

Clinical Research Article

SEVENTEEN CEREBRAL VENOUS THROMBOSIS CASES

*Nevin SÜTLAS, Aysun ÜNAL, Aysegül BARUTCUOGLU, Demet Yandim KUSCU**Bakirköy Hospital for Nervous Diseases & Psychiatry, 3rd Dept. of Neurology, Istanbul, Turkey*

ABSTRACT

Cerebral venous thrombosis (CVT) is less frequent than arterial thrombosis, but may leave sequele or may be fatal if not recognized and treated early. We reviewed the records of 17 patients aged 20 to 46 (mean = 34.5) years with CVT evaluated at our department between 1994 and 1999 retrospectively. All patients initially complained of headache. Thirteen had intracranial hypertension (papilledema with or without sixth nerve palsy), 13 had focal neurological deficits, 12 had seizures, 7 had confusion and 4 were in coma. Psychiatric symptoms were present in six patients. CVT occurred during post-partum period in seven patients. The predisposing factor was infection in six patients and hormonal dysregulation in two patients. Iron deficiency anemia was present in fourteen patients. Eleven of the patients had multiple venous sinus thrombosis and 8 of these patients revealed venous infarct with neuroimaging studies. Single sinus involvement was seen in six patients and none of them had venous infarct. Seven patients were treated with antibiotics, 2 patients were treated with anticoagulant and 7 patients were treated with combination of antibiotic and anticoagulant. Six patients recovered completely, 9 patients were left with sequel neurological deficits and two patients died. The outcome seems to be independent of age, sex, clinical features and treatment.

Key-words: venous thrombosis, clinical features, predisposing factors

Cerebral venous thrombosis (CVT) is a rare condition with a wide range of symptoms and clinical findings. CVT usually occurs in the setting of a known predisposition to venous thrombosis. Despite the continuing description of new causes, the proportion of unknown etiology remains high in recent series, between %20 and %35 (2). Predisposing factors include infections, pregnancy and puerperium, hypercoagulable states, acquired and congenital heart disease, red blood cell disorders, malignancies, connective tissue disorders, severe dehydration, liver disease, surgery, sex steroid administration and major trauma (13). Thyrotoxicosis has been reported in one patient (14). The use of magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) have led to accurate, rapid and non-invasive diagnosis of this condition. The clinical syndrome is thus being better defined, however its prognosis remains largely unpredictable. In the early literature, mortality ranged between 30% and 50% (2,12,15), whereas it is between 10% and 15% in more recent series (3,6,12). The cause of CVT should be treated on its own merit, in association with antithrombotic treatment (heparin, warfarin) and symptomatic treatment (anticonvulsants, analgesics, numerous methods used for reducing intracranial hypertension; mannitol, steroids, lumbar puncture etc). In the present study, we retrospectively reviewed 17 patients with CVT.

MATERIAL and METHODS

To assess the clinical characteristics, neuroradiological findings and outcome of patients with CVT, we reviewed the records of 17 CVT patients evaluated at our department between 1994 and 1999.

We reviewed demographic, clinical, radiological, laboratory, treatment (anticoagulation, antibiotherapy, mannitol, steroids, anticonvulsants) and outcome data. We focused on risk factors relevant for cerebral arterial ischemia and venous thrombosis, history of previous cerebral or systemic venous occlusive events, topography of involved cerebral venous structures and laboratory evidence of inflammatory or autoimmune conditions.

Screening with automated serum chemistries, complete blood count, erythrocyte sedimentation rate, prothrombine time and aPTT analysis was performed. In the majority of the patients, serological studies including rheumatoid factor, VDRL serology for syphilis, antinuclear antibodies, thyroxine, triiodothyronine and thyroid stimulating hormone were available. Selected patients were tested with cerebrospinal fluid analysis, electroencephalographic recordings, protein C activity and antigen, protein S antigen, antithrombin III and anticardiolipin antibodies.

All patients underwent neuroimaging studies, including craníal CT or MRI, MR angiography and MR venography.

No statistical analysis were performed because of the small size of the study population and increased probability of error.

