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Refractory status epilepticus in an elderly patient with cerebral venous thrombosis and chronic ischemic stroke

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ABSTRACT

Cerebral venous thrombosis was one of the diseases thought to be uncommon before non-invasive neuro-imaging techniques were introduced. Current statistics indicate that the annual incidence of cerebral venous thrombosis is 3-4 cases per million (1,2). The most frequent symptoms of CVT are epileptic seizures or even status epilepticus, that usually appear in the early stages of the disease (3,4). Recent studies show that the incidence of status epilepticus (SE) in the elderly has risen lately, causing lethal outcome in 38% of the patients, signifi cantly more than in young adults (14%) (11). Cerebral venous thrombosis (CVT) is a major cause of SE, 25% developing seizures in the early stages of the disease as the fi rst symptom of cerebral thrombosis (3,10). We present the case of an 86-year-old patient with de novo partial SE of the right limbs. The SE was generated by CVT with haemorrhagic transformation and chronic Sylvian stroke in a patient with multiple comorbidities.

Keywords: cerebral venous thrombosis, elderly, status epilepticus

Abbreviations:

SE – status epilepticus
CVT – cerebral venous thrombosis

INTRODUCTION

Cerebral venous thrombosis (CVT) was one of the diseases thought to be uncommon before the introduction of non-invasive neuro-imaging techniques. Current statistics indicate that the annual incidence of cerebral venous thrombosis is 3-4 cases per million, mostly occurring in the young population, especially women, which have predisposing factors such as pregnancy, puerperium or use of oral contraceptives (1,2). One of the major risk factors for CVT is the hypercoagulable state that can appear in infections, malignancy, pregnancy, use of oral contraceptives, myeloproliferative disorders, hyperlipidemia, diabetes mellitus and blood vessel abnormalities (2). One of the most frequent symptoms of CVT are epileptic seizures or even status epilepticus (SE), that usually appear in the early stages of the disease (3,4). Previous studies have shown that one-third of the patients with CVT experience focal or generalized epileptic seizures before having the diagnosis confirmed (5,6). SE in the elderly is very dangerous and lately, its incidence has risen. Recent studies show that mortality due to SE is higher in the elderly (38% of the cases) than in young adults (14%) (7).

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CASE REPORT

An 86 years old woman, with a medical history of diabetes mellitus, atrial fibrillation, thyroid neoplasm, ischemic stroke and recent pleurisy, was admitted to our departament through the emergency ward for unilateral right clonic seizures lasting more than 30 minutes, without full recovery of consciousness (status epilepticus). Upon admission her blood pressure was 150/100 mmHg, 120/min, neurological examination showed jacksonian seizures of the right upper limb, tetraparesis with the predominance of right hemiplegia, bilateral Babinski sign, comatose state (GSC = 6 points). Blood tests revealed the following: inflammatory syndrome: leucocytosis, elevated fibrinogen, ESR and CPR within the physiological range, creatinine: 1,38 ng/dl (NV: 0,89-1,76), TSH: 0,093 μIU/mL(NV: 0,4-4), anti-thyroglobulin and anti-TPO – within the physiological range, D-dimers: positive (800-1600 ng/ml) (NV: negative < 200 ng/ml). Lumbar puncture: the CSF parameters were not altered. Emergency cerebral CT scan highlighted only a chronic ischemic lesion in the left Sylvian territory. A cerebral MRI was performed at 72 hours after admittance, revealing: Left parietal cerebral venous

