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Role of rehabilitation in prevention of early thromboembolic complications in hemorrhagic stroke

STANESCU Ioana C.[12], BULBOACA Angelo[12], FODOR Dana Marieta[1], OBER Camelia Diana[3], GUSETU Gabriel[12], DOGARU Gabriela[12]

Corresponding Author: **FODOR Dana Marieta**: fodordana@yahoo.com

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1 . "Iuliu Hatieganu"University of Medicine and Pharmacy Cluj Napoca, Romania
2. Clinical Rehabilitation Hospital Cluj Napoca, Romania
3. Heart Institute "Nicolae Stancioiu" Cluj Napoca, Romania

Abstract

Hemorrhagic strokes (ICH) affects mainly young active people, with increasing incidence in developing countries. Mortality is high in acute phase, and patients are prone to complications related to stroke itself and to coexisting medical conditions. Patients with ICH are at high risk in developing deep venous thrombosis (DVT) with secondary pulmonary embolism (PE). Prevention of venous thrombotic events in hemorrhagic stroke patients requires intermittent pneumatic compression and preventive doses of low molecular weight heparins (LMWH) in high-risk patients. If DVT and /or PE occurs, the therapeutic management should balance the risk of recurrent cerebral bleeding and the life-threatening risk of PE, making the decision to start anticoagulation challenging. We present a case of a young patient with a large hypertensive capsulo-lenticular hemorrhage, who was diagnosed with pulmonary embolism 21 days after stroke onset. The decision was for anticoagulant treatment initial with LWMH, and switch to direct oral anticoagulants (DOAC) after 10 days; strict control of vascular risk factors of the patients (hypertension, diabetes and obesity) was achieved. Rehabilitation treatment, delayed until day 21, was recommended with progressive intensity. Evolution of the patient was favorable, with complete hematoma resorbtion under DOAC treatment at 10 weeks follow-up and important motor recovery. Rehabilitation program was intensive during this interval, and strongly contributive to neurologic improvement.

Key words: *intracerebral hemorrhage, pulmonary embolism, anticoagulant treatment, early rehabilitation ,*

Introduction

Intracerebral hemorrhage (ICH) accounts of 10-15% of strokes in European countries, with an incidence rate of 0.1-0.3/1,000/year (1). Mortality rates are high, 40 to 50%% in the first month, and are related to severity of neurological picture and to high rate of complications (2). In the first hours after bleeding onset, almost 40% of patients have hematoma expansion with deterioration of neurological status and conscience levels (3). After the first days, ICH survivors are prone to complications. Complications related to severity of motor deficit in bed-ridden patients are deep-venous thrombosis (DVT), pulmonary embolism (PE), aspiration pneumonia, pressure sores, urinary infections.

Deep venous thrombosis appears frequently in ICH patients, with variable incidence between 10 to 75% depending on the diagnostic method (4). Symptomatic DVT appears in 2-10% of acute stroke patients, the onset could be as early as the second day, and the peak of incidence being in the first week post-stroke (4). After using lower limbs ultrasonography as diagnostic method for DVT, its incidence increases at 15,9% at 10 days post-ICH (5). The most severe complication of DVT is pulmonary embolism (PE), which appears in 1-3% of patients in the first weeks and are responsible of 13-25% of early deaths after stroke (4).

Case presentation:

We present the case of a 46 years old women, which was transferred in a Rehabilitation hospital 3 weeks after a severe intracerebral hemorrhage. The patient had history of hypertension and diabetes mellitus. The stroke onset was brutal, with headache, vomiting, obtundation , right motor deficit and language troubles, and high blood pressure (BP) values: 240/130 mmHg. NIHSS (National Institute of Health Stroke Scale) score at admission was 22 points, indicating a severe stroke. An emergency native CT scan showed a left intraparenchymal bleeding (capsulo-lentincular hemorrhage) of 55/24/33 mm with midline shift of 3 mm **(Figure 1).**

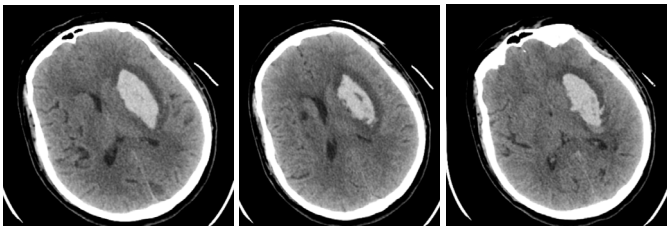

Fig. 1: Native cerebral CT scan (axial sections) showing acute left capsulo-lenticular hemorrhage with perilesional edema and midline shift; right old ischemic lacuna on anterior arm of internal capsule.

