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STUDY CLINICAL FEATURES AND SOME RISK FACTORS OF CEREBRAL VENOUS THROMBOSIS

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ABSTRACT

Background: Cerebral venous thrombosis (CVT) is a rare type of cerebrovascular disease that can occur at any age, including in neonates, and it accounts for 0.5% of all stroke. The widespread use of neuroimaging now allows for early diagnosis and has completely modified our knowledge on this disorder. CVT is more common than previously thought and it is recognized as a non-septic disorder with a wide spectrum of clinical presentations, numerous causes, and usually a favorable outcome with a low mortality rate. **Objectives:** Determine the clinical characteristics and risk factors of cerebral venous thrombosis. **Subjects:** 59 patients \geq 16 years of age were diagnosed cerebral venous thrombosis at Cho Ray Hospital during January 2010 to May 2012. In the control group, 57 patients with a periodic health examination were randomly selected at Cho Ray Hospital. **Method:** The prospective, cross-sectional descriptive study with the control group was conducted. **Results:** The common symptoms of CVT in this study were headaches (98.31%), paralysis (57.63%), seizure (50.85%), consciousness disorders (37.29%), cranial nerve paralysis (32.2%), papilledema (30.5%). Coagulation studies included the following tests: antithrombin, protein C, protein S, and factor V Leiden. The proportion of cases with congenital thrombophilia was 66.7%: with Odds ratios for CVT found to be 2.25 (95% CI, 0.93 to 5.46) for factor V Leiden mutation, 2.76 (95% CI, 0.8 to 9.49) for protein C deficiency, and 1.7 (95% CI, 0.5 to 5.6) for ATIII deficiency. The oral contraceptive pill appeared to be an important additional risk factor with odd ratio was 4.05 (KTC 95%, 0.88-25.1). **Conclusions:** Cerebral venous thrombosis is a challenging condition because of its variability of clinical symptoms and signs.

The spectrum of clinical presentations is non-specific and varied, such as headaches, paralysis, seizure, consciousness disorders, cranial nerve paralysis, papilledema. Inherited as well as acquired coagulation disorders are frequent causes. Acquired and congenital varieties of thrombophilia appear to be an important additional risk factor.

Keywords: *Cerebral venous thrombosis, risk factor, coagulation disorders.*

I. INTRODUCTION

Cerebral venous thrombosis (CVT), thrombosis of the intracranial veins and sinuses is a rare type of cerebrovascular disease that affects about 5 people per million and accounts for 0.5 % of all stroke. CVT was first recognized at the beginning of the 19th century and it was long thought to be an infective disorder that commonly affected the superior sagittal sinus and resulted in bilateral or alternating focal deficits, seizures, and coma, which usually led to death. In the past 25 years, the widespread use of neuroimaging has aided early diagnosis of CVT and has thus completely modified the current information we have on this disorder. CVT is now typically recognized as a non-septic disorder with various clinical presentations and a usually favorable outcome, with mortality was below 10%. MRI and magnetic resonance angiography are the best diagnostic methods for diagnosis and heparin is the first-line treatment. However, the diagnosis of CVT is still commonly overlooked or delayed because of the remarkable diversity of its clinical symptoms, modes of onset, and neuroimaging signs; furthermore, a cause cannot be found in about 15% of cases, the individual outcome may still be difficult to predict, and the disorder may occasionally worsen despite anticoagulation. CVT thus remains a diagnostic and therapeutic challenge.

The risk factors for CVT differ from those for arterial disease. The risk factors for venous thrombosis are linked to the Virchow triad of stasis of the blood, changes in the vessel wall, and changes in the composition of the blood, especially the first and third of these. Risk factors are usually divided into acquired (e.g. surgery, trauma, pregnancy, puerperium, lupus anticoagulant, malignant disease, and female hormones) and genetic (congenital thrombophilia). Laboratory investigation for markers of thrombophilia in patients with CVT may include the identification of various congenital defects of natural anticoagulant pathways (ATIII deficiency, protein C, protein S, and factor V Leiden being the most frequent).

