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original article

Spontaneous chronic subdural hematoma in young adult: the role of missing coagulation factors

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SUMMARY: **Spontaneous chronic subdural hematoma in young adult: the role of missing coagulation factors.**

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Aim. *Chronic subdural hematoma (CSDH) is typically in elderly and rarely in young people. To prevent complications and re-bleeding after surgical treatment of CSDH it is important to assess the risk factors as coagulation disorders especially in young patients (below 65 years) with no history of head trauma, alcohol abuse or anticoagulant therapy.*

Patients and methods. *This study consists of 16 patients (12 males, 4 females) with age ranging from 27 to 59 years (median 48,25 years) operated for CSDH. All patients are submitted to routine coagulation parameters pre-operatively and complete screening for unknown coagulation deficit in the follow-up.*

Results. *Factor VII was altered in 6 out of 16 patients and one patient had the alteration of the Von Willebrand factor. Recurrence occurred in 4 out of 16 patients and all of these patients were positive for factor VII deficiency. Three pts were in therapy with ASA. No patients were alcoholists or suffered from hematological disease.*

Conclusion. *In this study we documented that the decreased activity of VII factor may play a role in the pathophysiology and recurrence of spontaneous CSDH in young adults. We suggest that for young patients aged under 65 y.o. suffered from CSDH the screening of coagulation factors is useful to planning a safely and correct surgical therapy.*

KEY WORDS: Chronic subdural hematoma - Factor VII deficiency - Head trauma - Recurrence - Hematological disease.

Introduction

Chronic subdural hematoma (CSDH) is characterized by an "old collection" of blood and blood breakdown products in the subdural space typically in elderly and rarely in young people. The frequency is 58.1 cases per 100.000 population per year in patients over 65 years of age and only 3,4 cases per 100.000 population per year under 60 years of age (1). The symptoms often occur suddenly and mimic an ischemic stroke (2) with motor weakness, dysphasia, amnesia or decreased level of consciousness. Most patients have a favorable prognosis if proper surgical treatment is chosen.

The etiology remains unknown in over 25% of cases because many patients have not experienced a prior traumatic event (3, 4) and others only a mild trauma (5). The spontaneous re-bleeding from the membranes covering the CSDH (6-8) is the mechanism of increasing the hematoma and beginning of symptoms. Fragile neovessels in the membranes that cover the CSDH and an imbalance between activated coagulation and fibrinolysis have been discussed as possible causes of multiple re-bleeding events and the chronic nature of the subdural hematoma especially in young people (9). Other causes of poor outcome are ethylism and anticoagulant therapy (10).

To prevent complications and re-bleeding after surgical treatment of CSDH it is important to assess the risk factors as coagulation disorders especially in young patients with no history of head trauma, alcohol abuse or anticoagulant therapy (11). This study was designed to evaluate the possible correlation between coagulation disorders (i.e. disorders giving rise to enhanced bleeding tendency) and the occurrence of CSDH in young patients.

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Patients and methods

This study consists of 16 patients (12 males, 4 females) with age ranging from 27 to 59 years (median 48,25 years) operated for CSDH. The target age of patients population is below 65 years in accordance with the definition of elderly population of the World Health Organization (WHO) (12). Patients were admitted to our department for treatment of CSDH over a period of 3 years (2013-2016). The present record concerns patients with diagnosis of CSDH made by CT scan and operated in emergency at our department (Fig. 1). All patients are submitted pre-operatively to routine coagulation parameters (INR, PTT, PT, fibrinogen, platelets) and complete screening for unknown coagulation deficit in the follow-up (VII, VIII, XIII, von Willebrand factor and ristocetin co-factor). For this study the normal range of factor VII activity was 70-120%.

At admission patients' past medical history was recorded concerning alcohol abuse, anticoagulant therapy, hematological disease, head trauma; GCS scale and standard neurological evaluation was also performed. Under local anesthesia were performed a single burr hole craniotomy, irrigation with saline solution, evacuation of the hematoma and positioning of subdural closed system of passive or active drainage. Routine CT scan was performed 48 hours after surgery with subsequent drainage removal (Fig. 2). Patients were discharged on the 4-6th day post-surgery. CT scan and neurological examination were performed at 30th days after discharge.

