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## Does headache represent a clinical marker in early diagnosis of cerebral venous thrombosis? A prospective multicentric study

**Abstract** The main aim of this study is to look for early clinical markers of cerebral venous thrombosis (CVT). As headache represents the major clinical manifestation at presentation we focused our attention on this symptom. We present the preliminary results of a prospective multicentric study that includes cases diagnosed as CVT in the participating centres. We have so far studied 35 patients (5 males

and 30 females) from the ages of 18 to 78. The most frequent manifestation was headache (77.1%). It was more frequently localised (66.7%) and continuous (77.8%). The onset of pain was mostly acute–subacute (38.5%–50.0%) and the intensity moderate–severe (37.0%–51.9%). On univariate analysis, we found a positive correlation between CVT, acute headache onset ( $p=0.001$ ) and severe headache ( $p=0.004$ ). These preliminary results seem in accordance with our previous findings in the retrospective study, suggesting that CVT is more often associated with acute-onset headache of severe intensity.

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**Key words** Cerebral venous thrombosis • Headache • Early diagnosis

The perception of cerebral venous thrombosis (CVT) has changed dramatically over the past two decades. Although uncommon, CVT is more frequent than usually thought. It has no uniform pattern of presentation but a huge variety of signs and modes of onset and a variable severity [1]. Early diagnosis of CVT is crucial because its potential for recovery is considerably high, particularly if adequate therapeutic measures, including heparin, are taken early [2]. The main aim of this study is to look for early clinical markers of CVT. As headache represents the major clinical manifestation at presentation [3] we focused our attention on this symptom. We present the preliminary results of a prospective multicentric study that includes cases diagnosed as CVT between January 2003 and June 2004 in the participating hospitals (22 centres). It is based on the results of a previous retrospective study conducted in three hospitals in and around Milan ("S. Gerardo" Hospital of Monza, Niguarda Hospital and National Neurological Institute "C. Besta" of Milan). The study is sponsored by the "Associazione Neurologica Italiana per la Ricerca sulle Cefalee" (ANIRCEF) and by the "Associazione per una Scuola delle Cefalee" (ASC).

Only cases occurring in adulthood (i.e., over 15 years of age) were included in this study. We have so far studied 35

patients. CVT diagnosis was based on MRI associated with magnetic resonance angiography in 33 patients and on trans-femoral angiography in 2 patients. Thirty-two patients were admitted to the emergency room for clinical manifestations of CVT while three came from neurological ambulatory. To identify some of the characteristics of headache which may be useful in the early diagnosis of CVT we compared our patients with headache (27 patients out of 35) with a control population including 71 subjects consecutively admitted to the emergency room of the "San Gerardo" Hospital complaining of headache from 1st June to 31st July 2000. These subjects were comparable to our CVT patients with headache for age and sex (controls: 16.9% male, 83.1% female; mean age 44.7 years/CVT patients with headache: 14.8% male, 85.2% female; mean age 43.2 years). Five patients (14.3%) were male and 30 (85.7%) female. The mean age was 44.0 (range: 18–78). Onset was acute in 37.1% of cases, subacute in 48.6%, and chronic in 14.3% [1]. The most frequent sign was headache (77.1%). Nineteen patients (54.3%) presented focal deficits, 14 patients (40.0%) had seizures, 13 patients (37.1%) altered consciousness and 8 patients (24.2%) neuropsychological deficits. Headache was the initial symptom in 77.1% of cases (in one patient it was associated with dizziness, in one other with visual disturbances and in a third with both). In 19 patients out of 32 (59.4%), headache was among and sometimes the only reason of emergency room admittance. At onset it was more frequently localised (66.7%) and continuous (77.8%). The mode of onset of pain was mostly acute-subacute (38.5%–50.0%) and the intensity moderate-severe (37.0%–51.9%). Pain was worsened by physical exercise (33.3%), Valsalva's manoeuvre (25.9%), orthostatism (22.2%) and recumbency (7.4%). Twenty patients complained of accompanying symptoms such as nausea and/or vomiting, photophobia, phonophobia, visual blurring and dizziness. On univariate analysis (chi-square), we found a positive correlation between CVT, acute headache onset ( $p=0.001$ ) and severe headache ( $p=0.004$ ). The following aetiologic factors were found: oral contraceptives (34.3%), anaemia (14.3%), antiphospholipid antibody syndrome (11.4%), puerperium (8.6%), pregnancy (5.7%), extracerebral tumours (5.7%), hyperhomocystinemia (5.7%), protein-C deficiency (5.7%), protein-S deficiency (2.9%), antithrombin III deficiency (2.9%), activated protein C resistance (2.9%), infections (2.9%), piastriosis (2.9%) and meningiomas (2.9%). Nine patients had two or more risk factors. Putative aetiological factors were absent in 20.0% of cases. Twenty-five patients (71.4%) had complete recovery, nine (25.7%) had mild-moderate sequelae and one patient (2.9%) had severe sequelae. The treatments used were: heparin i.v. (51.4%), low molecular weight heparin (37.1%), oral anticoagulant therapy (8.6%) and locoregional thrombolysis (2.9%).

