CME

The spectrum of presentations of venous infarction caused by deep cerebral vein thrombosis

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Abstract—The classic features of thrombosis of the deep cerebral venous system are severe dysfunction of the diencephalon, reflected by coma and disturbances of eye movements and pupillary reflexes, resulting in poor outcome. However, partial syndromes without a decrease in the level of consciousness or brainstem signs exist, which may lead to initial misdiagnoses. The spectrum of clinical symptoms reflects the degree of venous congestion, which depends not only on the extent of thrombosis in the deep veins but also on the territory of the involved vessels and the establishment of venous collaterals. For example, thrombosis of the internal cerebral veins with (partially) patent basal veins and sufficient collaterals may result in relatively mild symptoms. Deep cerebral venous system thrombosis is an underdiagnosed condition when symptoms are mild, even in the presence of a venous hemorrhagic congestion. Identification of venous obstruction has important therapeutic implications. The diagnosis should be strongly suspected if the patient is a young woman, if the lesion is within the basal ganglia or thalamus, and especially if it is bilateral.

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MRI has improved recognition of thrombosis. Deep cerebral venous thrombosis (DCVT), i.e., of the internal cerebral veins, the basal veins (vein of Rosenthal), or the great cerebral vein (vein of Galen), affect 3 to 8% of patients, predominantly women.[1,2] Patients with DCVT often present with a rapidly declining course, altered level of consciousness, and long tract signs. Death or long-term sequelae are common.[3]

The clinical presentations of DCVT can be less severe, without affecting consciousness. As the radiologic signs of venous (hemorrhagic) infarction are not always easily recognized, such atypical clinical presentations may not be correctly identified.[4,5]

We describe the spectrum of clinical presentations in relation to the anatomy of the deep venous system.

Case 1. A 30-year-old woman with a history of frequent headaches consulted a neurologist in a regional hospital because of a progressive headache, located on the left side, for 2 weeks; it was accompanied by vomiting and became worse when she was up and about. She had noticed a right-sided visual defect that hindered her walking ability. She had been using nonsteroidal anti-inflammatory drugs (NSAIDs) without relief. Her only other medication was the oral contraceptive pill; she had no history of smoking.

Physical examination showed a fatigued young woman with a normal level of consciousness and a right-sided hemianopia. Brain CT and MRI showed a mass in the left thalamus, provisionally diagnosed as a tumor, after which the patient was referred to the neurosurgery department of our hospital.

Shortly after admission to our hospital the patient had a generalized tonic-clonic seizure. Repeated brain MRI and MR venography showed hemorrhagic infarction in the left thalamus and massive thrombosis of the deep venous system, including the internal cerebral veins, vein of Galen, and the left transverse and sigmoid sinuses (figure 1).

The patient's mother had a history of recurrent leg vein thrombosis, but full laboratory investigations were negative for all currently known varieties of thrombophilia and autoimmune disorders.

She was treated with anticoagulant therapy and made a good recovery; after 6 months her only residual symptoms were fatigue and episodes of headache.

Case 2. A 28-year-old woman presented to the neurology department in a regional hospital with right-sided weakness that developed within 24 hours preceded by a period of 1 month with fatigue, pain in the left ear, and fever. She did not smoke and used no medication apart from oral contraceptives. Brain MRI showed a lesion in the left thalamic region. Under a provisional diagnosis of a brain abscess caused by mastoiditis, antibiotic treatment was started and a mastoidectomy was performed, which failed to show an infection. Because of the persisting hemiparesis the patient was referred to our neurosurgery department for drainage of the abscess.

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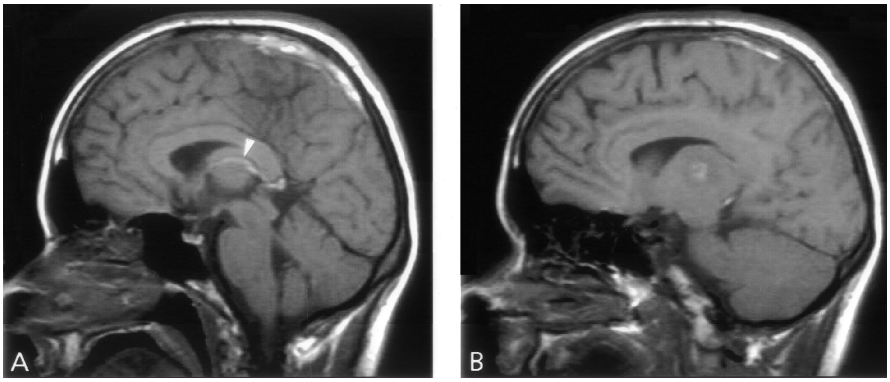