Results

All patients had preoperative normal standard coagulation parameters (INR, PTT, PT, fibrinogen, platelets). Haematomas were unilateral in 12 cases and bilateral in 4 cases. A definite history of head injury was obtained in 12 patients out of 16. In the follow-up the dosage of Factor VII (FVII) was abnormal in 6 out of 16 patients and one patient had the alteration of the von Willebrand factor. Recurrence occurred in 4 out of 16 patients (Figs. 3 and 4) and all of these patients were positive for factor VII deficiency. Three pts were in therapy with ASA. No patients have an history of cerebral vascular malformations, arachnoid cysts, were alcoholists or suffered from documented hematological disease. One patient with a history of politrauma occurred one month before admission, was operated in general anesthesia for subdural chronic hematoma and vertebral fracture with a short fixation (13, 14) not healed with corset. One patient was operated of vertebral fixation two months before admission for lumbosacral spontaneous pyogenic spondylodiscitis (15).

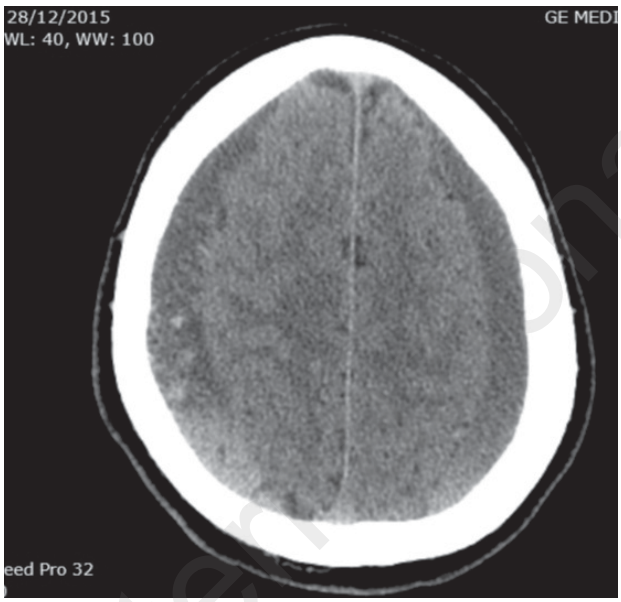

Figure 1 - Preoperative TC scan.

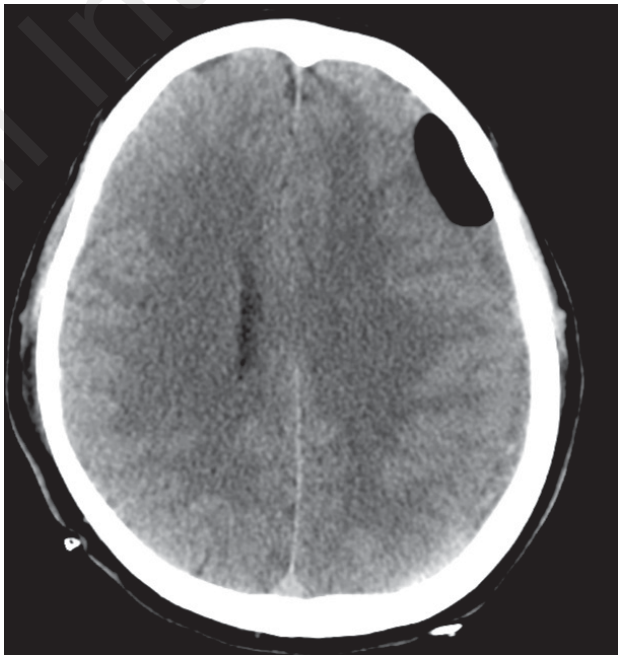

Figure 2 - Immediate postoperative TC scan.

Discussion

CSDH is one of the most common clinical entities in daily neurosurgical practice. It is characterized by a well defined and encapsulated collection between the *dura mater* and arachnoid membranes containing a mixture of fluid and coagulated blood in various stages (16, 17). The pathogenesis of CSDH begins with an head trauma often misunderstood with injury of micro-vessels and

