Review Article

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Neuro-Psychiatric Medicine : Old wine in new bottle

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ABSTRACT

Organic brain syndrome is the term loosely used for 'Neuropsychiatric Disorders' and most commonly for describing Delirium in clinical practice. Psychiatric manifestations cropping up in medically ill patients a physician set up makes the treatment difficult. Psychiatrists as well as Physician are the vital cogs in this management. This article reviews these conditions from a physician perspective with a thrust on delirium.

Key Words : Organic brain syndrome, Neuropsychiatric Disorders, Delirium

Introduction -

Historically organic disorders are described as disorders with identifiable pathological conditions while functional disorders are described as disorders without identifiable pathological conditions.

But now, Psychiatric disorder explanations are based on Bio-Psycho-Social model. With advancing neuro-imaging tools and sophisticated clinical testing, psychiatric disorders are increasingly being found to have solid biological basis likewise the 'Neurological disorders' have been proved to have significant psychiatric morbidity. Hence, These disorders are also described as neuropsychiatric disorders.

Alwyn Lishman used the term 'Neuropsychiatry' to define a discipline at interface of Neurology & Psychiatry that addressed disorders owing their origins to 'Brain malfunction of clearly identifiable nature'.[1]

For example, Stroke can be considered as a purely neurological disorder. But behavioral changes arising out of stroke would be better addressed under Neuropsychiatry discipline. A Neuropsychiatric disturbance is strongly colored by factors specific to the person and his environment. So, a physician not well versed in psychological symptoms would often find it difficult to manage the patient to his complete satisfaction. The following article would provide a framework in understanding and managing common neuropsychiatric disorders.

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Some commonly used terms in this context are[2] -

1. Confusional state : A state of disordered orientation. It usually means that patient is unable to think with his customary clarity & coherence.
2. Clouding of consciousness : Reduced clarity of awareness of environment. It is mildest stage of impairment in consciousness.
3. Coma : The deepest degree of stupor in which all consciousness is lost and there is very little spontaneous motor activity. Coma has grades of depth.
4. Delirium : is disturbance of consciousness with reduced ability to sustain or shift attention and is often associated with disorientation and perceptual disturbances. There is often impaired memory & language function as well.

Approach to any case of Neuropsychiatric disorder starts with a sound clinical assessment[1]

1. **History Taking :** A semi-structured format is easily available where all important points are covered and points of interest can be elaborated in detail as needed. A few minutes spent extra in detailed history taking are often well rewarded later. It is very important to obtain history from persons who're well acquainted with patient's lifestyle. This can include spouse, parents,

relatives and friends. It is often advisable to provide privacy and complete attention for accurate details.

2. **Physical Examination :** Other than of the presenting symptoms, a careful and complete physical examination can often uncover subtle signs and sometimes other unrelated illnesses. Often a patient labelled with psychiatric diagnosis get neglected for other problems and this can prove debilitating in long term.

3. **Mental State examination :**
   1. Level of consciousness
   2. Appearance & general behavior
   3. Mood
   4. Speech -clarity, coherence, volume, adequacy of response, relevance, content
   5. Perceptual disturbances - illusions or hallucinations
   6. Memory
   7. Insight

Tools to aid Diagnosis & management

1. Relevant blood investigations
2. Neuro-radiological assessment-e.g CT, MRI,PET
3. Psychometric testing- e.g MMSE,WMS
4. Electro-encephalography
5. Lumbar puncture

Amongst all these disorders, practically, the term Organic brain syndrome is synonymously used for Delirium.

A. Delirium -

Delirium is often encountered in hospitalized patients and it is a difficult puzzle . It is a bad prognostic sign with mortality rate as high as 50% on 1 year follow up[3]. It occurs in about 15 per cent of all general medical and surgical inpatients and a substantially higher proportion of those who are elderly[4]. It is common in those with severe illnesses, postoperatively. In intensive care and in other settings where patients are severely ill.

Common factors likely to lead to delirium[4].

- Advanced Age
- Sensory Impairments
- Metabolic Derangements
- Substance Abuse
- Pre-Existing Chronic Illnesses
- Addition Of More Than Three New Drugs

DSM-IV (Diagnostic and Statistical Manual IV) Criteria for Delirium[5] :

a. Disturbance of consciousness (i.e., reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention.

b. A change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a preexisting, established, or evolving dementia.

c. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.

d. There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition.

