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A rare localization of cerebral venous sinus thrombosis. Case report

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SUMMARY: **A rare localization of cerebral venous sinus thrombosis. Case report.**

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In this work the Authors report their experience on the treatment of a case of cavernous venous sinus thrombosis.

The diagnosis is clinical and neuroradiological, CT, MRN, cerebral angiography and orbital venography have aided in establishing the diagnosis during life.

Very interesting is the therapeutic approach.

KEY WORDS: Cerebral venous sinus thrombosis (CVST) - Cavernous sinus thrombosis (CST) - Anticoagulant therapy (AT) - Magnetic Resonance (MR) - Computerized Tomography (CT).

Introduction

Cerebral venous sinus thrombosis (CVST) is an uncommon condition with an often dramatic clinical presentation (1). A pro-thrombotic risk factor or a direct cause is about 85% of patients with CVST (2).

Genetic prothrombotic conditions [antithrombin deficiency (5), protein C and protein S deficiency (6, 7), factor V Leiden mutation (8), prothrombin mutation (9), homocysteinemia caused by gene mutations in methylenetetrahydrofolate reducatase (10)]; acquired prothrombotic states [nephritic syndrome, antiphospholipid antibodies (11), homocysteinemia (10), pregnancy (12), puerperium (12)]; infections (otitis, mastoiditis and sinusitis, meningitis and systemic infectious disease) (6); inflammatory disease [Systemic lupus erythematosus (13), Wegener's granulomatosis (7), sarcoidosis, inflammatory bowel disease (14), behcet syndrome (15)]; hematologic conditions [polycitemia primary and secondary (2), thrombocitemia (2), leukemia (16) and anemia including paroxysmal nocturnal hemoglobinuria (17)], drugs [asparaginase (6, 16) and oral contrapceptives (18)]; traumas or mechanical causes [head injury (19), injury to sinuses or jugular vein, jugular catheterization, neurosurgical procedures and lumbar puncture (20)], miscellaneous (dehydration, especially in children and cancer) (6) and high altitudes (21).

The first diagnostical procedure however is clinical and CVST should be considered when a physical examination reveals signs of superior orbital vein occlusion and the patient develops any combination of chemosis, ptosis, proptosis, orbital edema and diplopia associated to a variable involvement of cranial nerves II,III,IV,V and VI. Headache (retro-orbital pain) and fever may be present (3).

These local eyes signs and symptoms, in conjunction with a III, IV, or VI cranial nerve palsy, suggest the diagnosis of CVST. Progression from unilateral orbital signs to bilateral involvement is an ominous indicator that is essentially pathognomonic. Headache, often from sphenoid sinusitis, is present in >90% of the patients. It is typically as a unilateral and retro-orbital or frontotemporal orientation. Pain or paresthesias in the V_1/V_2 distribution occur less commonly. Diplopia can precede other symptoms. Extraocular muscle palsies will be present, and the sixth nerve is most commonly affected. Less often, Horner's syndrome or a dilated/sluggishly reactive pupil will be present. In the patient may be present meningismus and inflammatory CSF, although cultures are rarely positive. It is pos-

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sible a decrease in visual acuity or field cut; about 10% will experience permanent blindness. Careful testing will frequently elicit sensory deficits in V_1 and V_2.

Patients with advanced disease will appear toxic or lethargic. All patients suspected of having CST should undergo lumbar puncture and thorough examination by an otolaryngologist. In diabetic patients and those who fail to respond to antibiotics mucormycosis must be ruled out. Blood cultures are positive in many cases (4). During the past decade, increased awareness of the diagnosis, improved neuroimaging techniques, and more effective treatment have improved the prognosis (2). CT, RM, cerebral angiography and orbital venography have aided in establishing the diagnosis during life (3). MRI is a good imaging method for suspected CST (4, 24) however CT remains an excellent method for the examination of CST (4); the angiographic studies are generally not helpful in the diagnosis of CST (4). The most obvious treatment option is anticoagulation with heparin to arrest the thrombotic process and to prevent pulmonary embolism, which may complicate sinus thrombosis (25).

We want to report our case of a patient affects by CST treated with only anticoagulation therapy.