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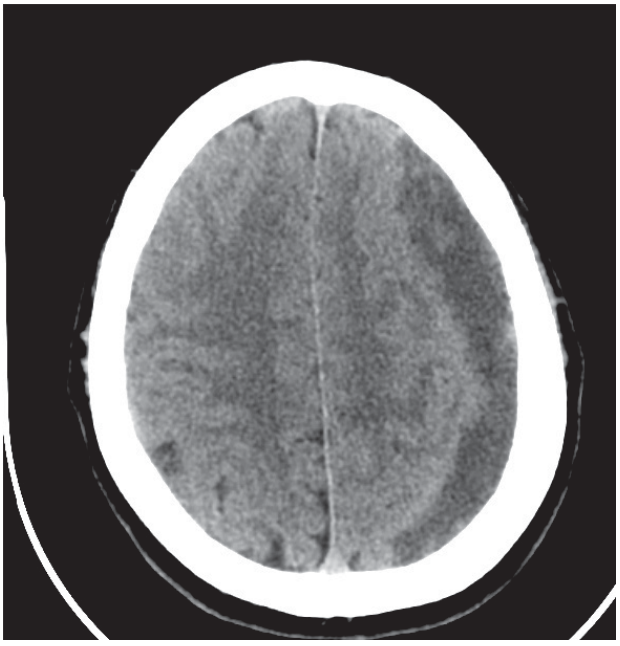

Figure 3 – Recurrence.

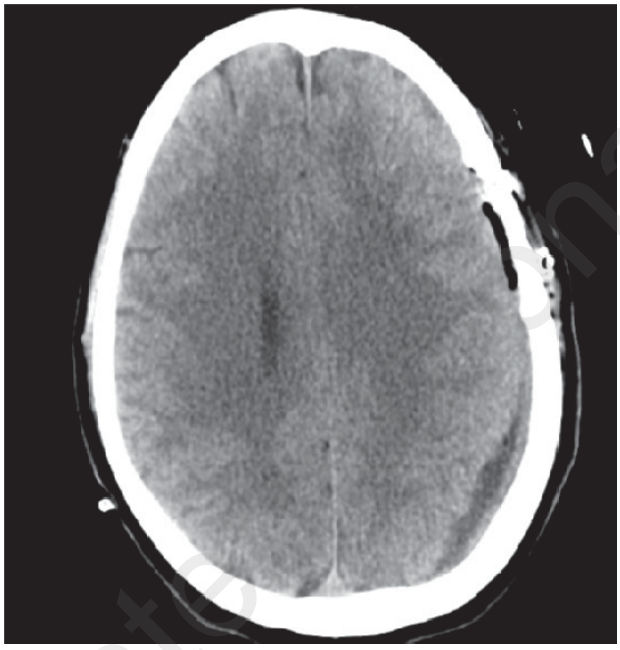

Figure 4 - Second operative procedure (craniotomy).

collection of blood in the subdural space. Spontaneous resolution may occur, but surgical evacuation is indicated in patients who deteriorate or do not improve. The most common surgical technique to treat CSDH is twist-drill craniotomy with a mortality rate of 2-4% (18). An early diagnosis and surgical drainage allow complete recovery in most cases with a recurrence rate reported to range from 2.3 to 33%.

One of the most frequent surgery complication of CSDH is the post-operative subdural re-bleeding. CSDH is considered to be a self-perpetuating inflammatory process involving the *dura mater*. It has been reported that a high concentration of inflammatory cytokines in the neomembrane of the subdural hematoma is correlated with the recurrence and this is more evident in patients with missing coagulation factor (19) or anticoagulant therapy. For these patients the treatment of choice is the replacement of the missing factor and/or suspension of therapy before surgery. In patients under 65 years with diagnosis of CSDH with no history of head trauma, anticoagulant therapy or alcoholic abuse it is reasonable to assume a coagulation disorder. In this series of patients under 65 years operated for CSDH 6 pts have a factor VII deficiency (37,5%) unknown before surgery.

FVII deficiency (20, 21) is the most common autosomal recessive coagulation disorder (1 in 500 000) and it is typically clinically heterogeneous, ranging in severity from lethal to mild, or even asymptomatic. FVII is hepatically synthesized and encoded by the FVII gene (*F7*) located on chromosome 13, 2.8 kb upstream of the FX gene. Both coagulant and antigenic plasma FVII levels are influenced by genetic and environmental factors (sex, age, cholesterol and triglyceride levels); FVII levels are also modulated by *F7* polymorphisms.

FVII deficiency is phenotypically variable: some patients do not bleed despite very low FVII activity, whereas others with similar levels experience frequent bleedings. Extensive hemarthrosis and gastrointenstinal (GI) and central nervous system (CNS) bleeds are among the manifestations in patients with severe FVII deficiency. Additional symptoms are epistaxis, muscle hematomas, postoperative bleeding and menorrhagia, with life- or limb-threatening bleeding being relatively rare.

However, CNS hemorrhage was reported to have a high incidence (16%) in a series of 75 patients (22, 23).