Clinical features :

- Impairment of consciousness : mild impairment of consciousness to near unconsciousness. Symptoms are often worse at night. There is disorientation in time, place, and the identity of other people.
- Appearance and behavior : Behaviour may be marked by agitation or hypoactivity, by a fluctuation between these states, or by a mixture of them for example, a drowsy patient plucking aimlessly at the bedclothes.
- Mood is frequently labile, with perplexity, intermittent periods of anxiety or depression.
- Speech : the patient may be incoherent.
- Perception : visual perception is the modality most often affected. Illusions and misinterpretations are frequent. For example, a patient may become agitated and fearful, believing that a shadow in a dark room is actually an attacker. Visual hallucinations also occur. The small living creatures which may be seen in delirium tremens are the best-known example. Auditory and tactile hallucinations also occur.

- Concentration is impaired, for example, errors on tests such as 'serial sevens subtraction' or 'days of the week backwards'.
- Memory disturbances are seen, with impaired registration (e.g. digit span), short-term recall (e.g. name and address), and long-term recall (e.g. current news items). After recovery from the illness there is usually (but not always) amnesia for the illness.
- Insight is usually impaired. The patient will have no understanding of why a psychiatric assessment has been requested

Management of Delirium

Delirium is a syndrome and not a disorder. The primary line of treatment is on effective management of underlying disease process.

a. Non-Medical Management[4] -

- Patients need reassurance and reorientation to reduce anxiety and disorientation; this should be repeated frequently.
- In hospital, a predictable and consistent routine should be planned. It may be that this is best provided by one to one nursing the patient in a quiet single room. Relatives and friends should be encouraged to visit frequently and help to reassure the patient. There should be enough light throughout the night to enable the patient to know easily where he is but not so much that sleep is disturbed.
- It is important to give as few drugs as possible, since these may worsen the delirium.
- Relatives find delirium upsetting and they require a clear explanation for the disorder so as to relieve their own anxiety and to help them to join in reassuring and reorienting the patient.

b. Medical Management[6] -

Starting low & going slow is important. To control Agitation and to calm down the patient, Haloperidol remains the most widely used agent. An Initial IM dose of 2.5 mg - 5 mg can be used. Due precaution is to be exercised when using this high potency antipsychotic as it can easily lead to dystonia or other extrapyramidal side-effects (EPS).If EPS occurs or patient already prone to EPS, it is advisable to use Promethazine 25 mg with Haloperidol. Alternative antipsychotics that can be used to control agitation are Olanzepine (available as IM injectable formulation too), Risperidone (available as oral solution), Aripiprazole or Quetiapine (Oral formulations only).

When shifting patient from Injectable to oral preparation, 1.5 times of injected dose may be used initially and later down titrated rapidly as patient stabilizes.

For managing Insomnia, short to intermediate half life benzodiazepines like Lorazepam are preferred .

B. Substance withdrawal :

Alcohol & other substance use not only complicates disease presentation but also adds a dimension of managing withdrawl symptoms in addition to routine patient management. Sometimes they might be the cause for hospital admission. This is even more complicated in patients getting admitted in emergency where the doctor has to often rely on his skills and experience as sufficient history details may not be available.

We'll be discussing about alcohol here as it is the commonest substance of abuse encountered in hospital setting. For other psychoactive substance use management, readers are requested to use appropriate resources.

I) Alcohol -

A person can be said to be dependent on alcohol if he's developed tolerance to the effects of alcohol, gets withdrawl symptoms (described below) when stops taking alcohol and continues to take alcohol despite knowledge of the physical, mental and social harm caused by it.

Clinical features of Alcohol withdrawl[5] -

A typical patient having alcohol withdrawl symptoms may present with some or all of the following signs and symptoms.

1) autonomic hyperactivity (e.g., sweating or pulse rate greater than 100)
2) increased hand tremor

3) insomnia
4) nausea or vomiting
5) transient visual, tactile, or auditory hallucinations or illusions
6) psychomotor agitation
7) anxiety
8) grand mal seizures

Alcohol withdrawl symptoms can start as soon as 2 hours after last drink but usually peak by 48-72 hours. A severe form of withdrawl called as Delirium Tremens (DT's) has mortality rate up to 5%.

