Association of British Neurologists

Self-Assessment Questions for consultants & trainees 2016

After a brief hiatus, it's back, and we enclose 10 more questions to educate, delight, infuriate and antagonise you all. There are no official CPD points, but you can self certify, and we encourage you to do so. I suggest that if done properly, this should account for about 5 to 6 hours work, including reading around the subjects.

Ideally, we encourage you to complete all 10 questions via SurveyMonkey link before downloading the answers pdf. Once you have completed the questions, you can access a CPD certificate.

We are very grateful to all of you who submitted questions, and if we did not use your question this time round, it may well appear in future exercises. And for those of who feel the questions are too dull/pedantic/hard/easy/wrong/bizarre, then put your typing where your mouth is and send me a question or two, we are always in need! All comments welcome.

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TEC Chair (on behalf of TEC)

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Question 1

A 27 year old woman presented after a presumed focal motor seizure with on-going right sided hemiparesis and expressive dysphasia. Five years earlier she had been treated for a left temporal lobe Anaplastic Astrocytoma WHO III, with surgical resection and radical radiotherapy (60 Gy) with subsequent regular surveillance MR imaging. She was taking levetiracetam for focal seizures and this had been increased 3 months earlier due to seizure recurrence. She also had headaches previously diagnosed as medication overuse headaches; attempted withdrawal of opiates had been unsuccessful. Due to the persisting focal neurology she was admitted.

Examination: GCS 14/15, apyrexial. Marked right-sided hemiparesis and expressive dysphasia. Comprehension limited to one stage commands.

Investigations

- MR head (12 hours after symptom onset), including diffusion weighted imaging: no evidence of tumour progression or acute infarction.
- EEG: no epileptiform changes.

On day 2 she had a witnessed focal seizure and the weakness and dysphasia persisted. On day 7, still with persisting signs, a repeat MR head with contrast was performed which demonstrated high T2 signal in the gyri around the left insular cortex with enhancement.

What is the most likely diagnosis?

Question 1 Answers

A CNS Tumour Progression
B Hemiplegic migraine
C Left middle cerebral artery territory stroke
D Prolonged Todd's paresis
E SMART syndrome

Suggested Answer

E

Explanation / Comments

SMART (Stroke-like Migraine Attacks after Radiation Therapy) syndrome is a rare disorder causing a transient, reversible (though not always complete) focal neurological deficit, headaches and seizures in patients whom have previously undergone cranial radiotherapy treatment. The interval between a SMART episode and radiation treatment, ranges from 1-35 years.

The presentation was in keeping with a stroke (sudden onset of an acute focal deficit). The seizure had not been witnessed but had been presumed by a relative. The DWI however 12 hours after onset was normal. On day 7 the MR performed revealed high signal along the perisylvian cortex on T2 weighted imaging with gyriform enhancement.

SMART is associated with characteristic MR findings – diffuse, unilateral, gyriform gadolinium enhancement. These findings reverse. The typical MR findings become apparent on day s2-7 (hence the unchanged MRI scan 12 hours after symptom onset).

She was known to have focal motor seizures complicated by Todd's paresis usually for 20-30 minutes. At day 7 the weakness persisted which was highly unusual. The MR then revealed new changes without any recent (more than 48 hours) seizure activity. The weakness continued for 4 weeks before slowly beginning to improve with no further seizure activity. At 6 weeks a repeat MRI with contrast showed complete reversal of the gyriform enhancement.

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Stroke-like Migraine Attacks after Radiation Therapy (SMART). Syndrome is not always completely reversible: A case Series. Black DF, Morris JM, Lindell EP, Krecke KN, Worrell GA, Bartleson JD, Lachance DH. AJNR 2013 Dec;34:2298-303

Acknowledgements / Consent (IF APPLICABLE)

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Question 2

A 66-year-old man with a background of hypothyroidism and irritable bowel syndrome presented to the ED with paraesthesia starting in the first two fingers of his right hand, spreading up his right arm into the right side of his face & mouth over a period of 10 minutes. Along with these symptoms he described his mouth feeling numb 'like after a dental injection'. He had 3 episodes in one day.

