CEREBRAL VEIN AND DURAL SINUS THROMBOSIS: AN EVALUATION OF 30 CASES

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ABSTRACT

Background and objectives: cerebral vein and dural sinus thrombosis (CVT) present a variety of non-specific clinical signs, but, due to the development of neuroimaging techniques, especially magnetic resonance imaging, their identification has increased in recent years, due to the development of neuroimaging techniques, especially of magnetic resonance imaging.

The aim of our study was to identify causes and risk factors, to describe the demographic, clinical, laboratory and neuroimaging data, and to evaluate the treatment and outcome of patients with C.V.T., comparing our experience with international literature.

Patients and methods: we included 30 patients (pts) with CVT, between January 1998 and September 2010. The diagnosis was based in all cases on neuroimaging features. The pts were examined at admission and after three months, using the mRS scores.

Results: mean age was 37.2 years (SD 8.6), sex ratio: male/female was 1/2. 80% of women were fertile. The main clinical manifestations were headache: 22 pts (73.3%), and papilledema: 16 pts (53.3%). The most frequent neurological syndrome at onset was intracranial hypertension with subacute evolution. CT showed direct signs of dural sinuses thrombosis: (dense triangle sign in 3 pts, delta sign in 7 cases); in 12 pts, we identified a venous cerebral infarct (indirect sign of dural sinuses thrombosis). MRI identified thrombosis of SSS in 21 pts, transverse sinus in 12 cases, cavernous sinus in 3 pts, cerebral edema in 18 pts. In 12 cases, we identified a venous cerebral infarct. 7 out of 30 MRI had a normal CT. DSA revealed isolated cortical veins occlusion, without sinus occlusion in 2 cases (CT, MRI, and MR-A were normal). Risk factors were identified in 22 pts (73.3%); congenital thrombophilia being the most common (9 pts). All pts received anticoagulant therapy. After 90 days from admission, complete resolution of symptoms was seen in 14 cases, minimal neurological deficits in 7 pts, and the death rate was 16.7% (5 pts).

Conclusions: CVT appear to be underdiagnosed in our region, due to low percentage of admissions for benign intracranial hypertension. CVT was common in women of fertile age, but oral contraceptive was not an important risk factor. The outcome was favorable with adequate therapy.

Key words: cerebral venous thrombosis, dural sinuses, anticoagulant therapy

BACKGROUND AND AIM

Cerebral vein and dural sinus thrombosis (CVT) are manifested by a variety of non-specific clinical signs, the only exception being thrombophlebitis of the cavernous sinus. C.V.T. appear to be rare, with a prevalence estimated between 2-7 new cases over 1,000,000 in general population, but, due to the development of neuroimaging techniques, especially of magnetic resonance imaging, their identification has increased in recent years. Their prompt diagnostic is very important, because time early diagnosis and adequate therapy have an essential impact on the disease's evolution, significantly reducing the risk for acute complications and sequelaes.

The aim of our study was to identify causes and risk factors, to describe the demographic, clinical, laboratory and neuroimaging data, and to evaluate the treatment and outcome of patients with C.V.T., comparing our experience with international literature.

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PATIENTS AND METHODS

We included 30 patients (pts) with CVT, that were admitted in our department between January 1998 and September 2010. 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 all cases taking into consideration factors such as: sex, age, etiology, clinical features, laboratory data and neuroimaging aspects (the identification of C.V.T. was made in all cases by computer tomography – CT, magnetic resonance imaging – MRI, magnetic resonance angiography – MR-A, and, in selected cases, by digital substraction angiography (DSA).

We recorded the pts at admission and after three months, using the modified Rankin scale (mRS) scores.

RESULTS

Total number of cases: 30. Sex ratio: women/men = 2/1 (20 women and 10 men); 16 women were fertile (80%). Mean age of the entire group was 37.2 years old (SD 8.6). Median delay from admission to neuroimaging examination was 4 days. Median hospitalization was 18 days.

Mode of onset:
- acute (<48 hours): 4 pts (13.3%);
- subacute (1-4 weeks): 20 pts (66.7%);
- chronic (>4 weeks): 6 pts (20%).