Figure 1. Case 1. (A) *Midline sagittal T1 shows that the normal flow void in the internal cerebral vein is replaced by increased signal intensity indicating recent thrombosis (arrowhead)* (B) *and a venous hemorrhagic infarction in the left thalamic region.*

Neurologic examination showed a normal level of consciousness and a right-sided hemiparesis predominating in the arm, with diminished sensation and a pathologic plantar response.

Revision of the brain MRI and repeat brain MRI and MR venography showed thrombosis of the left internal cerebral vein, the vein of Galen, the straight sinus, and the left sigmoid and transverse sinus (figure 2). The brain abscess in the left thalamic region in fact was a venous hemorrhagic infarct. The antibiotic regimen was discontinued and anticoagulation therapy was started. She made a favorable recovery, but after 1 year a mild hemiparesis and dysphasia persisted. The patient's mother had a history of repeated deep venous thrombosis but investigations showed no evidence of thrombophilia.

Case 3. A 53-year-old woman without previous medical history had a progressive headache, which had developed in the course of several days before admission to our hospital. According to her husband, on the day of admission she had been drowsy on awakening, spoke only in a monosyllabic fashion, and was incontinent of urine. For the rest of the day she had headache, acted indolently, and was unstable on her feet. There was no nausea or vomiting. She did not smoke and used no medication apart from oral contraceptives.

Neurologic examination showed disorientation in place and uninhibited behavior with a normal level of consciousness. Movements of the right hand were not fluent and her walking pattern was unstable. Brain CT showed a cord sign of both internal cerebral veins and subsequent brain