Various therapeutic options are available for FVII deficiency (24, 25), including FFP (fresh frozen plasma) and PCCs (Prothrombin complex concentrates) however FVII concentration in both are low and therefore they are not optimal treatments. Recombinant FVIIa is genetically engineered and considered the optimal replacement therapy as used at a low dose (10-30 μg/kg). Prophylaxis is debated in FVII deficiency but has been used in those with severe bleeding. There is continuing concern that factor VIIa may cause thromboembolic side effects largely because it is an activated factor given in doses to raise FVIIa levels more than 1000-fold. Evidence to date, however, suggests that recombinant FVIIa is both safe and effective. It is likely that the safety of the product is due to its selective location at the site of bleeding. Thrombotic events (myocardial infarction, stroke, pul-

monary embolism, and deep venous thrombosis) have occurred in patients with a predisposition to thrombotic complications such as diabetes mellitus, obesity, cancer, and atherosclerotic cardiovascular disease, and administration of recombinant FVIIa to such patients should be approached with caution. Adverse events have not been related to dose.

In the present study 4 patients out of 16 (25%) have a recurrence of hematoma; anyway, taking in account the limited sample size, it is remarkable that all recurrences occurred in patients with factor VII deficiency. In normal coagulating patients Stroobandt et al. (26) quoted a percentage of 22% of recurrence and Svien and Gelety a rate of 37% in patients undergoing craniotomy and 20% in those receiving a single burr hole for drainage (27). In our study, bilateral CSHD occurred in 20% of patients and this is comparable with rates between 16 and 20% of other series (28). In large studies (2, 29) a history of head trauma in CSDH is reported approximately in 50-80% of cases. We ascertained a traumatic origin of the CSH in 90% of patients. No major complications were observed and all operated patients healed.

Conclusion

In this study we documented that the decreased activity of VII factor may play a role in the pathophysiology and recurrence of spontaneous CSDH in young adults. We suggest that for young patients aged under 65 years suffered from CSDH the screening of coagulation factors is useful to planning a safely and correct surgical therapy.