Case report

A 35-year-old male patient with no significant medical history and no trauma history presented to Emergency Department following a several day of nausea, malaise and retro-orbital headaches with fronto-temporal orientation. After a worsening of these symptoms he presented to the emergency room. A neurological examination revealed a left proptosis, a left decrease of visual acuity and the left orbital edema, anisocoria with reduced reaction to light on the left eye; Horner's syndrome.

A general physical examination revealed nothing remarkable, no meningismus was present and no fever. Cerebrospinal fluid (CSF) from a lumbar puncture demonstrated normal glucose and protein levels. The peripheral white cell count was hight 18,530 and the other inflammatory indexes was in normal range. CSF, blood, and urine cultures were negative. The exams about the thrombotic risk were negative and a otorhinolaryngology consult did not reveal anything significant to the nose and paranasal sinuses.

Magnetic resonance imaging (MRI) revealed enlargement and abnormal enhancement of the left cavernous sinus, with enhancement and increased T2 signal. The patient completed the diagnostic exams with CT and angio CTscan. Figures 1-5 show the results of the MRI performed before treatment.

The patient was treated with only 20,000 I.U. of heparin in pump for five days and then 20,000 I.U. of heparin in pump associated with warfarin for seven days. He

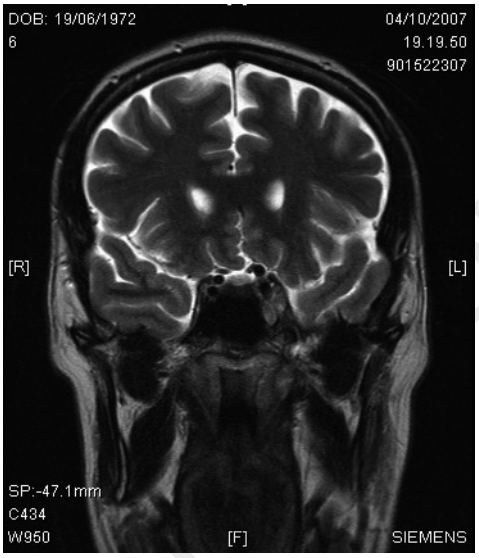

Fig. 1 - RMN images: coronal images pre-treatment.

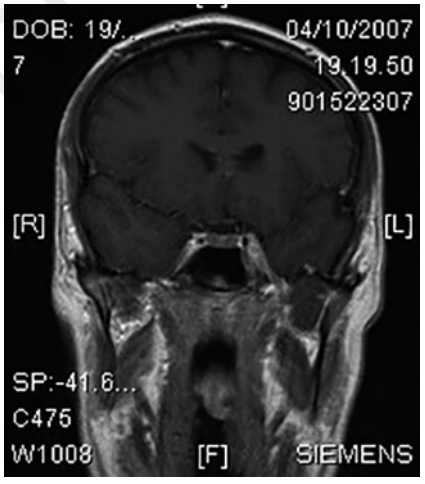

Fig. 2 - RMN images: coronal images pre-treatment.

continued the treatment with only warfarin according to I.N.R. (international normalized ratio) for eight weeks.

The patient improved just after one day of anticoagulant treatment.

MRI performed 1 week later demonstrated reversal of the previous magnetic resonance (MR) findings: marked increase in the caliber of the left cavernous sinus. Figures 6-7 show the successful results of the MRI examination after anticoagulant treatment. The patient was discharged after 12 days.

He completed a 8 weeks course of AT at home, with complete resolution of the Horner syndrome, headache and nausea. He continued at home the therapy with warfarin for four months. The blood examens of risk factors was negative.

