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Rizwan Taj

Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Mamoona Manzoor

Pakistan Institute of Medical Sciences, Islamabad, Pakistan

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PSYCHIATRIC DISORDERS IN NEUROLOGY

Prof. Rizwan Taj, Dr.Mamoona Manzoor
Psychiatry Department, Pakistan Institute of Medical Science

Correspondence to: Psychiatry Department Pakistan Institute of Medical Science G-8/3 Islamabad. Email:rizwantajpims@gmail.com
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ABSTRACT

Psychiatric disorders (PDs) are very frequent in neurological illnesses. Depression, anxiety and cognitive impairment are frequently seen in many neurological disorders such as stroke, Parkinson disease (PD), epilepsy and multiple sclerosis (MS). In addition, hallucinations, delusions, obsessive-compulsive disorder, sleep disorders, Impulse control disorders (ICDs), somatization, bipolar disorder, behavior problems and psychological problem are also seen. Depression in stroke and epilepsy has bidirectional relationship. Lesion location affects both frequency and severity of depression in stroke patients. Hallucinations and delusions are frequent in patients with Parkinson disease and epilepsy. In Parkinson's, these are associated with disease itself and are also secondary to treatment while in epilepsy, psychosis can be peri-ictal and interictal or post-ictal. Suicidal ideation are prominent in MS and epilepsy patients. Suicide is considered to be an important contributor to the increased mortality of persons with epilepsy. Features of depression and dementia may overlap with symptoms of neurological illnesses especially in multiple sclerosis, parkinsonism and stroke thus confounding the identification of these disorders. The presence of co morbid psychiatric illnesses in neurological patients should be of particular concern to physicians as they increase severity of neurological problem, lead to more functional impairment and increase mortality. Clinicians must aim to identify those patients with co morbid illness most likely to benefit from interventions and psychiatric or psychotherapeutic treatment should be provided to them. Psychiatric disorders (PDs) are very frequent in neurological illnesses. Depression, anxiety and cognitive impairment are frequently seen in many neurological disorders such as stroke, Parkinson disease (PD), epilepsy and multiple sclerosis (MS). In addition, hallucinations, delusions, obsessive-compulsive disorder, sleep disorders, Impulse control disorders (ICDs), somatization, bipolar disorder, behavior problems and psychological problem are also seen. Depression in stroke and epilepsy has bidirectional relationship. Lesion location affects both frequency and severity of depression in stroke patients. Hallucinations and delusions are frequent in patients with Parkinson disease and epilepsy. In Parkinson's, these are associated with disease itself and are also secondary to treatment while in epilepsy, psychosis can be peri-ictal and interictal or post ictal. Suicidal ideation are prominent in MS and epilepsy patients. Suicide is considered to be an important contributor to the increased mortality of persons with epilepsy. Features of depression and dementia may overlap with symptoms of neurological illnesses especially in multiple sclerosis, parkinsonism and stroke thus confounding the identification of these disorders. The presence of co morbid psychiatric illnesses in neurological patients should be of particular concern to physicians as they increase severity of neurological problem, lead to more functional impairment and increase mortality. Clinicians must aim to identify those patients with co morbid illness most likely to benefit from interventions and psychiatric or psychotherapeutic treatment should be provided to them. Psychiatric disorders (PDs) are very frequent in neurological illnesses. Anxiety and depression are most common, but hallucinations, delusions, obsessive-compulsive disorder and delirium or confusional state are also frequent comorbidity in many neurological conditions such as stroke, epilepsy, multiple sclerosis (MS), Parkinson disease (PD). With a growing body of research showing strong links between neurological and psychiatric illnesses, there is need to understand the co morbidity of psychiatric illnesses in neurological disorders.

STROKE

Stroke is the third leading cause of death in developed countries. Psychiatric syndromes associated with stroke lead to significant psychological distress, functional impairments, poor rehabilitation outcomes, and excess mortality. Most common psychiatric disturbances seen after stroke include cognitive impairment and dementia, depression,

mania, anxiety disorders, and pathological laughing and crying - now referred to as involuntary emotion expression disorder or IEDD. Vascular cognitive impairment and post stroke dementia, a condition that can be found in 20% to 30% of stroke patients.^(1,2) Cognitive evolution 2 years after stroke is rather heterogeneous, but a substantial number of patients remain stable or even improve 3 with time. The determinants of progression of cognitive impairment are still

