Neuropsychiatric Aspects of a Common Problem: Stroke

Anatolii Tsarkov & Petro Petlovanyi

Abstract—Stroke ranks second in the list of major causes of disability and death in the world. Stroke is the sudden onset of focal or generalized abnormalities of brain function caused solely by vascular causes that are associated with cerebral blood flow and last for more than 24 hours. Stroke can also be diagnosed if symptoms persist for more than 24 hours, but with a confirmation of neuroimaging studies, the ischemic area has been clearly located and documented, symptoms disappeared after thrombolytic therapy, or the patient died within 1 day of symptoms onset. Often, patients with stroke experience emotional and behavioral disorders. Their frequency varies depending on factors such as the patient’s age, gender, socioeconomic status, post-stroke disability, and cognitive changes that play a crucial role in patients’ well-being and can significantly affect the recovery process. This article describes common psychiatric presentations in patients in a post-stroke period. Some available evidence-based data on the treatment of these conditions and identified possible risk factors that influence their development are presented.

Index Terms—Stroke, Post-Stroke, Neuropsychiatry, Pathological Laughter and Crying, Catastrophic Reaction, Anxiety, Depression, Cognitive Impairment

I. INTRODUCTION

According to the World Health Organization (WHO) [1], “stroke is a clinical syndrome of rapid development of signs of focal or global loss of brain function lasting 24 hours or more or leading to death in the absence of non-vascular causes”. In the past decade, there has been a clear decline in morbidity and mortality from acute cerebrovascular accidents, which is due to improved control of hypertension and other risk factors, as well as improvement of urgent treatment interventions. However, the prevalence of this state remains very high. For example, in the US, more than half a million new cases of stroke occur every year, of which at least 140,000 end in lethal in an acute period [2]. Among those who have survived, more than 2/3 will suffer from a certain level of permanent disability that will require intensive rehabilitation [2].

Recent studies suggest that neuropsychiatric complications of acute cerebrovascular abnormalities have a negative effect not only on the social functioning, but also on the overall quality of patients’ life. The group of these disorders include: organic psychiatric disorders (dementia and cognitive impairment), post-stroke depression, anxiety, mania and bipolar disorder, catastrophic reaction, psychosis and pathological affect (pathological laughter and crying). The summary of these disorders with descriptions of their clinical presentations are presented in table 1.

II. DEMENTIA AND POST-STROKE COGNITIVE IMPAIRMENT

“Post-stroke cognitive impairment” means any cognitive disorder that has a connection with a stroke and found in the first three months after an acute impairment of cerebral circulation, which causes damage to brain tissue, but usually not later than one year after the stroke. Three-month interval introduced in the case of vascular dementia and is one of the evidences of a causal link between cerebrovascular disease and dementia.

Based on data from various studies, it has been reported that “post-stroke cognitive impairment” with varying degrees of severity is found in 40-70% of stroke patients, with about half of the patients, including those with mild stroke [3], [4]. The prevalence of dementia varies from 5 to 32% in the first 3-6 months after stroke and from 8 to 26% after 12 months [5], [6].

Research findings indicate that the highest risk of dementia is observed within the first 6 months after stroke [7]. Post-stroke dementia has a leading role in the structure of disabling conditions, and along with the incidence of cerebrovascular pathology, the medical and social relevance of this problem is increasing worldwide. Epidemiological data on the prevalence of post-stroke dementia vary depending on the site of the study and the diagnostic criteria used. The prevalence of dementia one year after stroke is estimated from 7% in population-based studies among first-stroke patients to 41% in groups of hospitalized patients with recurrent brain events [8]. The highest risk of dementia is observed in the first months after a stroke, possibly due to previously unrecognized and undiagnosed cognitive impairment.

After the first year, the incidence of new cases of dementia is increasing gradually between 1,7% and 3% annually. The longest follow-up study showed that in 25 years after stroke, dementia developed in nearly half of the patients. According to other researchers, a stroke has increased the risk of dementia by 4 to 12 times [9], [10]. The syndrome of persistent cognitive impairment as a result of organic brain damage develops in 25-30% of stroke patients, leading to a significant increase in the cost of their care and increases mortality among the cohort between two to three times. Traditionally, the focus in the treatment of stroke patients is on such forms of cognitive dysfunction as dementia or severe aphasia. Although milder and more moderate forms of cognitive impairments are much more common. Early detection of these disorders can help prevent further cognitive deficits and improve prognosis [11]. In general, three types of cognitive disorders that occur after a stroke can be distinguished by the degree and prevalence of cognitive

Published on 26 August, 2019.
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DOI: http://dx.doi.org/10.24018/ejmed.2019.1.3.64
The clinical significance of post-stroke cognitive impairment and dementia lies primarily in the poor prognosis in stroke patients [7]. Typical for patients with post-stroke dementia are higher mortality and higher risk of recurrent stroke. A less favorable prognosis can be explained by a number of factors: a broader vascular pathology of the brain, mainly comorbid somatic diseases (e.g., more frequent and severe cardiovascular diseases). Patients with dementia have more pronounced functional disorders (inability of self-care and impairment of performing of daily living activities).

