

PAPER

Headache as the only neurological sign of cerebral venous thrombosis: a series of 17 cases

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Background: Headache is the most frequent symptom in cerebral venous thrombosis (CVT), and usually the first. However, it has rarely been reported as the only symptom of CVT.

Objectives: To study the characteristics of patients in whom headache was the only presentation of CVT in the absence of intracranial hypertension, subarachnoid haemorrhage (SAH), meningitis, or other intracranial lesion.

Methods: From a prospective study of 123 consecutive patients with CVT only those with isolated headache and normal brain computed tomography (CT) scan and cerebrospinal fluid (CSF) examination were included in the present study. All patients underwent an extensive systematic aetiological work-up and were given intravenous heparin followed by oral anticoagulants. A detailed description of the headache was obtained.

Results: Headache was only sign of CVT in 17 patients. The lateral sinus was the most frequently involved sinus (n = 15). Onset of headache was progressive in 11, acute in 3, and thunderclap in 3 patients. Once established, the headache was continuous in 15, diffuse in four and unilateral in 13, usually ipsilateral to the occluded lateral sinus. No specific risk factor or cause was found. All had a favourable evolution.

Conclusion: The pathogenesis of isolated headache in CVT in the absence of intracranial hypertension, SAH, meningitis or intracerebral lesion is unknown but may involve changes in the walls of the occluded sinus. Hence MRI/MRV should be used to look for signs of CVT in all patients with recent headache (progressive or thunderclap) even when the CT scan and CSF examination are normal.

Cerebral venous thrombosis (CVT) is an uncommon cerebrovascular disease presenting with a remarkably wide spectrum of signs and mode of onset.¹ In all series, headache is the most frequently occurring symptom at any time, present in over 80% of cases,¹ and it is also the commonest initial symptom. The headache has no specific features and is almost invariably associated with other neurological signs such as papilloedema, focal deficits, seizures, disorders of consciousness, or cranial nerve palsies. These signs can be grouped into four main syndromes: isolated intracranial hypertension, focal syndrome, diffuse encephalopathy, and cavernous sinus syndrome.^{1–4} In rare cases of CVT, the headache is not accompanied by any clinical findings, but brain computed tomography (CT) scanning and/or cerebrospinal fluid (CSF) examination usually reveal conditions that explain the headache, such as subarachnoid haemorrhage (SAH), intracerebral infarction or haemorrhage due to the CVT, or meningitis related to the aetiology of CVT. Headache as the only presentation of CVT in the absence of such conditions is rare.^{5–8}

In this paper we present the characteristics of 17 patients—from a prospective series of 123 patients with CVT seen over four years at our institution—in whom headache was the only clinical presentation of CVT in the absence of intracranial hypertension, SAH, meningitis, or other intracranial lesion as assessed by head CT and/or CSF examination.

PATIENTS AND METHODS

The present study is based on a prospective cohort of 123 consecutive patients with CVT admitted to our department between December 1999 and July 2004, of whom 28 were included in the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT).⁹ Diagnosis of CVT was based on magnetic resonance imaging (MRI) combined with

MR venography (MRV), and/or helical CT venography and/or conventional angiography.¹

Patients were included in the present study if headache was the only manifestation of CVT in the absence of intracranial hypertension (no papilloedema and/or normal CSF pressure), SAH (no blood on CT scan and CSF examination), meningitis (normal CSF), or any intracerebral lesion on CT scan and/or MRI.

We obtained a detailed description of the headache including its mode of onset, location, severity, pattern, and evolution. The headaches were classified into different types according to the criteria of the International Headache Society (IHS). For all patients we recorded the past history of the headache and residual headache three months after CVT. A visual analogue scale (VAS) was used to record pain severity (severe headache = VAS \geq 7). Three modes of onset of the headache were defined depending on the time between the initial pain sensation and the most severe headache:

- “thunderclap”—sudden onset of an excruciating headache (VAS more than 8/10), reaching maximum intensity in less than one minute, and lasting more than one hour
- acute headache developing in less than 24 hours
- progressive over 24 hours. After 24 hours, the pain was characterised as continuous or intermittent (with headache free periods).

Abbreviations: CT, computed tomography; CSF, cerebrospinal fluid; CVT, cerebral venous thrombosis; ISCVT, International Study on Cerebral Vein and Dural Sinus Thrombosis; MRI/V, magnetic resonance imaging/venography; SAH, subarachnoid haemorrhage; VAS, visual analogue scale

All patients underwent an extensive systematic aetiological work-up in which we looked for the main causes and risk factors of CVT such as systemic diseases, malignancies, haematologic disorders, antiphospholipid syndrome, and local (infectious or non-infectious) causes. Treatment was based on intravenous unfractionated heparin, followed by oral anticoagulation for six months or longer according to the aetiology of CVT. All the patients were prescribed analgesics or narcotics according to the severity of their headache.