In Vietnam, there have been many studies on aspects of stroke. However, there are few studies on CVT, therefore we decided to study CVT with the objectives: Determine the clinical characteristics and risk factors of cerebral venous thrombosis.

II. METHODS

We selected 59 patients ≥ 16 years of age who was diagnosed cerebral venous thrombosis at Cho Ray Hospital during January 2010 to May 2012. In the control group, 57 patients with a periodic health examination were randomly selected at Cho Ray Hospital.

Data was investigated prospectively, cross-sectional descriptively with the control

group at Chợ Rẫy Hospital. Patients were included if a diagnosis of definite CVT had been made by a neuroradiologist either on CT scan after contrast enhancement showing the dense-triangle sign, or MR based on classical neuroradiological features. Patients underwent the following laboratory investigations, which increased in number over the study period as possible prothrombotic associations were reported: blood count, cholesterol, triglycerides, lipoprotein, fibrinogen, protein C, protein S, antithrombin III, , factor V Leiden. Details of the clinical presentation, laboratory and radiological investigations and long term clinical and radiological follow-up were obtained from the databases and were supplemented by return to the medical notes. All patients were seen at least once for a follow-up with a neurologist. Follow-up neuroimaging was undertaken at the discretion of the neurologist. Parenchymal changes were compared with the previous imaging and were classified as normal, improved or persistent. Venous sinus patency was assessed as normal, improved or persistent. We looked for distinctive features between venous and arterial strokes, in order to examine whether there were clues to the differential diagnosis.

Statistical analysis was performed using X^2 , T test and logistic regression (Stata version 8.0).

III. RESULTS

Clinical presentation

There were 59 patients enrolled from Cho Ray hospital. Mean age was 37.8 (mean, 37.8 ± 1.9) years. There were 33 (55.93%) females and 26 (44.7%) males; the females were 7 years younger than the males. The most common presenting features were headache, followed by focal motor deficits, seizures, and mental status changes. Unlike in arterial stroke, the symptom onset in CVT were subacute (2 days to 1 month; 79.7%), in some cases were acute (2 days or less; 11.8%) and the onset of symptoms were chronic (more than 2 months; 8.5%) (Table 1).

Table 1: Clinical features of CVT in 59 patients

Symptoms	Frequency (%)
Headache	58 (98.31%)
Motor deficits	34 (57.63%)
Seizures	30 (50.85%)
Metal status changes	22 (37.29%)
Cranial nerve abnormality	19 (32.2%)
Papilledema	18 (30.5%)
Sensorial deficits	5 (8.47%)
Aphasia	5 (8.47%)
Meningeal signs	3 (5.08%)
Vertigo	3 (5.08%)
Onset	
Acute	7 (11.8%)
Subcute	47 (79.7%)
Chronic	5 (8.5%)

Screening for thrombophilia

Table 2: Frequency of primary thrombophilia

Risk factors	Patients	Frequency of Positive Results* (%)
Protein S	16/53	30.2
Protein C	14/57	24.5
ATIII	11/57	19.3
V Leiden factor	23/47	48.9
≥ 2 risk factors	29/57	33.3
≥ 3 risk factors	5/56	8.9
4 risk factors	0	0

*Positive results mean either decreased protein C, protein S, antithrombin-III

Factors of acquired thrombophilia

Table 3: Status of administration with oral contraceptive drugs in female patients

contraceptive drugs	Number of patients		Total
	Experimental group	Control group	
Yes	10	3	13
No	23	28	51
Total	33	31	64

$\chi^2 = 4.2$; $p = 0.04$; OR = 4.05 (CI 95%, 0.88-25.1)

Table 4: Status of pregnancy in female patients

Pregnancy	Number of patients		Total
	Experimental group	Control group	
Yes	1	0	1
No	32	27	59
Total	33	27	60

$\chi^2 = 1.06$; $p = 0.361$

There was no statistically significant difference on CVT between pregnancy group and non-pregnancy group with $p = 0.361$.

