Journal of Pre-Clinical and Clinical Research, 2012, Vol 6, No 2, 105-110
www.jpccr.eu

Etiology, clinical manifestation and radiological findings in cerebral venous and sinus thrombosis

Anna Solińska[1], Ewa Dziurzyńska-Białek[1], Agnieszka Grudzińska-Raczek[1], Wiesław Guz[1], Ewa Kurys-Denis[2], Witold Krupski[2]

[1] *Department of Radiology in Provincial Hospital No 2 in Rzeszów, Poland*
[2] *2nd Department of Radiology, Medical University of Lublin, Poland*

Solińska A, Dziurzyńska-Białek E, Grudzińska-Raczek A, Guz W, Kurys-Denis E, Krupski W. Etiology, clinical manifestation and radiological findings in cerebral venous and sinus thrombosis. J Pre-Clin Clin Res. 2012; 6(2):105-110.

Abstract

Introduction. Cerebral venous sinus thrombosis (CVST) is a rare disease with a variety of symptoms, diagnosed primarily in imaging studies which allow early introduction of proper, causal treatment.

Objective. To analyze the epidemiological and clinical data and the results of imaging studies performed in patients diagnosed with this disease.

Material and method. The analyzed material consisted of a group of 16 patients (11 women and 5 men) who were examined with CT and MRI in the Department of Radiology and Diagnostic Imaging at Provincial Hospital No. 2, named after St. Jadwiga the Queen, in Rzeszów during the period October 2000 – October 2012, and who were diagnosed with CVST. At least one of the following imaging examination was performed in these patients: head CT scan with or without intravenous contrast administration, CT angiography of the head, head MRI with intravenous contrast agent, MR venography.

Results. CVST occurred most often in women in two age groups: 20 – 29 and 40 – 49-years-old. The most common risk factors were inflammatory lesions of the head and neck, and slightly less frequent in group of women, oral contraceptives and puerperium. In six patients

(**37**.5%) co-existence of at least two risk factors was observed: 1) thrombotic lesions more often localized in large, paired sinuses, 2) blood clots, observed in multiple locations in the majority of patients, i.e. in 13 patients (81.25%). The greater number of risk factors was associated with a more extensive range of DVT. In eight patients, changes in the sinuses and cerebral veins were associated with various changes in the brain tissue. The level of D-dimers in CVST may be normal. Diagnosis was usually made on the basis of CT angiography examination and, in the second place, on the basis of MR venography.

Conclusions. CVST is most common in young women. The most common risk factor is inflammation, and puerperium is the condition especially predisposing to parenchymal changes in the brain. The large sinuses are the most common locations for thrombosis. The shorter the duration of clinical symptoms and the more severe their presentation, the more extensive concurrent brain parenchyma changes. The correct level of D-dimers does not exclude the presence of CVST. CT angiography and MR venography are the most sensitive methods for detecting CVST, while MRI with contrast is the most sensitive method to detect parenchymal changes in the brain.

Key words

cerebral venous sinus thrombosis, CT venography, MR venography

INTRODUCTION

Cerebral venous and sinus thrombosis (CVST) is a rare disease that manifests itself in a variety of clinical symptoms. Neuroimaging studies play a decisive role in its diagnosis. Nowadays, owing to prompt diagnosis, adequate treatment can be immediately implemented, and is responsible for a significant reduction in mortality in the course of this disease in recent years.

The aim of this study is to analyze epidemiological and clinical data, as well as results of imaging studies performed in patients diagnosed with cerebral venous and sinus thrombosis.

Address for correspondence: Anna Solińska, Department of Radiology in Provincial Hospital No 2 in Rzeszów, Lwowska 60, 35-301 Rzeszów, Poland
E-mail: ahoma@poczta.onet.pl

Received: 20 October 2012; accepted: 19 December 2012

MATERIALS AND METHOD

The analyzed material consisted of a group of 16 patients (11 women and 5 men) who were examined with computed tomography (CT) and magnetic resonance imaging (MRI) in the Department of Radiology and Diagnostic Imaging at Regional Hospital No. 2, named after St. Jadwiga the Queen in Rzeszów, during the period October 2000 – October 2012, and who were diagnosed with CVST. At least one of the following imaging examinations was performed in these patients: head CT scan with or without intravenous contrast medium administration, CT angiography (CTA) of the head, head magnetic resonance imaging with intravenous contrast agent, MR venography.

