Mini-Review

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The etiologies of new cases of cerebral venous sinus thrombosis reported in the past year

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Summary **Cerebral venous sinus thrombosis (CVST) is an uncommon but life-threatening stroke subtype with extremely diverse clinical features, predisposing factors, brain imaging findings, and outcomes. Its predominant etiologies were known to be otomastoid, orbit, and central face cutaneous infections, pregnancy and complications associated with the postpartum period, and oral contraceptives. In recent years, however, infections have accounted for fewer cases while oral contraceptives, pregnancy and complications associated with the postpartum period, tumors, and coagulopathies have accounted for more cases of CVST. These conditions have become the predominant risk factors for CVST, but uncommon etiologies have also emerged. This review focuses on the new etiologies of CVST cases reported this year to broaden perspectives on the etiologies of CVST.**

Keywords: Cerebral venous sinus thrombosis, etiology

1. Introduction

Cerebral venous sinus thrombosis (CVST) is an uncommon but life-threatening stroke subtype caused by clotting of blood in cerebral venous or dural sinuses, and, in rare cases, cortical veins, with extremely diverse clinical features, predisposing factors, brain imaging findings, and outcomes (*1,2*). Predisposing clinical conditions usually combine to constitute an underlying etiology. It is a rare but potentially fatal cause of acute neurological deterioration previously related to otomastoid, orbit, and central face cutaneous infections, pregnancy and complications associated with the postpartum period, and oral contraceptives (*2*). With the advent of antibiotics and improved medical care for women, infections and the postpartum period have been controlled, so these conditions have accounted for fewer cases of CVST. In recent years, new risk factors for CVST have emerged as people are living longer. Here, papers published last year and common and uncommon etiologies of CVST at this time have been summarized in order to broaden perspectives on the etiologies of CVST.

2. Search strategy and data extraction

MEDLINE and PUBMED databases were searched for articles in English on etiologies of CVST, including case control, cohort, and case series studies and case reports published in peer-reviewed journals from September 2010 to October 2011.

3. Features and etiologies of CVST

The features and etiologies of CVST in cases reported this year are summarized in Table 1. Patients in these cases were of various ages, from neonates to 56-year-old; most susceptible were younger individuals and

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Table 1. Cerebral venous sinus thrombosis cases reported in the past year

Case number	Etiology	Age	Gender	First author (*Ref. No.*)	Published year
1	Unknown	41	F	Nimjee SM (*3*)	2011
2	Unknown	32	F	Levy M (*6*)	2011
3	Unknown	52	F	David Oehme (*10*)	2011
4	Unknown	18	F	Christopher T. Shah (*30*)	2011
5	Vaginal rings	28	F	Kolacki C (*4*)	2011
6	Vaginal rings	32	F	Fugate JE (*5*)	2011
7	High-voltage electrical burns	10	F	Singh G (*8*)	2011
8	Oral contraceptives	20	F	Min J (*7*)	2011
9	Oral contraceptives	21	F	Slankamenac P (*9*)	2011
10	Oral contraceptives	45	F	Wong VS (*31*)	2011
11	SIH	35	M	Dangra VR (*10*)	2011
12	SIH	26	M	Yoon KW (*13*)	2011
13	The postpartum period	19	F	McCaulley JA (*12*)	2011
14	Paroxysmal nocturnal hemoglobinuria	44	M	van Eimeren VF (*15*)	2011
15	Pregnancy	33	F	Ferreira MM (*16*)	2011
16	Mutations in factor V Leiden and MTHFR A1298C	56	F	Ozkurt S (*17*)	2011
17	Hyperthyroidism	8	F	van Eimeren VF (*15*)	2011
18	Choriocarcinoma	33	F	May T (*18*)	2011
19	Factor V Leiden mutation	12	M	Yilmaz S (*20*)	2011
20	Chemotherapy for acute lymphoblastic leukemia	4	M	Wang TY (*21*)	2011
21	HIV+ protein S deficiency	30	M	Modi M (*22*)	2011
22	Trauma	30	F	Fahim DK (*24*)	2011
23	Ruptured intracavernous carotid artery aneurysm	55	F	Aldea S (*25*)	2011
24	Dural scalp and intracranial hemangiomas	4 months	F	Nahed BV (*26*)	2011
25	Sickle-cell disease	42	F	Vassilopoulou S (*32*)	2011
26	Polycythemia	31	M	Raval M (*27*)	2011
27	Type I antithrombin deficiency	25	F	Sharpe CJ (*28*)	2010
28	Iron deficiency anemia	18 months	M	Habis A (*29*)	2010