Neurosurgical recommendation was for conservative treatment. Few hours after admission the patient became comatose, and was admitted to Intensive Care Unit. After specific treatment, neurological status slowly improved, the patient regained consciousness, but with persistent severe motor deficit (right hemiplegia) and language troubles. Elastic stockings, thigh-level, were used from the second day post-stroke to prevent thrombotic events.

A control CT scan at 7 days showed partial resorbtion of the hematoma **(Figure 2)**

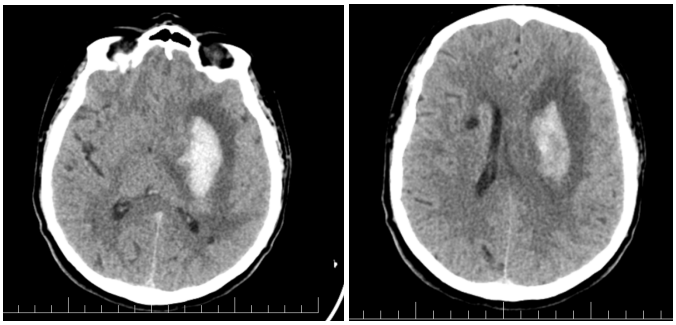

Fig. 2: Control cerebral CT scan at 7 days showing patrial hematoma resorbtion

Evolution was favorable, except one episode of agitation, chest pain, dyspnea and desaturation to 84%, 14 days after ICH onset, interpreted as aspiration pneumonia, and treated with antibiotics.

At admission on rehabilitation facility, clinical examination reveals an obese patient (body mass index (BMI) = 32), normal BP values (140/80 mmHg) and a swollen and painful right lower limb. Neurological examination showed an alert patient, with severe right hemiparesis (muscle force of 1/5 in upper limb and 3/5 in lower limb), severe expressive aphasia and impossibility to maintain sitting position.

Ultrasonography reveals acute extensive thrombosis of right popliteal and femoral veins. Biological parameters showed hyperglycemia, elevated C-reactive protein, increased values of D-Dimers and NT-pro-BNP (markers of high risk and limited recovery) (6), normal troponin. Pulmonary angio-CT scan reveals a massive and bilateral pulmonary embolism **(Figure 3).**

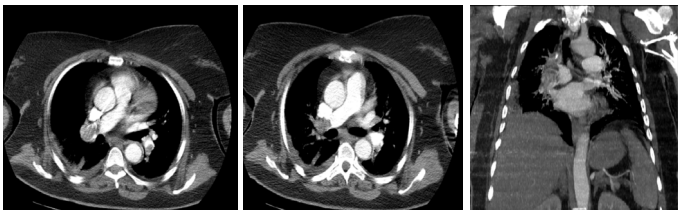

Fig. 3: Pulmonary angio-CT scan with contrast (axial sections-left, center, coronal sections-right) showing a thrombus in the right pulmonary artery (PA) and in a branch of left PA

For therapeutic management, evolution of intracerebral bleeding was assessed the sme day by a native cerebral CT scan, showing important hematoma resorbtion at 3 weeks after onset **(Figure 4).**

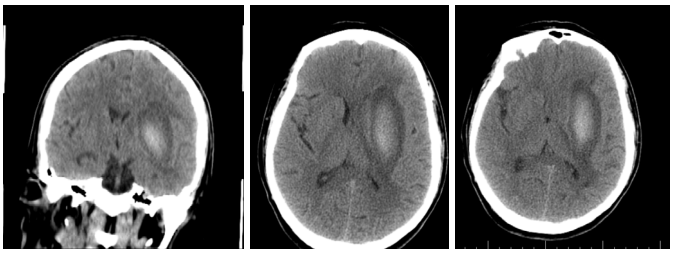

Fig. 4: Cerebral CT scan at 3 weeks showing important hematoma resorbtion

After the diagnosis of pulmonary embolism, the patient was transferred in Cardiology. She continued to be hemodynamically stable. Anticoagulant treatment was started, initially with LWMH, and after 10 days with a direct oral anticoagulant (DOAC), for 3 months period. Neurological status was constantly monitored, but the evolution was favorable.

After effective anticoagulation, the rehabilitation treatment was started, but with precautions, low intensity and constant surveillance. Bed-exercises were performed, consisting in passive mobilization -

joint range of motion exercises, straight leg raising exercises, stretching exercises and truncal posturing and facilitation techniques.
After 6 weeks (10 weeks after stroke onset) the patient neurological status was much improved: motor deficit scores 3/5 in proximal upper limb and 4/5 in proximal lower limb, the patient was able to walk for few steps with unilateral support. Language trouble also improved. Control CT scan one month after onset of anticoagulation showed complete resorbtion of hematoma **(Figure 5)**.

