disturbed sleep. She was taken to another psychiatrist on following day and prescribed tab haloperidol 15mg per day. However after one day (20th june) of the dose she developed current complaints in the form of fever, mutism, altered sensorium and rigidity and hence was brought to our medical emergency services. There was no history of First rank symptoms, any substance abuse or history suggestive of medical illness.

Past history- In Jan 2009, after 4 month of post partum period she had an episode characterized by sadness of mood, loss of interest and enjoyment in pleasurable activity, easy fatigability, decreased interaction with family member, sleep disturbance, pessimism, suicidal idea, decreased appetite and distuebed biological functions. She was diagnosed as case of severe depressive episode without psychotic symptoms in our OPD and started on tab Paroxetine 12.5mg per day, dose of which was increased up to 25mg per day on next visit. She showed improvement till March 2009 and left treatment of her own. She remained asymptomatic till Dec 2009.

In Dec 2009, she presented in our OPD with 6 months pregnancy along with complains of irritability, fluctuating psychotic symptoms like delusion of grandiosity, delusion of infidelity,

delusion of persecution, 2nd and 3rd person auditory hallucination with disturbed biological functions. She was diagnosed as a case of acute & transient psychotic disorder with symptoms of schizophrenia and put on tab Haloperidol 10mg per day. She showed improvement within one week (i.e. within 1 month of onset of symptoms) and maintained well till end of her delivery in March 2010. After that she followed in OPD with current episode.

Family history- no significant history suggestive of any psychiatric illness in family

Personal history- She is living with her in-laws. Her husband is working in private firm in Orisa. She is +2 pass. She has two daughters one daughter is 2 years old and another 4 month of age. She has normal menstrual cycles.

General Physical Examination- In emergency her pulse rate was more than 100/ min, blood pressure more than 140/90 but fluctuating and temperature was more than 39 degree Celsius. She had generalized rigidity in body.

On MSE she had passive attitude, did not speak, body was rigid, waxy flexibility, altered sensorium, dependent upon her family member for all her self care activity.

Management in Emergency Ward- Investigations revealed, leucocytosis (TLC >12,000), CPK MB- >900IU while other investigations LFT, TFT, SERFT, CSF study were in normal limit. With the available information, we kept the possibility of recurrent depressive disorder current episode severe with neuroleptic malignant syndrome (F33.2 with NMS). Her score on NMS rating scale[10] was 41/69. Since NMS was an emergency condition, psychotropics were discontinued and she was initially treated for NMS. Intervention in Emergency ward included supportive care and Tab Bromocriptine 10mg per day. By 28th of June (8 days since admission), she showed only slight improvement in rigidity and mutism, but no autonomic hyperactivity, no fever and improvement in NMS Score (NMS rating scale 15/69). Hence, she was transferred to psychiatry ward on 28/6/10. Mental state examination done at time of admission (Kirby's method)[11] showed passive attitude toward examiner, mutism, did not follow the command, constant behavior throughout the day, dependent upon her mother for her eating and excretory habits, rigidity and waxy flexibility. Score on Bush- Francis catatonia rating scale[12] was 18/69 at time of admission to our ward. Since the recent episode was depressive and current MSE showed only catatonic symptoms, she was put on Tab Escitalopram 10mg per day along with tab Lorazepam 3mg per day. Dose of tab Lorazepam was increased upto 6 mg per day within 7 days of admission in ward. She showed improvement in rigidity within two weeks of treatment but marginal improvement in mutism (Bush- Francis score was 10). MSE 2 weeks after admission to psychiatry ward revealed inappropriate smiling, poor speech output, irritability, visual and auditory hallucination of crawling snake on her bed. Tab Quetiapine 200mg per day was added keeping the possibility of acute transient psychotic syndrome unspecified for the current episode and anti-depressant was discontinued. Subsequently, dose was increased up to 400mg per day till 11th July. Patient had shown only slight improvement with treatment, so it was planned to start ECT. ECT was given on 10th and 17th of July.