Managing Alcohol withdrawl[6] -

1. An important point to be established through history is the quantity of alcohol consumption, timing and frequency of consumption and approximate hours since last intake as this will have prognostic implications.
2. Use of Thiamine is paramount in all alcoholics. To be given as Intramuscular injection 100 mg after test dose everyday. It is important to ensure sugar levels are good before giving Thiamine.
3. Use of other multi vitamins , especially B12, is must as most of these persons are nutrtionally deprived. Preferable to give injectable as oral absorption is erratic.
4. It is important to give high carbohydrate diet in these patients to reduce liver strain.
5. Benzodiazepines are main stay in managing alcohol withdrawl symptoms. With normal Liver function, long acting drug such as chlordiazepoxide is preferred. In case of compromised liver function, lorazepam is preferred due to its predominant renal excretion. Alcoholics have cross-tolerance to effects of BZD's hence they require fairly higher dosage. Once the patient is out of delirium, it is preferable to reduce doses by 20% everyday.
6. Beta blockers help in reducing autonomic hyperactivity and reducing gastric bleed, if present.
7. In case of perceptual disturbances, high potency antipsychotics like Haloperidol or Olanzepine (both available in injectable and oral formulations) in small repeated doses are preferred.
8. Withdrawl seizures may be treated with Diazepam. Anticonvulsants can be withdrawn within few months if no other risk factors are present.
9. Use of anti-craving drugs like topiramate, Acamprosate or Naltrexone may be started during withdrawl period itself once the symptoms are attenuated. Use of disulfiram is not indicated without making patient aware of consequences of alcohol-disulfiram reaction.

C. Traumatic Brain injury

Mild Trauma

Post-concussion syndrome[7,8] -

concussion is a mild traumatic brain injury , usually without loss of consciousness. There are no significant clinical findings and often gets ignored . The usual list of complaints include

Headaches
Dizziness
Fatigue
Irritability
Anxiety
Insomnia
Concentration difficulties
memory disturbances
noise and light sensitivity

Management -

1. Patient need to be given patient hearing and need to be explained that this is a time limited condition and most symptoms would disappear within 3 months.
2. Amitriptyline can be used for headache.
3. SSRI's and low dose BZD's can help in managing anxiety and depressive symptoms.

Severe Trauma

The prognosis following TBI is related to initial Glasgow coma scale score. The most commonly injured areas of the brain are the anterior poles of the frontal and temporal lobes, where they abut bony ridges of the skull.

The initial management of traumatic brain injury is surgeon's domain. The subacute phase is often managed by controlling delirium as outlined above.

Neuropsychiatry would be more closely linked with long term sequelae of TBI.Re-adjustment to a life with disability is hampered by many factors[8,9] viz.

a. reduced attention span and memory

b. emotional dysregulation

c. physical disability

d. specific cognitive deficits relevant to damaged area

Patients with left hemisphere lesions are more closely associated with overall psychiatric disability than right hemisphere lesions and patients with injury to the left temporal lobe were particularly at risk.

However, intellectual disorders were found more commonly after left hemisphere damage, while affective disorders, behavioural disorders and somatic complaints were more frequent after right hemisphere damage.

Injury to the frontal lobe can lead to distinct varieties of 'Frontal Lobe Syndrome' characterized by 'Apathy' or Disinhibition[10].

Apart from cognitive deficits relevant to area damaged, Depression remains a very common disorder in TBI. Appropriate identification and treatment remains vital in speeding patient recovery.

Managing TBI patients -

1. Agitation/Disinhibition[9,11]

Agitation or disinhibition are managed well with used of small dose antipsychotics. Care is to taken in keeping dose low and uptitrating slowly as these patients are more susceptible to side effects.

Benzodiazepines are to be avoided in view of risk of addiction as well as cognitive decline.

2. Depression/Anxiety[12]

Depressive symptoms often remain hidden in these patients due to inability of a clinician to separate the physical and psychological manifestations of neuronal damage. As many as 20% patients of TBI meet full criteria for depression as per DSM-IV-TR[7]. restricted expressive capability of the patient also delays diagnosis. Nevertheless, if the patient is showing below par recovery, a trial of antidepressants is advised.

3. Post Traumatic Stress Disorder[13]

The classical triad of re-experiencing the trauma, avoiding stimuli e.g. driving and hyperarousal symptoms like sleep disturbance, irritability are often seen in patients suffering TBI. Long term sequelae are likely to include Generalized anxiety disorder and phobias.

Other than medical management, a neuropsychiatrist professional plays an important role in explaining and guiding the family on the road to recovery. Special focus on care-giver burden often helps in better patient care and outcome.

D. Infections -

Any meningitis or encephalitis can have initial psychiatric presentation. Prominent amongst these are Herpes Simplex Encephalitis and Tuberculous Meningitis.

The symptoms often include anosmia, olfactory and gustatory hallucinations, and personality changes with aggressive behavior is not unknown. and can also involve bizarre or psychotic behaviors[14]. Treatment of the respective infection along with the initial behavioral management is needed.