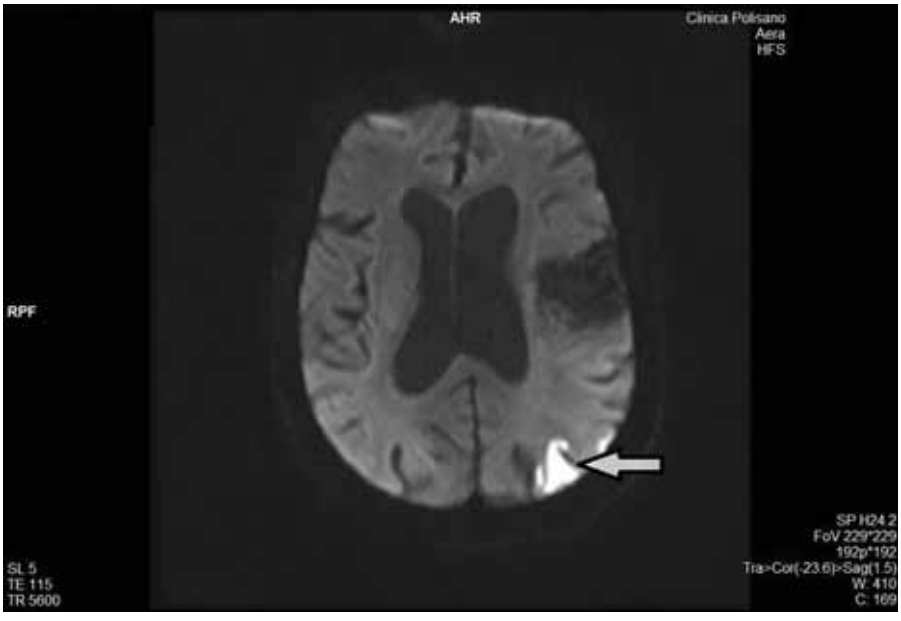

FIGURE 1. *Venous Cerebral Thrombosis – ep2d_diff_3scan_trace*

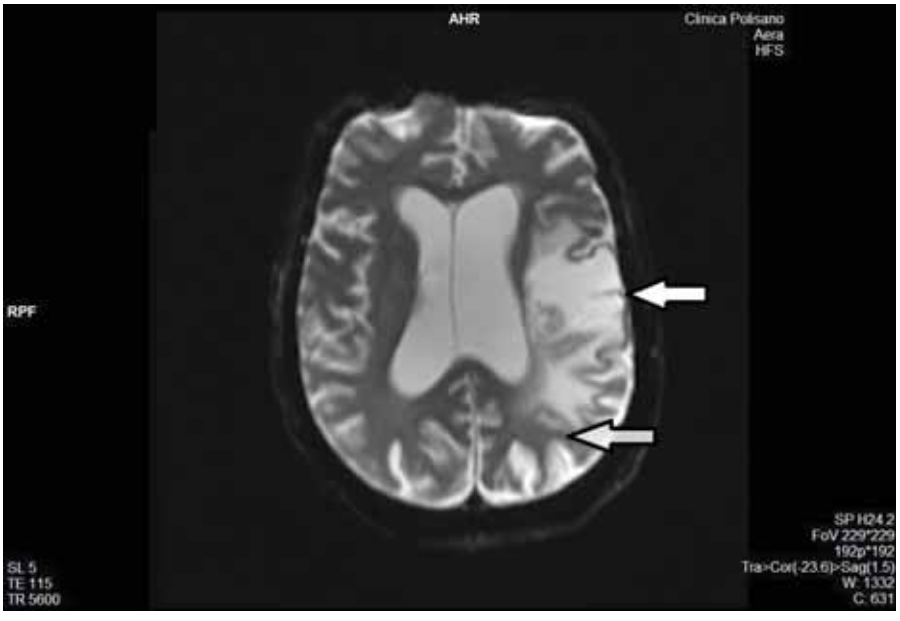

FIGURE 2. *Chronic left sylvian ischemia. Venous Cerebral Thrombosis – ep2d_diff_3scan_trace (ADC)*

