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Post-stroke hemiballismus: a series of two cases

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ABSTRACT

Background. Hemiballismus is a rare hyperkinetic movement disorder characterized by irregular, poorly patterned, high-amplitude involuntary movements of the limbs on one side of the body. While being usually a consequence of subthalamic nucleus lesions, hemiballismus is uncommonly associated with stroke in adults. Moreover, many debates remain regarding the physiopathology behind post-stroke hemiballismus and its optimal treatment.

Case reports. In this context, the article aims to present two intriguing cases of hemiballismus arising from ischemic stroke, illustrating the intricate interplay between vascular pathology and movement disorders. Case 1 involves a 72-year-old female presenting with sudden onset left hemiballismus following incomplete right middle cerebral artery infarction, who received intravenous thrombolysis and had a good outcome. Case 2, an 80-year-old female presenting with abrupt onset right hemiballismus, with a suboptimal therapeutic response but self-remission after three months. Considering the inconclusive imaging results, this case highlights the diagnostic challenges and dilemmas encountered in the management of post-stroke hemiballismus.

Conclusions. The authors propose a discussion by comparing the selected case reports with currently available data from the literature, focusing on the diagnosis and possible therapeutic strategies. These two cases underscore the importance of early recognition and tailored management of post-stroke hemiballismus, enriching the understanding of this movement disorder.

Keywords: hemiballismus, ischemic stroke, movement disorders, basal ganglia, post-stroke recovery

BACKGROUND

Post-stroke movement disorders are uncommon in adults. Despite limited data, it is considered that under 1% of stroke patients are expected to develop acute or delayed hyperkinetic movement disorders [1]. The clinical picture can be very variable, with cases of hemiballismus-hemichorea [2], tremor [3], myoclonus [4], and dystonia [5] being reported in the literature. Still, post-stroke hemichorea-hemiballismus was the most frequently encountered regardless of what larger cohorts were studied.

Based on the available epidemiological data, hemorrhagic strokes are more likely to be linked to movement disorders compared to ischemic strokes [6]. Another relevant aspect refers to the onset and progression of movement disorders following stroke, which exhibit significant variability. Chorea and hemiballismus tend to manifest earlier post-stroke, several hours to days, despite considerable heterogeneity within each movement disorder category [6]. This variability in timing may impact the duration required for partial motor function recovery and the development of aberrant neural circuitry. However, the good news is that the majority of acute-onset stroke-related movement disorders are resolved within six months [1].

While movement disorders following stroke are relatively infrequent and often transient, their identification remains crucial for localizing lesions and indicating potential underlying causes. In this regard, the posterolateral thalamus was the most frequently affected area, but the caudate, putamen, and globus pallidus are also involved [7].

Strictly related to post-stroke hemiballismus-hemichorea, hemiballismus is characterized by vigorous, high-amplitude, irregular movements of the limbs on one side of the body [8]. While chorea is defined as arrhythmic, non-repetitive, brief movements that typi-

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cally worsen with volitional movements [9], the distinction with hemiballismus in real-life situations can sometimes be challenging. It should also be considered that hemiballismus improves in the chronic post-stroke phase and can evolve into lower amplitude chorea [10].

In the context of many debates regarding the physiopathology behind post-stroke hemiballismus, its diagnosis, and optimal treatment, this article aims to present two interesting cases that highlight the intricate correlation between cerebrovascular disease and this rare movement disorder. Subsequently, the authors compare the two case reports with similar data available in the literature, with the final goal of increasing the understanding of this phenomenon, as well as the importance of its early recognition and adequate treatment.

CASE REPORTS

We report two cases of post-stroke hemiballismus patients who presented in the Second Neurology Clinic, "Prof. Dr. Nicolae Oblu" Emergency Clinical Hospital, Iasi, Romania, between December 2023 and February 2024.

