کارگاه‌های آموزشی مرکز اطلاعات علمی

مقاله نویسی علوم انسانی

اصول تنظیم قراردادها

آموزش مهارت های کاربردی در تدوین و چاپ مقاله
Cerebral Venous-Sinus Thrombosis: A Case Series Analysis

Nahid Ashjazadeh1, Afshin Borhani Haghighi2, Maryam Poursadeghfard2, Hoseinjan Azin3

Abstract

Background: Cerebral venous-sinus thrombosis is an uncommon form but important cause of stroke, especially in young-aged women.

Methods: We performed a retrospective descriptive-analytical study in which 124 patients with cerebral venous-sinus thrombosis, who referred to Nemazee Hospital, Shiraz University of Medical Sciences from January 2000 to March 2008, were included, and their demographic, etiologic, radiological and prognostic characteristics were evaluated.

Results: The patients' mean age was 34.01±10.25. Eighty seven (70.16%) were women and 37 (29.83%) were men. The most frequent clinical manifestations were headache, papilledema and seizures. Fifty seven (65.51%) women took oral contraceptive pills. Twenty of 57 women (35.08%) took the pill longer than one month to be able to fast in Ramadan or perform the Hajj ceremonies. In the mean time they developed cerebral venous-sinus thrombosis. Superior sagital sinus, with or without lateral sinuses, was the most involved area (70.96%). High mortality and morbidity rates (14.51% and 35.48%, respectively) were found in patients. Poor prognostic factors at the time of admission were stupor and coma (P=0.001) and evidence of hemorrhage in primary CT scan (P=0.005).

Conclusion: Taking oral contraceptive pills was a main factor associated with cerebral venous-sinus thrombosis. Clinical manifestations, prognostic factors, common involved sinuses and image findings of this study were similar to those of other studies. Health care policy makers should design a plan to warn susceptible women of the risk of cerebral venous-sinus thrombosis, and to educate them the ways to prevent it.

Iran J Med Sci 2011; 36(3): 178-182.

Keywords • Intracranial sinus thrombosis • oral contraceptives • stroke

Introduction

Cerebral venous-sinus thrombosis (CVST) is a potential life-threatening condition that requires rapid diagnosis and urgent treatment. Its epidemiology has changed over past few decades.1 Its increasing prevalence may be attributed to not only increased ease of diagnosis by modern imaging tools such as magnetic resonance imaging (MRI), but also to the increment of underlying causes including use of oral contraceptive pills
(OCPs). Cerebral venous-sinus thrombosis seems relatively more frequent in South Asia and Middle East. This study aims to report demographic, etiologic, radiological and prognostic characteristics of patients with CVST in Fars province in the south of Iran.

Materials and Methods

The study is a retrospective analysis of medical records of 124 patients with CVST, who referred to Nemazee Hospital, a teaching hospital affiliated with Shiraz University of Medical Sciences, from January 2000 to March 2008. Written informed consents were obtained from all patients. Patients with related CVST manifestations underwent cerebral MRI and magnetic resonance venography (MRV). Contrast digital subtraction venography was conducted in some patients with equivocal diagnosis. Patients whose presentations could be explained better by any other neurological diseases or those whose imaging revealed congenital hypoplasia of dural sinuses were excluded. Brain and paranasal sinuses MRI, high resolution computer tomography (CT) scan of chest, abdominal and pelvic organs, bone scan, and tumor marker measurement were performed to evaluate infections and malignancies. In addition to routine laboratory evaluations, sickle cell and sucrase lysis tests were done. Also, plasma concentrations of proteins C and S, and antibodies such as anticardiolipin, antinuclear, anti-double-stranded DNA and anti-beta2-glycoprotein were measured. Pathergy skin test and HLA-B51 antigen were evaluated in patients suspected to have Behcet's disease (BD). All patients with non-septic CVST, even those with hemorrhage, received intravenous heparin followed by oral warfarin for a period of six months. Thrombosis profile was recorded in all patients, and when a substantial cause of thrombophilia was found, warfarin was prescribed as a life-long treatment. The patients' demographic characteristics, clinical manifestations, laboratory finding, neuro-imaging investigations, treatment options and prognosis were also studied.

