ANTICOAGULATION COMPLICATIONS IN A PATIENT WITH PRIOR CEREBRAL VENOUS THROMBOSIS

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ABSTRACT

Cerebral venous thrombosis is a rare form of stroke treated with anticoagulant compounds both in the acute phase as well as in long term. We present the case of a 56 year old female that suffered two different forms of stroke in 2 years.

Keywords: cerebral venous thrombosis, intracerebral hemorrhage, vitamin K antagonists, hereditary thrombophilia, malignancy

BACKGROUND

Cerebral venous thrombosis is an atypical form of stroke. Most patients with this type of stroke recover fully after receiving anticoagulant treatment in the acute phase with *low*-molecular-*weight heparin* (LMWH) or unfractionated heparin (UFH) and afterwards with vitamin K antagonists (VKA). Only a small percentage of patients are left with significant disability (modified Rankin score > 3). (1,2) Duration for anticoagulation is determined taking in consideration the patient's risk factors for recurrence: gender, smoking, use of drugs (especially oral contraceptives), pregnancy or puerperium, inherited or aquired thrombophilias, systemic diseases, infections and malignancy. (3)

CASE REPORT

We report the case of a 56 year old woman who was admitted in the Neurology Department of Colentina Clinical Hospital in February 2015, after being brought by her family for generalized anxiety with confusion and behaviour disturbances with sudden onset on the previous night.

The patient's past medical history is significant for a right ovarian tumor and cervical cancer, both diagnosed in 2009. At the time of diagnosis the patient suffered a radical hysterectomy with bilateral anexectomy and later received chemotherapy, but the exact treatment regimen in unknown. The oncology physician also decided to perform a thoracic CT that found multiple lung micronodules of different sizes which, upon every 6 months reevaluation, were unchanged in size and appearance. The patient did not have any significant family history for malignancy.

In 2013 she was admitted in our neurology department for left temporal headache, nausea and paresthesias of the upper limbs. Imaging studies (native cerebral MRI and venography) revealed low signal intensity due to flow void at the level of the left transverse sinus and a 0.9 cm hyperintense lesion on T2 and FLAIR sequences which causes a

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filling defect at the same level (Figure 1 a, b). Subsequently she was diagnosed with left transverse sinus thrombosis which was considered to be secondary to a hypercoagulable state. She was screened for hereditary thrombophilias which revealed hyperhomocysteinemia, homozygous plasminogen activator inhibitor (PAI-1) and heterozygous methylenetetrahydrofolate reductase (MTHFR)-A1298C and C677T mutations. Anticoagulant treatment was initiated with acenocumarol. At the time she was now admitted she was still taking acenocumarol 5 mg two days in a row with one day 4 mg with a target INR value between 2 and 3. Last control of INR was two months ago and it was in range.

General examination was unremarkable, the patient was alert, responsive and still quite anxious, blood pressure and pulse were slightly elevated.

Neurological examination found slightly flattened nasolabial fold, evenly distributed left hemiparesis (4/5 MRC), with spasticity , brisk reflexes and Babinski sign present on the left. Routine blood tests were normal except for the INR value which was 5.2.

We performed an emergency cerebral CT scan which showed a well demarcated mass at the level of the frontal semioval center, 21/20 mm in size, predominantly hyperdense with a hypodense center. The scan also showed moderate perilesional edema, mass effect on the adjacent cerebral parenchyma and a midline shift of about 3 mm to the left. The CT images (Figure 2 a, b) were significant for intracerebral hemorrhage (ICH) either spontaneous or due to a possible bleeding metastasis and a recommendation was made for a brain MRI.

We performed an enhanced brain MRI which showed a frontal subcortical space occupying lesion with hypo/isointensity on T2-weighted and