poorly known. Age, previous cognitive decline, polypharmacy, and hypotension during admission are risk factors for progression.⁽⁴⁾ The predictor of cognitive change which has a protective role, is years of education.⁽⁵⁾ Post stroke dementia increases the risk for recurrent stroke and mortality.⁽⁶⁻⁸⁾ Appropriate management of vascular risk factors is an important preventive treatment strategy to decrease the risk of stroke recurrence and cognitive impairment. Effective secondary prevention could help to prevent or delay the onset of severe global cognitive impairment. Psychiatric disorders, mostly depression, are fairly common in stroke survivors. Depression and anxiety are significantly correlated to the patient's psychopathological profile. Some form of depression is considered to occur in at least one-quarter of patients in the first year after acute stroke⁽⁹⁾, with the period of greatest risk being the first few months after onset^(9,10,11). Lesion location is most important in determining frequency and severity of depression. Researches show that patients with left hemisphere frontal lobe infarctions who are within 2 years of the stroke, are at high risk for developing post stroke depressive disorders⁽¹²⁾. Other variables including functional physical impairment, intellectual impairment, quality of social support, and age contribute to or modify depression⁽¹³⁾. The presence of depression in stroke patients should be of particular concern to physicians as depression reduces the desire and capacity to participate in rehabilitation⁽¹⁴⁾, and affected people are less inclined to socialize (socialization is thought to be protective of mood disorders. It may put people at a greater risk of adverse health behaviors, such as poor adherence to medications. So physicians should be careful in identifying depression in patients for stroke. Remarkable features of emotional behavior, such as disinhibition, denial, indifference, overt sadness and aggressiveness, are not rare during the acute phase of stroke. Some of these early behaviors, such as denial, may relate to the late development of depression, anxiety and other disorders⁽¹⁵⁾. Anxiety disorders, especially agoraphobia, are relatively common (20% if diagnosed in the presence of depressive disorder), but are not related to lesion location or volume⁽¹⁶⁾. Emotional blunting or apathy has been reported to constitute a frequent sequel of stroke lesions. Apathy is found in about 23 % patients with acute stroke lesions and may coexist with important emotional and cognitive post stroke disturbances⁽¹⁷⁾. The hypo activity in the frontal lobe and anterior temporal regions may contribute to symptoms of apathy after stroke. Unilateral, usually sub cortical, strokes can also produce pathologic laughter⁽¹⁸⁾. Parkinsonism Parkinson's disease PD is the second most common neurodegenerative disease and is characterized by the cardinal signs of bradykinesia, rigidity, tremor at rest, and abnormalities of balance, posture, and gait⁽¹⁹⁾. The psychiatric symptoms and syndromes associated with Parkinson's disease are either those unrelated to Parkinsonism, reactive mental disturbances or psychiatric

symptoms caused by medication. Mild cognitive impairment (MCI) is common in patients with PD without dementia, affecting a range of cognitive domains, including memory, visual-spatial, and attention/executive abilities⁽²⁰⁾. Cognitive impairment in subjects with early, drug-naïve Parkinson disease (PD) is two times greater than the general population⁽²¹⁾. Although, Patients with PD and MCI had a higher risk of developing dementia than cognitively intact PD patients, suggesting that MCI in PD is an early manifestation of dementia⁽²²⁾. But prevalence of patients of PD developing dementia even in absence of initial MCI is much higher than general population, (about 75% in a study after 8 years). Patients with akinetic-dominant PD and hallucinations prior to the baseline evaluation are at higher risk of developing dementia than those with tremor-dominant parkinsonism and without hallucinations⁽²³⁾. Depression is common in PD, with a prevalence of 25% to 50% over the course of the illness and there may be overlap in the pathophysiology of the two conditions. As in the case of epilepsy and stroke, depression and PD appear to have a bidirectional relationship. That is, not only are patients with PD at greater risk to developing depression, but patients with a depressive disorder have been found to be at greater risk of developing PD.⁽²⁴⁾ Anxiety disorders, particularly generalized anxiety, panic, and social phobia, occur in up to 40% of patients with Parkinson's disease (PD) and often coexists with depression. Current evidence suggests that anxiety may not be a psychological reaction to the illness but rather may be linked to specific neurobiological processes accompanying PD.⁽²⁵⁾ Impulse control disorders (ICDs), including compulsive gambling, buying, sexual behavior, and eating, can occur as a complication of Parkinson's disease (PD). In addition, other impulsive or compulsive disorders have been reported to occur, including dopamine dysregulation syndrome (DDS) and punting. Male gender, younger age at PD onset, a pre-PD history of ICD symptoms, personal or family history of substance abuse or bipolar disorder, and a personality style characterized by impulsiveness are some of the risk factors for an ICD in patients of PD⁽²⁶⁾. Various studies have sought to identify obsessive-compulsive symptoms (OCS) in PD. Tomer et al.⁽²⁷⁾ described higher scores of OCS in PD; Alegret et al. found that patients with severe PD presented more obsessive traits than controls, and severity of OCS was related to the severity and duration of PD. Tomer et al. also observed an association between the severity of motor symptoms on the left side of the brain and OCS related to cleanliness and repetition, whereas they found OCS related to order/routine to be correlated with the right side⁽²⁷⁾. However Maia AF found that OCD, OCS, and related disorders were not higher in PD⁽²⁹⁾. Their findings revealed an association of some OCS with left side motor symptom predominance in PD patients, particularly for symmetry and ordering/arranging. allucinations and delusions are frequent in patients with Parkinson disease.

