

CEREBROVASCULAR FLEBOTHROMBOSIS. A REVIEW OF A FEW CASES

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ABSTRACT

Background: The clinical spectrum of the cerebral vein and dural sinus thrombosis (CVT) is wide and non-specific. With the development of neuroimaging techniques, their identification recently improved.

Objectives: To collect data, identify causes and risk factors, to evaluate treatment and outcome

Patients and methods: 67 patients were admitted between 1998-2008. Their demographic, clinical, radiological data were analysed. The diagnosis was based on MRI+MRA, and/or CT+DSA. Received treatments and outcomes (mRS) were recorded at admission, after 1st and 3rd month, respectively.

Results: Sex distribution was: 35 women, 32 men; their average age was 41.92 years; 24 out of 35 women were fertile. The major clinical manifestations included headache, in 40 patients, focal neurological deficit in 8 patients, papilledema in 10 patients. All patients underwent CT, MRI+MRA in 41 patients, DSA in 4 patients. The most frequent thrombosed sinus was superior sagittal sinus (30 patients). Risk factors were identified for 32 patients. After 90 days after admission, death rate was 5.97% (4 patients), and 73.84% made a recovery between 0-2 mRS.

Conclusion: CVT were underdiagnosed in our region (low percentage of admissions for benign intracranial hypertension). Even though the percentage of women of fertile age was great, oral contraceptives were not an important risk factor. Diagnostic methods and emergency management were not yet standardized enough, while anticoagulants were systematically used.

Key words: cerebral thrombosis, neuroimaging, risk factors, treatment

INTRODUCTION

Cerebrovascular flebothrombosis is a relatively rare disease, with an annual prevalence estimated between 2-7 new cases over 1,000,000 in general population. Its incidence was over underestimated before the development of new imagistic techniques. A prompt and accurate diagnostic of cerebrovascular flebothrombosis is mandatory, because the time factor and appropriate therapy have a major impact above the evolution of the disease, and reduce significantly the risk for acute complications and sequelae. Since the etiology and clinical manifestations are very variables, the imagistic techniques play a front-line role in the diagnosis process.

OBJECTIVE AND METHODS

The objective of this study was to describe the features of cerebral venous thrombosis (C.V.T.) in the department of neurology in Timisoara, between 01.01.1998 and 1.02.2008. The identification of C.V.T. was made by CT, MRI, MR-angiography (MRA), digital subtraction angiography (DSA) and/or anatomo-pathological examination.

Because the individual risk for C.V.T. is determined by genetic factors, but may be increased by numerous predisposing conditions and precipitating factors, we analyzed the cases taking into consideration factors such as:

- sex

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- age
- etiology
- clinical course, and
- neuroradiological aspects.

RESULTS

Total number of cases: 67

Sex ratio: women/men = 1.09/1 (35 women and 32 men); 24 women were fertile.

Mean age: entire group: 41.92 years old (women 40.72 years old; men 43.31 years old).

Median delay from onset to admission: 5 days

Median delay from admission to neuroradiological examination (CT, MRI, MRA, DSA): 4 days

Median hospitalization: 18 days

Mode of onset:

- acute (<48 hours): 34 patients (50.74%)
- subacute (1-4 weeks): 31 patients (46.26%)
- chronic (>4 weeks): 2 patients (2.98%)

Clinical aspects at onset:

- headache: 40 patients
- papilledema: 10 patients
- motor and/or sensory deficits: 4 patients
- seizures: 4 patients
- drowsiness, mental changes, confusion or coma: 6 patients
- aphasia: 3 patients
- multiple cranial nerve palsies: 10 patients
- cerebellar incoordination: 1 patient

CASE 1

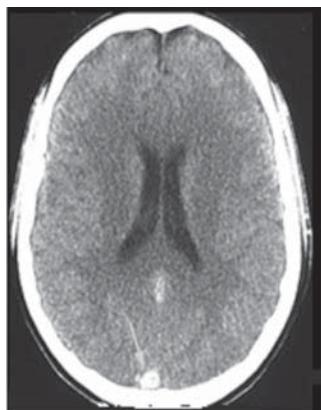


FIGURE 1. Unenhanced CT scan. Dense triangle in a recent S.S.S. thrombosis arrow. The thrombus is hyperdense. (Man, 44 years old, with headache, papilledema, left sixth nerve palsy)

