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Neuroimaging of Cerebral Venous Thrombosis (CVT) – Old Dilemma and the New Diagnostic Methods

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Background:

Cerebral venous thrombosis is a relatively uncommon neurologic disorder that is potentially reversible with prompt diagnosis and appropriate medical care. The pathogenesis is multifactorial and the disease may occur at any age. CVT is often associated with nonspecific symptoms. Radiologists play a crucial role in patient care by providing early diagnosis through interpretation of imaging studies.

Underdiagnosis or misdiagnosis can increase the risk of severe complications, including hemorrhagic stroke or death. The purpose of this study is to investigate radiological and clinical characteristics of cerebral venous thrombosis (CVT) based on material from 34 patients under care of our hospital.

Material/Methods:

A total of 34 patients were diagnosed with CVT from August 2009 until March 2015. A clinical and radiological database of patients with final diagnosis of CVT was analyzed.

Results:

Patient group included 22 women and 12 men at a mean age of 48.7 years (ranging from 27 to 77 years). In the study group 8 patients (23.5%) suffered from hemorrhagic infarction, whereas 16 patients (47%) were diagnosed with venous infarction without hemorrhage. Thirty patients (88%) had transverse sinus thrombosis.

Conclusions:

According to our study, CVT was more prevalent in women. Transverse sinus was the most common location. Among all age groups, the highest prevalence was seen in the fifth decade (n=14). Contrast-enhanced CT and MR venography were the most sensitive imaging modalities.

MeSH Keywords:

Intracranial Hemorrhages • Stroke • Venous Thrombosis

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Background

Cerebral venous thrombosis is a relatively rare disease that remains a diagnostic challenge due to its uncharacteristic clinical presentation.

The most common symptoms include headaches, nausea, vomiting, visual disturbances, loss of consciousness and, at times, neurological deficits. These symptoms may occur in

a course of numerous central nervous system pathologies. Venous strokes secondary to dural venous sinus thrombosis and cerebral venous thrombosis constitute 1% of all acute strokes [1].

In view of nonspecific clinical symptoms diagnostic imaging is of key importance for establishing proper diagnosis. Rapid diagnosis and appropriate treatment translates directly into better prognosis. High overall mortality (up

to 10%) observed in this condition and its subsequent decrease due to treatment makes imaging crucial for accurate diagnosis [1].

The goal of this work was to present radiological characteristics of venous sinus thrombosis and cerebral venous thrombosis as well as to identify the most sensitive methods of imaging.

Material and Methods

There were 34 cases of CVT diagnosed in a period from 08.2009 to 03.2015 at the Diagnostic Radiology Department of Central Clinical Hospital of the Ministry of Interior in Warsaw.

Computed tomography examinations in native and venous phases were performed using a 64-slice HI SPEED PRO General Electronic device, while magnetic resonance studies were completed with 1.5T Marconi and Toshiba, as well as 3T Philips Ingenia systems. The following MR sequences were performed: SE, FSE, GRE, FLAIR, DWI, while MR venography was done using TOF method and after contrast enhancement.

We subjected imaging studies to retrospective analysis, taking into consideration the location and extent of thrombotic changes, presence of ischemia, hemorrhagic foci and patients' epidemiological characteristics, including sex, age, risk factors and comorbidities.

Patients were divided into three categories depending on time from the onset of symptoms until the diagnosis in accordance with the classification suggested in the International Study on Cerebral Venous and Dural Sinuses Thrombosis (ISCVT), i.e. acute – less than 48 hours, subacute – 48 hours to 30 days, and chronic – over 30 days from the onset of symptoms.

Noncontrast computed tomography is usually the first-choice examination in the diagnostics of acute CNS disorders. Hyperdensity of dural sinus (Figure 1), cortical vein (cord sign) or deep veins is characteristic for CVT due to increased density of thrombus in comparison with the flowing blood [2–6]. These symptoms may sometimes coexist. One should remember that hyperdensity of dural sinuses or cerebral veins may be also seen in dehydration or with elevated hematocrit [5,6]. Transverse sinus thrombosis may be also mimicked by blood layered on cerebellar tentorium in a course of acute subdural hemorrhage or by epidural hematoma at the level of the sinus. Particular attention should be paid to neonates, in whom nonmyelinated brain or physiological polyglobulia might lead to overdiagnosis [5–7]. Unfortunately, sensitivity of this method is relatively low and it is estimated that thrombosis may be visualized in about 1/3 of cases, while in the remaining cases cerebral image is unremarkable [5,7]. Therefore, in patients with clinical suspicion of CVT or those with ambiguous results of initial CT imaging the diagnostics should be broadened to include CT venography. In this diagnostic method CVT presents with loss of contrasting in the thrombosed sinus – the empty delta sign (Figure 2) [2–7]. Contrast enhancement of the dura