III. POST-STROKE DEPRESSION

Depression is one of the most common neuropsychiatric complication in stroke. Despite the high prevalence and the negative impact on patient’s well-being, it is not diagnosed by physician in at least 50-80% of cases [13]. The prevalence of this condition was studied quite intensively, it depends on many factors. The average prevalence of depression in the acute period of stroke is 22% for severe depression and 17% for mild depression. In the outpatient group of patients, these indicators are as 23% for severe depressive episode and 35% for mild-moderate depressive presentation, and in general population 13% (for severe) and 10% (for mild) respectively.

In some categories of patients, to diagnose a post-stroke depression is quite difficult (e.g., in the presence of cognitive impairment or aphasia). Although in “Diagnostic and Statistical Manual of Mental Disorders, 5th Edition: DSM-5” (DSM-V) criteria for "mood disorders due to medical condition" are fully applicable, some researchers and specialists believe that certain symptoms are adequate for major depression (insomnia, loss of appetite or level of physical activity) can be observed in stroke patients with normal mood in the background of hospital stay, comorbid illnesses and medication action (or side effects) [14].

Therefore, although depression after acute cerebrovascular abnormalities cannot be completely diagnosed in people with comorbid perceptual and cognitive impairment, the DSM-V criteria for major depression are quite adequate. Such patient should experience depressed mood or apathy for at least 2 weeks and be accompanied by at least four of the following symptoms: decreased or increased appetite and weight, insomnia or hypersomnia, psychomotor agitation or slowing, loss of vital activity, feeling of uselessness and guiltiness, impairment of attention and concentration, recurrent suicidal ideation.

According to DSM-V criteria [14], [15], a diagnosis of mild depression requires the presence of more than two but less than five depressive symptoms, including depressed mood or loss of interest in life. Although it is not included in

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TABLE I: NEUropsychiatric disorders ASSOCIATED WITH STROKE

<table>
<thead>
<tr>
<th>No</th>
<th>Disorder</th>
<th>Prevalence of the disorder</th>
<th>Clinical Manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dementia and Impairment Post-Stroke Cognitive</td>
<td>Between 7% and 41% (depending on the criteria used) for dementia</td>
<td>Determined by the age, localization and the massiveness of lesions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Between 25% and 40% (depending on the criteria used) for post-stroke cognitive impairment</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Depressive Disorder</td>
<td>Between 10% and 35%</td>
<td>Change of mood and appetite, weight loss, insomnia and social withdrawal</td>
</tr>
<tr>
<td>3</td>
<td>Anxiety Disorder</td>
<td>28%</td>
<td>Anxiety is usually manifested by insomnia, excessive feelings about insignificant life problems, excessive fatigue, uncontrolled autonomic symptoms (high blood pressure, gastrointestinal dysfunction, tachycardia, hyperhidrosis), expectation of adverse social events</td>
</tr>
<tr>
<td>4</td>
<td>Mania and Bipolar Disorder</td>
<td>Rare, between 0,4% and 1,6%</td>
<td>Mania characterizes by elevation of mood, reduce sleep time, “grandiosity” and pressure of speech.</td>
</tr>
<tr>
<td>5</td>
<td>Catastrophic Reaction</td>
<td>19%</td>
<td>Outbreaks of aggressive behavior, anxiety and crying</td>
</tr>
<tr>
<td>6</td>
<td>Psychosis</td>
<td>Rare, approximately 3,1%</td>
<td>Hallucinations and delusions</td>
</tr>
<tr>
<td>7</td>
<td>Pathological Affective (Pathological Laughter and Crying) Presentation</td>
<td>15%</td>
<td>Emotional outbreaks are inadequate to the internal state</td>
</tr>
</tbody>
</table>

DOI: http://dx.doi.org/10.24018/ejmed.2019.1.3.64
the category of "depression due to general medical condition", this diagnosis can be used in stroke patients.