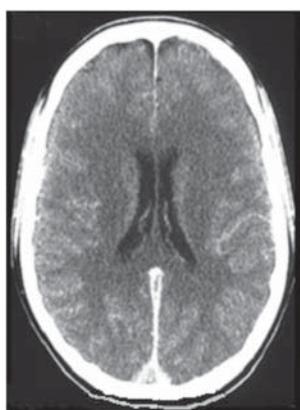


FIGURE 2. Enhanced CT scan in the same patient 10 days later. Empty delta sign. The thrombus is hypodense within the sinus, whose walls are clearly enhanced by the injection

CASE 2

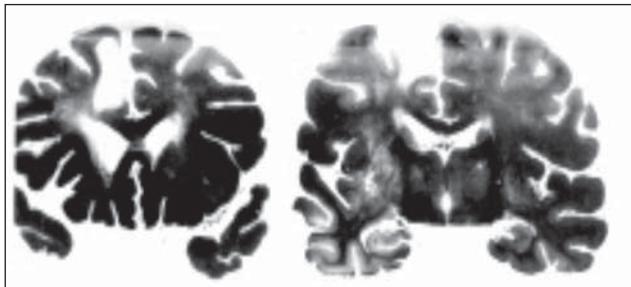


FIGURE 3. (left hemorrhagic infarct in S.S.S. thrombosis)

CASE 3

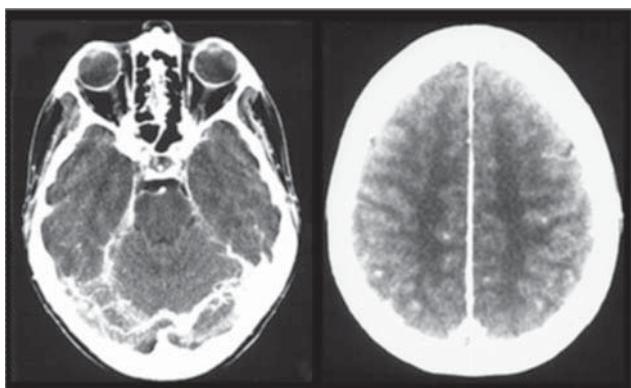


FIGURE 4. Enhanced CT scan (intense contrast enhancement of the tentorium associated with dilated transcerebral veins indicating a major venous stasis, in relation to an extensive S.S.S. thrombosis; empty delta sign). Women, 37 years old, puerperium with headache, papilledema and seizures.

Neurological syndromes at onset:

- intracranial hypertension (persistent and isolated)
 - subacute or progressive onset
 - focal neurological signs (deficits and/or seizures and/or altered consciousness)
 - sudden onset
 - cavernous sinus thrombosis
 - sudden onset
 - subacute encephalopathy
 - depressed level of consciousness
 - unusual presentations
 - subacute onset of multiple deficits with or without signs of increased intracranial pressure
 - TIA like
 - psychiatric disturbances (anxiety, depression).

Neuroradiological examinations:

- CT: 67 patients
- MRI+/-MRA: 41 patients
- DSA: 4 patients

CSF examination: 2 patients

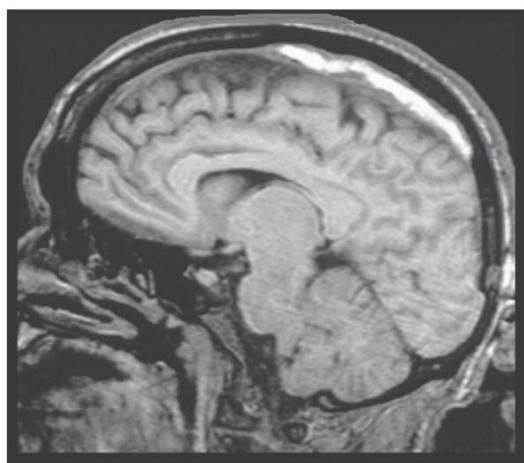
CASE 4

FIGURE 5. M.R.I., T1-weighted image. Hyperintense signal indicating subacute thrombosis of the S.S.S.; this pattern was found 14 days after the onset of symptoms: headache, seizures.