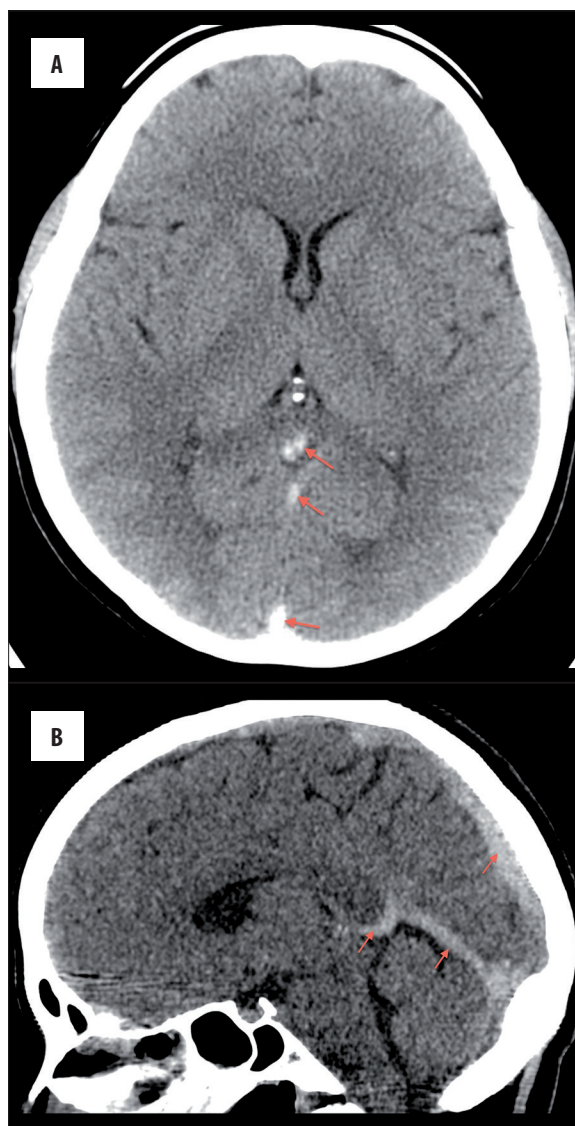


Figure 1. Unenhanced CT. Axial (A) and sagittal (B) images. Abnormal hyperattenuation in the superior sagittal sinus, straight sinus and internal cerebral veins.

matter and the blood flowing around hypodense thrombus is apparent in such cases. Lack of sinus contrasting does not always unequivocally indicate a thrombus; one should remember about possible anatomic variations, such as sinus hypoplasia/aplasia or presence of arachnoid granulations or fat in the sinus [5–9]. Careful analysis of 2D MPR and 2D MIP images is necessary for venography assessment. During image analysis particular attention should be paid to window settings – its width should be set at about 260 HU (W-260) and level at 130 HU (L-130), allowing for better visualization of sinuses located immediately next to the bone [5].

A digital image processing technique was used during the assessment of early ischemic lesions in CT examination in order to increase the sensitivity of detection of discrete differences in brain tissue densities in the areas with impaired venous drainage [10,11]. Digitally assisted evaluation of hypodense areas corresponding to edema,