Duration of the depressive episode after acute cerebrovascular accident was studied in several longitudinal studies. It was found that the average duration of severe depression was 34 weeks, and minor depression was only 13 weeks [16]. It has been reviled that most of the depressive episodes disappeared after 1 year from the first presentation [17]. However, in 30% of these patients, symptoms persisted after 1 year, in 25% after 2 years, and at 20%-3 years after the stroke. Although the average duration of major depression in this population of patients was no more than 9 months, there is a significant percentage of patients whose conditions last for several years.

Despite the fact that the causes of depression after acute neurovascular episode are mostly unknown, it is assumed that insufficient monoaminergic compounds play a major role in the lesion of the frontal lobe or basal ganglia. The lesions in the frontal lobe at the cortical level or at the level of the basal ganglia interrupt serotonin and norepinephrine pathways. It is associated with enhanced binding of serotonin receptors in the homolateral hemisphere. The interruption of the dopaminergic pathways is also relating to the pathogenesis of post-stroke depression.

At least three double-blind, placebo-controlled studies are currently available on the effectiveness of antidepressants in this category of patients. The first of them was conducted in 1984 [18]. It looked at the effect of nortriptyline in persons with acute cerebrovascular abnormalities compared to placebo group. There was significant improvement of patients with post-stroke depression who take nortriptyline. Among the side effects, delirium episodes have been revealed.

The other controlled study were 27 patients with post-stroke depression and with inadequate dexamethasone suppression test were treated with trazodone [19]. The patients clearly improved quality of their life after 2-3 months on their treatment. The Barthel scale was used to measure activities of daily living (ADL) of patients with post-stroke depression.

Efficacy and tolerability of a selective serotonin reuptake inhibitor (SSRI) citalopram in a controlled study of patients with acute cerebrovascular abnormalities were evaluated [20]. The reduction of depressive symptoms was noted after 3 and 6 weeks on citalopram.

Although other treatment options for post-stroke depression, including transcranial magnetic stimulation (TMC) and electroconvulsive therapy (ECT), are available and were tested in clinical settings, they were not evaluated in controlled trials. Antidepressants remain the first choice to correct this condition [21]. Since depressive symptoms have a negative impact on functional recovery, medications should be prescribed as soon as possible to avoid long-term complications. The duration of treatment remains essential (minimum of 5-8 weeks) for improving the prognosis.

IV. POST-STROKE ANXIETY

There is a stable connection between post-stroke depression and anxiety. In some studies, patients with acute stroke were found to meet the DSM-V criteria for generalized anxiety disorder (GAD), except the duration of this condition has to be more than 6 months. Most patients in this subgroup showed depressive symptoms.

These results were confirmed in a 3-year longitudinal study of 80 patients conducted by Astrom [22]. According to this research, the prevalence of anxiety in the acute phase of neurovascular accident was 28%, and this parameter did not significantly decrease after 3 years.

DSM-V defines a condition like "anxiety disorder due to another medical condition" [14]. The criteria for GAD require constant anxiety associated with at least three of the following symptoms: anxiety, decreased vital activity, worsening of concentration, irritability, muscle tension, sleep disorders that persist for at least 6 months [14].

Tomographic studies of patients with anxiety after acute cerebrovascular abnormalities suggest that those whose anxiety disorder comorbid with depression had a much higher incidence of cortical lesions compared with those who were depressed, in which the stroke sites had predominantly subcortical localization. In addition, the combination of "depression + anxiety" has been found to be more characteristic of left vascular ventricular lesions, while isolated anxiety is associated with involvement of the right cerebral hemisphere. According to Astrom [22], persistence of post-stroke anxiety disorder after neurovascular incident may be associated with atrophic changes.

Presence of anxiety disorder has a very negative effect on the functional recovery after acute cerebrovascular incident since anxiety in such situations is more than an immediate response to the disease. As already mentioned, the combination of post-stroke anxiety and depression is associated with prolonged persistence of the depression, which adversely affects the physical and social functioning of the individual.

Since there are no studies devoted to the systematic study of therapy of anxiety disorder in the context of cerebrovascular accidents, the only available information is derived from the findings based on the treatment of "non-stroke" patients. The most commonly used drugs are benzodiazepines, although they tend to accumulate side effects in the elderly patients. Therefore, it is desirable to use them after acute cerebrovascular abnormalities for a very short period of time. There is no data on the therapeutic efficacy of various classes of antidepressants in these patients.

V. MANIA AND BIPOLAR DISORDER IN A POST-STROKE PERIOD

Mania is a syndrome that along with depression is the main feature of bipolar disorder [14], [23]. It is characterized by an increased (elevated) mood, acceleration of the thinking process, speech (rate and volume) and motor (psychomotor) arousal (so-called, “manic triad”).