Table 5: Puerperium characteristics on female patients

Puerperium	Number of patients		Total
	Experimental group	Control group	
Yes	8	0	8
No	25	27	52
Total	33	27	60

$\chi^2 = 7.5$; $p = 0.006$

There was a statistically significant difference on number of patients with CVT between puerperium group and control group.

IV. DISCUSSION

Clinical presentation

In our study, the In the control group, 57 patients with a periodic health examination were randomly selected at Cho Ray Hospital. percentage of female patients with CVT was higher than the one of male patients with CVT (55.93% vs 44.7%), with the female/male ratio was 1/0.78. According to the study of Tanislav, among 39 patients with CVT, the

percentage of female patients was significantly higher than the percentage of male patients (71% vs 29%). According to the study of Khealani, among 109 patients, the percentage of female patients was higher than the percentage of male patients (53% vs 47%).

Overall, our study was similar to other studies of other authors with the percentage of female patients with CVT was higher than the percentage of male patients, especially female patients in childbearing age, this suggested that the risk of CVT may relate to pregnancy, puerperium and birth control drugs.

Mean age of patients in our study was 37.8, wherein percentage of patients aged from 21 to 50 was 82.46%, percentage of patients aged > 50 was 13.56%.

According to the study of Nguyen Ngoc Hung on 37 patients with CVT, the mean age was 38.7. A retrospective study on 48 patients with CVT of Terazzi et al. in 2004 showed that the mean age of CVT patients was 44.8. According to the study of Ferro, in 624 patients with CVT, there was 92.8% of patients < 65 years old.

Thus, according to above stated studies, the mean age of adult patients with CVT was 32.7 to 44.8. The result of mean age in our study was also within this range and was not significantly different to other studies of other authors worldwide.

In our study, the number of patients with subacute onset accounted for the highest percentage (79.7%) followed by acute onset. According to Paciaroni, onset of CVT is commonly subacute (2 days to 1 month) with 50-80% of all cases, but sometimes it suddenly occurs with acute onset (< 2 days) like stroke (20-30% of all cases). In some cases, the clinical symptoms of CVT are similar to cerebral tumors, and there are few cases CVT occurs with clinical signs are increased intracranial pressure, and chronic symptoms at the onset (>1 month), 10-20%. According to the study of Terazzi, in 48 patients with CVT, the percentage of patients with acute onset was 44%, subacute onset was 35% and chronic onset was 21%. In general, the onset characteristics of CVT are varied, but the majority of patients have subacute onset and our study data were equivalent to the results of Paciaroni's study.

Clinical fetures

Headache: In our study, headache was the most common with a rate of 98.31% of all cases. This result is similar to the result of the study of Le Van Thinh and Trinh Tien Luc with headache accounted for 88%. In general, it is like other studies of other authors, headache was the most common and presented with the highest rate in these studies.

Paraparesis: Similar to results of other studies of other authors, our study found that the symptom of paraparesis ranked the 2nd position after headache with a percentage of 57.63%. The level of this symptom were mainly 4th degree (25.5%), 3rd degree (13.5%), 2nd degree (10.6%). According to the study of Tanislav et al., this symptom also ranked the 2nd position after headache (69%) with a rate of 44%. In general, the percentage of patients with paraparesis symptom in our study was equivalent to results from others studies of other authors and the similar point is this symptom ranked that 2nd or 3rd position among other clinical signs.

Seizures: In our study, the percentage of seizures symptom ranked a 3rd position after headache and paraparesis. According to the study of Le Van Think and Trinh Tien Luc, seizures accounted for 32%, ranked the 3rd position after headache and cranial nerve paralysis. According to the study of Ferro, seizures accounted 39% in patients < 65 years old, and 45% in patients \geq 65 years old.