SIH means spontaneous intracranial hypotension. Vaginal rings mean contraceptives like NuvaRing (a combined vaginal contraceptive ring).

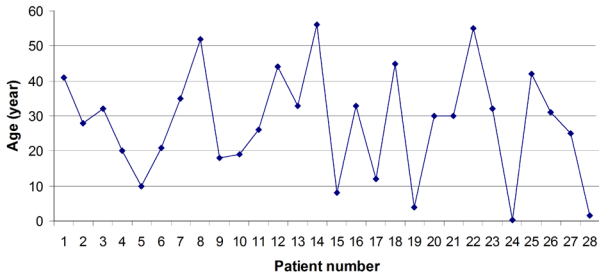

Figure 1. Age of onset in patients with cerebral venous sinus thrombosis.

women. The average age of onset (Figure 1) was 27.99 ± 12.22 years, females accounting for 71.4% of patients and males accounting for 28.6% (Female:Male = 2.5:1). The etiologies of cohort CVST cases reported this year varied. Joining known etiologies were some new risk factors. Contraceptive use accounted for 17.9% of cases and included oral contraceptives in 10.7% and use of a local contraceptive (NuvaRing) in 7.2%. Other common etiologies were hematological diseases (14.3%), a hypocoagulable state (7.2%), systemic cancer and other malignant hematological diseases (7.2%), a hypercoagulable state (type I antithrombin deficiency), and trauma (7.2%). Infection was rare as an etiology in these cohort cases while oral contraceptives were a predominant risk factor. There were, however, 14.3% of cases that had no clear etiology. Uncommon etiologies include spontaneous intracranial hypotension (SIH), hyperthyroidism, paroxysmal nocturnal hemoglobinuria, ruptured intracavernous carotid artery aneurysm, dural scalp and intracranial hemangiomas, sickle cell disease, polycythemia, and iron deficiency anemia (Table 1). Unknown etiologies account for 14.3% of cases of CVST, which is a rather high figure as a percentage of all etiologies, and this finding agrees with the results of a previous study (*1*).

4. Discussion

At this point, the predominant etiologies of CVST are oral contraceptives, hematological disorders, a hypercoagulable state, trauma, cancer, and pregnancy and complications associated with the postpartum period, but some newly emerged risk factors warrant more attention.

NuvaRing, a combined contraceptive vaginal ring, is a contraceptive widely used as an alternative to oral contraceptives with a purported advantage of allowing lower hormonal doses, thus potentially presenting less of a risk for venous thromboembolism (*4*). However, CVST has recently been noted in association with the use of a contraceptive ring, and these cases deserve attention (*4,5*). That is, both oral and local contraceptive use carry a risk of CVST. Emergency physicians should keep in mind that patients using NuvaRing have an increased risk of CVST. That said, there is still a need for large randomized and control studies of the

relationship between local contraceptive use and the onset of CVST.

SIH caused by a cerebrospinal fluid (CSF) leak is another reported risk factor for CVST. SIH may change the velocity of the cerebral blood flow and cause thrombosis (*10,13*).

However, case reports are just individual instances and do not represent general facts. Thus, newly emerging risk factors for CVST need to be studied further. In addition, unknown etiologies also account for a considerable number of cases of CVST (14.3%). Accordingly, the pressing challenge is to identify other potential risk factors for CVST.

In conclusion, the predominant etiologies of new cases of CVST were reported to be oral contraceptives and local contraceptives (*e.g.* NuvaRing), pregnancy and complications associated with the postpartum period, trauma, cancer, hematological disorders, and a hypercoagulable state. Infection is no longer a common etiology of CVST.

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