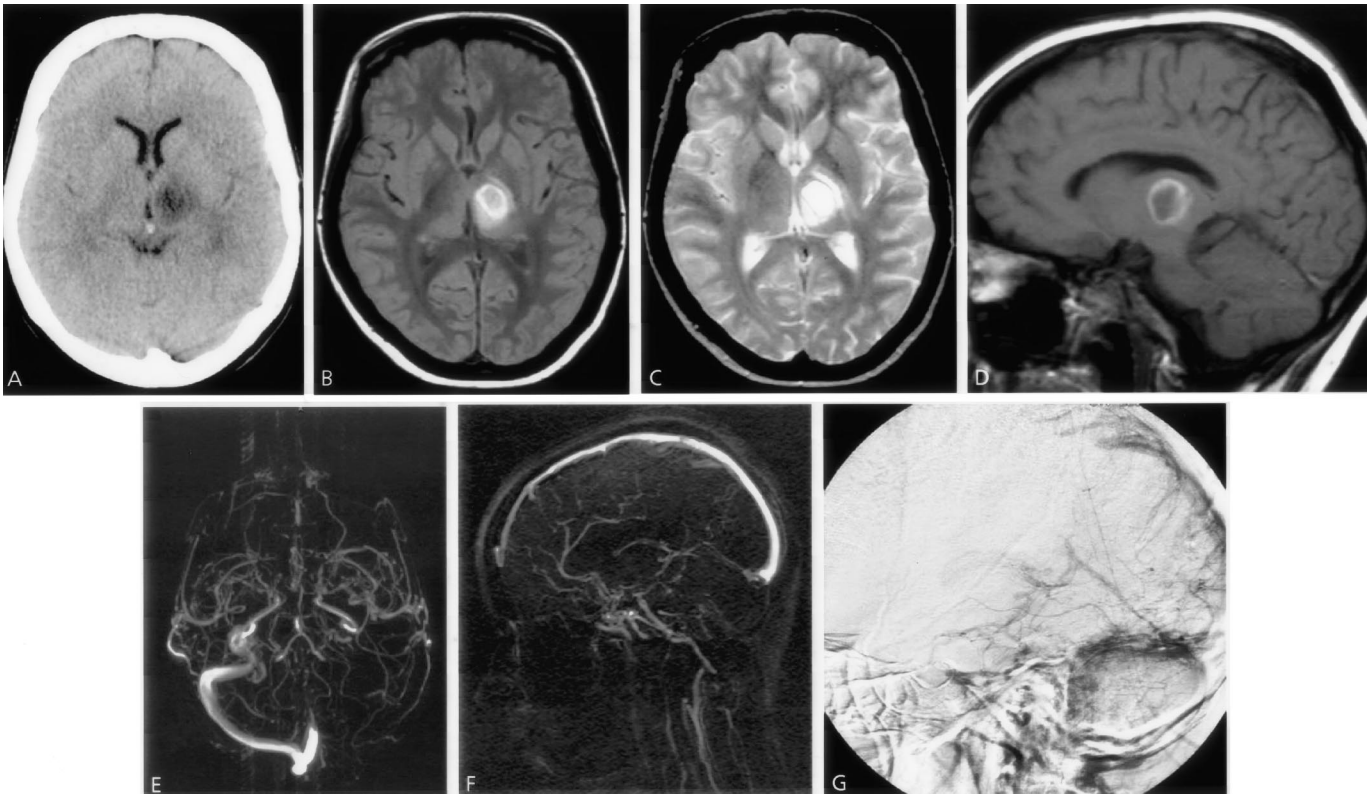

Figure 2. Case 2. (A) *Brain CT showing a hypodense lesion in the left thalamic region.* (B) *Axial MRI FLAIR,* (C) *T2, and* (D) *T1 showing edema with a hemorrhagic component in the left thalamus.* (E) *Axial and* (F) *sagittal MR venography and* (G) *sagittal digital subtracted catheter angiography showing partial filling of the internal cerebral veins, basal veins, vein of Galen, and straight sinus. The left sigmoid and transverse sinuses are absent.*

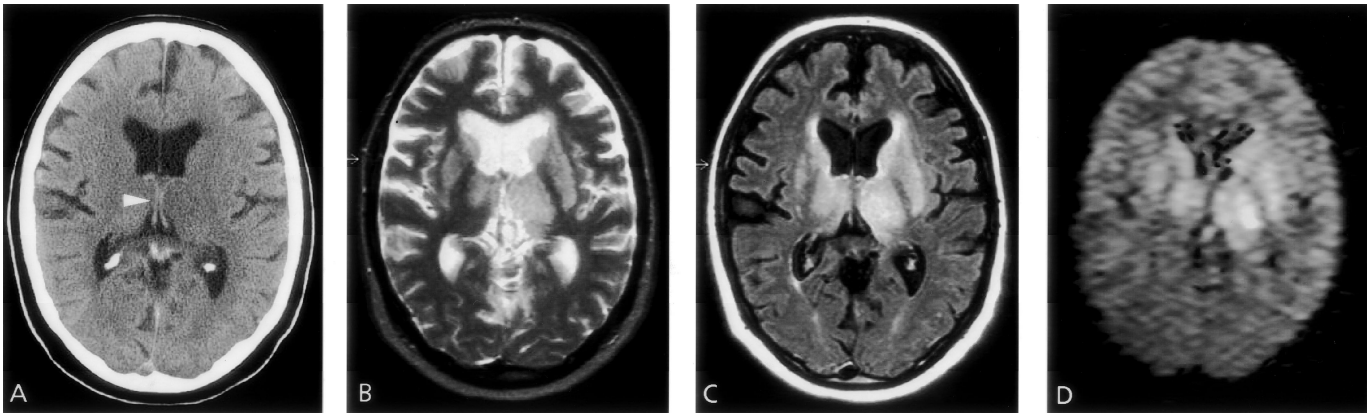

Figure 3. Case 3. (A) *Brain CT showing a dense vessel sign in both internal cerebral veins (arrowhead).* (B) *Axial MRI T2 SE,* (C) *MRI FLAIR, and* (D) *MRI DWI showing bilateral hyperintense lesions in the basal ganglia representing edema and venous infarction.*

MRI showed absence of flow voids in the internal veins as well as bithalamic hypodensities indicating venous infarction (figure 3). No additional MR or angiographic studies were done. Laboratory investigations were negative for thrombophilia and autoimmune disorders.

She was treated with anticoagulation therapy and recovered completely.

Case 4. A 53-year-old woman with premenstrual migraine in her medical history consulted a neurologist in a regional hospital because of a progressive loss of strength in the right arm and leg for 3 days, accompanied by speech difficulties and headache, located on the left side. She did not smoke and used no medication apart from oral contraceptives.