Over the next month, he continued to have almost daily episodes of tingling & numbness affecting his hand and face lasting 20 minutes. On one occasion he described an episode affecting his throat and being unable to speak for several minutes. He also complained a frequent "muzzy" headache. He was not normally a headache person and had never had similar symptoms. He did not think the tingling and numbness were linked to his headache which was more constant, lasting for days and low grade. He never lost consciousness with any of the attacks.

His blood pressure was 190/105. GCS 15/15. He gave a good account of his symptoms and had no focal neurological deficit.

What is the most likely diagnosis?

Q2 Answers

A Cerebral amyloid angiopathy
B Focal seizures
C Hypertensive encephalopathy
D Migraine
E TIA

Suggested Answer

A

Explanation / Comments

TIAs typically cause negative symptoms and do not spread slowly from one part of the body to the next. It is also very uncommon to have recurrent TIAs on a daily basis that do not result in a stroke.

The description could be in keeping with focal seizures but would not explain the headaches.

Migraine aura can cause positive symptoms that can spread from one limb to another. However new onset migraine aura at this age should prompt neuro-imaging to exclude a structural cause.

Hypertensive encephalopathy causes reduced level of consciousness, confusion and seizures. This patient did not have an encephalopathy.

MRI revealed typical changes of focal cortical superficial siderosis (cSS) but no lobar haemorrhage; this is increasingly recognised in patients with cerebral amyloid angiopathy. In this condition, there is deposition of β-amyloid protein in the leptomeningeal and cortical vessels, causing vessel wall damage leading to multifocal subarachnoid or intracerebral bleeding and increase risk of intracerebral haemorrhage.

About 20% of patients with cerebral amyloid angiopathy develop transient focal neurological events or 'amyloid spells'; these are especially likely if cerebral imaging shows cortical superficial siderosis.

Amyloid spells typically include both positive and negative symptoms and last up to 30 min. All patients describing atypical recurrent focal episodes— regardless of their exact nature—should have both blood-sensitive and diffusion-weighted MR imaging. Amyloid spells are frequently mistaken for seizures, migraines or TIAs, often delaying or missing the diagnosis of CAA.

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Question 3

A 42 year old right handed man presented with a 3 month history of right arm tremor. The tremor had begun in the context of an illness characterised by fever, malaise, myalgia, and generalised shaking which emerged abruptly one night and led to an acute admission. Routine blood tests, MSU, chest x-ray and unenhanced CT head scan were all unremarkable. His systemic symptoms settled within days.

His generalised shaking resolved whilst in hospital, but the right arm tremor persisted. He described it as continuous at rest and on action (although not worse on action). It interfered with social and occupational functioning but he remained at work as a customer adviser. He felt unusually tired. There were no other symptoms. His only past medical history was an episode of back pain when he was 21 that had kept him off work for 18 months before resolution. He was married with two children, and described no significant stress other than concern that he might be developing Parkinson's disease. His wife had noticed that there were periods when the tremor would stop for a few minutes at a time.

Examination revealed a 3-4 Hz tremor of the right hand. He found it impossible to make a simple rhythmical 2 Hz voluntary movement with his left hand even when copying the examiner doing the same task (cued task). When he was asked to make a tapping movement with his right foot the rhythm 'entrained' to the tremor in the right hand.

Lively debate ensued as to whether the tremor was organic or otherwise.

Which of the following is least helpful in establishing the clinical diagnosis?

Q3 Answers

A Absence of previous psychogenic/ functional symptoms.
B Emerging in context of physical illness.
C Entrainment.
D Inability to copy a cued rhythmical task with the unaffected hand.
E Sudden onset of tremor.

Suggested Answer

A

Explanation / Comments

The correct diagnosis in this case was psychogenic/functional tremor.