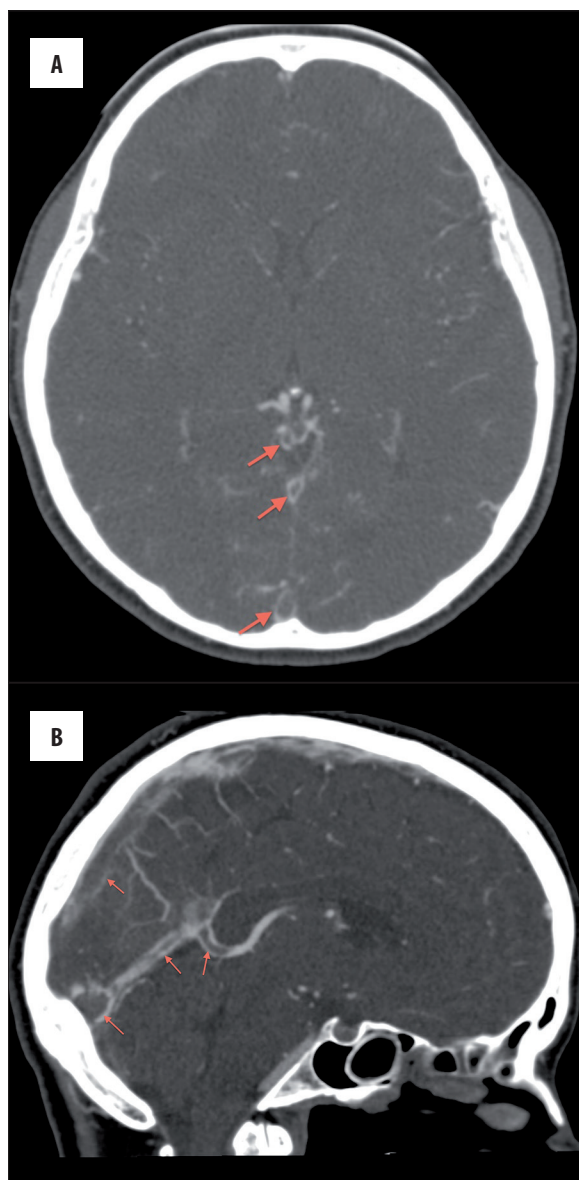


Figure 2. Contrast-enhanced CT. Axial (A) and sagittal (B) images. A central filling defect in the superior sagittal sinus, straight sinus and internal cerebral veins surrounded by intensely enhanced dura mater.

almost imperceptible in native CT images, may be potentially useful in identification of CVT-induced ischemic changes [10,11].

Magnetic resonance imaging constitutes an alternative or may be complementary to CT studies. Picture of a thrombus in MR examination depends on the time elapsed since its formation [12]. In the acute phase thrombus exhibits signal isointensive to that of surrounding brain tissue in T1-weighted images, while in T2-weighted images signal is hypointensive due to the presence of deoxyhemoglobin, which may be misinterpreted as normal blood flow within the sinus (Figure 3). In the subacute phase thrombus becomes hyperintensive – first in T1-weighted and subsequently in T2-weighted images (Figure 4). Change in signal intensity during this period is caused by deoxyhemoglobin

conversion to methemoglobin. Such a picture persists for about 5 to 30 days. During the chronic phase persistent thrombus is isointensive in T1-weighted and hyperintensive in T2-weighted images. At this stage signal intensity corresponding to a thrombus may be heterogeneous due to recanalization [1].

MR venography (MVR) technique has a well-founded position in the diagnostics of CVT. This study may involve intravenous administration of contrast medium in a manner analogous to CT venography or non-invasively, using 2D/3D TOF (time of flight) as well as 2D and 3D PC (phase contrast) techniques.

In the MRV with contrast, thrombus is visible in the lumen of a sinus as loss of signal. Outline of the sinus is often irregular and jagged with dilated collaterals. It should be noted that in T1-weighted images performed with this technique hyperintensive subacute thrombus may imitate blood flow through the sinus and standard sequences should be also assessed. MR venography with contrast does not depend on blood flow velocity, but inability to suppress signal from arterial vessels is an important limitation to the study [1].

TOF technique is dependent on the velocity of blood flow. In the presence of slow flow, the signal coming from the vessel is weak or very weak and may imitate closing [3]. In the subacute phase hyperintensive thrombus (methemoglobin) may mimic sinus blood flow. In the MRV PC method hyperintensity of thrombi in T1-weighted images is not a limitation. However, inability to visualize small veins is a disadvantage [1].

Study protocol should include DWI (diffusion weighted imaging) method. These sequences exhibit the highest sensitivity with regard to detecting early ischemic lesions and allow for differentiating between vascular and cytotoxic edema (ADC normalization/rise or ADC decrease, respectively) [13].

On the other hand, classic gradient echo sequences and, even more sensitive in this respect, SWI (susceptibility weighted imaging) sequences may be of great value in precise assessment of early hemorrhaging and thrombosis involving minute cortical veins [13].