Clinical aspects of onset:
- headache: 22 pts (73.3%);
- papilledema: 16 pts (53.3%);
- motor and/or sensory deficits: 14 pts (46.7%);
- seizures: 10 pts (33.3%);
- drowsiness, mental changes, confusion or coma: 5 pts (16.7%);
- aphasia: 3 pts (10%);
- multiple cranial nerve palsies (cavernous sinus syndrom): 3 pts (10%);
- cerebellar incoordination: 1 pt (3.3%).

Neurological syndromes at onset:
- intracranial hypertension (persistent and isolated), with subacute or progressive onset.
- focal neurological signs (deficits and/or seizures and/or altered consciousness), with sudden onset.
- cavernous sinus thrombosis, with sudden onset.
- subacute encephalopathy, with depressed level of consciousness.

After diagnostic in hospital, the modified Rankin Scale (mRS) scores of the pts were:
- level 1-2: 6 pts;
- level 3-5: 24 pts.

*Neuroimagistic examination*s:
- CT: 30 pts:

CT showed direct signs of dural sinuses thrombosis: dense triangle sign in 3 pts, empty delta sign in 7 cases. Indirect signs of dural sinuses thrombosis: venous cerebral infarction in 12 cases, cerebral edema in 18 pts, intense contrast enhancement of the falx and tentorium in 2 pts.
- MRI+/-MRA: 30 pts:

MRI showed thrombosis of SSS in 21 pts, transverse sinus in 12 cases, cavernous sinus in 3 pts. cerebral edema in 18 pts. In 12 cases, we identified a venous cerebral infarction. 7 out of 30 MRI had a normal prior CT.
- DSA: 2 pts.

DSA showed isolated cortical veins occlusion, without sinus occlusion (prior CT, MRI, and MR-A were normal).

Localization of thrombosis:
- one sinus: 6 pts (20%) (3 pts: cavernous sinus; 3 pts SSS);
- one sinus and cortical veins: 8 pts (26.7%);
- two or more sinuses and cortical veins: 14 pts (46.6%);
- cortical veins (without sinus occlusion): 2 pts (6.7%).

Laboratory data:
- Blood examination (including D-dimer levels, C-reactive protein, FV Leiden mutation, antiphospholipid antibodies, etc): 30 pts;
- Cerebrospinal fluid examination: 4 pts.

Etiology:
- *unknown:* 8 pts (26.6%);
- *known*: 22 pts (73.3%):
  - infectious causes: 5 pts (suppurative process of the upper one-half of the face: 3 pts; otomastoiditis: 2 pts);
  - noninfectious causes: 17 pts:
  - congenital thrombophilia: 9 pts (FV Leiden in 6 cases, FII G20210A, 2 pts, and MTHFR C677T in 1 case);
  - pregnancy or puerperium: 8 females;

- oral contraceptives: 4 females;
- visceral carcinomas: 3 pts;
- systemic lupus erythematosus: 2 pts.

Treatment:

- symptomatic treatment:
  - anticonvulsivant treatment: 10 pts;
  - lowering intracranial pressure: 16 pts: mannitol and diuretics.
- etiologic treatment:
  - wide spectrum combination antibiotics: 5 pts;
  - surgical treatment of the primary site of infection: 5 pts;
  - peculiar treatment in: malignacies: 3 pts; connective tissue diseases: 2 pts.
- antithrombotic treatment:
  - low molecular weight heparin (LMWH): all 30 pts received it after diagnosis, and 15 out of 27 pts which were discharged;
  - oral anticoagulant at discharge: 7 out of 27 pts discharged;
  - antiplatelet therapy at discharge: 5 out of 27 pts discharged.

Outcome at 3 months after admission in the hospital:

- deaths in hospital: 3 pts (10%) (massive hemorrhagic cerebral infarct 1 pt, pulmonary embolism 2 pts);
- deaths after discharge: 2 pts (6.7%) (pulmonary embolism);
- relapses of thrombosis: 4 pts (C.V.T. 1 pt, thrombosis of profound veins of the legs: 3 pts);
- seizures after discharge: 3 pts;
- after 90 days from admission, the modified Rankin Scale (mRS) scores were:
  - level 0-2: 21 pts;
  - level 3-5: 4 pts;
  - level 6: 5 pts.