RESULTS

Table I: Main characteristics of patients

Case	Age/Sex	Initial presentation	Site of Thrombosis	Parenchymal abnormalities	Predisposing factors	Management	Outcome
1	37/F	S, FND, ICH	TS, SS, JV	Temporal venous infarct	Inf+A	Ab, Ae, M, St	MND
2	33/F	H, FND, PS, Cnf	SS, TS, JV	Temporo-parietal haemorrhagic infarct	PP+A	Ab	Resolved
3	40/F	S, ICH, PS	SSS, TS, SS	No abn.	Inf	St, D, Ab, Ae	MND
4	23/F	ICH, FND	SSS	Eedema	PP+A	Ab	Resolved
5	29/F	S, ICH, FND	SSS, LS	Haemorrhagic infarct	A	Ae, Ab, Ac, St, M	MND
6	46/F	ICH, FND, PS, Cnf	Cavernous sinus	Fronto-temporo-parietal hemorrhagic infarkt	Inf+A	Ac, Ab, St, M	Exitus (10 th day)
7	39/M	ICH, FND	TS	No abn.	Inf	Ab	MND
8	31/M	ICH, FND	TS	No abn.	Inf+A	Ab, Ac	MND
9	37/F	S, ICH, PS, C, Cnf, FND	SSS, TS, DVS	Eedema	PP+A	Ac, Ab, Ae, M, St	Resolved
10	46/F	S, ICH, C	TS, SS, SSS	Frontal ischemia	HD + trauma +A	Ab, Ae, Ac, M, St	MND
11	39/F	S, Cnf, FND, H	SSS	No abn.	HD+A	Ab, Ae, Ac	MND
12	20/F	S, C, ICH, Cnf	TS, SS	Temporal hemorrhagic infarct	PP+A	Ab, Ae, M	Resolved
13	28/F	ICH, FND, S, PS, Cnf	SSS, TS, SS	Bilateral frontal infarct	PP+A	Ac, Ae, Ab, M	MND
14	26/F	ICH, FND, S, PS, Cnf	TS, SS, JV	Bilateral cortical and deep infarct	PP+A	Ac	MND
15	46/F	S, FND, H, C	SSS, TS	Parietal hemorrhagic infarct	HT+ HD+ A	Ab, M, St	Exitus (12 th day)
16	27/F	S, H	LS	No abn	PP+A	Ae	Resolved
17	40/F	S, ICH, FND	SSS, LS, SS	No abn	OC, Inf	Ae, Ac, St	MND

(S: seizure, FND: focal neurological deficit, ICH: intracraníal hypertension, PS: psychiatric symptom, H: headache, C: Coma, Cnf: Confusion, TS: Transverse sinus, SS: sigmoid sinus, JV: Jugular vein, SSS: sinus sagittalis superior, LS: Lateral sinus, DVS: Deep Venous

System , No abn: no abnormality, Inf: Infection, PP: Post-partum, A: Anemia, HD: Hormonal Disregulation, OC: oral contraceptive, Ab: Antibiotics, Ac: Anticoagulants, St [inorder to distinguish from S=seizure]: Steroid, Ae: antiepileptics, D: diuretic, M: Mannitol, MND: minimal neurologic deficit)

Table I lists the main characteristics of the patients. The seventeen patients comprised 2 men and 15 women (ratio : 0.13). Ages were between 20 years and 46 years. The mean age of the patients was 34.5 years.

All the patients initially complained of headache. Thirteen had intracranial hypertension (papilledema and/or sixth nerve palsy), thirteen had focal neurological deficits, twelve had seizures, seven had depressed level of consciousness and four were in coma. Psychiatric symptoms were present in six patients. Two of them had initially presented with psychiatric symptoms and misdiagnosed as post-partum psychosis and major depression. Fever ($> 37.5^{\circ}\text{C}$) was present in four patients.

CVT occurred during post-partum period in seven patients. The predisposing factor was nearby infection in five patients and lung tuberculosis in one patient. Two patients had hormonal dysregulation. Oral contraceptive use was present in one patient and we have found a nearby infection as another risk factor in that patient. Iron deficiency anemia was present in fourteen patients and in two of them we could not find another predisposing factor. Cholesterol was elevated in seven patient. None of the patients had antiphospholipid-antibodies or other auto-antibodies suggestive of collagen vascular disease.