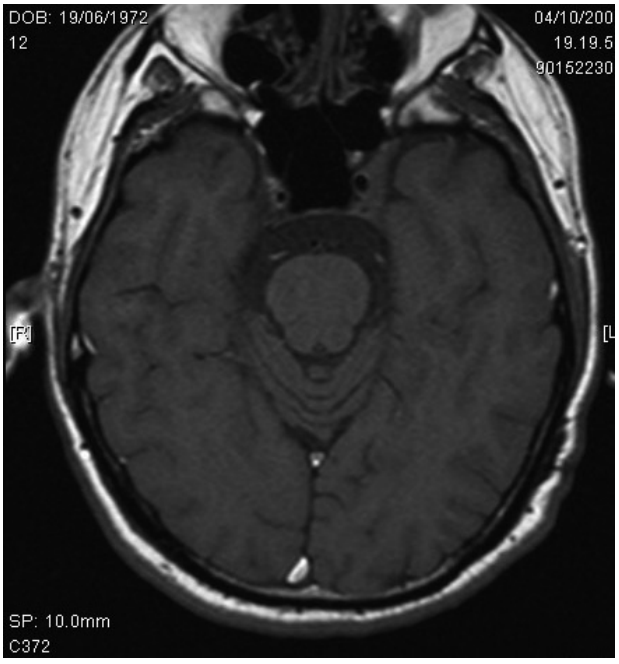

Fig. 3 - RMN images: axial images pre-treatment.

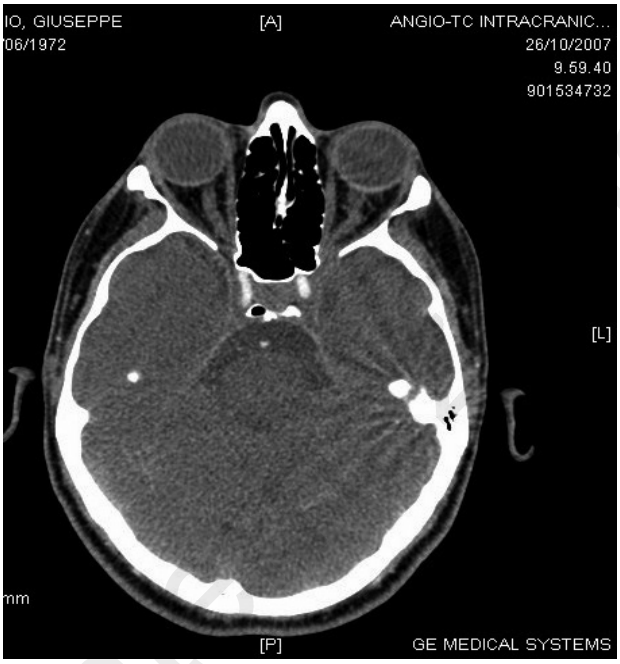

Fig. 4 - Angio-TC Axial image-initial sequence; pre-treatment.

Clinical follow-up to 1 year is normal and currently he is not under treatment.

Discussion

The cavernous sinus thrombosis (CST) - as confirmed by I. Gosk-Bierska et al. in 2006 - is a rare manifestation in the context of CVST (1). Lyons reported that Dease had first described the clinical entity of CST in 1778 (3).

Stam et al. estimated annual incidence is 3 to 4 cases for 1million population and up to 7 cases for million among children. About 75 percent of the adult patients are women (2).

Gosk-Bierska et al. proposed a study with one hundred fifty-four patients with diagnosis of cerebral venous sinus thrombosis, only six cases were affected by cavernous sinus thrombosis. These data reinforced the fact that in view of venous thrombosis of the cerebral sinuses, CST is the most rare, moreover according to some case reports (4, 23, 25-30) exposed in literature the cavernous sinus thrombosis (CST) are a very rare localization in the context of cerebral venous sinus thrombosis. The diagnosis, pathophysiology, and natural history of cavernous sinus thrombosis are dictated by the anatomy of the cavernous sinus. The VI cranial nerve is the only cranial nerve that actually runs within the cavernous sinus; all other cranial nerves of the cavernous sinus (III, IV, V_1, V_2) run within the lateral dural wall of the sinus. The intracavernous portion of the internal carotid artery (along with its accompanying sympathetic plexus) is the only other structure within the sinus. Each cavernous sinus receives blood from the orbit via the superior and inferior ophthalmic veins. There are no valves in any of the dural sinuses, which has important implications for the spread of thrombus. Because of its cen-