Results

The group consisted of 34 patients (22 women and 12 men). Mean patient age was 48.7 years (from 27 to 77 y.o.). Mean age in the female group (47.9 years) was somewhat lower than in the male group (50.3 years). In the whole studied group, 8 patients were in the acute phase of the disease, 16 in the subacute and 10 subjects were diagnosed in the chronic phase. Noncontrast CT was performed in 24 patients and dural sinus hyperdensity was visualized in 12 of them (50%). In CT venography absence of contrast in the sinus indicating a thrombus was noted in 23/24 of subjects (96%). Among conventional MR sequences the highest sensitivity was reported with the GRE sequence – 80% (25/31). In T2-weighted images and FLAIR sequences sinus thrombi were identified in 21/31 cases (67%), while in T1-weighted

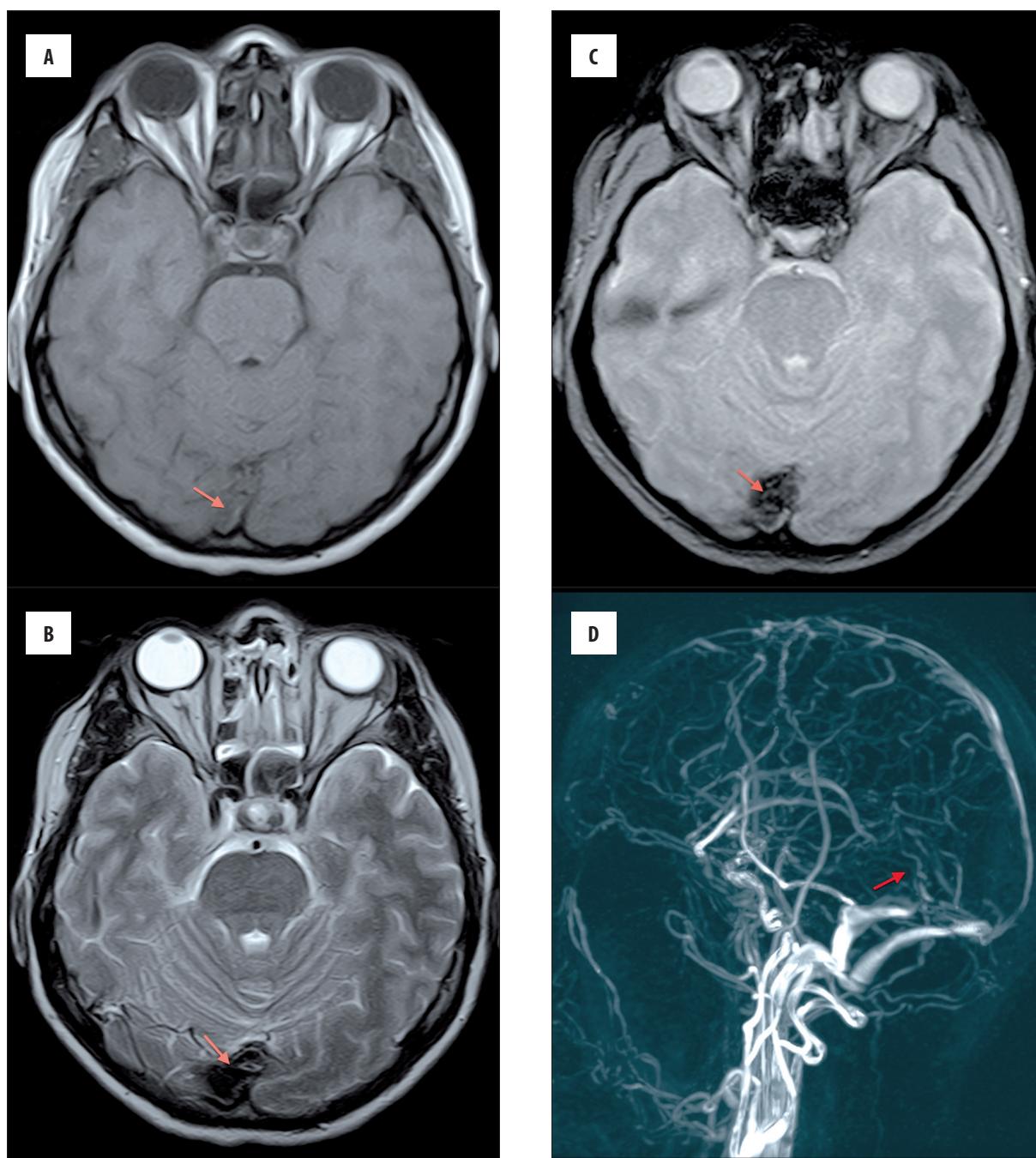


Figure 3. Axial T1-weighted (A), axial T2-weighted (B) and axial-GRE (C) MR images show acute thrombus of the straight sinus. Signal from the thrombus is isointense (A) and hypointense (B, C), compared with normal brain parenchyma. Sagittal TOF MR venography (D) shows no flow in the straight sinus.