E. Encephalopathy -

Encephalopathy can produce alterations in mental processes, behavior, and neurological functions. The diagnosis should be considered whenever recent and rapid changes in behavior, thinking, and consciousness have occurred. The earliest signals are likely to be impairment of memory, particularly recent memory, and impairment of orientation.

Encephalopathies associated with paraneoplastic syndromes are well associated with neuro-psychiatric presentations. common presentation will include depression, personality changes, hallucinations[14].

Limbic encephalitis can present with memory loss, sleep disturbances, confusion and seizures. It can develop over weeks leading to misdiagnosis as

psychiatric disorder[15].

Hashimoto encephalopathy & NMDAR associated encephalopathy can present with paranoid symptoms, bizarre behavior and mood swings.

F. Auto-immune -

A common auto-immune disorder having psychiatric manifestations is Systemic lupus erythematosus (SLE).

The major symptoms are depression, insomnia, emotional lability, nervousness, and confusion. Most psychiatric manifestations are seen within first 2 years of disease onset[16].

Treatment with steroids commonly induces further psychiatric complications, including mania and psychosis. Hence a careful approach in tandem with a psychiatrist is necessary.

G. Endocrine Disorders -

a. Diabetes Mellitus

The number of diabetics is exploding and there are many ways in which diabetes and psychiatric disorders, notably depression complement each other. Presence of depression is likely to lead to medication and life style non compliance and worse glycemic control. Uncontrolled sugar levels can increase levels of stress hormone cortisol which has been linked to depression[17]. DM also increases stress by putting a premium on life style modification and restrictive complications like neuropathy, retinopathy etc.

Other psychiatric illnesses like Schizophrenia & Bipolar disorder have elevated risk of diabetes through both, genetic association and second generation antipsychotic associated metabolic side effects.

b. Thyroid Disorders[18]

Somatic symptoms of hyperthyroidism include sweating, fatigue, heat intolerance, weight loss, weakness, fine tremor, and tachycardia. The psychiatric symptom pattern in hyperthyroidism most often resembles generalized anxiety, but depression, irritability, hypomania, and cognitive dysfunction are all common. In severe hyperthyroidism (thyrotoxicosis, "thyroid storm"), patients may be manic.

The somatic symptoms of hypothyroidism include weakness, fatigue, cold intolerance, weight gain, constipation, and somnolence. The psychiatric presentation of hypothyroidism closely mimics depression, but cognitive dysfunction is not uncommon. Severe hypothyroidism rarely presents with psychosis ("myxedema madness").

H. Dementia/pseudodementia[19] -

Dementias are disorders of the brain that affect multiple cognitive domains. Memory impairment is a key feature of many, but not all, dementia syndromes. Other cognitive domains that can be impaired include language, cognitive processing speed, visuospatial perception, reasoning, and executive functions. Behavioral and personality changes may also occur. Alzheimer's disease and cerebrovascular dementia are the most common types.

For neurosychiatric problems like aggressive behavior, sleep disturbances low dose Quitiapine 25-50mg/d or aripiprazole 2.5-5 mg/d are safer additions. Anticholinergic drugs , Benzodiazepines worsen the confusional behavior and should be best avoided.

Elderly patients might have memory complaints secondary to Depression ,often confused with Dementia, hence called pseudodementia. Unlike Dementia, it is of short duration, rapid progression, with negative cognition with compatible distressed behavior.

I. Seizures -

Epilepsy :

Psychiatric symptoms can present in relation to seizure-ictal /post ictal or in between the seizure episodes-interictal.

Postictal psychoses/delirium are the most common form of psychomorbidity in patients with epilepsy. The clinical presentation is distinctive, with a sudden onset of mixed psychotic and affective features, most notably agitation, following a brief lucid interval after seizures. Usually self-limiting,

treatment with antipsychotic medication is usually not indicated. However, the degree of agitation and behavioural disturbance may be such that hospital admission and sedation with benzodiazepines are required.

Psuedoseizures are episodes of unresponsiveness mimicking semiology of seizure commonly observed in young females but can be differentiated by the presence of precipitating stressor and attention seeking behavior as well as absence of injury, incontinence, sleep attacks[21].

Psuedoseizures should not be dismissed lightly. Trying to ascertain the reason behind such presentation helps in uncovering and treating significant psychiatric co-morbidity.

Conclusion -

Neuropsychiatric disorders are common and have vastly different presentations in general practice. Apart from medical management, support, counseling and behavioral modification remain essential part of giving these patients best possible outcomes. The team work of psychiatrist, physician/ Neurologist and trained supporting staff is essential for its management.

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