DISCUSSIONS AND CONCLUSIONS

C.V.T. appear to be underdiagnosed in our region if we compare our findings to the data supplied by international literature *(the multicenter International Study on CVT – I.S.C.V.T.*, *Bousser M.G., 2000),* due to low percentage of admissions of C.V.T. for benign intracranial hypertension, to non-specific clinical signs of the great majority of C.V.T., and to difficulties to access to MRI examination. (*Jianu et al, 2008*)

Despite the assiduous investigations performed, up to 25% of our patients with C.V.T. didn't have a clearly identifiable mechanism of intravascular thrombosis, results which are comparable with the data mentioned in international literature. (*Einhäupl K.M., Masuhr F., 1994)*

C.V.T. is a disease affecting especially young women (16 out of 20 were in the fertile period of their life). (*Cantu C., Barinagarrementeria F., 1993)*

The incidence of septic C.V.T. in our study was reduced (accounting for less than 20% of cases) like in similar studies from Western Europe. Pregnancy and puerperium were the most frequent causes for C.V.T. in young women in our region, data which are comparable with those of international studies. (*Cantu C., Barinagarrementeria F., 1993, Lamy C., et al, 2000*).

Oral contraceptives didn't represent an important risk factor for C.V.T. in Banat, like in some other studies (*Buchanan D.S., Brazinsky J.H., 1970*).

Detailed coagulation studies have only rarely been performed in series of C.V.T., and their results are conflicting. (*Bousser M.G., 2000*) The most frequent cause of C.V.T. in our study was congenital thrombophilia, data which are similar to Bousser studies. (*Bousser M.G., 2000*) There were published some studies regarding the role of antiphospholipidic antibodies as non-infectious cause of C.V.T. (*Camerlingo et al.,1995, Kahles et al., 2005)* The presence of antiphospholipidic antibodies was related to thromboembolic events, such as deep venous thrombosis, pulmonary embolism, myocardial infarct and cerebral ischemia. The importance of these various autoantibodies, regardless if they only represent a cause or a consequence, or only a coincidence, in thromboembolic events is still an item for debate. (*Tuhrim S., et al.1999)*

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

Since the etiology and the spectrum of its clinical manifestations were extremely wide, the neuroimaging techniques played a front-line role in the diagnosis process. CT scanning was the first neuroimaging examination carried out in pts with C.V.T, followed by MRI and MR-A. Isolated cortical vein thrombosis was overlooked, because of its difficult diagnosis. DSA was reserved only for cases whose diagnosis remained uncertain with MRI associated with MR-A.

Because CVT is an relatively uncommon disease, with a great variability in clinical signs, treatment is still controversial. The treatment of choice in our cases consisted of heparin (L.M.W.H), following the informations provided by the literature (*I.S.C.V.T.*, *Bousser M.G., 2000*)

C.V.T.'s outcome was usually favorable with early diagnosis and with adequate therapy (mRS scores were 0-2 for the majority of pts discharged), data which are comparable with those of international studies. (*De Bruijin S.F.T.M.,et al., 2001*)

The mortality rate (16.7%) was higher than the one mentioned in the reports from western countries (*Ferro J., et al., 2001*), because some of our patients presented factors classically considered to suggest a bad prognosis (an infection cause, focal symptoms and coma, presence of a hemorrhagic infarct and empty delta sign on CT scan (*Bousser M.G., 2000*).

CASE 1

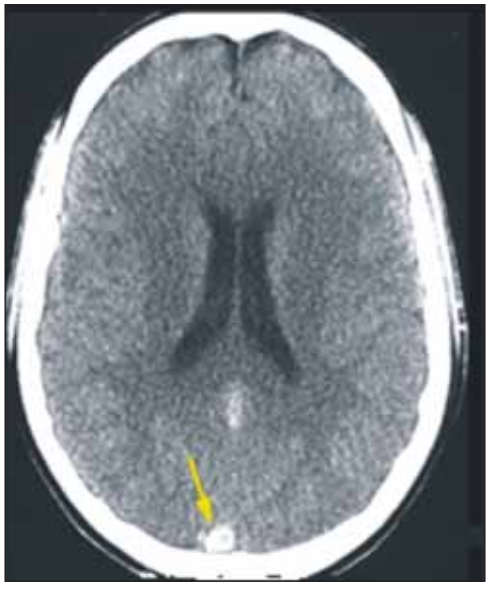


Figure 1 *(unenhanced CT scan). Dense triangle in a recent S.S.S. thrombosis. The thrombus is hyperdense (arrow).*