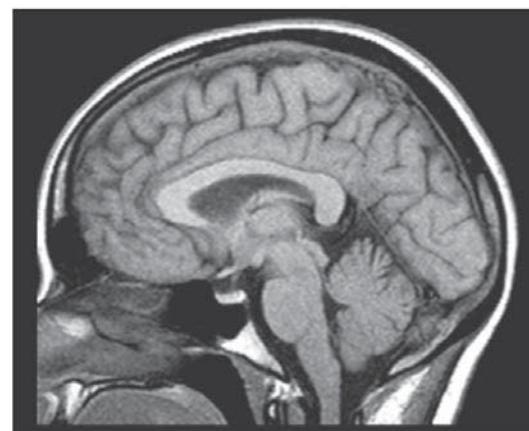


FIGURE 6. M.R.I., T1-weighted image. Hypointense signal indicating chronic thrombosis of the S.S.S.; same patient 1 month later.

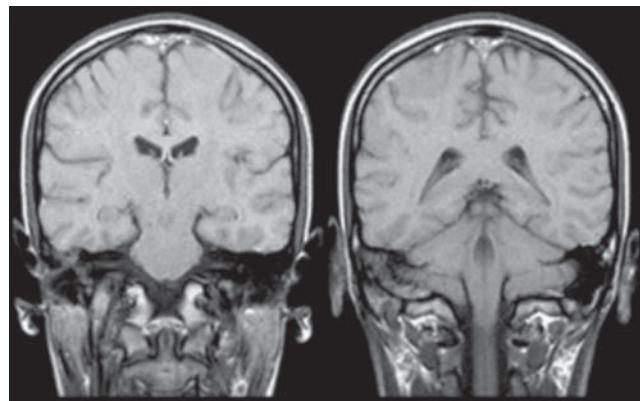
CASE 5

FIGURE 7. Woman, 32 years old, oral contraceptives with headache, papilledema, sixth nerv palsy, right hemiparesis. (S.S.S. thrombosis - M.R.I.)

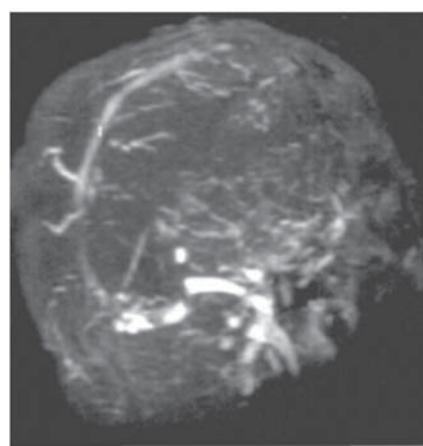
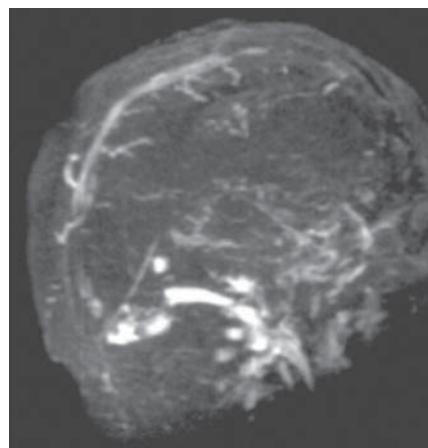
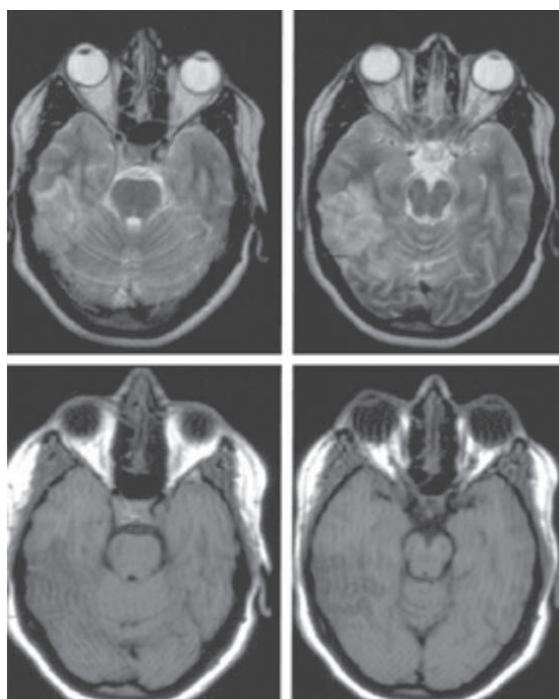
CASE 6

FIGURE 8. Women, 38 years old, puerperium with headache and seizures (partial right lateral sinus – L.S. – thrombosis with hypointense signal in T1 and hyperintense signal in T2-M.R.I.)