RESULTS

Of 28/123 patients (23%) who presented with headache as only neurological symptom on admission, 17 (14%; six men and 11 women; mean age 37.6 years, range 22–5; table 1) satisfied our inclusion criteria. Eight patients (47%) were recruited through the emergency headache centre and nine were admitted directly to the neurology unit.

The mean delay between onset and diagnosis was 13.1 days (range 0–30). The shortest delay (less than 24 hours) was observed in two patients with thunderclap headache and the longest in another two patients, of whom one had a progressive and the other an acute headache. One of the longest delays occurred in a patient with several episodes of thunderclap headache. Predisposing factors or causes of CVT were as follows: current oral contraceptive use ($n = 9$), antiphospholipid antibody syndrome with systemic lupus erythematosus ($n = 2$), thrombophilia due to protein S deficiency and/or factor V Leiden mutation ($n = 3$), and iron deficiency anaemia ($n = 2$). No cause was found in four patients, two of whom had a history of recurrent venous thrombosis. The sinus most frequent involved was the lateral sinus ($n = 15$), either isolated ($n = 8$) or in association with jugular vein thrombosis ($n = 4$) or with other sinuses ($n = 3$). The superior sagittal sinus was involved in four patients (isolated in two and associated with lateral sinus and deep venous system in the other two). An initial non-contrast CT scan was performed in 15 patients. It showed a definite spontaneous hyperdensity of one or several sinuses in nine patients and was normal in six patients (fig 1).

The main headache characteristics are given in table 2. Four patients had a history of migraine without aura before CVT. In three the headache differed from their usual

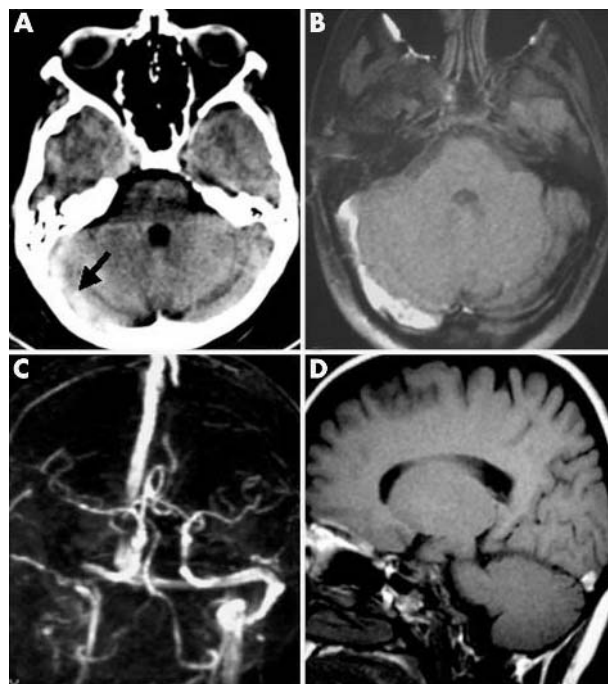


Figure 1 Patient 6. (A) Non-contrast cerebral computed tomography scan showing spontaneous hyperdensity of the right lateral sinus (arrow). (B–D) Cerebral MRI/MRV: hypersignal of the right lateral sinus on (B) axial fluid attenuated inversion recovery (FLAIR) images and (D) on sagittal T1-weighted images. (C) Right lateral sinus and jugular vein were not seen on cerebral MRV, confirming thrombosis.

migraine, and the time from onset to diagnosis was six to seven days. One patient had a headache that was initially similar to her usual migraine attacks but it persisted. She was evaluated 23 days after onset. The onset of headache was progressive over a few days in 65% ($n = 11$), acute in 17.5% ($n = 3$), and thunderclap in 17.5% ($n = 3$) of the patients. Once established, the headache was continuous in 88% ($n = 15$); two of these had superimposed attacks of

Table 1 Baseline characteristics of patients with isolated headache as only sign of CVT