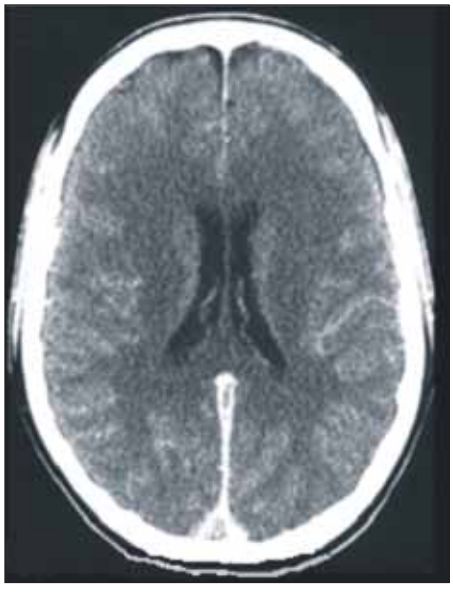
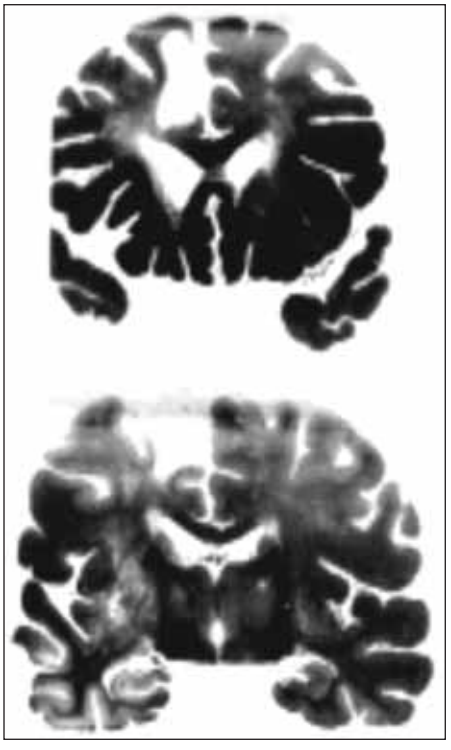


Figure 2. *Enhanced CT scan in the same patient 10 days later. Empty delta sign. The thrombus is hypodense within the sinus, whose walls are clearly enhanced by the injection.*

CASE 2



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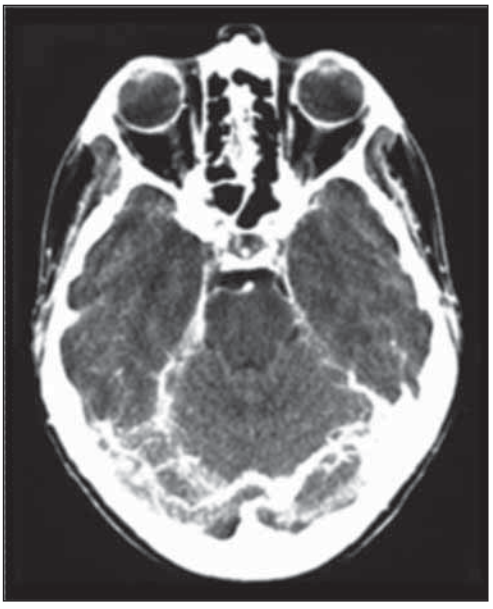


