

PROS AND CONS ABOUT THE ADMINISTRATION OF ANTICOAGULANTS IN PATIENTS WITH HEMORRHAGIC STROKE AND VALVULAR PROSTHESIS - CASE REPORT

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Abstract: The coexistence of hemorrhagic stroke with severe mitral valve disease, corrected by prosthetic valve, leads to problems in case management related to the anticoagulant therapy. A decision on therapeutic line, in such a situation, should take into account the ratio between the advantages/disadvantages in the administration of the anticoagulant, the generating mechanisms of these cardiovascular pathologies and the interference of the anticoagulant with these pathologies, the complications that may arise, of course all based on concrete and specific evolution of the patient. The patient C.I., aged 65, with mitral prosthesis, with chronic heart failure (CHF), New York Heart Association (NYHA) class III, aortic insufficiency, atrial fibrillation (AFI) and high pulse rate, (PR) hypertension (high blood pressure) grade III, with very high cardiovascular risk, Parkinson's disease stage II, with oral anticoagulant for 2 years, suffering a hemorrhagic stroke (confirmed by CT), resulted with right hemiparesis and vascular coma grade II. In the first 5 days, anticoagulant therapy - low molecular weight heparin (LMWH) is maintained, administered subcutaneously as recommended by the cardiologist, but Glasgow Coma Scale (GCS) = 8 points, stationary clinical course, thus being decided to cease the anticoagulant therapy, after interdisciplinary consultation (cardiologist, neurologist, neurosurgeon, intensive care specialist). In the following 3 weeks, the patient had a favourable evolution, with normalization of laboratory parameters, the occurrence of swallowing and cough reflexes, spontaneous opening of eyes, poor responsiveness to noxious stimuli, normalized thermal curve. Monitoring the size of intraparenchymal hematoma by repeated computed tomography (CT) shows a regression of it, especially after discontinuing anticoagulation treatment but maintaining the important mass effect on ventricular system. Despite the favourable evolution in the 27th day, the general condition worsened, requiring supportive measures. After 24 hours, the patient dies of cardiac arrest, the heart did not respond to resuscitation.

INTRODUCTION

Cardiovascular diseases are the leading cause of deaths globally, the World Health Organization (WHO) estimating that deaths, due to heart disease and stroke, are the most numerous.(1) In the world, cerebral hemorrhage accounts for 10-15% of total strokes, the incidence is double in Romania (30%). The mortality is high in the first 30 days from onset between 35-52%, of which approximately 50% die within the first 2 days.(2) By intracerebral hemorrhage, we understand the presence of spilled blood which infiltrates and dissects the brain tissue.(3) The bleeding process can be localized in the brain parenchyma, intraventricular or secondary intraventricular (cerebral hemorrhage with ventricular flooding), meningeal hemorrhage (subarachnoid) or cerebral meninges.(4) Intraventricular effraction (36-50% of cases) has as a consequence the increase of mortality rate (43% after 30 days versus 9% in the case of intraparenchymal bleeding) and the risk of poor prognosis.(5) Factors involved in the production, in most cases, of hemorrhagic stroke (HS) are: hypertension, aneurysm rupture, brain tumours, hemorrhagic transformation of cerebral infarction, anticoagulation therapy, venous cerebral thrombosis.(6)

Cerebral hemorrhage can be primary (80-85%) or secondary (15-20%) being extremely important to establish the type of bleeding for taking the correct therapeutic decision.(7) In

cardio-vascular pathology, hemorrhagic stroke and the severe mitral valvulopathy occupy important places in terms of the degree of damage, complications and prognosis, of patient's quality of life.

Cardiac abnormalities and electrocardiogram (ECG) changes are common in patients with acute stroke.(8)

AFI is a strong independent risk factor for stroke, as well as the age over 60, high blood pressure or left ventricular dysfunction (9) having an increased risk for stroke.

Cerebral edema may increase in the first 14 days, being the main cause of deterioration and early death in these patients by ground effect. Life-threatening brain edema occurs between the 2nd day and 5th day after stroke onset, but up to a third of patients can have neurological deterioration within 24 hours after the stroke onset.(10,11)

Valve replacement is the only treatment for severe mitral valvulopathy when the indication for correction is set (12) whereas the optimal anticoagulant regimen in the case of heart valve prostheses is that regime which makes the incidence of valve thrombosis and systemic embolism to be minimal for a minimum number of bleeding episodes.(13)

Thus, for mechanical prostheses, the optimal international normalized ratio (INR) is of 2.5-3.5, the lower level available being for aortic prostheses (2,3) and the higher level for mitral prosthesis.(3,5).

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Anticoagulation therapy group includes heparins, heparin monitoring being done by activated partial thromboplastin time (APTT), which is sensitive to the inhibitory effect of heparin on thrombin, of X and IX factors), the number of platelets, hemoglobin, hematocrit and the group of oral coumarin anticoagulants, the coumarin effect being monitored by Quick Time (QT-prothrombin time), today, being used in monitoring the coumarin effect and the INR.(14)

The association between the two diseases (valvular and hemorrhagic stroke) questions the opportunity of anticoagulant treatment.