Computed tomography studies were performed in a sequential acquisition, in layers with a width of 2.5 mm at the head basis and 5 mm in the rest of the brain. Ultravist 370, Omnipaque 400, and Iomeron 240 were used as non-ionic iodine contrast agents. For the head CT, in adult patients the intravenous contrast medium was administered at a dose of slightly less than 1 ml/kg body weight, about 50-60 ml in total. In children, the amount of contrast depended on the age and weight: in newborns slightly less than 3 ml/kg body weight, in infants and older children slightly less than 2 ml/kg body weight.

CT angiography scans of the head were performed with the standard protocol using the 'bolus test' technique. Contrast agent (Ultravist 370 or Iomeron 400) was administered with the use of an automatic syringe at the speed of 3.5 ml/sec and in an amount of 100 ml in adults, and with a lower rate of approximately 1.5 ml/sec in a dose of about 1.5 ml/kg body weight in children. Scanning delay after contrast administration was adjusted mainly for good contrast enhancement of the cerebral venous system.

MRI of the brain was performed in turbo spin echo (TSE) sequence, obtaining T1- weighted axial images, T2-weighted, axial, sagittal and frontal images, and axial FLAIR images. After contrast administration, the brain was imaged in T1-weighted images in all three planes of the TSE sequence. In order to contrast brain structures, 0.5 and 1.0 mmol, gadolinium-based contrast media were used in a dose of 0.1 mmol/kg body weight.

Vascular MRI studies were performed in TOF and PC techniques without the use of contrast enhancement; after obtaining native images in axial cross-section, multi-planar reconstructions (MPR) were further retrieved.

RESULTS

The study group consisted of 16 patients (11 women, 5 men). The disease occurred more frequently in the age groups 20–29-years-old and 40–49-years-old – half of the patients belonged to one of those groups. The above data shows that the patients who most frequently suffered from CVST were young women (20–29 years), as well as middle-aged women (40–49 years). In men, however, the most common age at onset was the period between 30–39-years-of age (Tab. 1).

Table 1. Age groups and gender in patients with CVST

Gender	No.	Age group	No.
Women	11 (68.75%)	0-9	2
		10-19	2
		20-29	3
		30-39	0
		40-49	3
		50-59	0
		60 and more	1
Men	5 (31.25%)	0-9	1
		10-19	0
		20-29	1
		30-39	2
		40-49	1
		50-59	0
		60 and more	0

The most common risk factor leading to the development of the disease were inflammatory lesions of the head and neck (including otitis media, mastoiditis, neck abscess, gangrenous teeth roots), occurring in 25% of patients, with second most common factors in the group of women were oral contraceptives and puerperium. In the group of young patients – up to 20-years-old – the dominant risk factors for CVST included inflammation of surrounding tissues and proliferative diseases. In six patients (37.5%), the co-existence of at least two risk factors was observed. In two patients, no risk factors could be identified (Tab. 2).

Table 2. Risk factors of CVST and patients' ages

Risk factors	Age group						
	0-9	10-19	20-29	30-39	40-49	50-59	≥ 60
Inflammatory lesions of head and neck	1	1	1	0	0	0	1
Dehydration	0	0	1	0	0	0	1
Oral contraceptives	0	0	1	0	2	0	0
Coagulation disorders	0	0	1	1	0	0	0
Puerperium	0	1	2	0	0	0	0
Malignancy	1	1	0	0	0	0	0
Trauma	1	0	1	0	0	0	0
Liver dysfunction	0	0	1	0	1	0	0
Thyroid disease	0	0	2	0	0	0	0

Thrombotic lesions more often localized in the large, paired sinuses. In the presented study group, these were specifically the sigmoid sinuses (29%), slightly less often the transverse sinuses (24%) and the unpaired superior sagittal sinus (21%). In the literature, the superior sagittal sinus is given as the most common site of thrombosis [1, 2, 3, 4, 5, 6, 7, 8, 9, 10]. The least common location were deep cerebral veins – only one patient manifested signs of such a thrombosis.

In the majority of patients (81.25%), blood clots were observed in multiple locations (symmetrical involvement of paired sinuses, for example, transverse sinuses, already considered as multiple). In only three patients, thrombi were present at a single location. The underlying background of their formation in two patients was cancer, and in one person coagulation disorders. Interestingly, in these three patients only in latter were single risk factors were identified. For more than 12 years, the authors of the presented study have not found a single case of isolated cerebral cortical veins thrombosis, it occurred only in conjunction with superior sagittal sinus thrombosis (Tab. 3).