In magnetic resonance venography studies it was seen that eleven of the patients had multiple and six of the patients had single venous sinus thrombosis. Nine of the patients with multiple venous sinus thrombosis, had venous infarct in MRI studies and five of them were hemorrhagic.

Seven patients were treated with antibiotics, two patients were treated with anticoagulant and seven patients were treated with combination of antibiotics and anticoagulant. Symptomatic treatment was also given besides these agents when necessary. One patient followed only with antiepileptic. We did not observe any difference between the outcome of patients on different treatment protocols.

DISCUSSION

CVT presents with a remarkably wide spectrum of symptoms. In contrast to the arterial stroke, which is diagnosed clinically in majority of cases, CVT has no single pattern of presentation. Therefore it cannot be diagnosed on clinical grounds and requires neuroimaging for its diagnosis. Headache is the most frequent symptom in patients with CVT. However patients presenting with headache as the only sign of CVT are rare (10,13) and it is usually seen in combination with other neurological signs (seizures, focal neurological deficit, signs of intracranial hypertension, etc). In our study group all the patients suffered from headache , and thirteen of them were associated with intracranial hypertension. Seven patients had confusion and four patients were in coma. Focal neurological deficit was present in thirteen patients (paresis in seven patients, dysphasia in three patients, hypoesthesia in three patients). Twelve of the patients had epileptic seizure, and three of them were in status epilepticus. Focal epileptic seizures were seen in five patients, complex partial seizure was seen in one patient. Generalised tonic-clonic seizure with focal beginning was seen in three patients. Six patients presented with psychiatric symptoms (agitation, irritability, depression, hallucination). One of them was diagnosed as post-partum psychosis and the other one diagnosed as major depression by psychiatrists. We think that this psychiatric presentation is significant because it has not become a part of the recognised clinical spectrum of CVT.

The numerous conditions that can cause CVT are pregnancy, postpartum state, surgery, head trauma, infection, paraneoplastic and autoimmune diseases and the use of oral contraceptive pills. Despite the continuing description of new causes, the proportion of cases of unknown etiology is between 20% and 35%. Although infection still constitutes a major identifiable cause in some recent series, it is well established that the incidence of septic CVT has been greatly reduced in developed countries since the introduction of antibiotics. Sinus thrombosis remains the most common form of septic thrombosis, usually following an infection of the middle third of the face due to *staphylococcus aureus*. Other sites of infection include sphenoidal and ethmoidal sinusitis, dental abscess and less often otitis media (2). In our review, the predisposing factor was nearby infection in five patients (otitis media in two patients, ethmoidal sinusitis in one patient, maxillary sinusitis in one patient, sphenoidal sinusitis in one patient) Lung tuberculosis was present in one patient . In young women CVT occurs more frequently during the postpartum period. This factor is more common in developing countries, but in developed countries the role of oral contraceptive pills is more important. CVT occurred during post-partum period in seven patients in our study and hormonal dysregulation was present in two patients. Oral contraceptive use was present in one patient but we found sphenoidal sinusitis as another risk factor in that patient, so it was difficult to decide the real predisposing factor. Red blood cell disorders, thrombocytopenia and coagulation disorders are the other known predisposing factors (3). Iron deficiency anemia was present in fourteen patients and in two of them we could not find another predisposing factor. It was unusual to see hypercholesterolemia in seven patients. The high levels of cholesterol was independent from steroid treatment. To our knowledge hyperlipidemia is a predisposing factor for arterial thrombosis but there is no report in the literature of hyperlipidemia inducing CVT. None of the patients had antiphospholipid-antibodies or other auto-antibodies suggestive of collagen vascular disease.