Localization of thrombosis:

- one sinus 47 patients (70.14%)
- two or more sinuses and cortical veins: 18 patients (26.86%)
- cortical veins (without sinusal occlusion): 2 patients (2.98%)

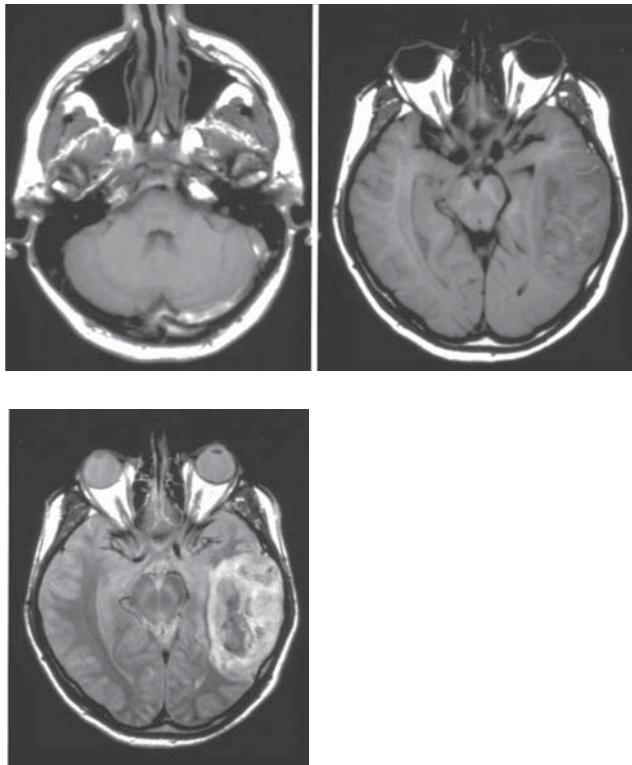
CASE 7

FIGURA 9. Men, 30 years old with headache and right hemiparesis (left L.S. and S.S.S. thrombosis and left T-P hemorrhagic infarct - M.R.I.)

Etiology of C.V.T.:

- unknown: 26 patients (38.80%)
- known: 41 patients (61.19%)
 - infectious causes: 19 patients (suppurative process of the upper one-half of the face, sinusitis, oto-mastoiditis) (fig. 10)
 - noninfectious causes: 32 patients (head injury, pregnancy or puerperium, oral contraceptives, visceral carcinomas, polycitemia verra, protein C deficiencies, systemic lupus erythematosus).

Seven patients presented two or more known etiologies.

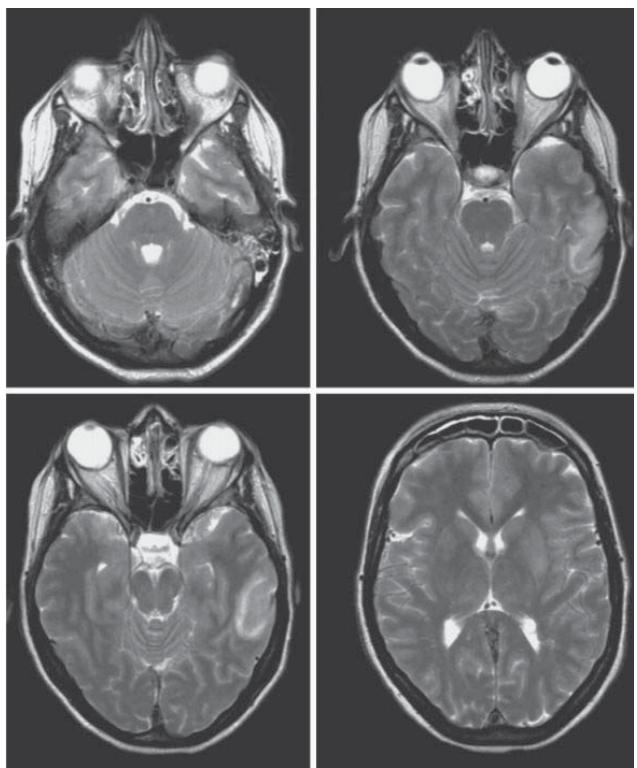
CASE 8

FIGURE 10. Man, 40 years old, mastoiditis (left T1-lenticular hemorrhagic infarct and straight sinus and S.S.S. Thrombosis)

