Neurologist-in-training

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Multiple choice questions

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Select the one correct answer.

1 The most characteristic feature in a patient with frontotemporal dementia is

A confabulation **B** disinhibition and hyperorality **C** early memory loss
D preserved insight into his or her disease **E** myoclonus

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2 A 45-year-old man of 80 kg with no past medical history has had generalised tonic-clonic seizure activity for 20 minutes, not been responding to i.v. injections of 300 mg thiamine (Benerva®), 50 ml of 5% glucose and two i.v. injections of 1 mg clonazepam (Rivotril®). What is the next medication?

A Valium 10 mg i.v. **B** Phenytoin (Epanutin®, Phenydan®) 1000 mg i.v.
C Phenobarbital (Gardenal®) 20 mg/kg i.v. **D** Phenytoin 15–20 mg/kg i.v.
E Propofol 2 mg/kg i.v.

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3 Huntington's disease

A is inherited in an autosomal-recessive way **B** is often accompanied by epilepsy
C is a disease of unknown cause **D** has low penetrance **E** shows anticipation

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4 Select the appropriate treatment for a 69-year-old woman with atrial fibrillation on anti-coagulation and no recent medical problems, who is brought to the emergency room 4 hours after onset of left facio-brachial hemiparesis, left hemianopsia and left hemine-glect. NIHSS is 16, blood pressure is 180/105, head-CT shows mild cortico-subcortical dedifferentiation in the right parietal region (less than ⅓ of MCA territory), INR is 1.1 and blood count is normal.

A i.v. thrombolysis with rt-PA
B i.a. thrombolysis with prourokinase if acute angiography shows an arterial occlusion in the middle cerebral artery territory
C Aspirine 100–300 mg
D Clopidogrel (Plavix®) 75 mg or dipyridamole/aspirine combination (Asasantine® 200/50)
E Heparin bolus 5000 units, followed by heparin infusion

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5 You choose to treat a patient with worsening respiratory and limb weakness due to proven myasthenia gravis with moderate dose corticosteroids. This treatment

A is the preferred long-term treatment of myasthenia
B should not be accompanied by Mestinon® treatment
C should be given intravenously
D may worsen myasthenia initially
E is contraindicated in elderly myasthenia patients

(For correct answers, see page 73)

Neuroradiology/Neuroanatomy

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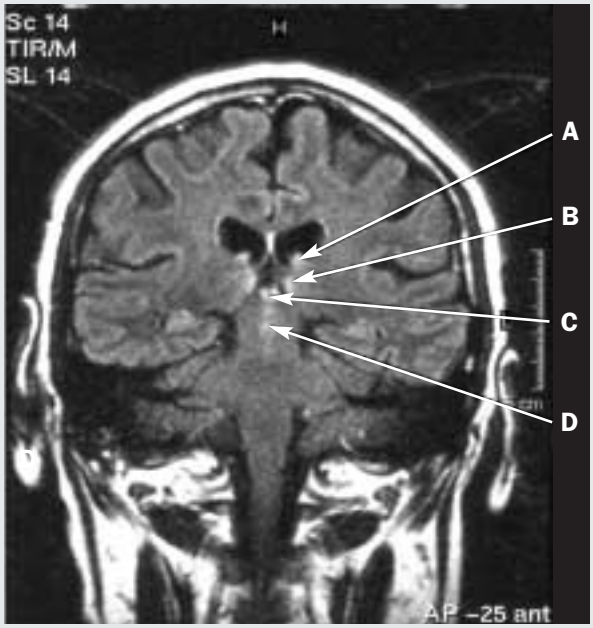

Identify the anatomical structures A–D on this FLAIR magnetic resonance image and make a diagnosis.

Figure kindly provided by A. Carruzzo and M. Chappuis, Hôpital des Cadolles, Neuchâtel, and J.-L. Dreyer, Institut de Radiologie, Neuchâtel.

(For correct answers, see page 73)

Read for you

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Should we use the new definition of TIA? When is a TIA a TIA?

Many clinicians felt that the classical definition of transient ischaemic attacks (TIAs) of "a sudden focal neurological deficit lasting for less than 24 hours, of presumed vascular origin ..." needed a revision. This is particularly true since there is a relatively poor correlation between the duration of the neurological deficit and the radiological and pathological findings, especially when the "transient" deficit lasts for more than 30–60 minutes. Furthermore, patients whose symptoms have not resolved after 1 hour are highly unlikely to be symptom-free after 24 hours and are therefore good candidates for acute treatment such as thrombolysis.

The new proposed definition is: "A TIA is a brief episode of neurological dysfunction caused by focal brain or retinal ischaemia, with clinical symptoms *typically lasting less than one hour*, and *without evidence of acute infarction.*"

Advantages of the new definition are:

1 It emphasises the very acute aspect of brain ischaemia and encourages physicians (and patients) to consider giving acute treatment without waiting several hours to see whether symptoms resolve spontaneously. This is especially important because it has been shown that the earlier the treatment is initiated the more the patient benefits.
2 There might be a better clinico-pathological correlation as TIAs lasting less than one hour are less likely to leave radiological or pathological lesions.

Problems with the new definition are:

1 It mentions an exclusion criterion of no "evidence of acute infarction" on imaging, but does (correctly) not require that each patient has an MRI. Consequently, a TIA in one patient might not be a TIA in another, depending on the imaging studies the patients may get.
2 The new time limit is given as "*typically* […] less than one hour" and remains voluntarily impre-

cise. Again, a TIA according to one physician's opinion might not be a TIA according to another physician.