Consciousness disorders: In our study, percentage of patients with consciousness disorders accounted for 37.29%, ranked the 4th position among other symptoms. Wherein, mild consciousness disorders was the most common with 30.5% while severe consciousness disorders accounted for 6.8%. According to the study of Bruijin in 59 patients with CVT (equal to the number of patients in our study), the percentage of patients with consciousness disorders was 39%. Wherein, mild consciousness disorders accounted for 23.7%, and severe symptom accounted for 15.3%. Overall, the percentage of CVT patients with consciousness disorders symptom in the studies of domestic and foreign authors was not as high as other symptoms, from 21% to 39%, the percentage of our study was within this range and similar to results of other authors.

Cranial nerve palsy: In our study, the percentage of patients with cranial nerve palsy was 32.2%. According to the study of Le Van Think and Trinh Tien Luc, the percentage of patients with cranial nerve palsy was 48%. According to the study of Paciaroni, the percentage of patients with cranial nerve palsy was 12%, this symptom commonly occurred in III, IV, V, VI, VII, VIII, IX, X and XI. These nerves could be injured separately or link to other nerves. Almost authors did not recognize cranial nerve analysis in their studies, this might be due to small sample size then they only recognized that patients had focal neurological deficits, such as in the study of Fink, this author only recorded that 60% of patients had focal neurological deficits. Overall, the cranial nerve palsy symptom on patients with CVT was not as common as other symptoms and accounted from 12% to 48%, the percentage in our study was 32.2%.

Papilledema: According to the results of our study, the percentage of patients with papilledema was 30.5%. This symptom varied depending on studies of other authors (table 4.39). According to the study of Stolz, papilledema accounted 40%. According to the study of Ferro, among 624 patients there was only 29% of patients < 65 years old and 14% of patients \geq 65 years old had this symptom, ranked after headache and positioning nerve sign and seizures. Overall, the percentage of patients with papilledema in our study was smaller than results from other studies, this could be due to the percentage of patients exhibited increased cranial pressure in our study was higher than results from studies of other authors.

Factors of primary thrombophilia

According to results of our study, patients with primary thrombophilia, V Leiden factor accounted for the highest percentage, followed by decreased protein S, decreased protein C, decreased ATIII. Compared to control group, we found that OR of protein C

was the highest, followed by V Leiden factor, ATIII. We could not calculate OR of protein S because there was no case with decreased protein S in control group.

According to the study of Bombeli, when analyzed 51 patients with CVT among 260 patients with venous thrombosis (cerebral veins, portal veins, retinal veins, upper limb veins, lower limb vein) and 120 healthy controls, he recognized that V Leiden factor accounted for the highest percentage 13.7% with OR 2.1 (CI 95%: 0.7-6), percentage of decreased protein S was 2% with OR 2.4 (CI 95%: 0.1-38.3); percentage of decreased protein C and ATII was 2%, he could not calculate OR of protein C and ATIII due to limitation of sample size. According to the study of Martinelli in 121 patients with CVT, the percentage of V Leiden factor was highest with OR = 4.7 (CI 95%: 1.8-11.8), followed by decreased protein C, decreased protein S and decreased ATIII. Due to limitation of sample size then the author calculated general OR = 6 for 3 factors decreased protein C, decreased protein S and decreased ATIII.

Thus, percentages of factors of primary thrombophilia in our study were higher than the results of other studies of domestic and foreign authors, this may relate to racial characteristics of Asians. In comparison with the factors of primary thrombophilia, we found that these disorders varied depending on each study and did not follow any basis. Thus, we can recognize that not only clinical characteristics of CVT were diverse but also primary risk factors were varied.

Factors of acquired thrombophilia

Among 33 female patients with CVT in our study, percentage of female patients using oral contraceptive drugs was 30.3%, percentage of pregnant patients was 3.03%, percentage of puerperium patients was 24.2%, no case was being treated by hormone replacement therapy. When compared to control group, we found that the risk of CVT in patients using oral contraceptive drugs was high with OR = 4.05 (KTC 95%: 0.88-25.1); we could not calculate OR for pregnancy, puerperium and hormone replacement therapy due to limitation of sample size.