With in 2 days of 2nd ECT, she showed marked change in her behavior. MSE revealed increased PMA, elevated mood, distractibility, authoritative speech, over talkativeness, tangentiality, flight of ideas and impaired abstraction with lack of insight. She started speaking in English which were unusual for her previous self. She would fight with family members on trivial issues, would be restlessness & have sleep disturbances. As her condition was worsening (BPRS13 36/148 and YMRS14 31/60), Tab lithium 900mg per day was added on 21st of

July and her dose of tab Quetiapine was increased to 800mg per day till 31st July. After increasing dose up to 800mg per day, she showed improvement in her symptoms. Score on BPRS scale had decreased from 36/148 on 18th July to 31/148 on 9th of Aug and score on YMRS decreased from 31 on 18th July to 12 on 9th July. She was euthymic at time of discharge (9th August) and on follow up visits in last one month.

DISCUSSION

Diagnostic dilemma: *changing phenomenology*

Patient's available history made it clear that her first episode was depressive and the second episode was acute and transient psychotic disorder. Her third episode lacked clarity. Initial part of this episode appeared as post partum depressive episode which was followed by symptom free period of one month. She however developed new set of symptoms (irritability, suspiciousness) and developed NMS within one day of onset of these symptoms (let's assume this as fourth episode). As her NMS resolved, catatonic symptoms emerged with no obvious affective/ schizophrenic symptoms. ECT then precipitated the fifth episode which was manic.

Her second episode, acute and transient psychotic disorder, had been one of the problems for reaching a comprehensive diagnosis. Although clinical experience suggests that in the affective disorders spectrum, the presenting clinical presentation features of manic episode often resemble ATPD[13], it often requires a period of time before the presumptive diagnosis of ATPD is revised to bipolar manic disorder. Manic patients often present with agitation, excitement, irritability and over activity all of which are common in ATPD.[14] Available literature on course of index episode of ATPD suggests that at 3 yr follow-up, 18 % of those diagnosed with ATPD have affective psychosis, 33% have either delusional disorder or schizophrenia and rest do not have any further episode.[15, 16] In Indian population, at mean 13.2 month follow-up 9.2 % had affective illness, 26.4% developed into schizophrenia and around 11.4 % had recurrent ATPD episodes.[17] We are not aware of incidence of ATPD episodes in bipolar disorder or as in present case- ATPD episodes that followed depressive illness. Although her ATPD episode was characterized by agitation, irritability, increased activity and grandeur delusion (fleeting in nature) her episode was typically polymorphic and did not evolve into a manic episode. In addition, the abrupt onset of episode, the presence of FRS (3rd person auditory hallucinations discussing about the patient), short duration of illness (< 1 month) and rapid response to treatment all conform to an ATPD episode. When later seen at other hospital this episode was possibly thought to be manic and hence patient was prescribed Valproate with possible diagnosis of bipolar affective disorder. It also appears that the episode of abnormal limb movements and altered consciousness after fall from stairs was neither a true seizure nor a post-traumatic seizure. It may have been a pseudoseizure.

Current episode started with postpartum depressive symptoms that resolved in 6 weeks and was followed by symptom free period of 1 month (without medication). She later had a single day period of symptomatology characterized by irritability, suspiciousness and sleep disturbance. Now, as per ICD-10, an episode is counted as new episode if the interval between episodes is more than 2 months or the symptoms are of the opposite polarity. The patients symptoms, however, cannot be classified as either manic, depressive (both do not meet the symptom or duration criteria) or may be adjustment disorder (she was forced to have medication when she did not feel the need to have them as she was symptom free). She subsequently developed NMS next day that resolved in a week but catatonic symptoms (either part of NMS or independent) continued. This catatonic period had no depressive mood or depressive cognition.

Indeed, she had visual hallucinations, auditory hallucination and inappropriate smiling, in this part of episode. Her symptoms 1 day prior to NMS, irritability, suspiciousness and biological dysfunction also continued. Considering her symptoms in 4th episode of illness, it is difficult to make out if they were a part of depressive episode i.e. continued 3rd episode or other psychotic illness. Since these symptoms lasted for less than a month and ICD-10 states psychosis to include purposeless motor activity, ATPD might be considered for diagnosis of this episode. Overall, this would be her second ATPD episode. However, the symptoms do not meet any specific subtype of ATPD. The subtype- 'other ATPD' allows for excitement but not stuporus catatonic symptoms. This episode makes a case-in-point on the raging debate of catatonia classification.[18]