Unfortunately, it remains unclear whether this new definition should be adopted worldwide now; although it is published in a very prestigious medical journal, it is only formulated as a "proposal" by leading American stroke neurologists; should it not have been published in the same place *after* an international consensus had been reached?

Independent of whether the patient has an "old-definition" TIA or a "new-definition" TIA (i.e. no matter how short symptoms last), the most important messages are that (1) TIAs should be considered as serious events, (2) acute ischaemic symptoms are a medical emergency, (3) an acute referral to the "best" treatment facility according to duration, type and severity of ischaemic symptoms is made, (4) a thorough search for a cause is undertaken and (5) that effective secondary prevention is assured.

References

Albers GW, Caplan LR, Easton JD, Fayad PB, Mohr JP, Saver JL, et al. Transient ischemic attack – proposal for a new definition. N Engl J Med 2002;347:1713–6.

Marler JR, Tilley BC, Lu M, Brott TG, Lyden PC, Grotta JC, et al. Early stroke treatment associated with better outcome: the NINDS rt-PA stroke study. Neurology 2000;55:1649–55.

Multiple sclerosis: which interferon regimen is "better"?

A randomised, controlled trial over 6 months found in patients with relapsing-remitting multiple sclerosis treated with IFNβ-1a (Rebif®) 44 µg s.c. three times a week a relapse rate of 25%, compared with 37% in patients treated with IFNβ-1a (Avonex®) 30 µg i.m. ($p = 0.0005$ for the odds ratio; Panitch et al.). However, the incidence of neutralising antibodies (25 vs 2%), injection-site reactions (83 vs 28%), abnormalities of liver enzymes and altered leukocyte counts was higher in the "more effective" group. The impact on disability was not assessed.

These results raise again the important question which dose, treatment frequency and route of administration are most effective and best tolerated. The trial of Panitch et al. still does not give a clear answer to these questions. It may be useful to the practising neurologist, however, for advising him and his patients on potential benefits and side effects of different regimens.

Reference

Panitch H, Goodin DS, Francis G, Chang P, Coyle PK, O'Connor P, et al. Randomized, comparative study of interferon beta-1a treatment regimens in MS: The EVIDENCE Trial. Neurology 2002;59:1496–506.

Neurologist-in-training

Answers to MCQ

1 **B:** Disinhibition with socially inadequate behaviour is an early characteristic finding in frontotemporal dementia. Prominent early memory loss is more typical of Alzheimer's disease, myoclonus might be seen in later stages of most dementias but should raise suspicion of prion diseases and metabolic encephalopathies.

2 **D:** One of the most frequent mistakes in treating convulsive status epilepticus is the underdosing of phenytoin. Intravenous valproate (Depakine®) loading might be an alternative, but is less well studied. As a next step, phenobarbital may be used if sufficient phenytoin-loading failed to stop the seizures. Dormicum (Midazolam®) or propofol infusions may also be considered instead of phenobarbital, but large controlled studies for these drugs in status epilepticus are currently lacking.

3 **E:** Huntington's disease is an autosomal-dominant trinucleotide repeat disorder (chromosome 4) characterised by chorea, cognitive and psychiatric manifestations. Anticipation (onset at an earlier age in the next generation) is a feature of most trinucleotide repeat disorders, mainly following transmission by the father.

4 **B:** Intravenous thrombolysis more than 3 hours after onset of ischaemic stroke is probably not efficient in the majority of patients. The PROACT-II study has, however, shown a benefit for patients with MCA-occlusion treated intraarterially in the 3- to 6-hour window. Oral anticoagulation is not a contraindication for thrombolysis in this patient because her INR is normal.

5 **D:** Because corticosteroids may worsen myasthenia gravis initially (typically after 5–7 days), many neurologists start with progressive doses and hospitalise these patients. Corticosteroids are also effective in elderly patients, but long-term treatment can usually be avoided (side effects!) with the help of other immunosuppressive treatment (such as azathioprine [Imurek®]).

Answers to Neuroradiology/Neuroanatomy

Anatomical structures:

A Fornix
B Dorsomedial thalamic nuclei
C Mamillary bodies
D Periaquaeductal grey

Diagnosis and commentary: Wernicke's encephalopathy. This 39-year-old alcoholic and epileptic man displayed two of the three features of the classical triad (confusional state, gait ataxia, but no oculomotor abnormalities). This disease is due to vitamin B_1 (thiamine) deficiency and may be missed if only one of the classical features is present or if the level of suspicion is too low (such as in patients with hyperemesis gravidarum or prolonged intravenous feeding). Pathologically, necrosis (sometimes haemorrhagic) is found in the paraventricular regions of the thalamus and hypothalamus, mamillary bodies, periaquaeductal region of the midbrain, floor of the fourth ventricle and superior cerebellar vermis. It is only recently that the MRI-features of this disease have been identified: diffusion-MR, FLAIR-MR, proton-density and to a lesser degree T_2-weighted images are more useful and may show abnormalities in the structures mentioned above.

Apparent diffusion coefficient (ADC) map revealed the high signal intensity lesions in bilateral medial thalami, suggestive of vasogenic oedema.

References

Kashihara K, Irisawa M. Diffusion-weighted magnetic resonance imaging in a case of acute Wernicke's encephalopathy. J Neurol Neurosurg Psychiatry 2002;73:181.

Shikata E, Mizutani T, Kokubun Y, Takasu T. "Iatrogenic" Wernicke's encephalopathy in Japan. Eur Neurol 2000;44:156–61.