The diagnosis of CVT is based essentially on neuroimaging techniques. Computed tomography (CT) is usually the first investigation performed on an emergency basis. Parenchymal abnormalities (hypodensities reflecting brain edema or infarction, hyperdensities suggestive of haemorrhagic infarcts and areas of gyral enhancement), small ventricles and contrast enhancement of falx and tentorium are the indirect non-specific signs. CT is normal in 30% of cases (1,2). The use of MRI and MRA has led to accurate, rapid and non-invasive diagnosis of CVT. MRI is also useful for showing parenchymal lesions secondary to the venous occlusion. In most cases, thrombosis affects several sinuses with or without cerebral veins. We have seen that eleven of the patients had multiple venous sinus thrombosis and eight of these patients had venous infarct in neuroimaging studies. Only one sinus involvement was present in six patients and none of them had venous infarct. In one patient there was total occlusion of arteria carotis interna because of cavernous sinus thrombosis. As a result of arterial occlusion, arterial infarct was present in MRI.

Treatment of CVT is based on the combination of intravenous heparin (followed by oral anticoagulants for 3-6 months), symptomatic treatment (anticonvulsants, analgesics, treatment of increased intracranial pressure) and treatment of the cause. Anticoagulation is still controversial in CVT treatment. However, heparin seems to be both effective and safe even in hemorrhagic lesions (2,4,5,8,11). In our CVT group, seven patients were treated with antibiotics, two patients were treated with anticoagulant and seven patients were treated with combination of antibiotics and anticoagulant. There was no difference between the prognosis of the patients in these three groups. Like some of the other studies made before (1,5,7), it is not statistically meaningful due to small number of patients.

The outcome of CVT remains largely unpredictable. It is not unusual to see deeply comatose or severely hemiplegic patients' recovery without any sequelae. Conversely, a patient with headache as the only presenting symptom can suddenly worsen with a dense hemiplegia if thrombosis spreads from a sinus to a cerebral vein. We have seen that in our study group six patients recovered completely, nine patients were left with sequel neurologic deficits and two patients died. One of the two cases died because of herniation secondary to fronto-temporo-parietal hemorrhagic infarct on the 10th day (case 6) and the other one died because of pneumonia on the 12th day (Case 15). Mortality rate (11.7%) was correlated with literature (3,6,12).

ONYEDI SEREBRAL VENÖZ TROMBOZ OLGUSU

ÖZET

Serebral Venöz Tromboz (SVT) beynin arteriyel hastalıklarına oranla az görülür, ama ölüm ve ağır sekeller yaratabilir. 1994-1999 yılları arasında yatırılan 20-46 yaşları arasında 15'i kadın, 2'si erkek 17 SVT tanısı almış hastanın dosyası değerlendirildi. Hastaların tümü basagrisinden yakınıyordu. Kafa içi basıncı artışı bulguları 13, fokal nörolojik bulgu 13, nöbet 12, konfüzyon 7, psikiyatrik belirtiler 6, ateş 4, koma 4 hastada vardı. Yedi hasta postpartum dönemde hastalanmıştı, 6 hastada ise komsu bir enfeksiyöz odak vardı. Hastaların 14'ünde belirgin anemi tespit edildi. Onbir hastada birden çok sinusta tıkanma olduğu, bunların sekizinde venöz enfarkt geliştiği görüldü. Tıkanması bir sinüse sınırlı olan 6 olgunun hiçbirinde venöz enfarkt gelişmemiştir. İki olguya antikoagülan, 7 olguya antibiyotik, 7 olguya ise antibiyotik ve antikoagülan tedavisi uygulandı. Altı hasta klinikten hiçbir patolojik bulgusu olmaksızın, 9 hasta bazı kalinti nörolojik bulgularla çıkarıldı. Yedi hasta öldü. Hastaların yaşı ve cinsiyeti ile hastalığın şekli, seyri ve prognozu arasında bir bağlantı yoktu. Tedavilerin ve klinik bulguların şekli ve şiddeti ile de prognoz arasında bir bağlantı kurulamadı.

Anahtar kelimeler: venöz tromboz, klinik bulgular, predispozan faktörler

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Correspondence

Dr. Aysun Ünal, Bakırköy Ruh ve Sinir Hastalıkları , Eğitim ve Araştırma Hastanesi, 3.Nöroloji Kliniği , Tel/Fax:0.212.5712451

[E-mail:bitam3@superonline.com](mailto:bitam3@superonline.com)

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