Management Issues: *NMS, Depression, Psychosis, Mania*

Frequent change and rapid escalation of dose (Haloperidol 15 mg) by private practitioner had resulted in neuroleptic malignant syndrome in this patient. NMS is more common with first generation high potency anti-psychotics, their rapid dose escalation or initiation at high dose, withdrawal of dopamine agonist and presence of any neurological insult.[19] NMS has also been correlated with symptoms of agitation, dehydration, restrain, iron deficiency and presence of catatonia.[20] Gupta et al, in a recent study found that NMS was more frequent in mood disorders (73.4%).[21] Interestingly, this study did not have patients who developed NMS with primary psychotic illness [F20-29]. Supportive medical therapy is mainstay of management of NMS, so she was treated in emergency under proper medical care. She was put on dopamine agonist which have role in treatment of NMS as reported by various meta analysis.[22] Although bromocriptine, used in her case for NMS, is known to cause psychosis,[23] patient was off this drug 2 days prior to admission to psychiatry ward.

During the initial part of her ward stay, we kept the possibility of depressive episode (with catatonia) because it had been just 1 month since her post-partum depressive episode to remit. We did start her on anti-depressant but later on as patient was improving from catatonic symptoms and her MSE findings revealed predominant psychotic picture, we decided to discontinue her antidepressant. However Lorazepam was continued (as discussed above, we were sure of catatonic state). We chose Quetiapine at this stage, for three reasons: (a) it is a well known second generation anti-psychotic and hence would be useful for treatment of ATPD, (b) it has been documented to be of utility in bipolar depression[24] and (c) quetiapine (and clozapine) is relatively safe in patients with prior history of NMS.[25]

Since the response to Lorazepam was inadequate and dose escalation of Quetiapine would require more time, ECT had to be considered. After her 2nd ECT, patient developed florid manic symptoms. Angst et al[26] and many other have noted significant number of patients that developed manic/ hypomanic episode following ECT. These switches may occur in any disorder for which ECT is being given but is more common in those with affective illness.[27,28] In the current case the patient was not in depressive state. Also, immediate discontinuation of ECT did not stop the manic episode from being developed. Interestingly the manic episode that developed did not have any delusion, hallucination or motoric abnormality.

Resolution of Diagnosis

Overall, the manic episode following ECT and 2 depressive episodes (one of which was post partum) suggested a bipolar diathesis rather than an underlying schizophrenic illness. However the two ATPD episodes (one definite and other unclear) are not adequately represented in this diagnosis. Using either the ICD-10 or DSM-IV, we could not fit all of these 5 episodes into a

single diagnostic entity. Considering that those with ATPD may have recurrent ATPD episodes, could this patient be having an independent ATPD (recurrent) with bipolar affective disorder? However, with constrains of ICD-10 we made a final diagnosis of Bipolar affective disorder with current episode of mania without psychotic symptoms.

Point in favor of **bipolar affective disorder-**

- More than two mood episode, two depressive and one manic
- Complete recovery in between episode(episodic illness)
- Fleeting type of psychotic symptoms
- NMS was more in favor of BPAD

Point against- presence of FRS in past

Point in favor of **unspecified psychosis**

- H/o delusion and hallucination
- First rank symptoms were present
- H/o Catatonia

Point against-

- Psychotic symptoms were not continuous in nature. These were fleeting in nature
- At least one month duration of illness was not fulfilled
- Depressive and manic episode pointed toward affective illness
- Did not fulfilled the criteria of schizophrenia

This case highlight number of issues like challenging the Kraepelinian dichotomy, problems related to catatonia classification and exposing constrains of ICD in terms in diagnosing ATPD, course specifiers and possibility of ATPD being independent of other psychiatric disorder. In addition, rare complication of treatment (NMS and ECT induced switch) and issues of treatment compliance were evident in this case. Clinical observations and researches have shown that individuals with psychiatric illness may have both prominent mood and psychotic symptoms - raising the possibility, that there is not a neat biological distinction between schizophrenia and bipolar affective disorder. Further, molecular genetic studies are beginning to challenge and overturn the traditional dichotomous view.[29]

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