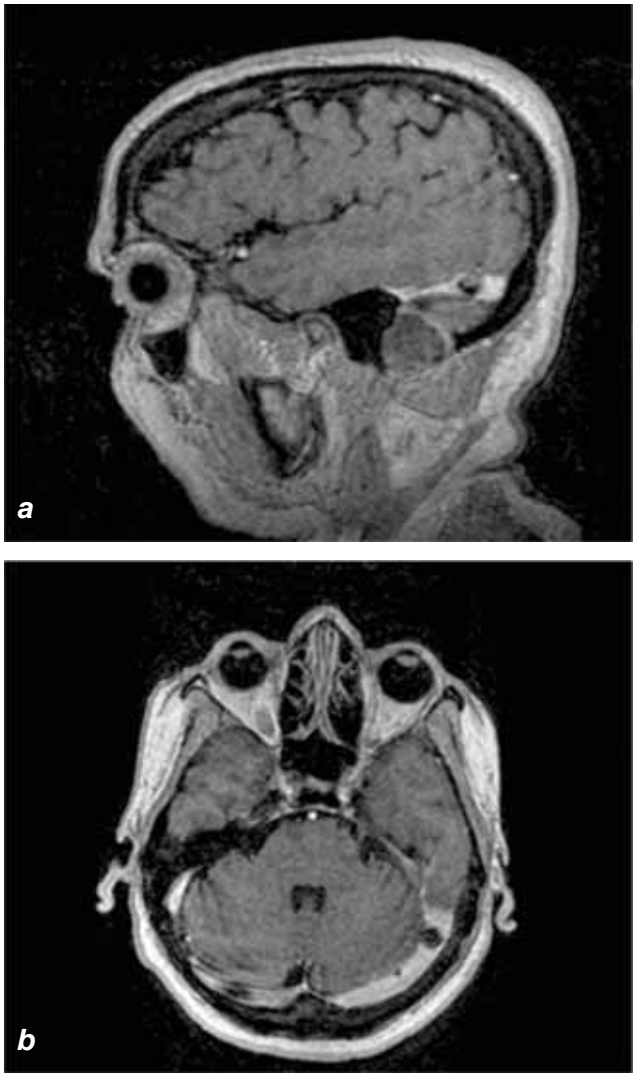


FIGURE 1. a, b *Coronal and axial FLAIR sequences after gadolinium enhancement show partially obstructed left transverse sinus with 0.9 cm hypointense area consistent with the appearance of a clot.*

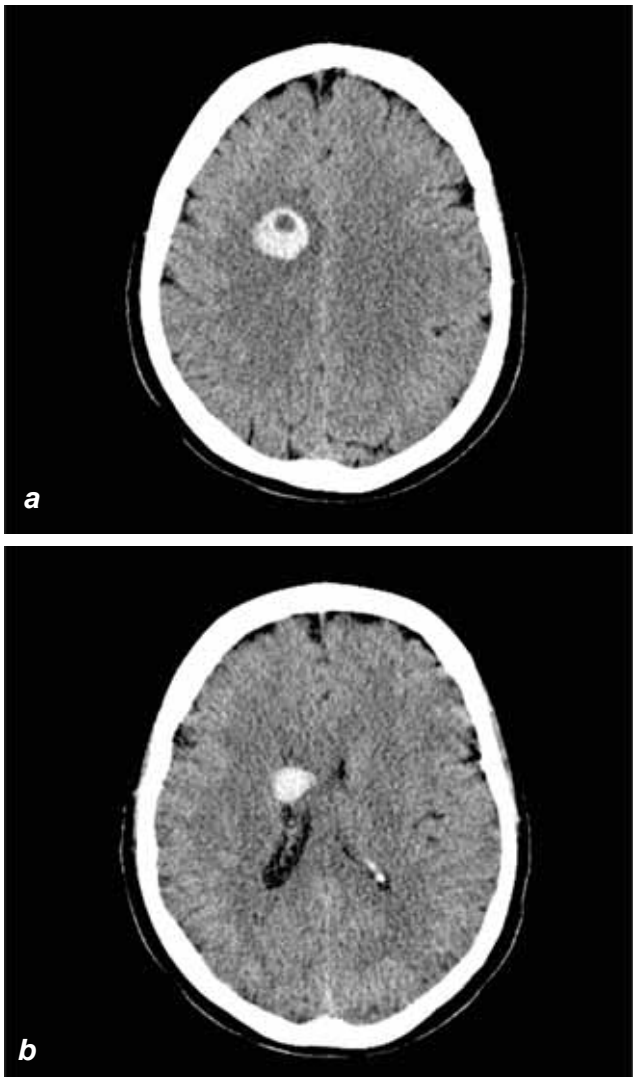
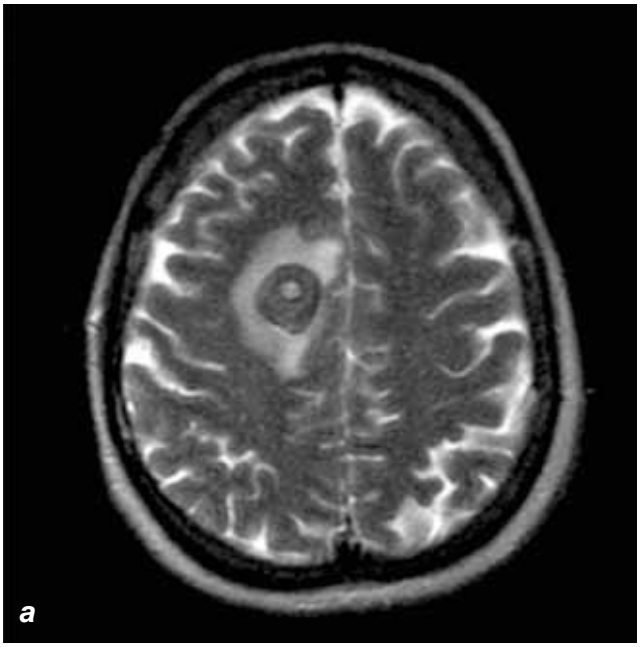