images in 19/31 subjects (61%). TOF MR venography and contrast MR were significantly better compared to standard sequences – 30/31 (96%) and 23/24 (95%), respectively (Table 1).

Thrombosis was most often present in the area of the transverse sinus – 30 cases (88%; 16 – left; 14 – right). In 22 patients thrombi were visualized in the sigmoid sinuses (64%; 12 – left; 10 – right). Involvement of internal jugular veins (n=10), superior sagittal sinus (n=8), deep cerebral veins (n=6), straight sinus (n=6) and cortical veins

(n=2) was less frequently observed. Radiological signs of ischemia were visualized in 16 subjects (47%), including 8 (23%) cases of secondary hemorrhagic transformation. In one case we observed significant mass effect and ventricular hemorrhage.

Discussion

True frequency of occurrence of venous sinus thrombosis and cerebral vein thrombosis is unknown, but it is estimated at 2–7 cases per million/year [14]. This pathology

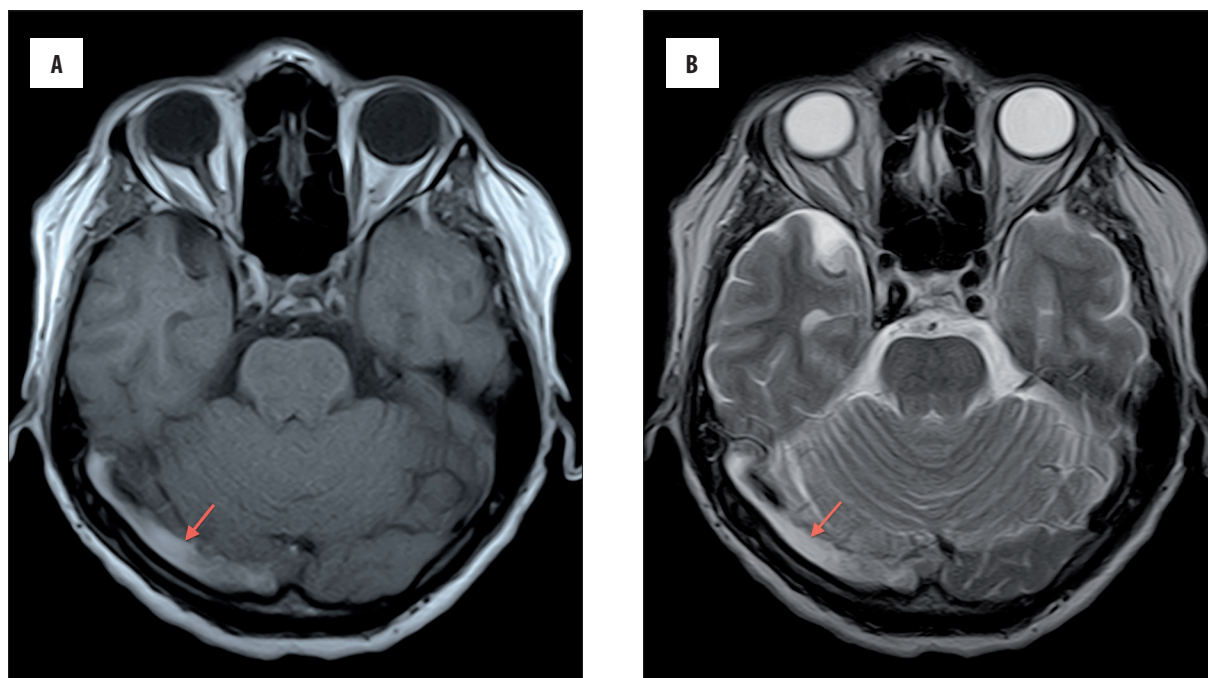


Figure 4. Subacute thrombus of the right transverse sinus. Axial T1-weighted (A) and axial T2-weighted (B) MR images show an area of abnormally increased signal intensity in the right transverse sinus.