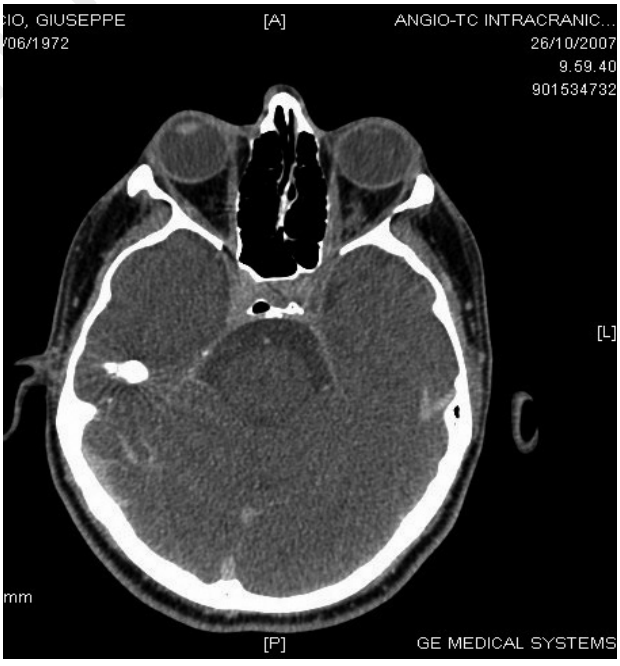

Fig. 5 - Angio-TC Axial Image tardive sequence; pre-treatment.

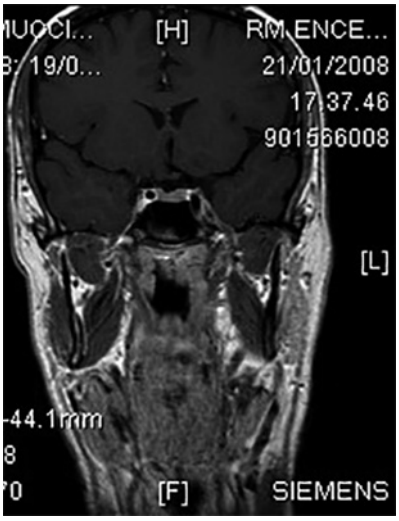

Fig. 6 - SE T1 Coronal image; post-treatment.

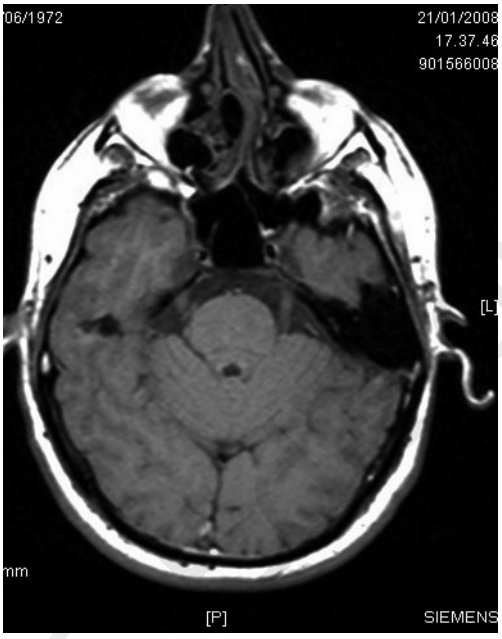

Fig. 7 - SE T1 Axial image; post-treatment.

tral location adjacent to the thin-walled sphenoid sinus and its myriad potentially bidirectional venous connections, the cavernous sinus is uniquely positioned to transmit a thrombus from the face or sphenoid sinus into the dural sinuses and central nervous system. Cranial nerves III, IV, VI, V_1, and V_2 and the intracavernous internal carotid artery (and its sympathetic plexus) are directly exposed to any inflammatory process in the cavernous sinus. The nearby optic nerve and V_3 are also at risk (4). MRI is the best imaging method for suspected CST. The signal intensities of the sinus can vary significantly as a result of infection, inflammation, and clot evolution. The cavernous sinus is enlarged, and the absence of flow void in the sinus suggests thrombosis. MRI in our case demonstrated parameningeal enhancement and increased T2 signal along the clivus and petrous apex. The progressive decrease in the diameter of the intracavernous internal carotid artery was also documented by MRI, as was its subsequent resolution. If CT or a simple MRI is unavailable, angio MRI remains an excellent method for the examination of CST. Angio-RM enhanced with contrast will show multiple filling defects from clot formation within the sinus. If the sinus is completely thrombosed, there will be complete lack of enhancement. The cavernous sinus is enlarged and asymmetric. Orbital venography could be effectively diagnose CST, but it is rarely used. It is important to remember that this entity remains a clinical and radiological diagnosis; MRI, CT, plain film radiology, and angiography are only confirmatory methods. Early recognition and treatment of CST are crucial. A delay in treatment can result in 100% morbidity, and delays can be avoided by an immediate and appropriately chosen anticoagulant treatment. CST can progress very rapidly (often in a few hours) (4). In patients with progressive disease, surgery should be considered. Even with appropriate surgical and medical treatment, cavernous sinus thrombosis can be fatal or result in serious complications. These complications, largely collected by case reports, can be infarction of the cerebrum, thrombosis of the internal carotid artery, cortical vein thrombosis, pituitary dysfunction, blindness, and cranial nerve palsies. The true incidence of these serious sequelae is unknown; they are documented as case reports or components of small series of CST (4).