Table 3. Localization of cerebral thrombotic lesions

Localization of cerebral thrombosis	Women	Men	Total
Superior sagittal sinus	5	3	8 (21.1%)
Inferior sagittal sinus	0	0	0
Transverse sinus	6	3	9 (23.7%)
Sigmoid sinus	7	4	11 (28.9%)
Internal jugular bulb	3	2	5 (13.2%)
Sinus rectus	2	1	3 (7.9%)
Deep cerebral veins	1	0	1 (2.6%)
Cortical veins	1	0	1 (2.6%)
			38 (100%)

In the presented group of patients it was observed that majority of risk factors were associated with more extensive CVST changes. This was true except, for one patient in whom even though only a single risk factor was identified (oral contraceptives), the thrombotic lesions were very extensive.

In eight patients (50%) changes in the sinuses and cerebral veins were associated with various changes in the brain parenchyma: venous infarct, haemorrhagic venous infarct or local swelling of the brain (Fig. 1). According to the literature, these changes occur in 10–57% of patients [1,2, 3, 4, 8, 11, 12].

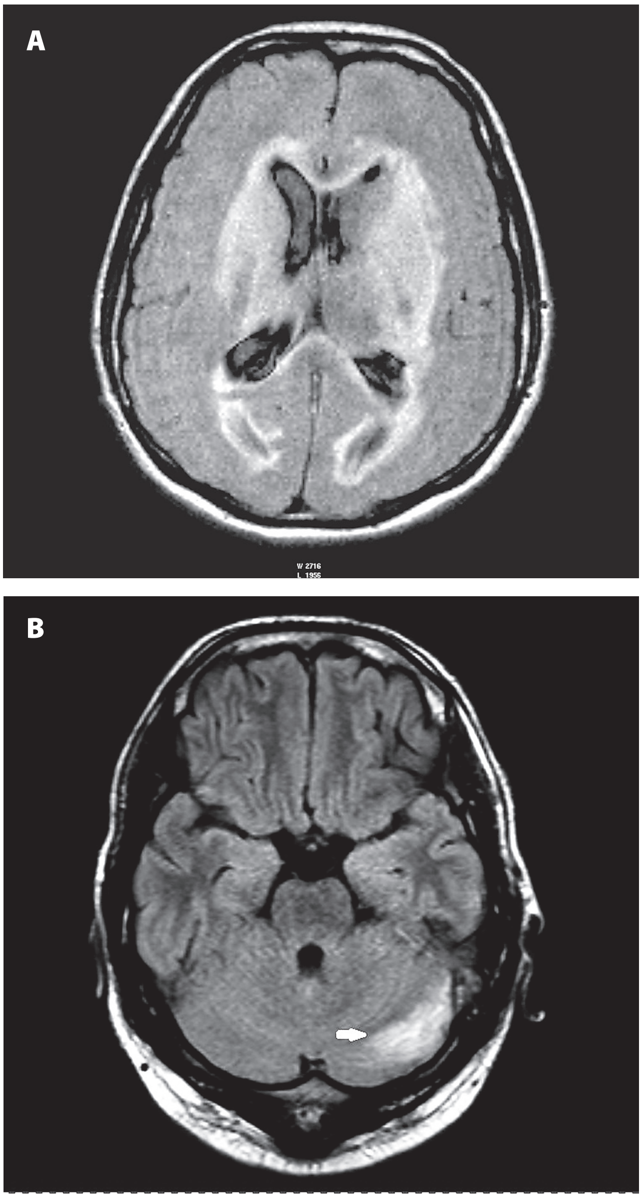

Figure 1 (A). FLAIR sequence, axial plane. Swelling changes in deep brain structures bilaterally in the course of CVST. **(B)** T1 weighted image, axial plane. Haemorrhagic venous infract in the left cerebellar hemisphere

The collected data shows that the shorter the duration of clinical symptoms and the more severe their presentation, the more extensive the accompanying changes in the brain. Among six patients who had sudden onsets of symptoms, in as many as four the imaging studies revealed brain parenchyma changes. It is especially important to note that this group included all three patients who had a thrombosis the puerperium. On the other hand, patients who showed a slow progression symptoms, less often had cerebral parenchymal changes, which is probably due to the possibility of the development of collateral circulation.

