Cerebral venous thrombosis (CVT) is an uncommon cerebrovascular disease presenting with a remarkably wide spectrum of signs and mode of onset. In all series, headache is the most frequently occurring symptom at any time, present in over 80% of cases, 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. 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.

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.

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). Diagnosis of CVT was based on magnetic resonance imaging (MRI) combined with MR venography (MRV), and/or helical CT venography and/or conventional angiography.

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 ≥ 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 22–50; 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 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
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 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, head-ache with normal CT scan and CSF examination. In two patients the headache was deceptive, mimicking migraine in one and cluster headache in the other.

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 (VAS 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 unknown whether stretching or irritation of nerve fibres at the walls of the occluded sinus is a possibility. It is also

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

<table>
<thead>
<tr>
<th>Patient</th>
<th>History of migraine</th>
<th>Onset</th>
<th>Evolution</th>
<th>Pattern</th>
<th>Severity (VAS)</th>
<th>Location</th>
<th>Associated signs</th>
<th>Headache at 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No</td>
<td>TH</td>
<td>Continuous</td>
<td>Constructive</td>
<td>10 Diffuse</td>
<td>Nausea and vomiting</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Migraine without aura</td>
<td>Progressive</td>
<td>Intermittent</td>
<td>Throbbing</td>
<td>8 RHC</td>
<td>Nausea and vomiting</td>
<td>Migraine without aura</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>No</td>
<td>Acute</td>
<td>Continuous</td>
<td>Throbbing</td>
<td>8 RHC</td>
<td>Nausea and vomiting</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>No</td>
<td>Progressive</td>
<td>Cluster-like attacks</td>
<td>Throbbing</td>
<td>8 UFO</td>
<td>Migraine without aura</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>No</td>
<td>TH</td>
<td>Continuous</td>
<td>Throbbing</td>
<td>9 RHC + RNP</td>
<td>Nausea and vomiting, phono/photophobia</td>
<td>Migraine with aura</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Migraine without aura</td>
<td>Progressive</td>
<td>Continuous</td>
<td>Throbbing</td>
<td>9 RHC + RNP</td>
<td>Nausea and vomiting</td>
<td>No</td>
<td>Migraine without aura</td>
</tr>
<tr>
<td>7</td>
<td>Migraine without aura</td>
<td>Progressive</td>
<td>Continuous</td>
<td>Throbbing</td>
<td>9 RHC</td>
<td>Nausea, phono/photophobia</td>
<td>TTH</td>
<td>TTH + migraine without aura</td>
</tr>
<tr>
<td>8</td>
<td>No</td>
<td>Progressive</td>
<td>Continuous</td>
<td>Throbbing</td>
<td>8 RHC</td>
<td>Nausea, phono/photophobia</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>No</td>
<td>Progressive</td>
<td>Continuous</td>
<td>Throbbing</td>
<td>6 RHC</td>
<td>Nausea and vomiting</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>No</td>
<td>Progressive</td>
<td>Continuous</td>
<td>Throbbing</td>
<td>10 UFO</td>
<td>Migraine without aura</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>No</td>
<td>Progressive</td>
<td>Continuous</td>
<td>Throbbing</td>
<td>10 RHC</td>
<td>Nausea and vomiting</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>No</td>
<td>Progressive</td>
<td>Continuous</td>
<td>Throbbing</td>
<td>9 RHC-UNP</td>
<td>TTH</td>
<td>Migraine without aura</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>No</td>
<td>Acute</td>
<td>Continuous</td>
<td>Throbbing</td>
<td>9 Diffuse</td>
<td>Nausea</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>No</td>
<td>Acute</td>
<td>Continuous</td>
<td>Throbbing</td>
<td>6 RHC</td>
<td>Nausea and vomiting</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Migraine without aura</td>
<td>Progressive</td>
<td>Continuous + several episodes of TH</td>
<td>Throbbing</td>
<td>9 Diffuse</td>
<td>Migraine without aura + episodic TTH</td>
<td>Migraine without aura</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>No</td>
<td>TH</td>
<td>Continuous + several episodes of TH</td>
<td>Throbbing</td>
<td>9 Diffuse</td>
<td>No</td>
<td>Migraine with aura</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>No</td>
<td>Progressive</td>
<td>Continuous</td>
<td>Throbbing</td>
<td>3 RHC</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

UFO, left-fronto-orbital; UHC, left hemorhiamus; RNP, right neck pain; RHC, right hemorhiamus; RNP, right neck pain; TH, thunderclap headache; TTH, tension-type headache.
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”.\textsuperscript{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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\textbf{REFERENCES}