Anticoagulant therapy for cavernous sinus thrombosis is controversial. Because the condition is very rare, the only data available are retrospective case reports with varying treatments and patient populations (3). Anticoagulation with heparin is the treatment of choice in the large majority of patients with CVT. The use of systemic heparin to treat CVT was initially reported by Lyons in 1941 (3). Current clinical guidelines are that patients without contraindications for anticoagulation therapy should receive either low-molecular weight heparin or dose-adjusted intravenous heparin (23). This practice is supported by a randomized controlled trial evaluating heparin therapy versus a placebo for CVT (24).

Effective corticosteroid use is limited to cranial nerve dysfunctions caused by inflammation and to the prevention of Addisonian crisis in patients with severe associated pituitary dysfunction (3).

The use of the anticoagulant therapy with antibiotics is about those cases when there is an evidence of local infections (4, 26-29).

Endovascular treatment for this type of lesion remains a particular option, but currently there exists only preliminary evidence for this type of treatment, and it certainly cannot be justified as a routine therapeutic option. The-

refore their use should be reserved for patients whose condition worsens despite adequate anticoagulation therapy, or whose initial clinical presentation is such that they are at high risk for an unfavorable outcome (23).

Conclusion

Cavernous sinus thrombosis is a very rare but dangerous entity difficult to diagnose. A lot of risk factors can cause this particular cerebral thrombosis. However a prothrombotic risk factor or a direct cause is found only in about 85% of patients with CST. Nonetheless, diagnosis and anticoagulant treatment with heparin in pump and warfarin are crucial. Morbidity and mortality are high even with appropriate therapy; delay too in treatment can be catastrophic. In our case the imaging showed the cavernous sinus thrombosis. The patient was treated with success with anticoagulant therapy. We preferred to treat him with anticoagulant therapy not because we thought that there was a clear connection between the presence of sinus cyst and breast cave, so comforted by opinion of otorhinolaryngology specialist. Then the fundamental interdisciplinary management of this disease so rare as complex.