Patient	Sex	Age	Time from onset to diagnosis (days)	Predisposing factor/cause	Site of thrombosis	Non-contrast CT scan
1	M	40	<1	No	SSS, RLS, DVS	Spontaneous hyperdensity
2	F	26	23	Oral contraception	SSS, RLS, DVS	Spontaneous hyperdensity
3	M	40	2	Recurrent venous thrombosis	LLS	–
4	F	41	15	SLE + APL	LLS, LJV	Normal
5	F	32	<1	Oral contraception	RLS, RJV	Spontaneous hyperdensity
6	F	33	6	Oral contraception	RLS, RJV	Spontaneous hyperdensity
7	F	31	6	Oral contraception	LLS	Spontaneous hyperdensity
8	F	29	15	Gastric carcinoma, oral contraception, iron deficiency anaemia	RLS	Normal
9	F	26	30	Oral contraception	RLS	Spontaneous hyperdensity
10	F	30	20	SLE + APL	LLS, DVS	Spontaneous hyperdensity
11	M	56	7	Recurrent venous thrombosis	LLS	Spontaneous hyperdensity
12	F	51	15	Oral contraception, factor V Leiden mutation	LLS, LJV	Normal
13	M	57	11	Protein-S deficiency, factor V Leiden mutation	RLS	–
14	F	38	30	Oral contraception	LLS	Normal
15	M	51	6	Factor V Leiden mutation	SSS	Normal
16	F	22	27	Oral contraception, iron deficiency anaemia	SSS	Normal
17	M	37	10	No	RLS	Spontaneous hyperdensity

APL, antiphospholipid syndrome; DVS, deep venous system; F, female; LJV, left jugular vein; LLS, left lateral sinus; M, male; RJV, right jugular vein; RLS, right lateral sinus; RVT, recurrent venous thrombosis; SLE, systemic lupus erythematosus; SSS, superior sagittal sinus.

Table 2 Characteristics of the headache in patients with cerebral venous thrombosis

Patient	History of migraine	Onset	Evolution	Pattern	Severity (VAS)	Location	Associated signs	Headache at 3 months
1	No	TH	Continuous	Constrictive	10	Diffuse	Nausea and vomiting	No
2	Migraine without aura	Progressive	Intermittent	Throbbing	8	RHC	No	Migraine without aura
3	No	Acute	Continuous	Throbbing	8	LHC	Nausea and vomiting	No
4	No	Progressive	Cluster-like attacks	Throbbing	8	LFO	Ocular redness	TTH
5	No	TH	Continuous	Throbbing	9	RHC + RNP	Nausea and vomiting, phono/photophobia	Migraine with aura
6	Migraine without aura	Progressive	Continuous	Throbbing	9	RHC + RNP	No	Migraine without aura
7	Migraine without aura	Progressive	Continuous	Throbbing	9	LHC	Nausea, phono/photophobia	TTH + migraine without aura
8	No	Progressive	Continuous	Throbbing	5	RHC	Nausea, phono/photophobia	No
9	No	Progressive	Continuous	Throbbing	6	RHC	Nausea and vomiting	No
10	No	Progressive	Continuous	Throbbing	10	LFO	No	No
11	No	Progressive	Continuous	Throbbing	10	LHC	Nausea and vomiting	No
12	No	Progressive	Continuous	Throbbing	9	LHC+LNP	No	TTH
13	No	Acute	Continuous	Constrictive	9	Diffuse	Nausea	No
14	No	Acute	Continuous	Constrictive	6	LHC	Nausea and vomiting	Migraine without aura
15	Migraine without aura	Progressive	Continuous + several episodes of TH	Throbbing	9	Diffuse	Nausea, phono/photophobia	Migraine without aura + episodic TTH
16	No	TH	Continuous + several episodes of TH	Throbbing	9	Diffuse	No	Migraine with aura
17	No	Progressive	Continuous	Constrictive	5	RHC	No	No

LFO, left fronto-orbital; LHC, left hemicranium; LNP, left neck pain; RHC, right hemicranium; RNP, right neck pain; TH, thunderclap headache; TTH, tension-type headache.

thunderclap headache. Two patients had intermittent headache: one with unilateral and throbbing “migraine-like” headache, the other with “cluster-like” attacks of severe orbital pain lasting 30 minutes.

The headache was throbbing in 76% (n = 13) and severe in 76% (n = 13) of the patients. It was diffuse in 4, unilateral in 13, and associated with homolateral neck pain in 3 patients. Nausea, vomiting, and/or phono/photophobia was present in 59% (n = 10). All patients except one with isolated unilateral lateral sinus thrombosis had a unilateral headache, ipsilateral to the thrombosis. One patient with right lateral sinus thrombosis had a diffuse headache. Patients with jugular vein thrombosis had ipsilateral neck pain.