Case 1

A 72-year-old woman presented with extensive, wide-amplitude, irregular, and continuous involuntary movements in the left limbs, accompanied by orolingual automatisms, symptoms with sudden onset three hours before arrival in the Emergency Department (ED). The patient's history was unremarkable, except for cervical-dorsal and lumbar disc pathology, without chronic drug treatment. Physical examination revealed normal weight, dorsal kyphosis, three neurofibroma-like lesions at the anterior cervical level, BP=160/100 mmHg, HR=100 bpm, and psychomotor agitation. Neurological examination revealed ballism of the upper and the lower left limbs, orolingual automatism, characterized by repetitive and sustained involuntary prolonged spastic movements of the tongue, facial and masticator muscles, hypertonia of the left limb, congenital convergent strabismus of the right eye, without any other pathological neurological findings. We performed a brain CT, which showed no acute ischemic or hemorrhagic lesions, ASPECTS score = 10, leukoaraiosis, and cerebral atrophy. Vital signs were normal on admission. Laboratory findings were within normal limits. According to the Romanian guidelines, intravenous thrombolysis with Alteplase was performed, and no adverse effects were encountered. As hemiballismus was maintained after thrombolysis, Haloperidol treatment was started, with eventual mitigation and resolution of the involuntary movements 24 hours later. The control brain CT scan was performed one day after thrombolysis and highlighted no ischemic or hemorrhagic lesions. A brain MRI was subsequently performed, showing lacunar strokes located in the right frontal-parietal lobe and cerebral atrophy but no acute ischemic lesions. As the extensive paraclinical investigation did not reveal arrhythmias, the patient was treated with clopidogrel 75 mg and atorvastatin 40 mg and discharged home. No similar episodes have been recorded up to the present. This case shows the occurrence of post-stroke haloperidol-responsive hemiballismus with fast resolution and satisfactory outcome.

Case 2

An 80-year-old patient presented with involuntary, large-amplitude, vigorous movements in the right upper limb, symptoms with sudden onset three days before arrival in the ED. Apart from chronic smoking, no prior medical history and no chronic treatment were mentioned. Physical examination revealed an overweight, hemodynamically and respiratory stable patient, with excoriating lesions at the level of the right upper limb as a result of trauma secondary to the involuntary movements. The neurological examination revealed a conscious, cooperative, and fully oriented patient with ballistic and chorea movements in the right limbs, predominantly in the upper right limb, diminished at rest and accentuated with voluntary

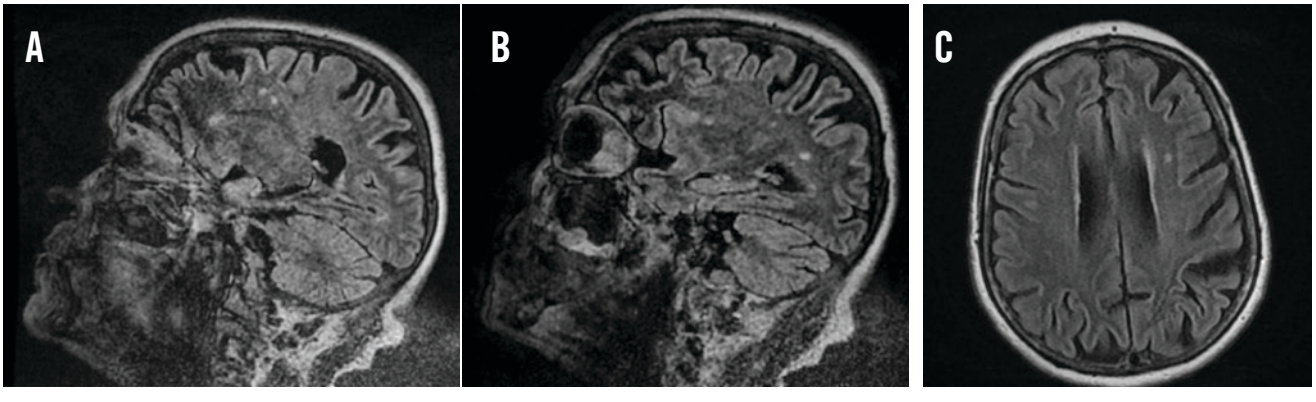

FIGURE 1. (A), (B) – T2 FLAIR brain MRI sagittal sequences showing several lacunar infarcts; (C) - T2 FLAIR brain MRI axial sequence showing one lacunar infarct in the left hemisphere

