

Neurologist-in-training

The aim of this section is to prepare the neurologist-in-training for the FMH examination, to confront her or him with specific problems of everyday neurological practice and to give him or her updates on recent controversies in clinical neurology.

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Neurological MCQ

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1 Which of the following antiepileptic drugs is not considered a “large-spectrum” agent?

- A valproate B gabapentine C zonisamide D topiramate E lamotrigine

2 Please indicate the incorrect statement regarding drug–drug interactions.

- A Phenytoin and dexamethasone have a reciprocal influence on their blood levels.
 B Valproic acid increases pregabalin bioavailability.
 C Carbamazepine may reduce statins' efficacy.
 D Phenytoin's serum free fraction may increase in case of renal function impairment.
 E Phenobarbital is a very potent cytochrome inducer.

3 Please indicate the wrong sentence regarding pharmacodynamics.

- A Phenytoin, carbamazepine and lamotrigine principally act as modulators of sodium channels' function.
 B Barbiturates exert some anti-NMDA (glutamate) activity.
 C Topiramate shows anti-AMPA (glutamate) properties.
 D Zonisamide lacks influence on the carboanhydrase system.
 E Levetiracetam binds on a synaptic vesicle.

4 Which of the following statements is false?

- A Topiramate and zonisamide increase the risk of nephrolithiasis.
 B Valproic acid causes glaucoma.
 C Carbamazepine should not be combined with clozapine because of the risk of leucopenia.
 D Carbamazepine, valproic acid, gabapentine and pregabalin induce weight gain.
 E Lamotrigine is a mood stabiliser.

5 Which sentence is correct?

- A Serum drug levels should regularly be checked during carbamazepine and valproic acid treatment.
 B High-dose topiramate (>200 mg daily) is safe regarding efficacy of hormonal anti-conceptual treatment.
 C During pregnancy significant bioavailability variations may be encountered with lamotrigine, oxcarbazepine and levetiracetam.
 D Very low serum levels of carbamazepine are always related to bad compliance.
 E Regarding risk of foetal malformation, valproic acid and phenobarbital are probably the safest antiepileptic drugs.

(For correct answers, see page 439)

Neuroimaging

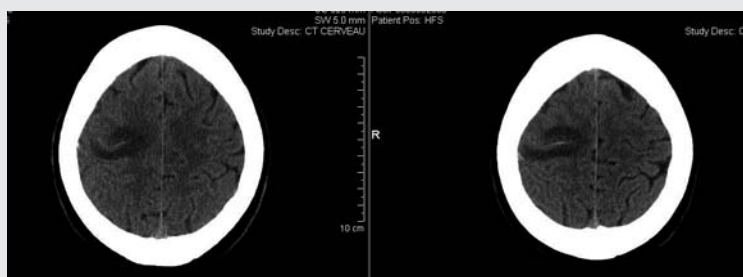
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A 41-year-old black woman, living in Switzerland since 20 years, presents to the emergency room with a history of unusual headaches since 48 hours (moderately intense, bi-frontal, non-pulsating, without nausea or photophobia) and one episode of a short, transitory loss of contact

with a few jerks of the left arm. On examination, she is slightly somnolent and shows a moderate left-sided ataxic hemiparesis. Her BMI is 28 kg/m², she does not smoke, and she has a hormonal anti-conceptual patch.

Her native brain CT scan is depicted below:



What is your diagnosis?

Figure 1
Brain CT scan.

(For correct answers, see page 439)

Read for you

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Minimally conscious state, persistent vegetative state and related conditions: static or dynamic?

Vegetative state (VS) is characterised by persistent absence of interaction with the environment, i.e. lack of any voluntary response to external stimuli and any ocular fixation longer than 5 seconds, with preserved sleep-wake cycles, spinal, brain-stem and startle reflexes. This condition is regarded as persistent (PVS) if lasting for longer than 3 months (US) or 6 months (UK) after anoxic and 12 months after traumatic brain injury [1, 2]. Minimally conscious state (MCS) is defined as a condition in which patients appearing in vegetative state occa-

sionally and inconsistently show some signs of conscious behaviour, and it is regarded as a possible transition from vegetative state to a more conscious state.

It is generally believed that subjects in prolonged vegetative state almost completely lack chances of regaining consciousness and that they do not have the possibility of performing conscious elaboration of external stimuli. Recent application of functional imaging to these patients has challenged this view. A British-Belgian group studied a young woman in definite vegetative state for 5 months after a car accident with brain functional MRI (fMRI) [1, 3]. Instructed to imagine playing tennis, she showed activation of the supplementary

motor area, a region known to be involved in the planning and coordination of complex movements, which was indistinguishable from imaging of healthy individuals. Furthermore, thinking of walking in her apartment elicited an activation of parietal regions underlying spatial orientation, again like normal controls. The authors view these responses as a proof of a conscious elaboration of the tasks.

Another group elegantly studied a 39-year-old patient who unexpectedly recovered from a condition of MCS lasting 19 years after traumatic brain injury [4]. They were able to show that fractional anisotropy (which is believed to reflect the myelination of white-matter tracts) increased in the dorsal paramedian brain regions, in parallel with an increased glucose metabolism in PET scan in the same areas. These regions are believed to play an important role in the functional network necessary for awareness [2, 4].