In all patients, the severe headache started to improve in a few days. It disappeared within two weeks in two thirds of the patients and within one month in the rest. At three months, the four patients who had migraine before continued to have attacks of migraine and two had associated tension-type headache. A new onset of migraine with aura was observed in two patients and of tension-type headache in one.

DISCUSSION

In a prospective series of 123 patients seen over a four year period at our institution, 17 (14%) had headache as the only manifestation of CVT in the absence of intracranial hypertension, SAH, meningitis, or intracranial lesions. This reflects a recruitment bias in favour of, firstly, CVT (our centre had the largest number of patients in ISCVT⁹) and, secondly, headache (our emergency headache centre deals with 7500 patients per year).

A remarkable feature of this series is the unusually high frequency (88%) of lateral sinus involvement either alone or associated with jugular vein or other sinus thrombosis. It is unlikely that isolated lateral sinus thrombosis was over-diagnosed because absence of flow on MRV was required in association with increased signal on MRI T1- and T2-weighted images for the diagnosis. This allowed us to differentiate it from lateral sinus hypoplasia.¹⁰ Whether the isolated lateral sinus thrombosis would have continued to remain isolated or whether it was the initial manifestation of a thrombotic process that might have extended to other sinuses remains debatable. However, it is noteworthy that the delay between the onset and diagnosis was not significantly different in the patients with isolated lateral sinus thrombosis from the patients with lateral sinus thrombosis associated

with other sinuses. In contrast, superior sagittal sinus thrombosis (the superior sagittal sinus is the most frequently involved in large CVT series) was detected in only four patients, most likely because headache in superior sagittal sinus thrombosis is associated with signs of intracranial hypertension, focal deficits, or disorders of consciousness. This also equally applies to bilateral lateral sinus thrombosis which usually induces intracranial hypertension. Apart from the site of thrombosis, all other characteristics (age, sex, aetiology) were similar to those of CVT in general. By definition, the prognosis was good, but again, it is not possible to conclude if the patients would have recovered spontaneously or whether heparin played a favourable role.

There was no uniform pattern of headache in this series. The most frequent characteristics were: recent rapidly progressive onset (less than 30 days) of severe headache (VSA above 8/10); persistent course (15/17); unilateral location (13/17); and throbbing quality (13/17). Three patients presented with thunderclap headache: one had superior sagittal sinus thrombosis, one had extensive thrombosis (superior sagittal sinus, lateral sinus, and deep venous system) and one had lateral sinus and jugular vein thrombosis. So thunderclap headache may occur in CVT in the absence of subarachnoid or intracerebral haemorrhage. Two of these patients had a spontaneous hyperdense sinus on CT scan that was suggestive of CVT, but the third had a completely normal CT scan. This demonstrates the importance of MRI/MRV in patients who have a thunderclap headache with normal CT scan and CSF examination. In two patients the headache was deceptive, mimicking migraine in one and cluster headache in the other.

Non-contrast cerebral CT scan is usually performed as the first investigation in patients with a recent persisting headache. The essential CT finding in our series was the spontaneous hyperdensity of the thrombosed sinus, present in 60% of patients. This sign, known as the “dense triangle” in superior sagittal sinus thrombosis,¹¹ may be seen in any sinus. However it is frequently missing or difficult to recognise with certainty, and there are false positives, particularly in children or in patients with haemoconcentration.¹²⁻¹³ Hence, MRI/MRV is required when this sign is lacking or doubtful.

The mechanism of headache in CVT in the absence of intracranial hypertension, SAH, meningitis, or intracranial lesion is unknown. Stretching or irritation of nerve fibres in the walls of the occluded sinus is a possibility. It is also

possible that a local inflammatory reaction occurs with dilatation of vessels in the sinus walls as suggested by the frequent contrast enhancement surrounding the clot, known as the “empty delta sign”.¹⁴

In conclusion, isolated headache can be the only clinical sign of CVT in the absence of intracranial hypertension, SAH, meningitis or intracerebral lesion. In such cases CVT mostly involves a lateral sinus, either alone or in association with other sinuses. The headache is usually progressive over a few days, severe, persistent, unilateral and throbbing, but a few patients have sudden onset or even a thunderclap headache. The pathogenesis of the headache is unknown but may involve changes in the walls of the thrombosed sinus. Plain CT scan frequently shows a hyperdense sinus, but it is normal in 40% of patients. This points to a need for MRI/MRV in all patients with recent headache—progressive or thunderclap—with normal CT scan and CSF examination.

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