movements, right Babinski sign, no subjective or objective sensory deficits, no cranial nerve impairment. Laboratory tests showed leukocytosis accompanied by erythrocytosis and thrombocytosis in the context of polycythemia vera but no other pathological modifications. EKG showed sinus rhythm. Brain CT performed at presentation in the ED excluded hemorrhagic lesions. The subsequent brain MRI detected multiple lacunar infarcts located in both hemispheres but not involving the basal ganglia (see Figure 1). Antiplatelet and lipid-lowering therapy was started, with Haloperidol as the initial treatment for the hemiballismus. Despite partial response to therapy, the patient maintained involuntary movements in the right upper limb up to three months after discharge. This case shows the occurrence of post-stroke hemiballismus due to multiple ischemic lesions affecting several neuronal networks outside the basal ganglia, highlighting the atypical correlation between lesion location and clinical picture. Moreover, the long-term prognosis was good; despite a suboptimal response to drug therapy, the hemiballismus self-remitted after three months.

DISCUSSION

Ischemic strokes usually manifest with motor deficits, sensory problems, or cranial nerve impairments; however, in rare cases, the only clinical manifestation can be hyperkinetic movement disorders, with hemiballismus-hemichorea the most frequently diagnosed. In this article, the authors present two cases of post-ischemic stroke hemiballismus, completing the existing literature on this topic. Despite a relatively sufficient number of reported cases, there are still many unknowns related to the physiopathology and optimal therapeutic approach in stroke-related movement disorders.

Reviewing the functional anatomy of the brain, the basal ganglia serve as the critical area prominently involved in the onset and evolution of post-stroke movement disorders. While the detailed presentation of the basal ganglia circuits is found in other recent works [11], the complex feedback loop between the cortex and the several components of basal ganglia is of interest to our topic [12]. Abnormal hyperkinetic movements result from small vessel disease and lacunar infarcts affecting these regions. While the classical approach correlates hemiballismus to subthalamic nucleus lesions, data from clinical cohorts shows that other subcortical areas may be equally involved. Worth mentioning is the retrospective conducted by Onder & Comoglu, which demonstrated that advanced age and caudate lesions were crucial determinants of the occurrence of hemiballismus in post-stroke patients [13]. However, in some patients, including one of our case reports, no vascular lesions were detected in the basal ganglia, in contrast to the clear clinical signs of hemiballismus. This demonstrated the involvement of other brain areas and possibly more complex molecular/neurotransmitter pathways in the pathophysiology of movement disorders related to stroke. Alteration within the basal ganglia output synchronization and in the GABAergic system [14] could be possible explanations for these cases, with a generalized impact at the central nervous system level. The effective drugs that modulate dopaminergic and GABAergic circuits are additional proof of the involvement of brain regions outside the basal ganglia in post-stroke movement disorders [15].