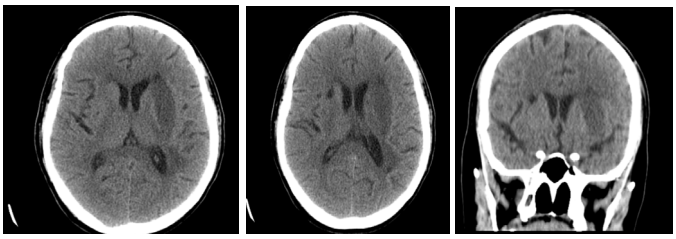

Fig. 5: Cerebral CT scan at 7 weks from ICH onset, showing complete resorbtion of bleeding

Lower limb ultrasonography showed complete recanalization of femoral and popliteal veins. The patient continued ambulatory rehabilitation treatment.

Discussion:
Patients with ICH, especially in women, have a higher risk of developing venous thrombotic events (3). Our patient was also obese and diabetic, she was comatose for few days with a severe neurological deficit (hemiplegia) and a high NIHSS score (22 points) – all factors demonstrated to favor venous thrombosis.
Prevention of PE and DVT in patients with recent intracerebral bleeding is not without risks. Intermittent pneumatic compression of lower limbs starting from the first day after stroke is recommended by guidelines (3). But this method alone is not enough for patients with immobility caused by severe neurologic deficits. The use of unfractionated heparin (UFH) or low-molecular-weight heparin (LWMH) subcutaneously could increase the risk of recurrence of intracerebral bleeding. Current guidelines recommend the use of low dose subcutaneous LWMH of UFH after bleeding cessation - documented by CT/MRI - in immobile patients, at days 1 to 4 post-ICH, for prophylaxis of venous thrombotic events. (3).
The efficacy of prophylactic treatment has been studied in a metaanalysis of 1000 ICH patients; DVT incidence has decreased from 4,2% in untreated patients to 3,3% and PE rate decreased from 2,9% in patients without UFH/LWMH treatment to 1,7% in treated patients. But, in 8% of treated patients, hematoma enlargement has been observed, compared to a 4% rate in untreated patients, and the mortality was not significantly reduced (7).
In our patient, only compression stockings have been used, without LMWH administration, possibly due to large volume of hematoma with risk of bleeding recurrence. Current guidelines stated that elastic stockings reduced the occurrence of asymptomatic DVT after ICH only if associated to intermittent pneumatic compression; elastic stockings alone are not efficient (3).
Also, severity of clinical picture and alterations in consciousness in our patient delayed early mobilization procedures, which could be protective factors against venous thrombotic complications. In our case, rehabilitation onset was delayed until the patient was neurologically stable, and passive mobilization and posturing were performed after 7 days post-stroke. First attempt to achieve sitting position was done 15 days after ICH.
Recovery after intracerebral hemorrhage occurs early, but the onset of rehabilitation treatment is usualy delayed by patient's severe neurological condition. In the literature, there are studies who demonstrated that early rehabilitation interventions in ICH patients will decrease the number of reported adverse events in the first 3 months (8, 9). Another study demonstrated that very early mobilization and mild kinesitherapy procedures – in the first 48 hours after stroke – is safe, and reduces the number of patients which experienced more than 2 adverse events during the 6 months after ICH (31% of patients in very early rehabilitation group versus 83% of patients in the group with rehabilitation onset after 7 days). Reduced rate of complications was seen for pneumonia and pulmonary embolism, and mortality rate at 3 months was reduced also with early onset of rehabilitation. However, the study excluded severe ICH patients, like our case (10). However, a recent Cochrane systematic review showed that very early mobilization of patients in the first 24 hours after ICH onset was not effective in prevention of immobility-related complications,

such as venous thrombosis, and did not improve recovery process (11).

When our patient was admitted to rehabilitation facility, deep venous thrombosis and pulmonary embolism were diagnosed. Rehabilitation procedures were once more delayed until implementation of efficient anticoagulant treatment. First signs of pulmonary embolism were manifested at day 14 post-ICH, but diagnosis was established effectively one week later by angio-CT scan (12).