There are some typical features in that the tremor started suddenly and in the context of a physiological triggering event, in this case rigors as part of a viral illness. There are also some features that might be thought to be less typical. He is a man, although studies show that for psychogenic/functional movement disorders there is only a slight excess of females. He doesn't present with a history of life stress or lots of other somatic symptoms (such as pain or gastrointestinal symptoms). However, studies show that life stress is often not detectable in patients with psychogenic/functional problems and its absence should not put you off the diagnosis. Conversely, mistakes are sometimes made when clinicians presume incorrectly that a symptom is psychogenic/functional because it started in relation to a recent life event. 'Secondary gain' is a non-specific phenomenon that occurs in patients with disease as well as psychogenic/functional symptoms and is often absent.

Psychogenic or functional movement disorders should be diagnosed on the basis of positive features of the tremor itself rather than on psychological factors found in the history. His tremor behaved in a way that could only be explained by this diagnosis. The patient was unable to make a rhythmical movement with his unaffected hand, and could not explain why, even though such a task is easy for most children and patients with an 'organic' cause of unilateral arm tremor. When he attempted a voluntary movement of his unaffected leg he developed 'entrainment'- the frequency of the leg movement became the same as the tremor in the arm. In some patients the tremor itself will entrain to the frequency of the tapping. A final response, which he didn't have, would have been for the tremor in the affected limb to cease altogether or change significantly in frequency during rhythmical voluntary movements in an unaffected limb. Other signs of psychogenic/functional tremor include transient pause of the tremor during ballistic movements of an unaffected hand, highly variable frequency (although variable amplitude is less helpful) or the presence of worsening tremor with weight loading or immobilisation. Other psychogenic/functional signs such as global weakness, give-way weakness or Hoovers sign (weakness of hip extension which returns to normal with contralateral hip flexion against resistance) may be present.

In this case the clinician explained to the patient that the diagnosis was 'functional tremor', showing him the physical basis on which this diagnosis was based and providing self-help information. It was emphasised to the patient that this was a genuine problem not related to a neurological disease but instead related to a

persistence of abnormal brain function triggered by the rigor and not 'all in his mind'. The patient was relieved that he didn't have Parkinson's disease and the tremor gradually settled over 2 months without the need for any further treatment other than neurological review and reassurance. In other cases referral to a liaison or neuro-psychiatrist for additional treatment may be helpful but ongoing neurological involvement is often helpful until the patient becomes confident about their diagnosis.

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Question 4

A 17 year old right handed female presented with two recent events. After a late night at a party, her mother noticed her at breakfast staring forward for a few seconds before her head twisted to the right. After a short grunt, she recovered. The patient recalled feeling confused but nothing else. She was taken to the ED where observations, ECG and bloods were all normal. CT Head was reported as normal.

Two days later she had difficulty seeing the right side of the television screen. The images became jumbled and replaced by red and orange indistinct shapes. This resolved, but she still had difficulty seeing to the right for a further 10 minutes. There was no headache.

In the past two years she had become clumsy and noticed small jerks in her arms, particularly in the morning. Recently the jerks had become more frequent and occurring in the evening as well. She had become low in mood and tearful, and was uninterested in school work.

Her birth and development were normal, but her mother reported a ten minute febrile convulsion when 2 years old. There was no history of intracranial infections or head injuries. There was a family history of breast cancer and the mother's great aunt had died in her 20s with 'bad epilepsy'. She admitted to smoking and drinking 10-15 units infrequently at parties, but denied taking recreational drugs.

Examination revealed occasional low amplitude myoclonic jerks in both arms. Finger-nose pointing elicited dysmetria and she was ataxic on tandem gait. Examination was otherwise normal. MMSE was 29/30.

EEG showed a well-organised background with multiple spike and wave discharges with photosensitivity.

Which diagnosis would best explain the symptoms?

Q4 Answers

A Juvenile Myoclonic Epilepsy
B Lafora Body Disease
C Occipital lobe Epilepsy
D Sporadic Creutzfeldt-Jacob Disease
E Unverricht-Lundborg Disease

Suggested Answer

B

Explanation / Comments

This patient presents with worsening myoclonus and ataxia, a focal seizure with altered consciousness, a possible occipital seizure and low mood.

Unverricht-Lundborg Disease (Baltic myoclonus) is autosomal recessive and the most common progressive myoclonic epilepsy. Age of onset is 6-15 years with stimulus-sensitive myoclonus and generalised tonic-clonic seizures the presenting features in most patients. Cerebellar dysfunction and dementia are late features.