Statistical Analysis

Findings were analyzed using Statistical Package for Social Sciences (SPSS software version 11.5). The data are reported as mean±SD for quantitative variables, and as count and percent for qualitative variables. Chi-square test was used to analyze qualitative findings. A P value of ≤0.05 was considered statistically significant.

Results

The mean age of the participants was 34.01±10.25. Eighty seven (70.16%) were women and 37 (29.83%) were men. Eleven (8.87%) had septic CVST and 113 (91.12%) had non-septic cerebral venous thrombosis (CVT). The most frequent clinical manifestations were headache in 116 (93.54%), papilledema in 48 (62.3%), seizures in 28 (36.4%), neurological deficit in 44 (35.48%), and decreased level of consciousness in 31 patients (25%).

Table 1 shows the most common findings in 124 patients with CVST. Twenty out of 57 women (35.08%) took OCPs to prevent menstruation to be able to perform Ramadan fasting and Hajj ceremony. Common thrombosed intracranial sinuses are presented in figure 1.

Table 1: Common findings in 124 patients with cerebral venous sinus thrombosis

| Etiology                        | Etiology subsets | Male | Female | Total |
|---------------------------------|------------------|------|--------|-------|
| Hormone related                 | OCP              | 0    | 57     | 57 (45.95%) |
|                                 | Pregnancy, postpartum | 0    | 10     | 10 (8.06%) |
| Rheumatologic diseases          | BD               | 5    | 2      | 7 (5.64%)  |
|                                 | APLS             | 2    | 2      | 4 (3.22%)  |
|                                 | SLE              | 0    | 2      | 2 (1.61%)  |
| Infections cause                | Mastoiditis      | 3    | 1      | 4 (3.22%)  |
|                                 | Otitis media     | 2    | 2      | 4 (3.22%)  |
|                                 | Sinusitis        | 2    | 1      | 3 (2.41%)  |
| Thrombophilic state             | Protein C deficiency | 1    | 1      | 2 (1.61%)  |
|                                 | Protein S deficiency | 1    | 1      | 2 (1.61%)  |
|                                 | Mixed hyperhomocysteinemia and | 1    | 0      | 1 (0.80%)  |
|                                 | Protein C deficiency | 11   | 1      | 12 (9.67%) |
| Others                          | Trauma, malignancy, liver disease,… | 11   | 1      | 12 (9.67%) |
| Undefined                       |                  | 9    | 7      | 16 (12.90%) |
| Total                           |                  | 37   | 87     | 124 (100%) |

OCP: oral contraceptive pill, BD: Behcet’s disease, APLS: antiphospholipid antibody syndrome, SLE: systemic lupus erythematosus
Eighteen (14.51%) patients passed away. Poor prognostic factors at the time of admission were stupor or coma (P=0.001) and parenchymal with or without subarachnoid hemorrhage in first CT scan (P=0.005). Recurrent thrombosis developed in 12 patients (9.67%) and consisted of recurrent CVST in one patient (0.80%), lower extremity deep vein thrombosis (DVT) in 10 patients (8.06%) and hepatic vein thrombosis in one patient (0.80%).

**Discussion**

A number of previous studies demonstrated increasing incidence of CVST in Iran. Such an increased profile prompted us to investigate the underlying causes of CVST in Iranian people. The present study is similar to some previous ones in terms of female predominance, clinical manifestations, and the involved sinus of CVST.3-10

The use of OCPs might be the main factor associated with CVST in our study. The combined OCPs increase the risk of CVST, and odds ratio increases to 30.0, 79.3 and 19.5 in the presence of V Leiden factor, prothrombin mutation or hyperhomocysteinemia, respectively. Twenty women (35.08%) took OCP for a duration longer than one month to prevent menstruation during religious ceremonies such as Ramadan fasting or Hajj, and developed CVST during the period of the drug use. A similar finding has been reported in other parts of Iran, but not in other countries. Dehydration during Ramadan fasting and immobilization during long journey of Hajj pilgrims are other factors in these situations. Hyperhomocysteinemia is a known risk factor for venous thrombosis. It results from low socioeconomic conditions secondary to deficient nutritional status, low plasma folate and vitamin B12 levels, which are associated with an increased risk of CVST in some developing countries.12,13