Treatment:

1. symptomatic treatment:
 - anticonvulsant treatment: 23 patients
 - lowering intracranial pressure: 67 patients (mannitol and diuretics)
2. etiologic treatment:
 - wide spectrum combination antibiotics: 46 patients
 - surgical treatment of the primary site of infection: 2 patients
 - peculiar treatment in:
 - malignancies: 1 patient
 - connective tissue diseases: 1 patient
 - hematologic disorders: 6 patients
3. antithrombotic treatment:
 - unfractionated heparin (UH): 36 patients
 - low molecular weight heparin (LMWH): 31 patients
 - oral anticoagulant at discharge: 47 out of 65 patients discharged
 - antiplatelet therapy at discharge: 18 out of 65 patients discharged

CASE 9

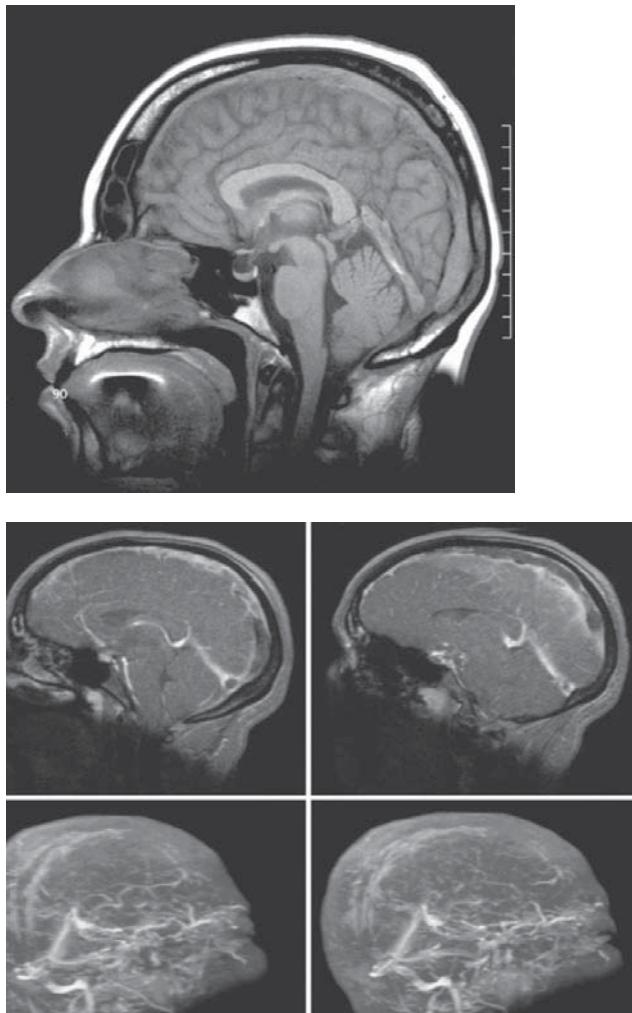


FIGURE 11. Woman, 22 years old, puerperium with headache and papilledema (S.S.S., left L.S. and torcular herophili thrombosis)

Short term outcome:

- deaths in hospital: 2 patients (2.98%) (massive hemorrhagic cerebral infarct 1 patient, pulmonary embolism 1 patient)
- deaths in first month after discharge: 4 patients (5.97 %) (pulmonary embolism)
- relapses of thrombosis: (C.V.T – 4 patients, thrombosis of profound veins of the legs – 6 patients): 10 patients
- seizures after discharge: 6 patients
- after 90 days from admission, the modified Rankin Score (mRS) was:
 - level 0-2: 48 patients
 - level 3-5: 13 patients

DISCUSSIONS AND CONCLUSIONS

Lately, there were published some studies regarding the role of antiphospholipidic antibodies as

non-infectious cause of C.V.T. They represent a group of heterogeneous antibodies targeted toward phospholipids and phospholipid-proteic complexes. The presence of antiphospholipidic antibodies was related with thrombo-embolic events, such deep venous thrombosis, pulmonary embolism, myocardial infarction and cerebral ischemia. The importance of these various auto antibodies, regardless if they only represent a cause or a consequence, or only a coincidence, is still an item in debate. Several studies from a few years ago have analyzed the relationship between the antiphospholipidic antibodies and myocardial and cerebral infarction, but their results are non-conclusive. These non-conclusive results are due, at least, because different selection criteria or different testing methods. Moreover, an important number of studies have concentrated above the anticardiolipin antibodies, neglecting the possible importance of some lupus anticoagulants, much more important for clinic.