There was no correlation between the extent of thrombotic changes and the occurrence of cerebral lesions. In three of four patients with the most extensive thrombotic changes, imaging studies revealed no parenchymal changes (Tab. 4).

Table 4. Correlation between extent of cerebral thrombotic changes and risk factors; presence of parenchymal cerebral changes and duration of symptoms and risk factors

Patient	Age	Localization of thrombotic changes	Duration of symptoms	Presence of cerebral changes	Risk factors
K.N.	19	TS	1 week	+	malignancy
T.K.	7	SS + B	1.5 weeks	-	otitis media
S.Ag.	5	SSS	acute (seizures)	+	malignancy
P.L.	41	SSS + TS + SS	10 days	+	oral contraceptives, liver disorders
P.Ł.	26	SSS + TS + SS + RS	4 weeks	+	trauma, liver disorders, gangrenous teeth roots
D.S.	30	SSS	several days	+	coagulation disorders
C.J.	2	SS + B	acute (trauma)	-	trauma
S.J.	67	SS + B	acute (loss of consciousness)	-	dehydration, otitis media
K.D.	43	SSS + TS (P i L)+ SS + B + SR	4 days	-	oral contraceptives
B.K.	25	SSS + TS (P i L) + SS (P i L) + SR	3 months	-	oral contraceptives, thyroid disease, coagulation disorders
D.M.	40	SSS + TS + SS + B	a few days	-	unknown
P.U.	49	TS + SS	2 weeks	-	unknown
S.An.	25	SSS + CV	acute (loss of consciousness)	+	puerperium
M.S.	16	TS + SS	acute (seizures)	+	puerperium, neck abscess
D.D.	23	DCV + SR	acute (consciousness disorders)	+	puerperium, thyroid disease
N.M.	38	TS + SS	1,5 weeks	-	Unknown

The following abbreviations are used in the table to specify the names of dural sinuses and cerebral veins: SSS – superior sagittal sinus; ISS – inferior sagittal sinus; TS – transverse sinus; SS – sigmoid sinus; RS – sinus rectus; B – internal jugular bulb; CV – cortical cerebral veins; DCV – deep cerebral veins.

The observation was noted, and must be particularly highlighted, that among laboratory tests the level of D-dimers, which is always abnormal in the course of deep vein thrombosis (DVT) in extra-cerebral localization, may be normal in the case of CVST. Their level was normal in as many as 25% of patients in the studied group. This is consistent with observations described in the literature [1, 12, 13] (Tab. 5).

Table 5. Level of D-dimers

D-dimers level	No. of patients
Normal	4 (25%)
> normal	6 (37.5%)
No data	6 (37.5%)

The majority of patients (13) had MRI examination with contrast medium. Slightly fewer patients (9) underwent CT angiography examination. In the studied group of patients, the diagnosis was usually made primarily on the basis of CT angiography examination, and in the second place, on the basis of MR venography. In no case was the diagnosis made solely on the basis of CT without contrast administration, although in three cases CVST was suspected on the basis of this study. The most sensitive method for detecting cerebral changes associated with CVST was contrast MRI examination. In only one patient, cerebral changes were also perceptible in CT with contrast administration (Tab. 6).

Table 6. Imaging of CVST in different diagnostic methods

Diagnostic method	No. of patients with a study performed	Result (No. of patients)			
		Normal	Suspicion of CVST	Diagnosis of CVST	Cerebral associated changes
CT without CM	6	5	3	-	-
CT with CM	7	-	2	2	1
CTA	9	-	-	6	-
MR + CM	13	1	-	4	7
MRV	7	-	-	5	-

DISCUSSION

Cerebral venous and sinus thrombosis is a relatively rare, but potentially life-threatening disease. Its incidence is approximately 2-4 cases per million per year [1, 2, 10, 12]. Due to the very wide range of causal factors of CVST (there are over 100 described in the literature) and extremely variable clinical presentations, the diagnosis of the disease is based mainly on imaging studies [6, 10, 11].

The most important risk factors include coagulation disorders (27-70%) [14, 15]. Somewhat less frequent, but equally important underlying background states, are infections, especially those of the nasopharynx and middle ear, and proliferative diseases; in women, oral contraceptives, pregnancy and childbirth. Less frequent causes include dehydration, trauma, and certain medications.