References

1. Kudo H, Kuwamura K, Izawa I, Sawa H, Tamaki N. Chronic subdural hematoma in elderly people: Present status on Awaji Island and epidemiological prospect. Neurol Med Chir (Tokyo). 1992;32:207-9.
2. Adhiyaman V, Asghar M, Ganeshram KN, Bhowmick BK. Chronic subdural haematoma in the elderly. Postgraduate Medical Journal. 2002;78:71-5.
3. Gelabert-Gonzáles M, Iglesias-Pais M, García-Allut A, Martínez-Rumbo R. Chronic subdural haematoma: surgical treatment and outcome in 1000 cases. Clin Neurol Neurosurg. 2005;107(3):223.
4. Albanese A, Tuttolomondo A, Anile C, et al. Spontaneous chronic subdural hematomas in young adults with a deficiency in coagulation factor XIII. Report of three cases. Journal of Neurosurgery. 2005;102:1130-2.
5. Mori K, Maeda M. Surgical treatment of chronic subdural hematoma in 500 consecutive cases: clinical characteristics, surgical outcome, complications,and recurrence rate. Neurologia Medico-Chirurgica. 2001;41: 371-81.
6. Lee KS. Natural history of chronic subdural haematoma. Brain Injury. 2004;18:351-8.
7. Yamashima T, Yamamoto S, Friede RL The role of endothelial gap junctions in the enlargement of chronic subdural hematomas. Journal of Neurosurgery. 1983;59:298-303.
8. Weir B. The osmolarity of subdural hematoma fluid. J Neurosurg. 1971;34(4):528-33.
9. Kawakami Y, Chikama M, Tamiya T, Shimamura Y. Coagulation and fibrinolysis in chronic subdural hematoma. Neurosurgery. 1989;25:25-29.
10. Wintzen AR, Tijssen JG. Subdural hematoma and oral anticoagulant therapy. Archives of Neurology. 1982;39:69-72.
11. König SA, Schick U, Döhnert J, Goldammer A, Vitzthum HE. Coagulopathy and outcome in patients with chronic subdural haematoma. Acta Neurologica Scandinavica. 2003;107:110-6.
12. World Health Organization (2002). Active Ageing: A Police Framework. A contribution of the World Health Organization to the Second United Nations World Assembly on Ageing. Madrid, Spain, April, 2002.
13. Dobran M, Iacoangeli M, Di Somma L, Di Rienzo A, Colasanti R, Nocchi N, Alvaro L, Moriconi E, Nasi D, Scerrati M. Neurological outcome in a series of 58 patients operated for traumatic thoracolumbar spinal cord injuries. Surgical Neurology International. 2014 Aug 28;5 (suppl 7).
14. Dobran M, Nasi D, Brunozzi D, Di Somma L, Gladi M, Iacoangeli M, Scerrati M. Treatment of unstable thoracolumbar junction burst fractures: short-segment pedicle fixation with inclusion of fracture level versus long-term instrumentation. Acta Neurochir. (Wien) 2016 Oct;158(10):1883-9.
15. Dobran M, Iacoangeli M, Nasi D, Nocchi N, Di Rienzo A, Di Somma L, Colasanti R, Vaira C, Benigni R, Liverotti V, Scerrati M. Posterior titanium screw fixation without debridement of infected tissue for treatment of thoracolumbar spontaneous pyogenic spondylodiscitis. Asian Spine J. 2016 Jun;10(3):465-71.
16. Shim YS, Park CO, Hyun DK, Park HC, Yoon SH. What are the causative factors for a slow, progressive enlargement of a chronic subdural hematoma? Yonsei Medical Journal. 2007;48:210-7.
17. Ito h Yamamoto S, Saito K, Ikeda K, Hisada K. Quantitative estimation of hemorrhage in chronic subdural hematoma using the 51 cr erithrocite labeling method. J Neurosurg. 1987;66(6):862-4.
18. Ernestus RI, Beldzinski P, Lanfermann H, Klug N. Chronic subdural hematoma: surgical treatment and outcome in 104 patients. SurgNeurol. 1997;48(3):220-5.
19. Bosche B, Molcanyi M, Noll T, Kochanek M, Kraus B, Rieger B, El Majdoub F, Dohmen C, Löhr M, Goldbrunner R, Brinker G. Occurrence and recurrence of spontaneous chronic subdural haematoma is associated with a factor XIII deficiency. Clin Neurol Neurosurg. 2013 Jan;115(1):13-8.
20. Mariani G, Bernardi F. Factor VII Deficiency. Semin Thromb Hemost. 2009;35(4):400-406.
21. Palla R, Peyvandi F, Shapiro D. Rare bleeding disorders: diagnosis and treatment. Blood. 2015;125:2052-2061.
22. Napolitano M, Giansily-Blaizot M, Dolce A, et al. Prophylaxis

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in congenital factor VII deficiency: indications, efficacy and safety. Results from the Seven Treatment Evaluation Registry (STER). Haematologica. 2013;98(4):538-544.

23. Mariani G, Herrmann FH, Schulman S, Batorova A, Wulff K, Etro D, Dolce A, Auerswald G, Astermark J, Schved JF, Ingerslev J, Bernardi F. International Factor VII Deficiency Study Group. Thrombosis in inherited factor VII deficiency. J Thromb Haemost. 2003 Oct;1(10):2153-8.
24. Roberts HR, Monroe DM, White GC. The use of recombinant factor VIIa in the treatment of bleeding disorders. Blood. 2004;104:3858-3864.
25. Napolitano M, Giansily-Blaizot M, Dolce A, Schved JF, Auerswald G, Ingerslev J, Bjerre J, Altisent C, Charoenkwan P, Michaels L, Chuansumrit A, Di Minno G, Caliskan U, Mariani G. Prophylaxis in congenital factor VII deficiency: indications, efficacy and safety. Results from the Seven Treatment Evaluation Registry (STER). Haematologica. 2013 Apr;98(4):538-44.
26. Stroobandt G, Fransen P, Thauvoy C, Menard E. Pathogenetic factors in chronic subdural haematoma and causes of recurrence after drainage. Acta Neurochir (Wien). 1995;137:6-14.
27. Svien HJ, Gelety JE. On the surgical management of encapsulated subdural hematoma. A comparison of the results of membranectomy and simple evacuation. J Neurosurg. 1964;21:172-177.
28. Oyama H, Ikeda A, Inoue S, Shibuya M. The relationship between coagulation time and bilateral occurrence in chronic subdural hematoma. No To Shinkei. 1999 Apr;51(4):325-30.
29. Cameron MM. Chronic subdural hematoma: a review of 114 cases. J Neurol Neurosurg Psychiatry. 1978 Sept; 41(9): 834-839.

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