Lafora Body disease is an autosomal recessive disease characterised by myoclonus, epilepsy, early cerebellar dysfunction and dementia. It is the second most common progressive myoclonic epilepsy. Symptom onset is age 12-17 years preceded by normal physical and mental development. Isolated childhood febrile and non-febrile seizures occur in many patients. Prominent seizure types are myoclonus and occipital, though other focal seizures with altered consciousness, atonic and atypical absences may all occur. Ataxia and cognitive decline, heralded by emotional disturbance, appear early. Diagnosis is confirmed by detecting Lafora bodies in skin biopsy specimens, but this is likely to be superseded by analysis of the EPM2A gene, yielding a known mutation in 80% of patients with Lafora's disease. At onset, it is difficult to differentiate from idiopathic generalised epilepsies particularly **Juvenile Myoclonic Epilepsy** (JME). EEG changes can also be very similar. JME is characterised by myoclonic jerks on awakening, but generalised tonic-clonic seizures and typical absences are typical. Focal seizures and progressive cerebellar dysfunction are rare.

Occipital Lobe Epilepsy alone does not account for the complex of clinical features.

The characteristic clinical picture in **sporadic Creutzfeldt-Jacob disease** (sCJD) is one of rapidly progressive dementia that can present as low mood with associated neurological features, particularly cerebellar ataxia, pyramidal signs and myoclonus. Visual disturbance and hallucinations are also well recognized. However the mean age of sporadic Creutzfeldt-Jacob Disease is much older with most cases presenting between 50 and 75 year although patients as young as 14 have been reported. Disease duration is typically short, with a median of 6 months from onset to death. Only 14% of cases survive longer than a year and only 5% live for 2 years or more. EEG classically shows periodic, triphasic sharp wave complexes at a frequency of 1/s, usually generalised throughout the trace.

Question setter:

Question 5

A 36 year old man presented with an 18 month progressive history of involuntary movements. There was no family history of similar problems. He had two sons and two daughters. Examination revealed generalised chorea.

A genetic test for Huntington's disease (HD) was requested. The results were reported as follows:

HTT allele 1: 15 CAG repeats
HTT allele 2: 33 CAG repeats

Which of the following is correct concerning this result?

Q5 Answers

A The diagnosis is HD and each of his children is at 50% risk of inheriting HD.

B The diagnosis is HD; his sons are each at 50% risk; the risk to his daughters is increased but less than 50%.

C His symptoms are not caused by HD; each of his children has a 50% risk of HD.

D His symptoms are not caused by HD; the risk to his children of developing HD is increased but less than 50%.

E No useful information can be derived from the result.

Suggested Answer
D
Explanation / Comments
He has an intermediate allele which does not cause HD in the proband but may expand when passed to offspring. The risk to children cannot be accurately assessed. It is increased, but less than 50% and independent of the gender of the child. An alternative cause for his symptoms is required.

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Question 6

A 56-year-old man on a general surgical ward was referred for a neurological opinion. As a young man, he required multiple GI operations for Crohn's disease, but this had been quiescent for some years; he also has ankylosing spondylitis. He had no family history of note and current medication included NSAIDs and sulphasalazine.

He was admitted under the surgeons with a six month history of weight loss, abdominal pain and watery diarrhoea. Investigations were non-diagnostic, and he had a laparotomy at which some adhesions were found, but no evidence of active inflammatory bowel disease. His symptoms settled, but he failed to mobilise after surgery, because of dizziness.

Further history revealed erectile dysfunction for five years and 10 years of urinary frequency and nocturia, attributed to "prostate trouble". He admitted to having intermittently felt dizzy on standing for at least three years, and to "blacking out" on three occasions in the last year when getting out of bed at night.

On examination, there were no signs apart from poor constriction of the pupils to light. Power, sensation and reflexes were normal and there were no signs of parkinsonism. He was unable to stand for more than a few seconds, because of postural hypotension: 160/90 lying, 65/undetectable standing.

Blood and urine tests done on the surgical ward were normal or negative. An ECG showed sinus rhythm with no R-R variation on respiration.