The prevalence of mania after a stroke is not exactly known, but according to some authors, is about 1% [24]. Cases of the development of mania are also described in other neurological diseases: multiple sclerosis, post-traumatic encephalopathy, epilepsy, Parkinson's disease, etc. [25], [26]. The concept of “secondary mania associated with organic brain damage” and its diagnostic criteria was proposed in
1978 [27].

Diagnostic criteria for secondary mania are: a) symptom duration of at least 1 week; b) high and irritable mood; c) 2 of the listed symptoms are present: hyperactivity, increased volatility, acceleration of the flow of thought, ideas of greatness, reduced need for sleep, distractibility, reckless behavior, lack of history of manic, depressive and other mood (affective) disorders, as well as symptoms of cognitive impairment (e.g., delirium) associated with mania.

Steffens and Krishnan [28] proposed the definition of post-stroke or vascular mania. This is a mania that develops in certain clinical conditions. These conditions include stroke or transient ischemic attack (TIA), symptoms of focal brain damage. Later, Wijeratne and Malhi [29] revised this definition. Vascular mania is a form of mania that begins in patients 50 years or older after acute cerebrovascular accidents (TIA or stroke) or with at least two vascular risk factors (arterial hypertension, hyperlipidemia, coronary heart disease, diabetes mellitus), as well as taking into account additional criteria, including changes according to neuroimaging investigations and neuropsychological studies.

According to a meta-analysis conducted in 2011 [30], which included 49 studies in the last 50 years, 74 cases have been described in the world literature. Robinson [31] deliberately examined 700 patients after a stroke and found only 3 cases of mania. The same number of patients was noted earlier, in 1986 [32], while examining 661 patients. In other words, in the above studies, the frequency of mania after a stroke ranged from 0.4 to 1.6%. In some cases, mania occurred within the framework of post-stroke bipolar disorder [33]. Mania may be developed in different periods of stroke: from acute to 2 years after the onset of the illness [30].

Manic episode often develops as a result of right-side strokes. Many authors explain this connection by the defeat of the right cortico-basal ganglia-thalamo-cortical loop (CBGTC loop), which are responsible for controlling the affective (mood) sphere and behavior, as well as motivation and spontaneity [30]. This finding is consistent with data on a high frequency of post-stroke depression, a state opposite to mania, with left-sided lesions [30]. However, in the literature there are reports of cases of the development of mania after strokes of various localizations. Probably, a significant role in the development of mania belongs to the phenomenon of dysfunction of the brain, not directly damaged, but associated with the site of damage by the system of pathways [34].

VI. CATASTROPHIC REACTION AFTER STROKE

Description of “catastrophic reaction” was made by Goldstein [35]. This covers a series of symptoms (anxiety, aggressiveness, negativism, and guiltiness) that occur in patients with brain lesions and triggered by inability of the body to cope with physical and cognitive deficits [36]. In other words, catastrophic reaction after a stroke is an acute psychological reaction to stress associated with the inability to perform daily tasks as a result of a neurological deficit.

Clinically, the syndrome is characterized by increased anxiety, a decreased mood and aggressiveness. The lack of a link between the severity of the neurological deficit and the development of a catastrophic reaction indicates a link between the development of the latter and focal brain damage (more often left-sided). Goldstein has developed a scale (Catastrophic Reaction Scale) to assess the presence and severity of this syndrome. It was found that catastrophic reactions occur in at least 19% of patients after an acute stroke [37]. Moreover, these symptoms are reliably associated with major depression and lesions of basal ganglia. It is believed that the disorder represents the release of depressive manifestations against the background of subcortical lesions of the anterior cerebral regions. Catastrophic reaction as a behavioral manifestation of pathological thinking, emanating from the regions of the right hemisphere, due to damage of the speech centers and the paralimbic regions of the dominant hemisphere.

The best treatment of catastrophic reaction is prevention. It often develops in the background of aphasia with reduced fluency. Therefore, speech therapy for such patients has to be considered. Speech therapy in post-stroke patients should be used in a spontaneous mode to avoid prolongation of the rehabilitation period.

VII. PSYCHOTIC EPISODE (PSYCHOSIS) IN A POST-STROKE PERIOD

Psychosis, mainly in the form of hallucinations and delusions, remains a rare neuropsychiatric complication of stroke. A group of researchers screened people over 60 years of age who were admitted in a neurological department during the 9-year period and found only 5 people with such complication [38]. All of them showed right-sided frontal and parietal lesion. Moreover, a significant number of these patients were seen with convulsions.