Generally, the diagnosis of stroke-related hemiballismus is straightforward, being based on clinical observation alone. The role of imagery techniques, although essential in the acute stroke setting, can be misleading in acute onset movement disorders related to stroke. Proof of this situation is our second case report, where 3T MRIs were also done in the follow-up phase and showed inconclusive results. The absence of a clearly detectable lesion in the basal ganglia suggests that the subthalamic nucleus is not the only brain area involved in generating hemiballismus. Searching the literature, even pure cortical strokes without any subcortical or basal ganglia involvement can lead to hemiballismus-hemichorea. In this regard, we mention the case of a 72-year-old man with vascular risk factors (hypertension, diabetes, atrial fibrillation) presenting with acute right-sided hemiballismus-hemichorea secondary to an acute parietal-occipital lobe infarct [16]. In order to explain the variability of stroke location leading to the same clinical signs, the existence of a sophisticated network connecting various brain regions, including the basal ganglia and subthalamic nucleus, was hypothesized. Disruption of this complex circuitry is thought to give rise to the characteristic movements observed in post-stroke hemiballismus. A more extensive study based on lesion network mapping, conducted in 29 cases of stroke-induced hemiballismus, showed that the causative lesions were localized within a unified network sharing functional connectivity with the posterolateral putamen [17]. Whether other possible brain areas may be involved in the onset of hemiballismus remains an open question, considering the high individual factors and the unique brain's capacity for plasticity.

The last debatable aspect of post-stroke hemiballismus is its adequate treatment, as there are currently no established guidelines in this direction. One explanation for the lack of a standardized approach could be the transient character of stroke-related movement disorders. In our case reports, involuntary movements disappeared after less than a month without specific drugs targeting the basal ganglia circuitry. Still, there is a broad literature on pharmacological and non-pharmacological therapies suitable for post-stroke hemiballismus. Dopamine receptor blockers, particularly halo-

peridol, were long considered the main drugs with satisfactory outcomes in hemiballismus patients [18]. According to one older study, more than 50% of patients receiving haloperidol experienced resolution of hemiballismus in under 15 days [19]. As haloperidol has its limitations, other therapeutic options were tested, with clonazepam and diazepam two promising alternatives [20]. Antiseizure medication, such as topiramate or valproic acid, was also considered in particular cases and demonstrated efficacy; however, the literature on this topic is scarce [21]. Tetrabenazine, acting primarily as a reversible high-affinity inhibitor of monoamine uptake into presynaptic neurons, leads to monoamine (particularly dopamine) depletion and is a potent medication in hyperkinetic movement disorders [22]. Used mainly in chorea, tetrabenazine is also a choice in stroke-related hemiballismus.

Finally, non-pharmacological therapies should also be considered, particularly in severe, long-lasting post-stroke hemiballismus that responds poorly to the abovementioned drugs. Surgical treatment referred in the early days to functional stereotactic surgery aimed to produce lesions in specific brain areas, such as contralateral zona incerta, the ventrolateral thalamus, or the medial pallidum [23]. While short-term resolution was achieved, in the long term, a significant percentage of patients undergoing surgery reported residual hyperkinetic movement disorders. Nowadays, deep brain stimulation (DBS) is preferred. A recent systematic review includes details about DBS as a treatment for stroke-related movement disorders, including hemiballismus [24]. The selected targets for DBS were the internal globus pallidus, the ventral intermediate nucleus of the thalamus, and the subthalamic nucleus. Both monopolar and bipolar stimulation can be used, with high-frequency stimulation being preferred in most cases. While improvement is significant, complications such as speech impairment and infections should also be considered. Based on the available literature data, DBS for stroke-related movement disorders seems to be effective and safe for the patients and a feasible option even several years after a stroke [24].

CONCLUSION

Despite its rarity, hemiballismus is a possible clinical manifestation of an acute stroke, even when the ischemic lesions are not located in the subthalamic nucleus. The two case reports highlight the most relevant aspects neurologists should consider when diagnosing and treating stroke-related hemiballismus.

Reviewing the currently available literature, three main debatable aspects need further exploration in the near future. Firstly, the pathophysiological mechanisms are still incompletely understood, and hypotheses based on sophisticated networks connecting various brain regions, including the basal ganglia, need further clarification. Secondly, there is an increasing need to enhance the role of advanced imaging techniques in clinical diagnosis and research related to post-stroke hemiballismus, with the final aim of better understanding of the involved neural pathways. Finally, systematized guidelines regarding pharmacological and non-pharmacological stroke-related movement disorders should be established.

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The authors declare no conflict of interest.

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