Headache is a common complaint in the emergency room and is a fairly aspecific symptom [4]. However, occasionally headache can be the manifestation of ominous and sometimes elusive disorders, such as CVT [5]. In fact,

headache can represent the sole clinical manifestation at the onset or during the course of the disease [6]. The International Headache Society (IHS) defined criteria for the diagnosis of headache attributed to CVT [7]. According to the IHS Classification, headache in CVT has no specific characteristics. In our study we found a positive correlation between CVT, acute headache onset ( $p=0.001$ ) and severe headache ( $p=0.004$ ). These preliminary results seem in accordance with our previous findings in a retrospective study, suggesting that CVT is more often associated with acute-onset headache of severe intensity. These features, especially in patients with underlying prothrombotic conditions, which have to be investigated with a meticulous anamnesis also in the emergency department, should lead to consideration of the diagnosis of CVT and to the requirement of neuroimaging examinations. As CT scan is normal in patients with proven CVT in 10%–20% of cases [6], MRI must be performed when clinical suspicion remains after a normal or non specific CT scan.

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**Patients are from** San Gerardo Hospital, Monza: E. Agostoni, S. Iurlaro, E. Beghi, P. Santoro, A. Aliprandi; San Paolo Hospital, Milano: N. Masetto; Niguarda Hospital, Milano: A. Guccione, A. Ciccone, A. Gatti, I. Santilli; Polyclinic of Messina: M. Autunno, R. Di Leo; San Raffaele Hospital, Milano: B. Colombo, P. Rossi; Civil Hospital, Brescia: T. Di Monda, R. Rao, P. Liberini; Mauriziano Hospital, Torino: M. Gionco, P. Cristofanelli, A. Febbraro, C. Labate, M. Maniscalco, L. Sosso, F. Trenini; Polyclinic of Modena: P. Cortelli, D. Grimaldi; San Bortolo Hospital, Vicenza: F. Perini; Moscati Hospital, Avellino: F. D'Onofrio

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## References

1. Bousser MG (2000) Cerebral venous thrombosis: diagnosis and management. *J Neurol* 247:252–258
2. Ferro JM, Correia M, Pontes C et al (2001) Cerebral vein and dural sinus thrombosis in Portugal: 1880–1998. *Cerebrovasc Dis* 11:177–182
3. Ameri A, Bousser GM (1992) Cerebral venous thrombosis. *Neurol Clin* 10:87–111
4. Svenson J, Cowen D, Rogers A (1997) Headache in the emergency department: importance of history in identifying secondary etiologies. *J Emerg Med* 15:617–621
5. Dodick D (1997) Headache as a symptom of ominous disease. What are the warning signals? *Postgrad Med* 101:46–50, 55–56, 62–64
6. Bousser GM, Ross Russel R (1997) Cerebral venous thrombosis, Vol 1. Saunders, London
7. Classification and diagnostic criteria for headache disorders cranial neuralgias and facial pain of the Headache Classification Committee of the IHS (2004) *Cephalalgia* 24[Suppl 1]