FIGURE 2. a, b *Native CT scan of the brain shows right frontal hyperdense lesion with hypodense center (bull's eye sign). The lesion is well demarcated, with slight perilesional edema and mass effect on neighbouring structures.*

FLAIR sequences, with central hyperintensity on T2 images suggestive for a subacute hematoma. Diffusion weighted images show slight hyperintensity. (Figure 3 a, b, c, d, e)

The patient received osmotherapy with mannitol, antiedema therapy with dexamethasone 6 mg daily and anticonvulsive therapy and was referred to a neurosurgical unit for further evaluation.

Due to the raised suspicion for metastasis and the history of the patient, the neurosurgical team decided to operate the patient and excise the mass for biopsy. Gross examination of the surgically re-



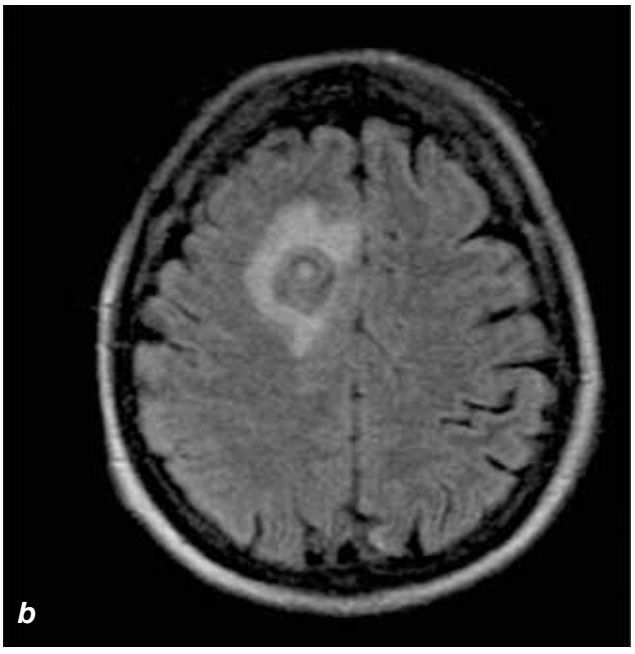
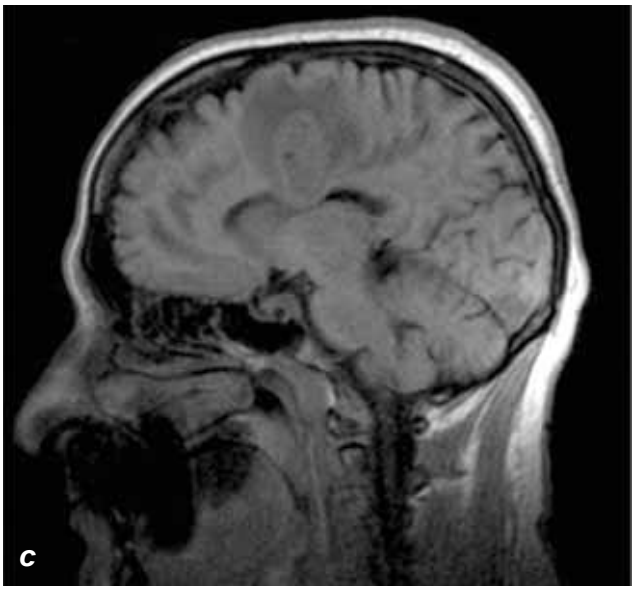
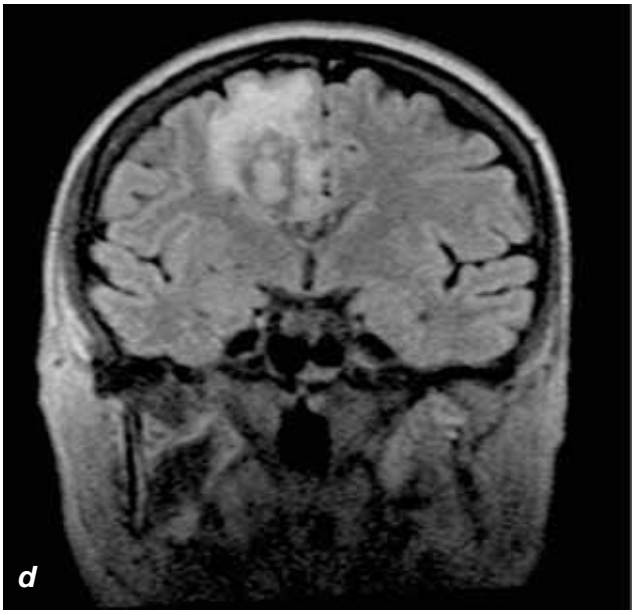