CASE REPORT

We present a patient aged 65, with multiple cardiovascular risk factors, with pathological personal history: a metal prosthesis in the mitral position, chronic heart failure (CHF), NYHA class III, aortic insufficiency, atrial fibrillation with high stroke, hypertension grade III with very high cardiovascular risk, Parkinson's disease stage II with oral anticoagulant administered for 2 years (Sintrom), associated with other background medication: COVERSYL, Betaloc Zok, Azilect, Neupro, digoxin, furosemide, who was brought in the emergency units, then in the intensive care department for sudden alteration of consciousness, associated with right plegic hemi body.

At admission in intensive care, GCS = 8 points, haemoglobin (Hb) = 15.7 mg / dl, NL (WBC number) = 8100 / mm³, INR = 4.51, Quick time (QT) = 11%, activated partial thromboplastin time (APTT) = 26, total bilirubin (TB) = 5.4 mg%, direct bilirubin (DB) = 0.31%, indirect bilirubin (IB) = 5.09 mg%, N-terminal end of the prohormone brain natriuretic peptide (NT-proBNP) = 1767 pg / mL, urea, creatinine, glutamic-oxalacetic transaminase (GOT), glutamic-pyruvic transaminase (GPT) normal-values, while the CT scan showed: external right intraparenchymal capsular acute hematoma as 6.3 / 3.3 cm., with mass effect on the right lateral ventricle (LV); midline ventricular system (VS), diffuse cerebral edema.

The anticoagulant therapy continued according to the cardiologist's indications by administering injections with small molecule heparin for 3 days but the patient's condition did not improve (GCS = 8 points). As a result, following interdisciplinary checkups (cardiologist, neurologist, neurosurgeon) anticoagulation therapy was ceased, low doses being maintained for thromboembolism prophylaxis.

Two days after ceasing the anticoagulant, GCS = 9 points (at day 7) and from the 8th day to the 25th day, GCS = 10 points, getting the patient to open his eyes spontaneously, to watch, to have swallowing reflexes, to cough, to react poorly to noxious stimuli, in the 4th day: BT = 5.4; BD = 0.72; BI = 4.72; in the 5th day: BT = 2.52; BI = 1.70; BD = 0.87, then the values were normalized in the 6th day, INR, QT, these days having APTT values within normal limits.

From the first day, there was maintained a systolic blood pressure (SBP) around 150 mmHg, a blood glucose value of 130-140 mg/dl, the head being raised at 30°, SpO₂ (oxygen saturation) = 99-100% with additional O₂ facial mask, a diuresis of 1700 to 2500 ml/day.

In the first 48 hours, Ringer liquid and NaCl 0.9% were administered after that, enteral nutrition, monitoring of gastric stasis, and parenteral nutrition. There were monitored throughout the confinement the ASTRUP parameters [(pH, HCO₃ (bicarbonate), Na (sodium), K (potassium), Cl (chlorine), etc.], and central venous pressure (CAV); after setting the central venous catheter on the right subclavian vein, they were maintained within normal limits.

On the 7th day, the second CT control was performed: subarachnoid hemorrhage (SAH). Right temporo-parietal intraparenchymal hematoma of 6.8 / 3.4 cm, with significant mass effect on the right LV. SV moved to the left of the midline by 6 mm. Flood haemorrhage in antlers T (temporal) and O (occipital) of the lateral ventricles.

After completing the second CT, it was administered 20% Mannitol initial bolus 1g/kg, and then, every 6 hours, 0.5 g/kg, for 72 hours, associated with loop diuretics (furosemide 10 mg every 30 minutes after Mannitol administration) and glucocorticoids for 4 days according to the treatment schedule described in "Specific management of critical patient".

In terms of temperature, it began to grow, reaching in 5-9 days, only in the morning, a value of 38°C, while leukocytes also grew, by 16,900/mm³, in the 10th day, then started to decrease.

Chest X-ray was also performed, which revealed: sternal cerclage, valvular metallic prosthetic in mitral position. Central venous catheters (CVC) in the distal end at VCS level. Without evolutionary pleural lung lesions. Cord with bulging cardiac bay.

In repeated tracheobronchial cultures there were found infections such as *Proteus* spp., *Enterobacter* spp., *Pseudomonas aeruginosa*, and in the urine culture: *Candida* sp., for which antibiotics were established according to pathogen susceptibility.

Besides antibiotics, positioning the head at 30°, maintaining normothermia, glucose, and neurotrophic and neuromodulating medication, vitamin therapy, analgesics and antipyretics, sedatives, Ca channel blocker, anti-arrhythmic, there were practiced physiotherapy and massage measures, stockings, changing the patient's position in bed every 2 hours, antieschar mattress.