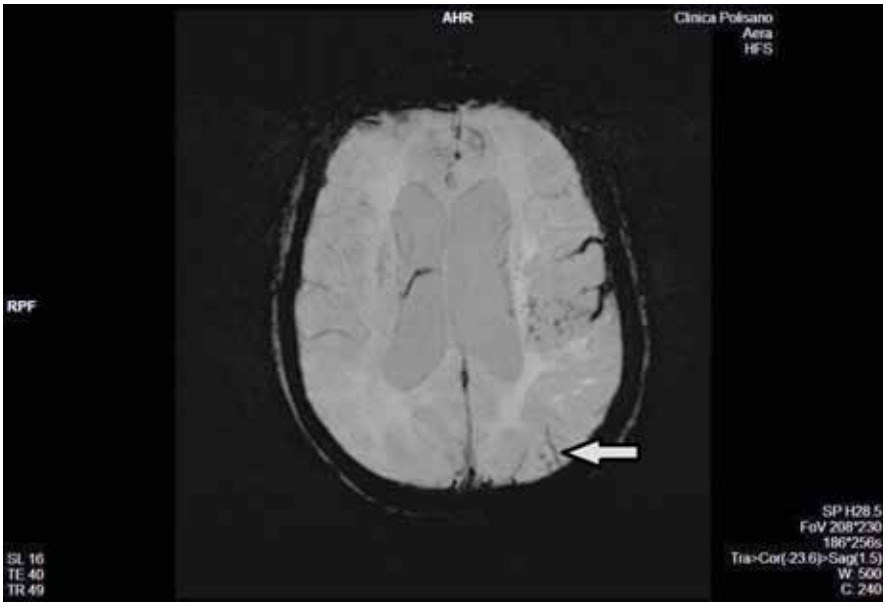

FIGURE 3. *Petechial haemorrhages, cortical venular ectasias – MIP*

thrombosis with petechial hemorrhages (Fig. 2, Fig. 3). Right vertebral artery with reduced calibre. Left Sylvian ischemic chronic stroke (Fig. 1). In our opinion, the cause of the SE was the CVT with petechial hemorrhages that imposed anticoagulant treatment with low molecular weight heparin, associated with first line antiepileptic drugs, benzodiazepines (diazepam IV 5 mg with a dose of 2 mg/min, repeated once every 10 minutes). As second line medication, we used Levetiracetam iv (LEV IV 1000 mg diluted in 100 mL saline solution 0,9% initially slowly injected in about 30 minutes, then continuously in PEV with 2000mg LEV). Phenytoin could not be administered because of the risk of hypotension followed by cardiac failure. The seizures lasted for over 9 hours despite all the given treatment and have finally yielded after 2 ml of Propofol were administered in bolus. After 13 days, in spite of receiving intense supportive treatment and antiepileptic drugs (Levetiracetam 2000 mg administered on the nasogastrial tube), the patient fell into a deep coma, followed by cardio-respiratory failure, cardiac arrest, and death.

DISCUSSION

Status epilepticus (SE) that is resistant to two antiepileptic drugs is defined as refractory status epilepticus (RSE). RSE is commonly acknowleged after the failure of the first (benzodiazepines) and second line treatments (phenytoin, valproate or phenobarbital, levetiracetam), or if the seizures last for more than 60 minutes (12). In most cases, focal convulsive seizures cease spontaneously and quickly, whereas status epilepticus is a major neurological emergency which causes high mortality, especially in the elderly (7). The causes of SE are various, 21% of the elderly experience SE for the first time because of a cerebral venous thrombosis or stroke (8). A hypercoagulable state is one of the major causes of CVT. One of the reasons patients have a hypercoagulable state are infections (2). In our case, the coexistance of thyroid neoplasm along side a pulmonary infection caused a hypercoagulable state that induced cerebral thrombosis. One of the symptoms of CVT are seizures or even status epilepticus that usually appear in the early stages of the disease (3). Previous studies have shown that most of the patients experience seizures before the confirmation of the diagnosis (5), same as the case reported by us, where the cerebral venous thrombosis was not confirmed initially by the emergency cerebral CT scan, but only after 72 hours by the cerebral MRI (Fig. 1). The particularity of our case is the association of two lesions with epileptic potential, a chronic ischemic lesion in the left Sylvian territory and an acute lesion – a left venous parietal infarction, with haemorrhagic transformation. Treatment options in elderly patients with SE have not been well studied and an optimal management protocol has not been elucidated (7), therefore this group of patients has a high mortality and low

chances of recovery. A more recent prospective study has shown that SE is an important source of morbidity and early mortality in patients with CVT (4). Previous studies have shown that in 25% of the cases SE was the first symptom of the stroke. After the first SE episode, the overall mortality is more than 20% (10). STESS (Status Epilepticus Severity Score) is a score that predicts the prognosis of status epilepticus, being favorable between 0-2 points. Our patient had a very high STESS score (5 points out of 6), consequently a bad prognosis. As it was recently pointed out (The Innsbruck Colloquium on SE, April 2–4 2009), there is a clear need for more data on RSE, since despite its clinical impact, current knowledge relies almost exclusively on retrospective assessments, and its management on small series and experts opinions. Recent studies have shown that in time, SE is refractory to treatment (6), proving the efficacy of the anesthesia (especially Propofol) in yielding seizures, therefore 1% of the patients could develop PRIS (Propofol Infusion Syndrome) (12). If Propofol is administered more than 48 hours, there is a risk of Propofol Infusion Syndrome with acidosis, elevated plasmatic lipids, cardiac arrest, kidney failure (often fatal).