A small percentage (5.64%) of our patients had BD. The prevalence of BD is 16 in 100,000 people in Iran. The frequency of neurological manifestations in Behcet’s disease ranges from 5% to 30%.16,17 Borhani-Haghighi et al. reported that 22% of patients with Neuro-Behcet's disease developed CVST. This might justify the high frequency of the disease as an underlying cause of CVST in Iran. Some patients of this study had primary antiphospholipid antibody syndrome (APLS) and systemic lupus erythematosus (SLE). The role of antiphospholipid antibodies and other lupus anticoagulants in the evolution of CVST has been previously reported.17,18 Thrombophilia conditions including deficiency of proteins C and S appeared in 6.5% of the patients. One of our patients, who was also reported by Borhani-Haghighi et al. had a rare sporadic combined hyperhomocysteinemia and protein C deficiency.

The mortality and morbidity rates in our patients were higher than some previous studies. The mortality rate was 14.51% in the present study, whereas that of patients with CVST in an international study on cerebral vein and dural sinus thrombosis (ISCVT) was 8.3%.9 Higher mortality in the present study might be
due to the referral nature of our center, which
excluded patients with milder course as well as
the lack of neuro-intensive care units. Presence
of coma or stupor ($P=0.001$), parenchymal
hemorrhage ($P=0.005$) at the time of ad-
mission, and cancer were common predictors
of high mortality rate in this study and other
previous studies.$^{3,6,8,20}$

Increased morbidity in the present study
(35.48%) compared to that of ISCVT (26.92%)
may be attributed to retrospective nature of our
study in a clinic-based follow-up. Headache,
oneg optic atrophy and focal neurological deficits
were major sequels, which were similar to those
reported in Azin et al.$^3$ and Hameed et al.$^{21}$

Extracranial venous thrombosis in our study
was approximately two times more than what
was reported in a study by Ferro et al.$^6$ (8.06%
vs 4.3%). Predisposing factors for recurrent
thrombosis were malignancy, postpartum
state, OCP, BD, SLE, and APLS. This study
sheds new light on the subject, and suggests
using important methods including organ mobi-
лизация and prophylactic anti-coagulative drugs
in patients with cerebral venous-sinus thrombo-
sis. It also emphasizes prompt diagnosis and
treatment of thrombophilic conditions to prevent
thrombosis formation more than before.

Conclusion

The findings of the study indicate that the use of
OCPs was a main factor associated with CVST.
Clinical manifestations, prognostic factors, in-
volved sinuses and imaging findings of our
study were similar to those of other studies.
Mortality and morbidity rates were high in our
patients (14.51% and 35.48%, respectively).
Moreover, the findings may suggest that health
care policy makers should design a plan to warn
susceptible women of the risk of CVST and
educate them the ways to prevent it.

Acknowledgment

We would like to thank Ms. Hosseini and Ms.
Gholami from Shiraz Neurosciences Research
Center for their kind assistance.