A new study of British scientists conducted a systematic review of post-stroke psychosis, their clinical characteristics, prevalence, localization, treatment, risk factors and outcomes from 1975 to 2016 [39]. According to the authors of the work, previous reviews of post-stroke neuropsychiatric complications did not focus on post-stroke psychosis, despite the obvious clinical significance. Perhaps this was the reason why this condition is not described in the clinical guidelines for the treatment of post-stroke mental disorders.

Neuropsychiatric symptoms after a stroke are quite common and seriously affect the quality of life. The average age of post-stroke psychoses is 66.6 years. This pathology is more common in men than in women. An interesting fact is that post-stroke psychoses were characterized by a delayed onset (according to some sources, the average onset time was from 6.1 months to 10 years). In addition, the neurological status for most stroke patients had “typical manifestations” (more often left-sided weakness, headache, left-sided decrease in vision or blindness, and slurred speech). However, a significant number of patients did not have any neurological manifestations.

The most common psychotic spectrum disorders were delusional disorder, schizophrenia-like psychosis and mood disorders with psychotic symptoms. Lesions are usually localized in the right hemisphere, especially in the frontal, temporal, and parietal regions, as well as the right caudate nucleus. In all these cases, the right middle cerebral artery was most often affected. At the same time, a total of hemorrhagic strokes were observed in 18.1% of patients.
whereas 79.8% of patients had ischemic strokes.

Post-stroke psychosis associated with poor functional outcomes and high mortality. However, the studies included in the review had poor methodological quality, which imposed significant limitations on the results (out of 2442 studies, only 76 met the inclusion criteria). In addition, the delayed onset of post-stroke psychosis can serve as a “target sign” for early therapeutic intervention. Therefore, further research is urgently needed on the safety and efficacy of antipsychotic drugs in this patient group.

In general, this disorder was well responsive to antipsychotic medications, in particular atypical class.

VIII. PATHOLOGICAL AFFECT (PATHOLOGICAL LAUGHTER AND CRYING) PRESENTATION

It is characterized by frequent and easily provocative episodes of crying and / or laughter that do not correspond to situations and do not reflect causative emotions. According to several studies, this condition occurs in at least 15% of patients with acute cerebrovascular abnormalities [40].

Patients may start to show emotion for no reason and without control, or their emotional response may be disproportionate to the importance of a reason that can cause frustration. A person is usually not able to stop herself/himself for a few minutes. Episodes may appear out of limits to the environment and with regard to negative emotions - the patient, for example, can laugh uncontrollably when angry or upset.

A cardinal feature of the disorder is a pathologically low threshold for the manifestation of the behavioral reaction of laughter, crying, or both emotions. The patient often shows episodes of laughter or crying without apparent motivation or in response to stimuli that would not cause such an emotional response before the onset of the underlying neurological disorder. In some patients, the emotional response is exaggerated by intensity, but the provoked stimulus coincides with the nature of the surrounding environmental circumstances. For example, a stimulus of sadness provokes a pathologically exaggerated state of rampant crying.

However, in some other patients, the nature of the emotional picture may be incompatible and even contradict the emotional state of the provocative stimulus. For example, a patient may laugh in response to sad news or cry in response to very mild irritants. In addition, after provoking the situation, episodes can go from laughing to crying or vice versa.

The Pathological Laughter and Crying Scale (PLACS) has already been developed to evaluate such a violation. For its therapy, the main drugs are antidepressants - both tricyclic (nortriptyline) and serotoninergic (citalopram and sertraline).

IX. CONCLUSION

There are numerous neuropsychiatric complications that accompany stroke. The most common among them are post-stroke cognitive impairment, depression and anxiety, and these conditions are often comorbid each other. In addition to detrimental effects, they are associated with a clear localization of lesions and adversely affect the restoration of physical functions during rehabilitation.

The same can be said about catastrophic reaction, pathological affect (pathological laughter and crying) and post-stroke psychosis. Given their prevalence, it should be noted that these neuropsychiatric presentations remain insufficiently investigated. In addition to using preventative strategies for stroke, treating its neuropsychiatric symptoms have the best potential for improving the prognosis and quality of life in such patients.

ACKNOWLEDGMENT

Authors wish to acknowledge continuous help and support of Professor Trevor Kaile (Dean, School of Medicine, University of Zambia - UNZA), Doctor Ravi Paul (Head of Department, Department of Psychiatry, University of Zambia - UNZA), and Doctor Margaret Chibowa (Senior Medical Superintendent, Chainama Hills College Hospital), who made writing this paper possible.

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DOI: http://dx.doi.org/10.24018/ejmed.2019.1.3.64