Headache, resistant to painkillers, or of different nature and location is the symptom most commonly reported by patients (74–95%) [6, 16]. A wide spectrum of symptoms also includes various neurological deficits, seizures (*petit mal* or *grand mal*) and various degrees of consciousness disorders, including loss of consciousness.

The primary mechanism of changes in the brain tissue seems to be an increased venous pressure. The process is initiated by the formation of a thrombus and its spreading to the cortical veins, which leads to the creation of two types of changes:

- vasogenic oedema – due to increased venous pressure, blood-brain barrier disruption and infusion of brain tissue with a large amount of fluid/blood;
- cytotoxic oedema – resulting from local ischemia caused by increased capillary pressure (=reduction of capillary flow), reduced arterial perfusion pressure, and damage to intracellular ion channels.

Both of these processes lead to oedema neurons, characteristic features of venous involvement in the disease which are possible to visualize on MRI images. CVST is described as a continuous process in which the balance between the processes of coagulation and fibrinolysis is disturbed in favour of the former, which leads to expansion of the venous clot over time. This slow increase in the size of the clot and the presence of extensive collateral circulation usually explains the gradual emergence of symptoms, sometimes lasting even for several months. Venous stroke is characterized by predominant presence of edematous not necrotic changes in the brain tissue, which explains the potential for withdrawal of symptoms and full recovery [4, 8, 9, 10, 11, 16].

Cerebral venous and sinus thrombosis most often involve the following vessels: superior sagittal sinus (62–72%) (Fig. 2), transverse sinuses (41–45%), sinus rectus (15–18%), superficial veins of the brain (6–17%), internal jugular veins (8–12%), deep cerebral veins (10–11%), cavernous sinus (1.3%), and least often – cerebellar veins (0.3%). In about one third of cases, more than one sinus is involved in the disease. In the next 30-40% of cases, thrombosis occurs both in the sinuses and in the cerebral or cerebellar veins [4, 6, 8, 11, 12].

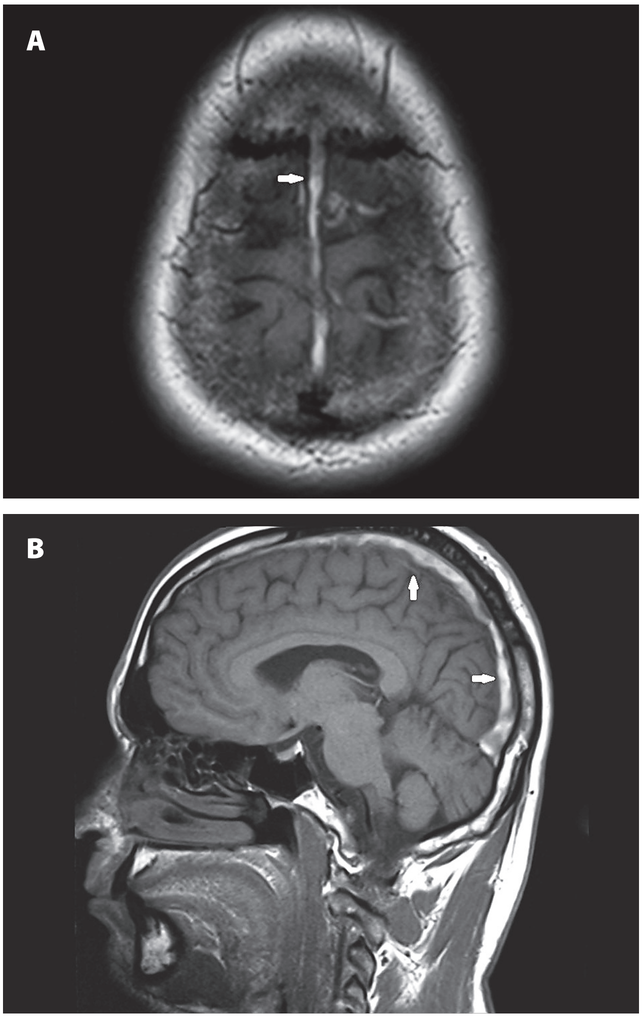

Figure 2 (A). T1-weighted image, axial plane. (B) T1-weighted image, sagittal plane. Hyperintense thrombus in the superior sagittal sinus