CONCLUSIONS

CVT rarely appears in elderly people, having a severe prognostic and being very dangerous because of its high morbidity and mortality. Further clinical trials are needed to understand the options for the treatment of SE in this special age group. In the newest guide of CVT treatment, it is recommended that D-Dimers should be assessed before neuroimaging in patients with suspected CVT (13). It is suggested that MRI is reliable for the confirmation of the diagnosis (13). In the next few years numerous observational studies and treatment trials on several uncertain issues (e.g. thrombectomy, direct oral anticoagulants, decompressive surgery, without pregnancy after CVT, duration of oral anticoagulation), will increase the level of evidence that currently supports the management of CVT (13).

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REFERENCES

1. **Stam J.** Thrombosis of the Cerebral Veins and Sinuses. *N Engl J Med* 2005; 352: 1791-98.
2. **Itrat A., Shoukat S., Kamal A.** (2006). Pathophysiology of cerebral venous thrombosis – an overview. *JPMA. The Journal of the Pakistan Medical Association,* 56(11), 506-508.
3. **Ferro J.M., Correia M., Rosas M.J., Pinto A.N., Neves G.** Cerebral Venous Thrombosis Portuguese Collaborative Study Group [Venoport]. Seizures in cerebral vein and dural sinus thrombosis. *Cerebrovasc Dis* 2003; 15(1-2):78-83.
4. **Masuhr F., Busch M., Amberger N., Ortwein H., Weih M., Neumann K. et al.** Risk and predictors of early epileptic seizures in acute cerebral venous and sinus thrombosis. *Eur J Neurol* 2006; 13(8):852-6.
5. **Ferro J.M., Canhão P., Bousser M.G., Stam J.** Barinagarrementeria F; ISCVT Investigators. Early seizures in cerebral vein and dural sinus thrombosis: risk factors and role of antiepileptics. *Stroke* 2008; 39(4):1152-8.
6. **Nergiz H., Hatice K.Ö., Ürfettin H., Metin E., Ataman S.** Epileptic Seizures Related to Cerebral Venous Sinus Thrombosis: Clinicoradiological Findings and Cases of Delayed Diagnosis, 10.5505/epilepsi.2014.30502
7. Status Epilepticus in the Elderly, Lu-An Chen, Shuo-Bin Jou, International Journal of Gerontology 10 (2016) 2e5
8. **DeLorenzo R.J., Hauser W.A., Towne A.R. et al.** A prospective, population-based epidemiologic study of status epilepticus in Richmond, Virginia. *Neurology.* 1996; 46:1029e1035.
9. **Rumbach L., Sablot D., Berger E. et al.** Status epilepticus in stroke: report on a hospital-based stroke cohort. *Neurology.* 2000; 54:350e354.
10. **Waterhouse E.J., DeLorenzo R.J.** Status epilepticus in older patients: epidemiology and treatment options. *Drugs Aging.* 2001; 18:133e142.
11. **Varelas P.N., Claassen J.** Seizures in critical care.3rd edition, Springer Eds -Switzerland; 2017
12. **Kjersti NesheimPower, HansFlaatten, Nils ErikGilhus, Bernt A. Engelsen,** Propofol treatment in adult refractory status epilepticus. Mortality risk and outcome, https://doi.org/10.1016/j.eplepsyres.2011.01.006
13. **J.M. Ferro, M.G. Bousser, J.M. Coutinho, I. Crassard, F. Dentali, M. Di Minno, A. Maino, D. Aguiar de Sousa, J.** Stam and European Stroke Organization, European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis – endorsed by the European Academy of Neurology, 20 August 2017, DOI: 10.1111/ene.13381.