FIGURE 3. a, b *Axial FLAIR and T2-weighted images show the lesion as being hypointense, inhomogenous, with a hyperintense center with the appearence of a "bull's eye".*





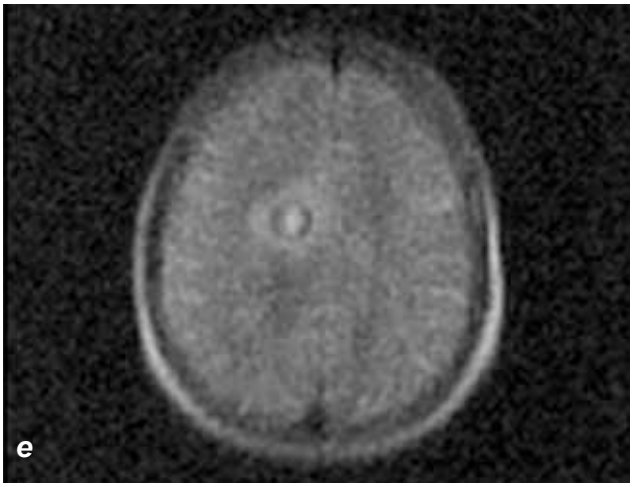


FIGURE 3 c. *Sagittal T1-weighted image (T1W) shows isointense to hypointense lesion in the right frontal lobe with surrounding moderate vasogenic edema.*
d. *Coronal FLAIR sequence – hyperintense center with hypo/isointense halo and surrounding edema.*
e. *Diffusion weighted imaging (DWI) shows slight hyperintensity in the right frontal lobe.*

sected material revealed a purple, friable, blood clot. This was consistent with the histological findings.

A brain CT scan was performed postoperatively which was considered to be within normal parameters with slight right frontal pneumocephalus in the resected area.

In conclusion, the patient suffered an intracerebral hemorrhage due to cumarinic overdosing.

Postoperative evolution was favorable. Taking into account risk factors, AVK therapy was restarted one month after the surgical cure, and patient was advised to make more often controls of INR.

DISCUSSION

Our patient is positive for more than one risk factor (female, previous malignancy, inherited thrombophilia) and as a result, a decision was made in favor of long term anticoagulant treatment in order to prevent cerebral venous thrombosis recurrence, keeping the INR within a target range between 2 and 3. (4) Recurrence of CVT is rare, under 5%, but these patients also have an increased risk of venous thrombosis at other sites. Risk for thrombosis recurrence is highest in the first year after anticoagulation discontinuation. (5)

The differential diagnosis of the most recent neurological episode, from a clinical and radiological point of view included CVT recurrence, metastasis and intracerebral hemorrhage due to cumarinic overdose. (6) As a consequence a decision was made, with the joint effort of the neurological and neurosurgical units, to excise the mass in order to exclude a possible tumoral origin.

Spontaneous intracerebral hematomas are quite frequent, accounting for up to 15% of strokes in developed countries. (7) Anticoagulation related intracerebral hemorrhages have the same frequency as spontaneous ones, leading certain authors to state that use of vitamin K antagonists might be just a risk factor and not a causal one. (8) Outcome is determined taking into consideration the patient's age, GCS score, hematoma position and size, and presence and amount of intraventricular hemorrhage. (9) Recently Wang et al. reported an algorithm which could predict the risk of hematoma growth in acute ICH, using baseline ICH volume, recurrent ICH, AVK treatment at symptom onset, intraventricular extension and number of hours from onset to computed tomography, but further validation is needed. (10)

Management options for VKA related ICHs are multiple and the American Heart Association guidelines state that the use of vitamin K administered intravenously withfresh frozen plasma or prothrombin complex concentrate is the preferred course of action. INR should be monitored closely until values are within the normal range. (9,11)

Surgical treatment is still considered controversial, early neurosurgical management could limit parenchymal injury, but cost-benefit analysis should take into account surgical risks.11

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