CT with and without contrast administration, CT angiography, MRI with contrast medium and MRI venography are all used in the diagnosis of CVST. In the past, classic angiography was the basic diagnostic method. It is now mainly used as a therapeutic method during local thrombolysis or mechanical clot removal. In CT examination without contrast medium, the symptoms of CVST are very subtle. A blood clot is directly visible as an increase of sinus density – 'hyperdense sinus symptom'; in the case of a hyperdense superior sagittal sinus it is called the 'delta sign', or in case of a vein – a 'string sign'. Indirect symptoms of a blood clot include concurrent changes in the brain parenchyma, such as hypodense ischemic areas, hyperdense bands of extravasated blood – haemorrhagic venous infarction. Extremely rarely cortical veins thrombosis occurs as an isolated subarachnoid hemorrhage (SAH) located on the brain convexity [6, 15, 17, 18, 19].

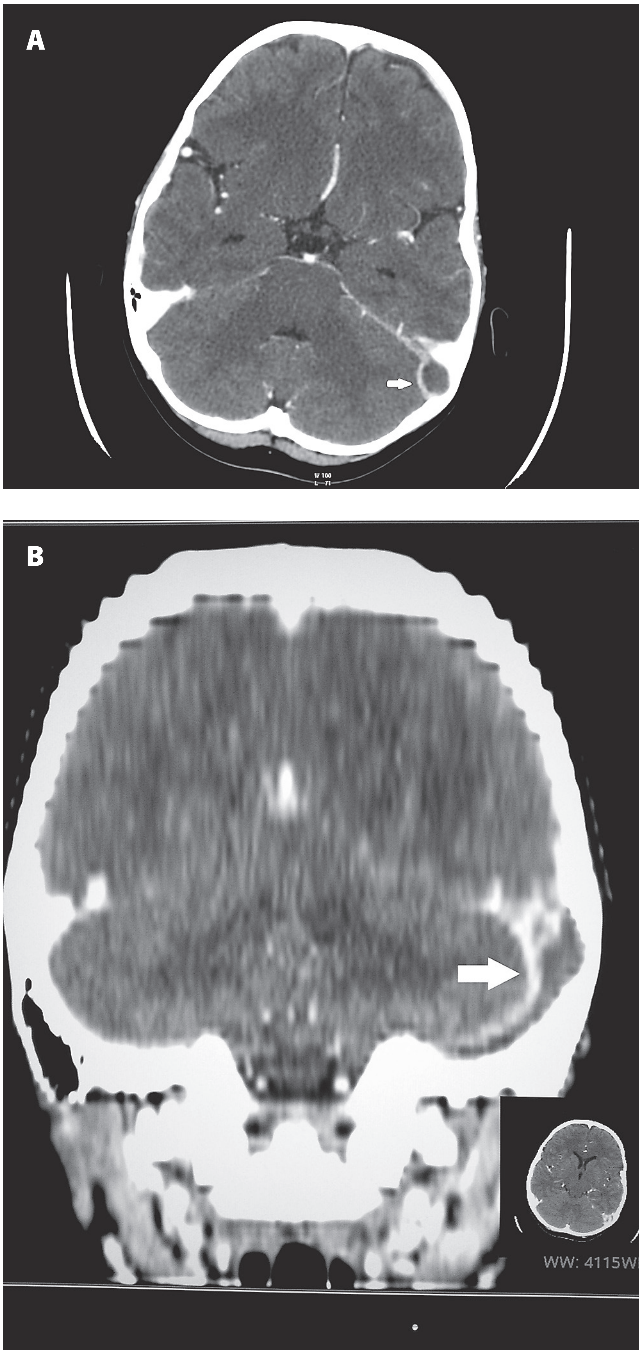

Figure 3. Angio-CT (A) axial plane, (B) coronal plane. Lack of contrast filling in the left sigmoid sinus – thrombus

In CT with contrast administration, the 'empty delta sign' can be additionally seen. It involves the absence of contrast enhancement of the thrombus located in the superior sagittal sinus and surrounded by hyperdense blood. In addition, in 20% of cases, enhancement of the cerebellar tentorium and cerebral falx can be observed. Enhancement of cortical gyri (proving disruption of the blood-brain barrier) and the presence of tortuous, collateral vessels are less often seen [4, 6, 8, 11, 15, 16, 18].

The CT angiography in the venous phase (CT venography) shows areas of lack of contrast filling in the sinuses. These should be differentiated from the presence of physiological arachnoid granulations, sometimes imitating the presence of a thrombus (Fig. 3) [1, 6, 18].