Neurologic examination showed a normal level of consciousness and a right-sided hemiparesis predominating in the arm, and aphasia.

Brain CT and MRI showed a lesion in the left thalamic region with no contrast enhancement (figure 4). Although the lesion was not compatible with (arterial) ischemia she was treated with anticoagulation therapy. There was a spontaneous recovery to only minimal dysphasia but after 4 weeks she had hallucinations which were successfully treated with antipsychotic drugs. After 5 weeks she underwent diagnostic conventional angiography which initially showed no abnormalities. Soon after the angiogram she developed three cortical ischemic lesions in arterial territories resulting in transient mutism and mild left-sided paresis. Under a provisional diagnosis of a brain tumor the patient was referred to our hospital for further analysis.

Revision of the brain MRI and angiography and repeat brain MRI showed partial thrombosis of the straight sinus and the left internal cerebral vein. The lesion in the left thalamic region had decreased in size and was in fact a venous infarct. Full laboratory investigations were negative for thrombophilia and autoimmune disorders. She is currently admitted for clinical revalidation.

Discussion. The case histories illustrate that partial syndrome exists and can be survived with surprisingly few sequelae.[6]

Many risk factors have been identified for intracranial venous thrombosis in general.[3,7-10] Oral contraceptives, pregnancy, and the puerperium are the most common factors reported in the literature; these are associated with DCVT in two-thirds of patients.[11] The oral contraceptive pill was the only identifiable factor that might have contributed to our patients' illness, but since its use is so common among women in the reproductive age this association is difficult to interpret.[12]

The deep venous system collects into channels that course through the walls of the ventricles and basal cisterns and converge on the internal cerebral, basal, and great veins (figure 5). The territory served

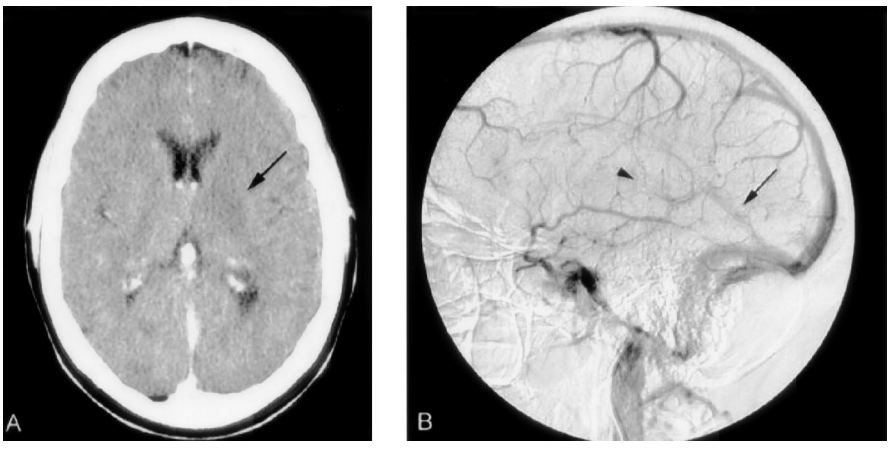

Figure 4. Case 4. (A) *Brain CT showing a hypodense lesion in the left thalamic region with no contrast enhancement.* (B) *Sagittal digital subtracted catheter angiography showing partial filling of the internal cerebral vein, and straight sinus.*