If venous thrombosis or pulmonary embolism are diagnosed in a patient with acute or subacute intracerebral hemorrhage, the therapeutic management in challenging. Pulmonary embolism is a life-threatening condition, and requires urgent treatment. Patient was hemodynamically stable, so there were no indication for thrombolysis or mechanical thrombectomy. Systemic anticoagulation or cava vein filter (IVC) placement are recommended by guidelines; the choice between the two methods depend of ICH onset, absence of active bleeding, cause of ICH and patient's status (3). Anticoagulation treatment was the only available option for treatment of pulmonary embolism in our hospital (12) .

The major threat was ICH recurrence during anticoagulant treatment, which could lead to the worst prognosis. Without anticoagulant treatment, annual recurrence rate of ICH was between 0 and 8,6%. Contrarily, recurrence rate of ICH during anticoagulant treatment is higher: 2,6 to 8.7% anualy (13). Rebleeding is influenced by uncontrolled values of BP, by serum cholesterol levels, diabetes mellitus poorly controlled, smoking and alcohol abuse (13).

In our patient, after initiating anticoagulant treatment, frequent neurological assessments were performed during hospital stay, to detect early signs of rebleeding. Also, BP values were under strict control by medication (between 130-140/70-80 mmHg), excessive lowering of cholesterol was avoided, and glycemic values were also maintained under control by readjusting oral medication.

Recovery after ICH occurs within the first few months post-stroke, earlier than in ischemic stroke. This is the reason why rehabilitation treatment should be started as soon as possible after intraparenchymal hemorrhage. Sensory function, trunk posture involved in sitting and standing, and lower limb motor deficit are recovering fast, but show a stationary evolution after three months. Upper limb motor deficit and walking ability are still improving after that interval, until six months after stroke. An important predictor for motor recovery is the integrity of the pyramidal tract, which can be measured by transcranial magnetic stimulation (TMS) or diffusion tensor tractography (DTI) (14).

In acute phase of ICH, there is a general lack of research on early rehabilitation methods and on effect of mobilization. Recommended standard interventions in acute ICH are bed exercises, such as joint range movements, posturing, passive leg raising, stretching and facilitation exercises. Out-of-bed mobilization training should begin when the patient is neurologically stable, usually in the early-subacute phase; it consist in standing-facilitation techniques: supine to sit manoeuvers, sitting on the edge of bed without support, standing with support, walking with aid.

Duration of anticoagulant treatment according to guidelines will be 3 months in this case of "provoqued" PE (15). Due to important burden of risk factors in our patient, therapies should aim also to prevent further cerebral and cardiovascular complications of hypertension and diabetes. Rigorous control of existing risk factors (hypertension, diabetes, obesity) is essential, by lifestyle changes such as diet and physical activity, and medication. A recent therapeutic option favors dietary use of antioxidants, which could be involved in the prevention of cardiac ischemia and diabetes complications (16, 17).

In early subacute (< 3 months) and late subacute (3 to 6 months) phases of ICH recovery, the rehabilitation program should continue with maximal intensity, aiming to obtain a maximal recovery of motor and sensory deficits, as well as language troubles (18).

In the chronic phase after hemorrhagic stroke, the maximal plateau for motor, sensory and language recovery has been obtained. However, gait improvement with increasing of the walking distance could be achieved during rehabilitation in a balnear resort (19). In a balnear facility there is a combination of therapeutic factors: climatic factors, carbonated mineral waters and moffetes, which have been used in the prevention and rehabilitation of cardiovascular diseases and strokes (20). Important improvements in the quality of life of cronic-ICH

patients could be obtained by pursuing rehabilitation procedures in a balnear resort, at 6 month interval (21). However, other studies have demonstrated that between 1 and 2 years after stroke onset, disability (measured by modified Rankin score mRS, and activities of daily living ADL) did not improve after rehabilitation, and could even worsen in specific categories of patients (22,23).

Conclusion:

Pulmonary embolism is a life-threatening and not very rare complication of hemorrhagic stroke. Prophylaxis of venous thrombotic events require use of pneumatic intermittent compression from the first 24 hours, and low weight molecular heparins after bleeding cessation (day 2-4). It is possible that early rehabilitation and mobilization in the acute phase of ICH, if bleeding is stopped and patient's condition is stable, is helpful in decreasing the incidence of immobility-related complications. Further studies are required to assess the impact of early rehabilitation on motor recovery, psychological condition and complication rate in patients with moderate and severe intracerebral hemorrhage. Pulmonary embolism requires treatment, even in patients with recent cerebral bleeding; multidisciplinary approach is mandatory for appropriate therapeutical choice; and further studies in this field are required.

Informed consent

An informed consent was obtained from the patient participating in the study.

Declaration of conflict of interests

The authors declare that there is no conflict of interest regarding the publication of this paper.

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