References

1. Gosk-Bierska I, Wysokinski W, Brown RD Jr, et al. Cerebral venous sinus thrombosis Incidence of venous thrombosis recurrence and survival. Neurology. 2006;67:814-819.
2. Stam J.¬ Thrombosis of the cerebral veins and sinuses. N Engl J Med. 2005;352:1791-1798.
3. Levine SR, Twyman RE, ¬Gilman S.¬ The role of anticoagulation in cavernous sinus thrombosis. Neurology. 1988;38:517-522.
4. Kriss Timothy C, Kriss Vesna Martich, Warf Benjamin C. Cavernous Sinus Thrombophlebitis: Case Report Neurosurgery. 1996;39(2):385-389.
5. Bousser MG, Chiras J, Bories J, ¬Castaigne P. Cerebral venous thrombosis. A review of 38 cases. Stroke. 1985;16:199-213.
6. deVeber G, Andrew M. Cerebral venous thrombosis in children. N Engl J Med. 2001;345:417-23.
7. Enevoldson TP, Russel RW. Cerebral venous Thrombosis. N Engl J Med. …
8. Ludemann P, Nabavi DG, Junker R, et al. Factor V Leiden mutation is a risk Factor for cerebral venous sinus thrombosis : a case-control study of 55 patient. Stroke. 1998;29:2507-10.
9. Reuner KH, Ruf A, Grau A, et al. Prothrombin gene G20210->A transition is a risk factor for cerebral venous thrombosis. Stroke. 1998;29:1765-9.
10. Cantu C, Alonso E, Jara A, et al. Hyperhomocisteinemia, low folate and vitamin B12 concentrations, and methylene tetrahy-drofolate reductase mutation in cerebral venous sinus thrombosis. Stroke. 2004;35:1790-4.
11. Carhuapoma JR, Mitsias P, Levine SR. cerebral venous thrombosis and anticardiolipin antibodies. Stroke. 1997;28:2363-9.
12. Cantu C, Barinagarrementeira F, Cerebral venous thrombosis associated with pregnancy and puerperium: review of 67 cases. Stroke. 1993;24:1880-4.
13. Vidailhet DJ, Piette JC, Wecksler B, Bousser MG, Brunet P. Cerebral venous thrombosis in systemic lupus erhythematosus. Stroke. 2000;31:1274-82.
14. Daif A, Awada A, al-Rajeh S, et al. cerebral venous thrombosis in adults: a study of 40 cases from Saudi Arabia. Stroke. 2000;31:1274-82.
15. Farah S, Al-Shubaili A, Montaser A, et al. Behcet's syndrome: a report of 41 patients with emphasis on neurological manifestations. J Neurol Neurosurg Psychiatry. 1998;64:382-4.
16. Wermes C, Fleischhack G, Junker R, et al. Cerebral venous sinus thrombosis in children with acute lymphoblastic leukemia carrying the MTHFR TT677 genotype and further prothrombotic risk factors. Klin Padiatr. 1999;211:211-4.
17. Hillmen P, Lewis SM, Bessler M, et al. Natural history of paroxysmal nocturnal hemoglobinuria. N Engl J Med. 1995;333:1253-8.
18. Martinelli I, Sacchi E, Landi G, et al. High risk of cerebral-vein thrombosis in carriers of a phrothrombin-gene mutation in users of oral contraceptive. N Engl J Med. 1998;338:1793-7.
19. Stiefel D, Eich G, Sacher P. posttraumatic dural sinus thrombosis in children. Eur J Pediatr Surg. 2000;10:41-4.
20. Wilder-Smith E, Kothbauer-Margreiter I, Lammle B, Sturzenegger M, et al. Dural puncture and activate protein C resistance: risk factors for cerebral venous sinus thrombosis. J Neurol Neurosurg Psychiatry. 1997;63:351-6.
21. Basnyat B, Cumbo TA, Edelman R. Acute medical problems in the Himalayas outside the setting of altitude sickness. High Alt Med Biol. 2000;1:167-74.
22. Snyder TC, Sachdev HS. MR imaging of cerebral dural sinus thrombosis. J Comput Assist Tomogr. 1986;10:889-891.
23. Einhäupl K, Bousser MG, de Bruijin SF, et al. EFNS guideline on the treatment of cerebral venous and sinus thrombosis. Eur J Neurol. 2006;13:553-559.
24. Einhäupl K, ¬Villringer A, Meister W,¬ Mehraein S, Garner C, ¬ Pellkofer M, ¬et al. Heparin treatment in sinus venous thrombosis. Lancet. 1991;338:597-600.
25. Newman CB, Pakbaz RS, Nguyen AD, Kerber CW. Endovascular treatment of extensive cerebral sinus thrombosis. Case report. Journal of Neurosurgery. 2008.
26. Gupta A, Jalaly S, Bansal RK, Grewal SP. Anterior ischemic optic neuropathy and branch retinal artery occlusion in cavernous sinus thrombosis J Clin Neuroophthalmol. 1990 Sep;10(3):193-6.
27. Geggel HS, Isenberg SJ. Cavernous sinus thrombosis as a cause of unilateral blindness. Ann Ophthalmol. 1982 Jun;14(6):569-74.
28. Ogundiya DA, Keith DA, Mirowski J. Cavernous sinus thrombosis and blindness as complications of an odontogenic infection: report of a case and review of literature. J Oral Maxillofacial Surg. 1989 Dec;47(12):1317-21.
29. Kalangu KK. Cavernous sinus thrombosis: report of eight consecutive comatose patients. East Afr Med J. 1995 Dec;72(12):791-5.
30. Bradley C. Lega, Daniel Yoshor. Postoperative dural sinus thrombosis in a patient in a hipercoagulable state Case report. Journal of Neurosurgery. 2006 Nov;105(5):772.