In MRI, on T1- and T2-weighted images, the signal intensity of a thrombus depends on the time elapsed since its formation. In the acute phase (0-5 days), the clot signal is mainly isointense on T1-weighted and hypointense on T2-weighted images, which can mimic the normal flow void in the patent sinus – this image may lead to diagnostic error. In the subacute phase (5-30 days), the thrombus signal is increased on both T1-and T2-weighted images – this is the phase in which diagnosis is the easiest, because the hyperintense signal on T1-weighted images in sinuses and veins is always abnormal. In the chronic phase (more than 30 days), the image is often misleading and the signal varies. On T1-weighted images it is usually isointense and iso- or hiperintense on T2-weighted images. After contrast enhancement the thrombus is seen as a non-enhanced structure in the sinus lumen ('empty delta sign' similar to CT with contrast) (Fig. 4), with the exception of a chronic (organized) thrombus, which can show enhancement, but which is not important from the clinical point of view. The MRI examination shows clearly all changes in the brain parenchyma, even as discreet as small vascular oedema [2, 6, 11, 12, 14, 16, 18, 20, 21].

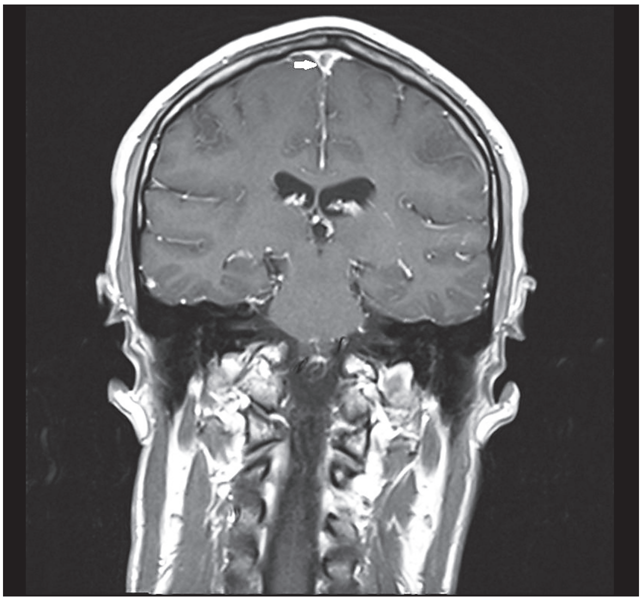

Figure 4. T1-weighted image + CM, coronal plane. 'Empty delta sign'

MR venography can be performed without an intravenous contrast agent (the blood flow is assessed in the TOF and PC method), or with contrast administration (contrasting of the vessel lumen is then assessed). As in CTA examination, lack of lumen filling or a complete stoppage of flow (blood or contrast) are observed (Fig. 5) [6, 8, 11, 18].

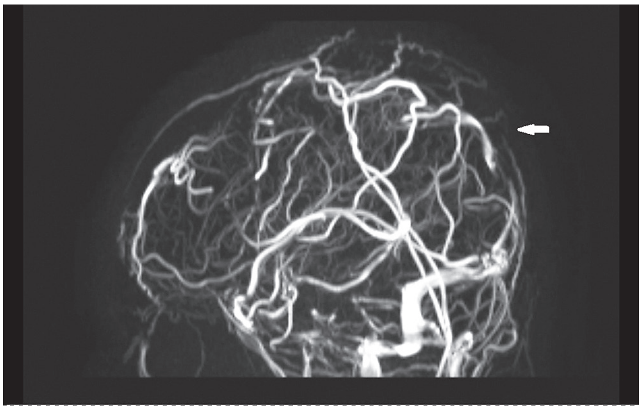

Figure 5. MR venography, sagittal plane. Lack of flow in the superior sagittal sinus – thrombosis

CONCLUSIONS

1. CVST is most common in young adults (up to 50 years of age), more often in women.
2. Among the risk factors, inflammatory changes play the most important role in the pathogenesis of the disease.
3. The vast majority of thrombotic lesions localize in the large sinuses.
4. The shorter the duration of clinical symptoms and the more severe their presentation, the more extensive parenchymal (accompanying) changes in the brain.
5. Puerperium is the state that particularly predisposes to parenchymal changes in the brain.
6. The correct level of D-dimers does not exclude the presence of CVST.
7. CVST is usually diagnosed in CT angiography and MR venography, and the accompanying brain parenchyma changes are best depicted in MRI with contrast administration. CT scan without contrast medium shows the lowest efficacy in diagnosis, which is associated with presence of only subtle radiological signs, and for this reason, and especially in the case of this examination, professional experience is extremely important.