Hallucinations, usually of visual modality, occur in about 30% of patients with PD, and delusions have been found in 10%.⁽³⁰⁾ In a recent study,⁽³¹⁾ visual hallucinations were reported in 26% of patients with PD. Hallucinations and delusions in patients with PD were reported before the introduction of dopaminergic therapy but are usually considered to represent behavioral complications of drug treatment.⁽³⁰⁾ Some evidence^(30,31,32) suggests that dementia, advanced age, administration of high daily doses of levodopa, premorbid psychiatric illness, and multidrug therapy are risk factors for psychotic symptoms in PD. Knowledge of these phenomena and their association with other clinical characteristics of PD is important for the diagnosis and treatment of patients and can provide information regarding the future needs for health care. Sleep problems are much more common in PD patients and correlate with increased severity of disease, levodopa dose, rigidity score, and bradykinesia score.⁽³³⁾ Inappropriate crying and laughing (also termed pseudobulbar affect (PBA)) are present in most movement disorders, but especially prevalent in parkinsonism. PBA patients have more chronic depressive symptoms and tiredness⁽³⁴⁾. Nonmotor features of PD such as dementia, depression, and psychosis may result in significant disability.⁽³⁵⁾ Furthermore, many PD symptoms overlap with features of depression and dementia including symptoms of withdrawal, lack of motivation, flattened affect, decreased physical activity, or bradyphrenia, thus confounding the identification of these behavioral and cognitive disorders

EPILEPSY

Psychiatric illnesses are very commonly associated with epilepsy. Mood disorders are the most common culprit (24–74%), particularly depression (30%), followed by anxiety disorders (10–25%), psychoses (2–7%) and personality disorders (1–2%). This comorbidity appears to be related to endogenous and exogenous (including iatrogenic) factors and to the severity and chronicity of epilepsy. Conditions such as schizophrenia-like psychosis of epilepsy and interictal dysphoric disorder are represented only in epilepsy⁽³⁶⁾. Depression is more frequent in patients with epilepsy compared to the general population. Population studies revealed a frequency of depression varying from 9% to 22% in patients with epilepsy, while hospital series usually report higher rates of depression (27% to 58%) for patients with epilepsy⁽³⁷⁾. For some authors, this prevalence is higher (60–80%) in patients with refractory TLE, although this is still controversial⁽³⁶⁾. Patients with longer duration of epilepsy are at higher risk of having depression. Relationship between epilepsy and depression is bidirectional⁽³⁸⁾. Thus, patients with epilepsy are more likely to develop depressive disorders, and patients with a history of depression or suicide attempt have a higher risk of developing epilepsy. Depres-