A French group has recently described a 48-year-old woman with akinetic mutism for 2 years following anoxic injury who was unexpectedly observed to become more active after administration of zolpidem for insomnia [5]. Formal neuropsychological testing confirmed a dramatic improvement of her motor and language performances, whereas PET imaging showed an activation of the anterior cingulate and orbitofrontal regions under zolpidem treatment, areas that are well known to mediate attention and motivation. Finally, a Taiwanese report points to dramatic improvement of motor and language functions in a patient with central pontine myelinolysis after zolpidem administration [6]. These observations suggest that this agent might block inhibitory sub-

cortical networks, possibly at the level of the basal ganglia, thus reversing an over-inhibited state [5], and more generally influence the impaired brain-stem-midline arousal system.

These paramount observations, even if they should be interpreted with caution because involving only single patients, open a wide door to a reassessment of our "certainties" regarding persistent vegetative state and conditions of impaired activation, and might hopefully contribute to a decisive improvement of clinical management of these conditions. Of course, ethical concerns related to the possible change of routine care in this setting will also need to be specifically addressed.

References

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- 3 Owen AM, Coleman MR, Boly M, Davis MH, Laureys S, Pickard JD. Detecting awareness in the vegetative state. *Science.* 2006;313:1402.
- 4 Voss HU, Uluç AM, Dyke JP, Watts R, Kobylarz EJ, McCandliss BD, et al. Possible axonal regrowth in late recovery from the minimally conscious state. *J Clin Invest.* 2006;116:2005–11.
- 5 Brefel-Courbon C, Payoux P, Ory F, Sommet A, Slaoui T, Raboyeau G, et al. Clinical imaging evidence of zolpidem effect in hypoxic encephalopathy. *Ann Neurol.* 2007;62:102–5.
- 6 Wang WT, Chen YY, Wu SL, Wei TS, Liu SY. Zolpidem dramatically improved motor and speech function in a patient with central pontine myelinolysis. *Eur J Neurol.* 2007;14:e9–e10.

Answers to MCQ

1 B 2 B 3 D 4 B 5 C

Answers to neuroimaging

The patient had a superficial cerebral vein thrombosis over the right convexity, located just anterior to the central sulcus (the latter is easily identifiable on the left hemisphere, on the right – more rostral – CT image), with a surrounding oedema. Therefore, it is not surprising that she experienced a complex partial seizure with left-arm clonic jerks. Headache is also a very common symptom of cerebral vein thrombosis. Regarding the aetiology, there was no abnormality of the coagulation parameters, no infections and no drepanocytosis. Thus, a causative role of the hormonal treatment was finally retained. The patient was anticoagulated for 6 months, and the evolution was very favourable.

Pathophysiologically, the oedema resulting from a vein thrombosis is not cytotoxic, but rather vasogenic; this explains the good prognosis once the vein is recanalised. Looking at the ADC maps (fig. 2), one may in fact appreciate that the oedema surrounding the thrombosis is hyperintense, whereas an acute cytotoxic oedema normally appears hypointense (dark).

Finally, the T_2^* images (fig. 3) show a couple of hypointense dots next to the lesion, corresponding to methemoglobine and therefore suggesting some petechial haemorrhage. It is important to underscore that this does not represent a contraindication to therapeutic anticoagulation in this setting.

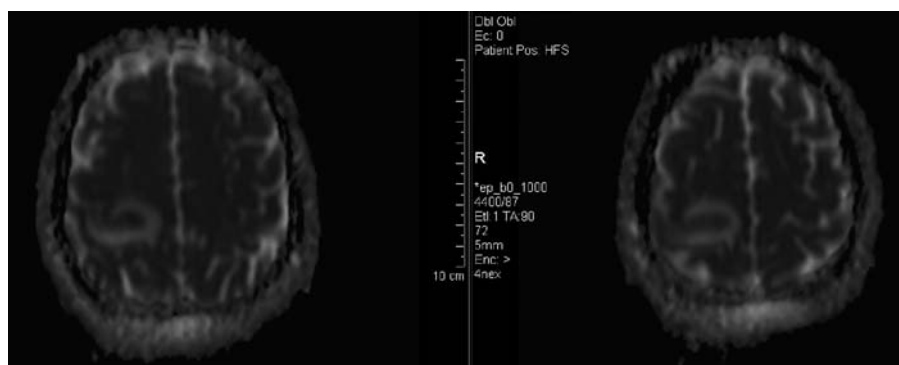


Figure 2
Brain MRI, ADC.

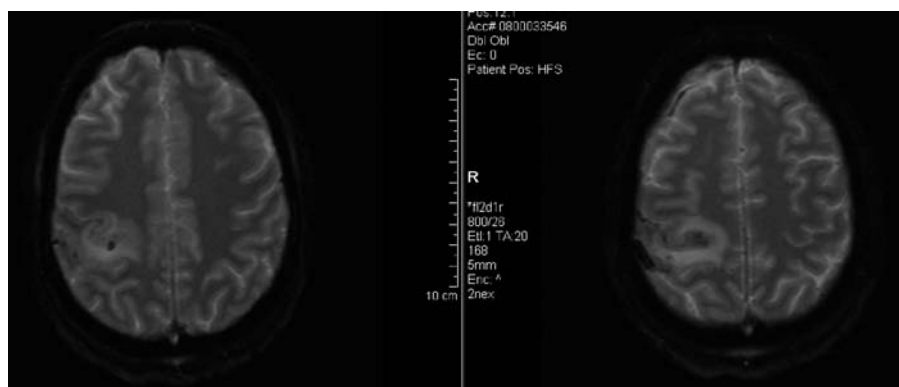


Figure 3
Brain MRI, T_2^* .