REFERENCES

1. Sapsonik G, Barinagarrementeria F, Brown RD Jr, et al. Diagnosis and management of cerebral venous thrombosis. A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke 2011; 42(4): 1158-1192.
2. Supeł E, Łęczycka A, Szary C, et al. Septic cerebral sinus thrombosis. Case report. Pol J Radiol. 2009; 74(2): 63-67.
3. Breteau G, Mounier-Vehier F, Godefory O, et al. Cerebral venous thrombosis. 3-year clinical outcome in 55 consecutive patients. J Neurol. 2003; 250(1): 29-35.
4. Allroggen H, Abbott RJ. Cerebral venous sinus thrombosis. Postgrad Med J. 2000; 76(891): 12-15.
5. Prakash S, Bansal BC. Cerebral venous thrombosis. J Indian Acad Clin Med. 2000; 5(1): 55-61.
6. Szurowska E, Szarmach A, Dubaniewicz-Wybieralska M, et al. Zakrzepica zatok żylnych w badaniach obrazowych (Diagnostic imaging approaches to cerebral sinus venous thrombosis). Udar Mózgu 2009; 11(1): 13-22 (in Polish).
7. van Gijn J. Cerebral venous thrombosis: pathogenesis, presentation and prognosis. J R Soc Med. 2000; 93: 230-233.
8. Rodallec MH, Karinik A, Feydy A, et al. Cerebral venous thrombosis and multidetector CT angiography: tips and tricks. Radio Graphics 2006; 26 Suppl 1: 5-18.
9. Itrat A, Shoukat S, Kamal AK. Patophysiology of cerebral venous thrombosis – an overview. J Pak Med Assoc. 2006; 56(11): 506-508.
10. Kimber J. Cerebral venous sinus thrombosis. Q J Med. 2002; 95(3): 137-142.
11. Leach JL, Fortuna RB, Jones BV, et al. Imaging of cerebral venous thrombosis: current techniques, spectrum of findings, and diagnostic pitfalls. Radio Graphics, 2006; 26 Suppl 1: 19-43.
12. Linn J, Pfefferkorn T, Ivanicova K, et al. Noncontrast CT in deep cerebral venous thrombosis and sinus thrombosis: comparison of its diagnostic value for both entities. Am J Neuroradiol. 2009; 30(4): 728-735.
13. Bousser MG, Ferro JM. Cerebral venous thrombosis: an update. Lancet Neurol. 2007; 6(2): 162-170.
14. Walecki J, Bulski T, Sklinda K. Choroby naczynipochodne ośrodkowego układu nerwowego. In: Walecki J. Postępy Neuroradiologii. Polska Fundacja Upowszechniania Nauki, Warszawa, 2007. p. 472-512.
15. Kozic D, Zarkov M, Semnic RR. Overlooked early CT signs of cerebral venous thrombosis with lethal outcome. Acta Neurol Belg. 2010; 110(4): 345-348.
16. Crassard I, Bousser MG. Cerebral venous thrombosis. J Neuro-Ophthalmol. 2004; 24(2): 156-163.
17. Chang R, Friedman DP. Isolated cortical venous thrombosis presenting as subarachnoid hemorrhage: a report of three cases. AJNR Am J Neuroradiol. 2004; 25(10): 1676-1679.
18. Poon CS, Chang JK, Swarnkar A, et al. Radiologic diagnosis of cerebral venous thrombosis: pictorial review. AJR Am J Roentgenol. 2007; 189(6 Suppl): 64-75.
19. Crombe D, Haven F, Gille M. Isoalated deep cerebral venous thrombosis diagnosed on CT and MR imaging. A case study and literature review. JBR-BTR, 2003; 86(5): 257-261.
20. Idbaih A, Boukobza M, Crassard I, et al. MRI of clot in cerebral venous thrombosis: high diagnostic value of susceptibility-weighted images. Stroke, 2006; 37(4): 991-995.
21. Boukobza M, Crassard I, Bousser MG, et al. MR imaging features of isolated cortical vein thrombosis: diagnosis and follow-up. AJNR Am J Neuroradiol. 2009; 30(2): 344-348.