sion has greater negative impact on quality of life than seizure frequency or the number of prescribed antiepileptic drugs⁽³⁹⁾. In addition, depression in epilepsy is associated with reduced seizure control⁽⁴⁰⁾. Although mood disorders represent a frequent psychiatric comorbidity among patients with epilepsy, data regarding bipolar disorders are still limited. Emerging evidence suggests that mood instability, mixed irritability, or even mania is not uncommon in patients with epilepsy⁽⁴¹⁾. Patients with epilepsy may be subject to an increased risk of premature death from the underlying cause, or from the epilepsy in itself. Mortality in patients with newly-diagnosed epilepsy is found to be high, mainly due to the underlying cause⁽⁴²⁾. Suicide is considered to be an important contributor to the increased mortality of persons with epilepsy. The collective data of different studies yield an average rate of approximately 1.2% of deaths due to suicide among people with epilepsy, compared with 1.1–1.2% in the general population. Potential risk factors for suicide are primary mood disorders, family issues, physical health, personality, life stress, previous suicidal behavior, and access to firearms. Assessing severity of risk helps to determine the appropriate level of intervention. Epileptic psychoses are categorised as peri-ictal and interictal according to their relationship with the occurrence of seizures. However, while post ictal psychosis constitutes a rather homogenous clinical entity, interictal psychosis is apparently quite heterogeneous. The treatment of peri-ictal or acute mental disorders is based on epileptic seizure control, while the treatment of interictal or chronic disorders has more in common with managing disorders which are purely psychiatric in origin. In addition to improving the patient's quality of life and reducing disability, achieving strict control over seizures may also prevent the development of interictal psychosis. Longer evolution of seizures and the presence of bilateral hippocampal sclerosis may increase propensity to develop psychoses in patients with refractory partial epilepsy⁽⁴⁴⁾. Memory problems are one of the chief complaints of patients with temporal lobe epilepsy (TLE). Epileptic seizures might trigger neurodegenerative changes leading eventually to memory impairments⁽⁴⁵⁾. Interictal epileptiform discharges are associated with neuropsychological disorders like cognitive impairment and behavioral problems even in absence of clinical epilepsy⁽⁴⁶⁾. Obsessive-compulsive symptoms OCS are more likely to develop in patients with epilepsy than in healthy people. The development of OCS appears to elicit psychosocial problems directly or indirectly by provoking depression or uncontrolled seizures⁽⁴⁷⁾. Children with seizures are at risk for behavior problems. Studies show that children with seizures were 4.7 times more likely to have a behavior problem as compared with controls⁽⁴⁸⁾. The specific behaviors and traits that were most problematic for children with seizures are being hyperactive (cannot concentrate, easily confused, impulsive, obsessive, and restless) and depend-

ent (clings to adults, cries a lot, demands a lot of attention, too dependent on others). Multiple Sclerosis (MS) Multiple Sclerosis is a chronic autoimmune demyelinating disease of the central nervous system. In the variable course and progression of symptoms in this disease, patients may experience episodic, chronic, or progressive symptoms including fatigue, pain, spasticity, loss of use of their arms and legs, loss of vision, impaired bowel and bladder function, and sexual problems. Symptoms of depression, anxiety and sleep impairment are common in MS patients. Less studied symptoms such as somatization, obsession, compulsion, interpersonal sensitivity, anger-hostility, phobic anxiety, paranoid ideation, psychoticism, low self-esteem and distorted eating attitudes are also more frequent compared to the healthy controls. Symptoms increase as degree of disability rises and ambulatory capacity declines⁽⁴⁹⁾. Neuropsychiatric symptoms of MS can be grouped into two categories: cognitive and mood. Amongst the latter, the most widely noted are depression, bipolar disease and pseudobulbar affect. Other psychiatric symptoms include irritability, apathy, disinhibition and euphoria. Individuals with MS have a prevalence of depression, that is higher compared to the general population. Prevalence of significant depressive symptoms in MS has been reported as 41.8% with 25% meeting criteria for major depressive disorder⁽⁵⁰⁾. Suicidal ideation is prominent in MS patients with the prevalence of 30%. Bipolar disease is also 2-3 times more common in this population⁽⁵¹⁾. Cognitive deficits occur in at least half of all adult individuals with MS. Recent studies have highlighted deficits in attention, executive function and working memory in the pediatric age group, even in the absence of significant physical impairment⁽⁵²⁾. Such cognitive loss may be a consequence of disease affecting the maturation process of the white matter pathways in the frontal lobe. Prevalence of poor self-reported sleep quality as well as sleep disorders, such as insomnia and restless legs syndrome, is higher in patients with MS compared with the general population. Poor sleep quality has been associated with greater disease severity, pain, and poorer mental and physical quality of life in patients with MS⁽⁵³⁾. Insomnia symptoms are commonly associated with depression and anxiety, and thus may cause or exacerbate sleep disturbance in patients with MS⁽⁵⁴⁾. Demoralization is particularly complex in the context of MS because of the intermittent nature of the condition, which can make it particularly difficult to cope with. Over time many MS patients find it increasingly difficult to adapt psychologically to new episodes and that this can adversely impact their relationships and psychosocial functioning.

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Dr. Rizwan Taj: Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review

Dr. Mamoona Manzoor: Data collection, data analysis, manuscript writing, manuscript review