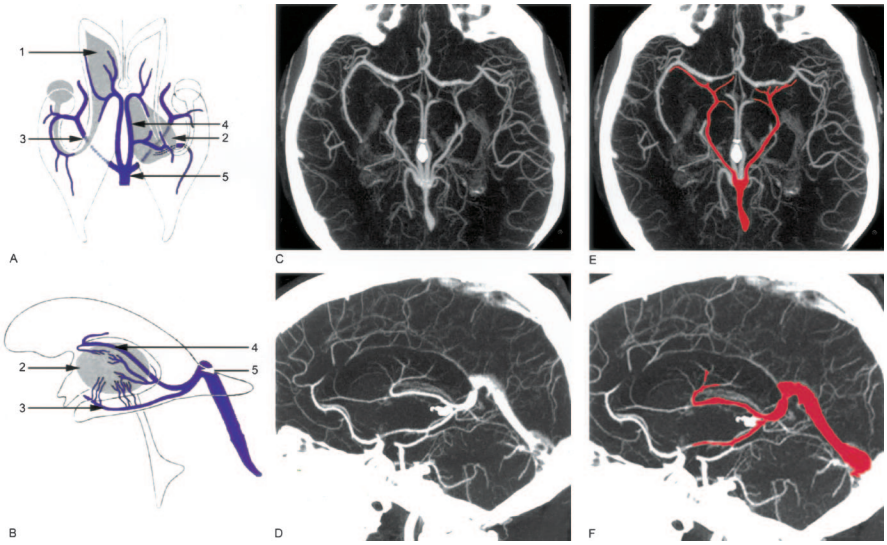

Figure 5. Anatomy of the deep cerebral venous system. (A, B) *Axial and sagittal view of deep venous system and basal ganglia: 1. caudate nucleus; 2. thalamus; 3. basal veins (veins of Rosenthal); 4. internal cerebral veins; 5. great cerebral vein (vein of Galen).* (C, D) *Axial and sagittal maximum intensity projection (MIP) images of the deep venous system.* (E–F) *Axial and sagittal MIP images; the deep venous system is demarcated in red.*

by these veins and their tributaries includes not only the choroid plexuses and the deep gray matter of the thalamus and striatum, but also the periventricular white matter and corpus callosum, hippocampus and the cortical areas of the limbic lobe (cingulate and parahippocampal gyri), the visual cortex, the diencephalon and rostral brainstem, and part of the cerebellum.[13-16] The basal vein is connected not only to the great vein of Galen, but also to the superior petrosal sinus (via the lateral mesencephalic vein), and in the adult configuration also to the cavernous sinus and pterygoid plexus (via the deep and superficial sylvian veins) and sometimes to the straight or lateral sinus via a tentorial sinus.[15,17-19] Because of these anastomotic interconnections, only simultaneous obstruction of the great vein of Galen and basal veins will effectively obstruct deep venous outflow. The functional role played by the centroperipheral anastomoses is difficult to ascertain in a given individual.

The clinical picture of thrombosis of the deep venous system is often dominated by severe dysfunction of the diencephalon, with coma and disturbances of eye movements and pupillary reflexes, with poor outcome. However, the degree of venous congestion depends on the extent of thrombosis in the deep veins, the territory of the involved vessels, the establishment of venous collaterals, and the duration of the thrombotic occlusion.

When collaterals are insufficient, massive cerebral edema with venous infarction may develop; this applies to DCVT as well as to dural sinus thrombosis. Whether hemorrhagic infarction develops depends on the intensity of venous congestion.[20]

The radiologic hallmarks the different variants of deep venous obstruction have in common are first that cortical involvement is limited to the limbic lobe and the visual cortex and second that the subcortical white matter is spared.

The diagnosis in patients with relatively mild symptoms of DCVT can be difficult also from a radiologic point of view because the appearances mimic those caused by more common lesions such as cerebral tumors, brain abscess, or top of the basilar infarcts.[5,21-23] Bilateral arterial infarcts classically occur in paramedian areas and usually demarcate more slowly than venous infarcts. Areas of venous congestion or infarction tend to have irregular edges instead of the sharper geometric margins with an arterial infarct.[24] Congestion from cerebral venous obstruction is associated with vasogenic edema on diffusion-weighted MRI,[25] unlike arterial infarction. If hemorrhage occurs in venous infarction it tends to spread from the center to the periphery, whereas in arterial infarcts it usually starts at the edges. Tumors and abscesses show more pronounced mass effect and contrast enhancement.

Additional neuroimaging findings in DCVT are hydrocephalus and a cord sign on noncontrast CT scanning, described as a spontaneously increased density of cerebral veins, usually observed during the acute phase of the disease. This early but very transient sign is caused by the hyperdense thrombus in the veins (figure 4).[26] Although MRI allows direct visualization of thrombus in both the deep veins and dural sinuses, MR angiography/venography is the most useful adjunct to MR brain imaging in order to distinguish DCVT from bithalamic lesions from other causes.[22]

Although the evidence is not conclusive, anticoagulant treatment for cerebral sinus thrombosis appears to be safe and is associated with a potentially important reduction in the risk of death or dependency.[27] As patients with DCVT might benefit from anticoagulant therapy or early application of direct endovascular thrombolytic therapy, even in the presence of a hemorrhage, it is important to make the correct diagnosis at an early stage.[28-31]

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