According to the study of Tran Thanh Tung, among 21 female patients with deep vein thrombosis, the percentage of patients related to administration of oral contraceptive drugs was 13.8%, percentage of abortions was 10.3%, no case was recognized as relating to pregnancy and hormone replacement therapy. According to the study of Dentali, this was a meta-study of previous studies, found that among 263 female patients with CVT, percentage of patients using oral contraceptive drugs was 58.9%. When compared to control group, OR = 5.59 (KTC 95%: 3.95 to 7.91). It might be due to in this study the author mainly assessed risk factors of contraceptive drug administration then he did not refer to the risk of pregnancy and puerperium on CVT.

Overall, on female subjects, all studies showed that administration of oral contraceptive drugs and puerperium were related to CVT. Especially in 2 studies of Martinelle and Bruijin, the percentages and OR relating to administration of oral contraceptive drugs were very high, this might be due to female subjects in these study

aged from 18 to 54 then the possibility of using contraceptive drugs were very high.

V. CONCLUSIONS

Clinical and cerebral imaging characteristics of CVT: Onset of CVT is very diverse, wherein, subacute onset accounted for the highest percentage (79.7%), acute (11.8%). Clinical characteristics of CVT were varied and nonspecific with common symptoms were headache 98.31%, paraparesis 57.63%, seizures 50.85%, altered consciousness 37.29%, cranial nerve palsy 32.2%, papilledema 30.5%. Other symptoms were less common such as sensory disorders 8.47%, language disorders 8.47%, meningitis syndrome 5.08% and vertigo 5.08%. Symptoms commonly occurred on severe patients were altered consciousness, coma, brain parenchymal injury accompanying hemorrhage.

Frequency of patients with primary thrombophilia was 66.7%, with V Leiden factor had OR = 2.25 (CI 95%, 0.93-5.46); decreased protein C had OR = 2.76% (KTC 95%, 0.8=9.49); decreased ATIII had OR = 1.7 (CI 95%, 0.5 -5.6); decreased protein S could not calculate OR but the difference between 2 groups was statistically significant. Percentage of patients with acquired thrombophilia was relatively common with 57.6%, with patients using oral contraceptive drugs had OR = 4.05 (KTC 95%, 0.88-25.1); pregnant and puerperium patients could not be calculated OR but the difference between 2 groups was statistically significant.

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PERSPECTIVES OF PUPILS ON MENTAL HEALTH PROBLEMS AMONG SECONDARY SCHOOL PUPILS IN CAN THO CITY

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ABSTRACT

Background: *Secondary school can be a stressful period for adolescents, having to cope with many life changes. The study aimed to explore perceptions of mental health status, risk factors for mental health problems among Vietnamese secondary school students. Methods:* *A qualitative design was used to address the main study question. Data was collected by means of in-depth interviews and focus group discussions (FGDs) among secondary school students. All interviews and FGDs were audio-taped, transcribed and analyzed for the identification of emerging issues using qualitative techniques of progressive coding, analytic memoing and ongoing comparison. Results:* *Our study confirms the need to pay attention to mental health of pupils in Vietnam. Depression, anxiety, stress, suicidal thoughts and suicide attempts were seen as major problems by students. Mental health problems were mainly associated with academic pressure, resulting from an overloaded curriculum and pressure from teachers and parents to succeed. Conclusions:* *Vietnamese secondary school pupils feel that their mental health status is poor, because of many risk factors in their learning and living environment. The need now is to investigate further to identify and apply strategies to improve students' mental health.*

Keywords: *Mental health, Depression, Anxiety, Stress, Academic pressure, Student*

I. INTRODUCTION

There has been a rapidly growing public awareness of mental health problems, such as stress, anxiety, depression and suicide among adolescents [1]. Psychopathology and life stress may play major roles in suicidal behaviours, especially among rural adolescents. Some 17.6% of secondary school pupils in a study in the north and 34.0% of first year university students in another study in Can Tho City in the south reported feelings of sadness and hopelessness every day for two weeks in the past 12 months [2]. Four studies reported a high rate (10%) of students who had considered attempting suicide in the past 12 months [3, 4]. Prevalence rates of suicidal behaviour increased significantly