On the 27th day, in the morning, the general health condition suddenly worsens, spontaneously INR = 2.01, QT = 30%, GPT = 130u / I GOT 57U / I, GCS = 8 points, the rest of the analysis being normal. It was performed cardiac ultrasound that revealed: valvular metallic prosthetic in mitral position was functional without pericardial fluid. Ejection fraction (EF) = 55%. The right and left cavities having normal size, but the CT shows: right fronto-parietal hematoma with resorption edema having important mass effect on SV. Ventricular flooding. Current diameter of the hematoma 6/2,9cm. VL moved to the left midline by 12 mm. SV asymmetrically moved.

In the afternoon of the 27th day, around 6 p.m., BP = 60/40 mmHg, inotropic support was initiated (+) 5-7 ml/h, with dose adjustments in order to maintain an average value of BP around 70-80 mmHg (6.7), and around 11 p.m., breaths became ineffective, SpO₂ = 77%, thus it was decided oro-tracheal intubation (OTI) and mechanical ventilation, inotropic support also being continued (+).

In the morning of the 28th day, the patient has cardiac arrest under mechanical ventilation and inotropic support (+) by severe bradycardia. Resuscitation was initiated, asystole throughout the resuscitation, the heart did not respond to resuscitation, observing the resuscitation guidelines.(15)

DISCUSSIONS

The particularity of the case lies in the coexistence of the two major cardiovascular diseases, anticoagulant therapy being essential for proper functioning of the prosthetic valve and for preventing major complications (valve thrombosis, systemic embolism), while for hemorrhagic stroke, the anticoagulant is contraindicated, having the risk of hematoma expansion or the occurrence of further bleeding.

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Such a case requires interdisciplinary management and prompt therapeutic intervention.(16,17,18)

Regarding drug therapy, considering AFI prevention either valvular or nonvalvular: oral anticoagulation (INR 2, 0-3, 0) reduces the risk of recurrent stroke in patients with nonvalvular AF (whether permanent, chronic or paroxysmal) (19) and with most other cardiac sources of emboli. The optimal time in which to start anticoagulation is controversial.(20)

Patients with prosthetic heart valves, with or without AF, should receive long-term anticoagulation therapy with a target INR based on the prosthesis type (bioprosthetic valves: INR 2.0-3.0; mechanical valves: INR 3, 0 to 4.0).(21)

In our case, where anticoagulation was contraindicated for cerebral hemorrhage, but indicated for valvular prosthesis (two associated pathologies where anticoagulation is controversial), agreement was reached on anticoagulant medication withdrawal, as shown above, reaching INR in a few days to normal levels, supporting the following hypothesis (conclusion and from studies): subcutaneous unfractionated heparin administered in low or moderate doses (22) did not show an overall benefit of anticoagulation initiated 24-48 hours after stroke onset. However, the prevention of low-dose subcutaneous administration of heparin (5000 IU twice/day) or LMWH is indicated in patients with high risk of venous thrombosis, peripheral or pulmonary edema (for example due to immobilization, obesity, diabetes, history of stroke).(23),(24)

Cardiac arrhythmias, particularly atrial fibrillation, are common after stroke; heart failure, myocardial infarction and sudden death are also recognized complications.(25),(26)

In studies conducted, there occurred the following typical components of stroke emergency unit: diagnostic and evaluation methods (including imaging - CT), rapid methods to determine nursing needs and treatment, quickly established medical care, consisting of early mobilization, prevention of complications and treatment of hypoxia, hyperglycemia, fever and dehydration.(27) In our patient, blood glucose levels did not exceed 150 mg/dl, the temperature was stabilized at 37° C, the oxygen saturation was between 98-99%, daily physiotherapy and massage, following the critical patient care protocols, (28,29,30,31) without omitting that, in severe injuries, thermoregulation suffers dramatic disorder.(32,33)

Bringing into balance the advantages/disadvantages of anticoagulation therapy management, its suppression brought improvement of the general health status, without affecting heart function and operating status of the mitral valve revealed by cardiac ultrasound and INR remained in permissible limits.

CONCLUSIONS

1. Hemorrhagic stroke and severe valvulopathy are two significant cardiovascular diseases.
2. The association between the two diseases generates significant difficulties in case management from the perspective of anticoagulant therapy.
3. Such a case in which the two diseases are accompanied by an ample cardio-vascular pathology requires interdisciplinary management.
4. Good collaboration between specialists, correlated with clinical and laboratory data, ensures making accurate decision regarding anticoagulation therapy.
5. In our case, the cessation of anticoagulant therapy did not affect heart function, brain function being favoured.
6. The unfavourable evolution of the case, despite sustained interdisciplinary care and partial recovery of brain function is due, most likely, to multiple cardiac pathologies with high cardiovascular risk overlapping respiratory pathology.

7. Mortality in cardiovascular diseases, especially in the association between hemorrhagic stroke and ischemic heart or valvular pathology remains high, despite the observance of developed diagnostic and treatment protocols and outstanding efforts to manage these cases.

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