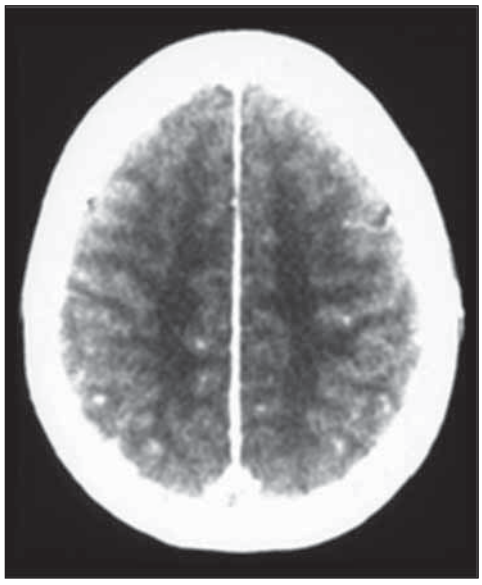


Figure 4. *Enhanced CT scan (intense contrast enhancement of the tentorium associated with dilated transcerebral veins indicating a major venous stasis, in relation to an extensive S.S.S. thrombosis; empty delta sign).*

CASE 4

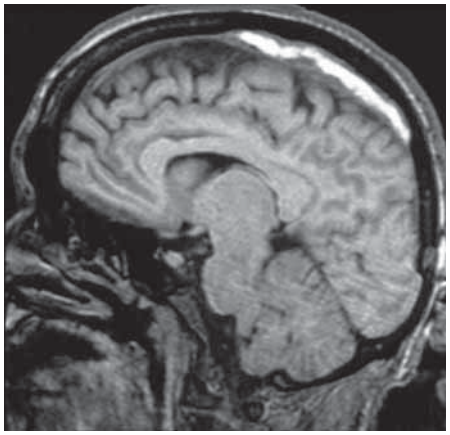


Figure 5. *M.R.I., T1-weighted image. Hyperintense signal indicating subacute thrombosis of the S.S.S.; this pattern was found 14 days after the onset of symptoms.*

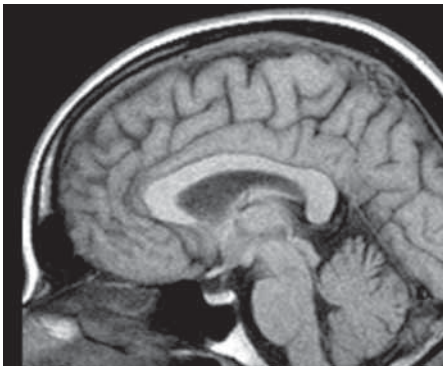


Figure 6. *M.R.I., T1-weighted image. Hypointense signal indicating chronic thrombosis of the S.S.S.; same patient, 1 month later.*

CASE 5

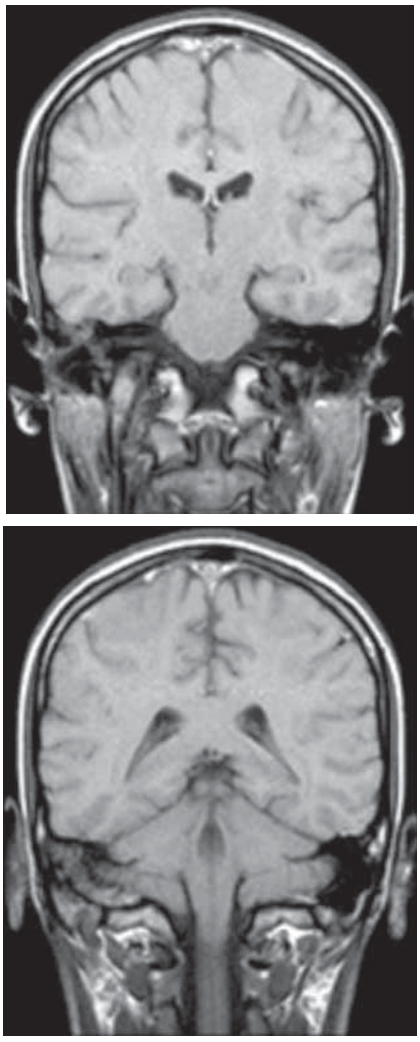
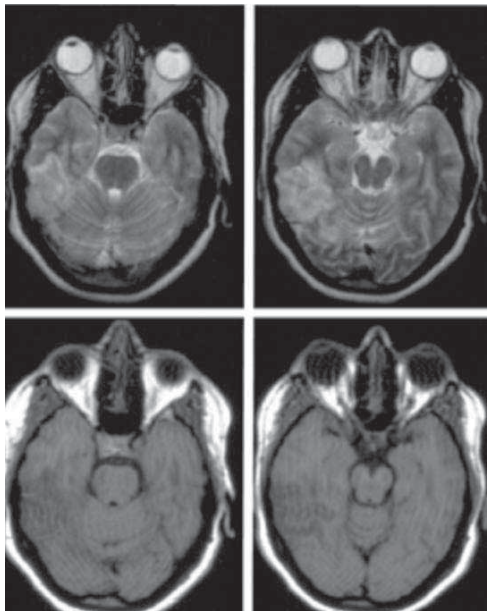