Nevertheless, the first step in the evaluation of the determinant role of antiphospholipidic antibodies in the pathogenesis of the cerebral ischemia is to show an increased prevalence of these antibodies in patients with ischemic stroke.

Kahles et al. (Kahles et al, 2005) have shown a potential role of IgG antiphosphatidylserine and IgA anti-beta-2-glicoprotein in the etiology of stroke. With the exception of cryptogenic stroke, there is a tendency toward positive association, but without significance, between the lupus anticoagulant and IgM antiphosphatidilinositol. At the follow-up examinations, the lupus anticoagulant has persisted only at the patients with lupus.

Kahles's results confirm the conclusions of some other anterior studies which have revealed an independent association between the ischemic stroke, IgG antiphosphatidylserine and IgA anti-beta-2-glicoprotein I. Regarding the IgG and IgM antiphosphatidylserine, Thurim et al (Thurim et al, 1999) have found a risk ratio of 3.2 at patients with stroke of various etiologies vs. normal subjects. Moreover, at young patients with cerebro-vascular disease of undetermined etiology, some researchers have showed an increased prevalence of antiphosphatidylserine.

For answering to the question if antiphosphatidyl antibodies play a major role in stroke occurrence, the presence and concentrations of these antibodies must be compared between the groups of patients with ischemic stroke of unknown etiology vs. the group of patients with a certain etiology. Kahles et al, in their study, didn't discover a relevant difference

regarding IgG antiphosphatidylserine and IgA anti-beta-2-glicoprotein between the two groups.

Pathophysiologically, there is a small probability that the presence of antiphospholipidic antibodies in stroke patients to be only an epiphomena. Camerlingo et al (Camerlingo et al., 1995) have found a significantly increased prevalence of anticardiolipin antibodies at patients with stroke in the first 6 hours from the symptoms onset. This result sustains the idea of a causing role of these antibodies, and not a consequence of stroke. The lack of a strong relationship between antiphospholipidic antibodies in stroke patients of a well known etiology may suggest that these antibodies represent moreover a co-factor and not an independent cause of stroke.

Despite the assiduous investigations performed, up to 33% of our patients with C.V.T. do not have a clearly identifiable mechanism of intravascular thrombosis, results which are comparable with the data obtained from literature. (Einhapl K.M., Masuhr F, 1994)

C.V.T. is a disease of all ages, especially for young women (24 out of 35 women were in fertile period of their life). (Cantu C., Barinagarrementeria F, 1993)

The incidence of septic C.V.T. in our study is reduced (accounting for less than 26% of cases) like in similar studies from West Europe.

Pregnancy and puerperium (Lamy C, Hamon J.B., Coste J et al, 2000) are the most frequent causes for C.V.T. at young women in our region.

Oral contraceptives (Buchanan D.S., Brazinsky J.H., 1970) do not represent an important risk factor for C.V.T. in Banat.

The most frequent syndrome identified in C.V.T. is one of subacute and progressive onset of intracranial hypertension; a second pattern includes the sudden onset of focal neurological signs (deficits and/or seizures).(Bousser M.G., 2000)

The treatment of choice consists of heparin (U.H or L.M.W.H).(Rousseaux P., Bernard M.H., Scherpereel B et al, 1978)

C.V.T.'s outcome is usually favorable (mRS = 0-2 for the majority of patients discharged).(De Brujin S.F.T.M., DE Haan R.J., Stam J, 2001)

The mortality is 8.95%, comparable with the results obtained by other authors. (Ferro J.M., Correia M., Pontes C et al, 2001)

CT scanning is the first neuroimaging examination carried out in patients with C.V.T.

Isolated cortical vein thrombosis is overlooked, because of its difficult diagnosis.

C.V.T. can be diagnosed by MRI and MRA (41 patients).

DSA is reserved for cases whose diagnosis remains uncertain with MRI+MRA (4 patients).

C.V.T. in Banat remains an under evaluated disease as appeared to the information provided by the literature (I.S.C.V.T.) (non-specific clinical signs of C.V.T. and MRI difficult to access). (Jianu et al 2008)

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