Conflict of Interest: None declared

References

1. Siddiqui FM, Kamal AK. Incidence and
epidemiology of cerebral venous thrombo-
sis. $J$ Pak Med Assoc 2006; 56: 485-7.
2. Saadatnia M, Tajmirriahi M. Hormonal con-
traceptives as a risk factor for cerebral
venous and sinus thrombosis. Acta Neurol
Scand 2007; 115: 295-300.
3. Azin H, Ashjazadeh N. Cerebral venous
sinus thrombosis—clinical features, predis-
posing and prognostic factors. Acta Neurol
Taiwan 2008; 17: 82-7.
4. Saadatnia M, Mousavi SA, Haghhi S,
Aminorrroaya A. Cerebral vein and sinus
thrombosis in Isfahan-Iran: a changing pro-
file. Can J Neurol Sci 2004; 31: 474-7.
5. Rahimi Z, Mozafari H, Bigvand AH, et al.
Cerebral venous and sinus thrombosis and
thrombophilic mutations in Western Iran:
association with factor V Leiden. Clin Appl
Thromb Hemost 2010; 16: 430-4.
6. Ferro JM, Canhão P, Stamm J, et al. Progno-
sis of cerebral vein and dural sinus thrombo-
sis: results of the International Study on
Cerebral Vein and Dural Sinus Thrombosis
(ISCVT). Stroke 2004; 35: 664-70.
7. Stamm J. Thrombosis of the cerebral veins
and sinuses. N Engl J Med 2005; 352:
1791-8.
8. Masuhr F, Mehraine S, Einfäulpi K. Cere-
bral venous and sinus thrombosis. J Neurol
2004; 251: 11-23.
9. Ameri A, Bousser MG. Cerebral venous
thrombosis. Neuro Clin 1992; 10: 87-111.
10. Daif A, Awada A, Al-Rajeh S, et al. Cere-
bral venous thrombosis in adults: A study
of 40 cases from Saudi Arabia. Stroke
1995; 26: 1193-5.
11. Saadatnia M, Haghhi S, Ziaei J, et al.
Oral contraceptive pills misuse and cere-
bral vein sinus thrombosis: a growing
health problem in Isfahani women. J Neurol
2004; 251: 300.
12. Nagaraja D, Noone ML, Bharatkumar VP,
et al. Homocysteine, folate and vitamin
B(12) in puerperal cerebral venous throm-
sis. J Neurol Sci 2008; 272: 43-7.
13. Cantu C, Alonso E, Jara A, et al. Hygro-
myocysteina, Low folate and vitamin B12
concentration, and methylene tetrahydro-
folate reductase mutation in cerebral ve-
nous thrombosis. Stroke 2004; 35: 1790-4.
14. Davatchi F, Shahram F, Akbarian M, et al.
Behcet’s Disease: Analysis of 3443 cases.
APLAR Journal of Rheumatology 1997; 1:
2-5.
15. Ashjazadeh N, Borhani Haghighi A, Saman-
goie Sh, Moosavi H. Neuro-Behcet’s dis-
ease: a masquerader of multiple sclerosis. A
prospective study of neurologic manifesta-
tions of Behcet’s disease in 96 Iranian pa-
tients. Exp Mol Pathol 2003; 74: 17-22.
16. Borhani-Haghighi A, Samangoowie S, As-
jahzadeh N, et al. Neurological manifesta-
tions of Behcet's disease. *Saudi Med J* 2006; 27: 1542-6.

17 Uthman I, Khalil I, Sawaya R, et al. Lupus anticoagulant, factor V Leiden, and methyltetrahydrofolate reductase gene mutation in a lupus patient with cerebral venous thrombosis. *Clin Rheumatol* 2004; 23: 362-3.

18 Lee MK, Kim JH, Kang HR, et al. Systemic lupus erythematosus complicated with cerebral venous sinus thrombosis: a report of two cases. *J Korean Med Sci* 2001; 16: 351-4.

19 Borhani–Haghighi A, Sabaeiyan B, Nejabat M, Omrani G. Coexistence of Hyperhomocysteinemia and Protein C Deficiency in the Development of Sinus Thrombosis a Case Report. *Iranian Journal of Endocrinology and Metabolism* 2006; 8: 345-51.[In Persian]

20 Canhão P, Ferro JM, Lindgren AG, et al. Causes and predictors of death in cerebral venous thrombosis. *Stroke* 2005; 36: 1720-5.

21 Hameed B, Syed NA. Prognostic indicators in cerebral venous sinus thrombosis. *J Pak Med Assoc* 2006; 56: 551-4.
کارگاه‌های آموزشی مرکز اطلاعات علمی

مقاله نویسی علوم انسانی

اصول تنظیم قراردادها

آموزش مهارت های کاربردی در تدوین و چاپ مقاله