Table 1. The comparison of the imaging techniques' sensitivity of thrombus detection.

	The frequency of occurrence	Sensitivity
Abnormal signal intensity within the dural sinus on T1-weighted images	19/31	61%
Abnormal signal intensity within the dural sinus on T2-weighted images	21/31	67%
Abnormal signal intensity within the dural sinus on FLAIR sequences	21/31	67%
Abnormal signal intensity within the dural sinus on GRE sequences	25/31	80%
Absence of signal at TOF MR venography	30/31	96%
Filling defect within the dural sinus at contrast-enhanced MR venography	21/22	95%
Hyperdens dural sinus on unenhanced CT	12/24	50%
Filling defect within the dural sinus at contrast-enhanced CT venography	23/24	96%

affects both sexes, although it is more prevalent among women of childbearing age [15]. Possible causes of this disease include: pregnancy, postpartum period, oral hormonal contraceptives, hormone replacement therapy, dehydration, trauma, essential thrombocytosis, thrombophilia, or other hypercoagulability syndromes (antithrombin III, protein S and protein C deficiency, factor V Leiden, polycythemia), collagenoses, paraneoplastic syndromes and neoplasms as well as systemic and local inflammatory states [14,15]. Around 10% of cases are associated with local damage to a vessel wall in a course of local inflammation (sinusitis, mastoiditis), trauma or neoplastic infiltration [1]. Frequent occurrence of thrombosis is related to coexistence of two or more risk factors [16]. Despite having identified over 100 possible factors that might predispose to CVT, etiology remains unknown in about 20–25% of cases [1].

Impaired venous drainage leads to elevation in capillary pressure and decreased perfusion. As a result, venous pressure in the region affected by thrombosis increases, there is a risk of blood-brain barrier interruption and secondary brain edema. Angioedema is of greater importance in this case than cytotoxic edema [17]. Venous stroke, which may be accompanied by bleeding, develops in about 50% of CVT cases [14]. Depending on the location and extent of thrombosis, disease course may be acute – 30% (less than 2 days), subacute – 50% (2–30 days), or chronic – 20% (over 30 days) [13]. Modern radiological diagnostics include a range of effective imaging techniques that play a key role in establishing the diagnosis of CVT, enabling early implementation of proper treatment and improved survival [18].

Cerebral venous thrombosis leads to venous infarction in about 50% of cases and anticoagulation is the treatment of

choice. Thus, rapid and accurate diagnosis directly influences patient prognosis [19].

Distribution of venous drainage areas in the cerebrum is subject to variation. However, there are some characteristics that may guide us to proper diagnosis: areas of ischemia bilaterally involving deep structures (cerebral deep vein thrombosis) or parasagittal regions (sagittal sinus thrombosis), as well as uni- and bilateral changes in peripheral areas of brain lobes or the temporal lobe (cortical vein thrombosis). It should be noted that among patients after surgery in the posterior cranial fossa (e.g. auditory nerve schwannoma) thrombosis of the vein of Labbe might occur if the temporal lobe had been lifted. Venous infarctions are also more prone to undergo hemorrhagic transformation, which may provide an additional clue about proper diagnosis. However, venous system variants should not be mistaken for venous thrombosis. Asymmetry of transverse sinuses with dominating right sinus is a common finding. In other cases we may observe unilateral obstruction of posteromedial segment of the left transverse sinus [5]. Particular care should be paid to deep cerebral vein thrombosis due to the fact that

its early symptoms in head CT may be very discrete and may be easily overlooked. It most frequently involves both internal cerebral veins, Galen's vein and straight sinus – in such cases they present with hyperdensity in noncontrast CT and are usually accompanied by decreased density in both halves of the thalamus, possible hemorrhages in that area and effaced borders between deep gray matter and white matter. In the presence of clinically suspected venous thrombosis with normal brain image in noncontrast CT studies, performing CT venography or MR examination with venography should be considered [5].

Conclusions

In the analyzed group of patients CT and MR venography were comparable and exhibited the highest diagnostic sensitivity. Both methods constitute the "gold standard" in the diagnostics of CVT. Due to a retrospective nature of our work we did not manage to establish optimal study protocols depending on the phase of the disease. It seems that prospective analysis on a greater number of patients might lead to developing a method with diagnostic sensitivity exceeding that of previous studies.

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