Figure 7. *Woman, 32 years old, oral contraceptives with headache, papilledema, sixth nerv palsy, right hemiparesis. (S.S.S. thrombosis - M.R.I.)*

CASE 6



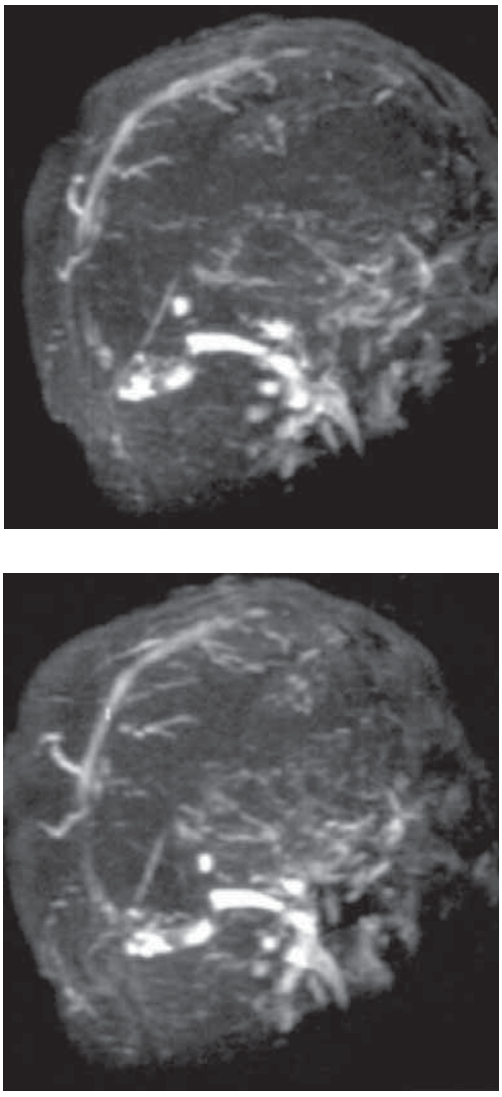
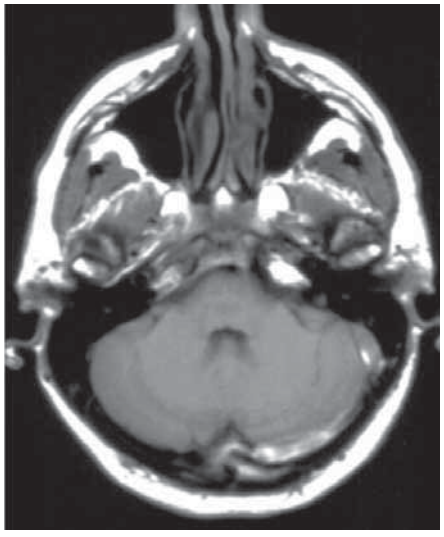


Figure 8. *Women, 38 years old, puerperium with headache and seizures (partial right lateral sinus – L.S.-thrombosis with hypointense signal in T1 and hyperintense signal in T2- M.R.I.)*

CASE 7



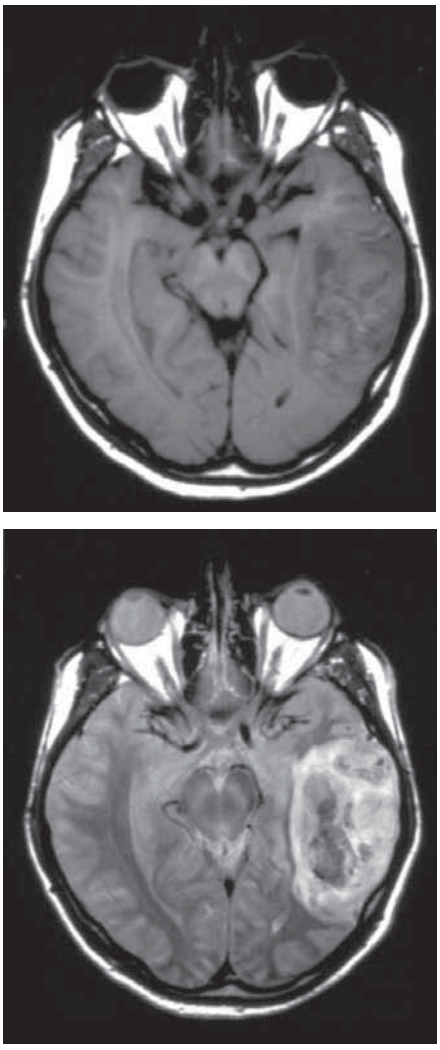
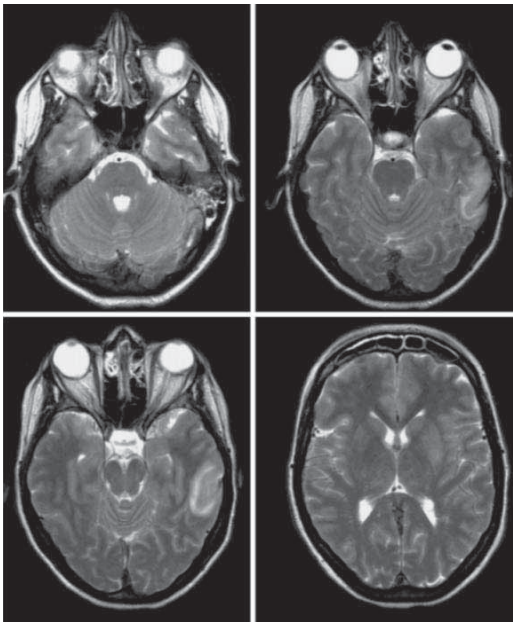


Figure 9. *Men, 30 years old, with headache and right hemiparesis (left L.S. and S.S.S. thrombosis and left T-P hemorrhagic infarct - M.R.I.)*

CASE 8



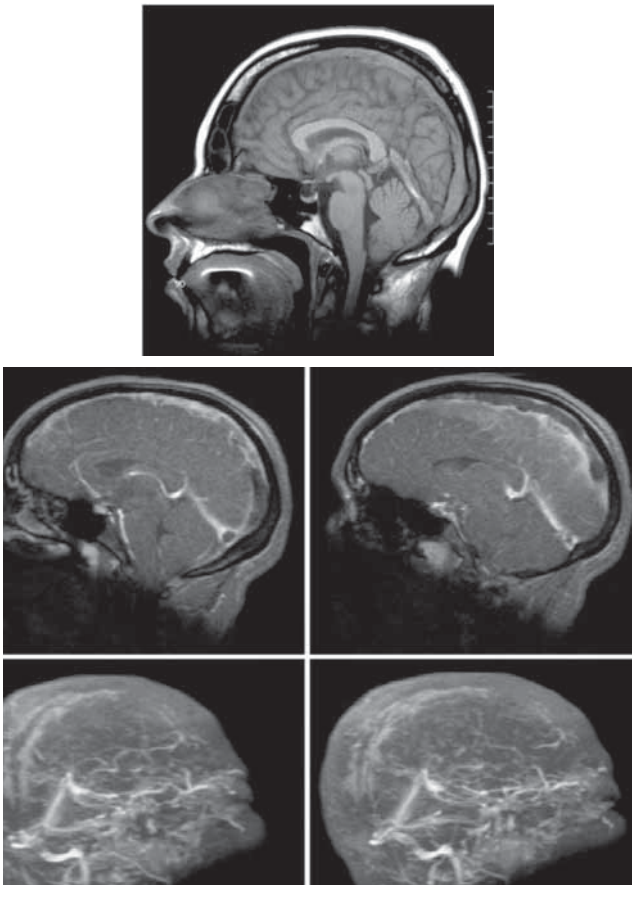


Figure 11. *Woman, 22 years old, puerperium with headache and papilledema (S.S.S., left L.S. and torcular herophili thrombosis).*

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