Which diagnosis best accounts for the clinical picture?

Q6 Answers

A Autonomic neuropathy due to amyloidosis secondary to chronic inflammation
B Autonomic neuropathy secondary to primary amyloidosis
C Multiple System Atrophy
D Primary autoimmune autonomic neuropathy
E Sjogren's syndrome

Suggested answer

D

Explanation / Comments

He has pure autonomic failure, without clinical evidence of a neuropathy.

The first diagnostic issue is whether this is peripheral or central. The circumstantial evidence suggests that it is peripheral because a central aetiology (MSA) would, after ten years, have evolved definite symptoms and signs of parkinsonism or cerebellar deficits. A tyramine test can usefully distinguish these two on the basis that denervation of the vascular bed (in a neuropathy) can lead to receptor hypersensitivity and hence a hypertensive response to tyramine that would not be seen in a central cause of autonomic failure.

Top of the list of causes of an autonomic neuropathy would be diabetes (which has been excluded here) and then primary amyloidosis. The median survival of patients with primary amyloidosis and a neuropathy is 13-35 months, so he is doing rather too well for that condition. Amyloidosis secondary to chronic inflammatory diseases does not cause an autonomic neuropathy.

A recent survey highlighted the disproportionate autonomic involvement seen in the neuropathy associated with Sjogren's syndrome, but this was never seen as an isolated phenomenon for as long a time as in this case. The history is too long for an autonomic Guillain-Barre or a paraneoplastic autonomic neuropathy. The entity of "autonomic CIDP" does exist, but without clinical signs of a neuropathy, seems unlikely here. Rare and unlikely causes in this context are the various hereditary autonomic neuropathies, infectious diseases with autonomic involvement (Chaga's and HIV), and toxins (marine toxins, organic solvents).

Primary autoimmune autonomic failure is relatively newly described. It is caused by antibodies to the ganglionic acetylcholine receptor (a serum test for which is available from Angela Vincent's laboratory), which cause a similar syndrome in animals. Patients can have autonomic failure for decades without clinical signs of a neuropathy. Even in the face of a long history, plasma exchange is well worth a try. Reasonable responses have also been achieved with IVIG. As well as the standard treatments of orthostatic hypotension (amongst which should now be included midodrine), it has been suggested that L-DOPS (L-threo-3,4-dihidroxyphenylserine) is especially beneficial in these patients.

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Acknowledgements / Consent (if applicable)
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Question 7

A 60 year old right-handed teacher was referred by an Ophthalmologist after presenting with gradually-progressive difficulty with vision. On some occasions visual field testing had revealed a left homonymous visual field defect, but this was inconsistent and his visual acuities were normal. Extensive investigation by ophthalmology had revealed no cause.

The patient struggled to explain his symptoms. He first noticed difficulties with vision around two years previously when driving, particularly at night. Over subsequent months he found parking increasingly difficult. He had difficulty with reading and had stopped work as he found he could no longer mark pupils' work. Over recent months he had experienced embarrassing situations where he has been unable to recognise the faces of people he had known for years. He reported no other cognitive difficulties, corroborated by his wife, and was otherwise well.

He had well-controlled type 1 diabetes mellitus, treated with insulin. There was no family history of visual or neurological disorders.

On examination he had insight into his problems and was able to converse appropriately. Speech was normal. Fundoscopy was normal, and there was no visual field defect on confrontation testing. He was able to correctly name objects in the room, but struggled to name objects in photographs. Examination of the remaining cranial nerves and limbs was unremarkable, and gait normal.

He scored 86/100 on an Addenbrooke's Cognitive Examination III, the breakdown as follows:

- Attention 18/18
- Memory 25/26
- Fluency 13/14
- Language 26/26
- Visuospatial 4/16

Which of the following results would be most in keeping with the suspected clinical diagnosis?

Q7 Answers

A. EEG showing periodic sharp wave complexes
B. Elevated CSF phosphorylated tau and decreased CSF amyloid β42
C. MR head showing established left parietal infarct
D. Positive anti-neuronal antibodies
E. SPECT showing frontal hypoperfusion

Suggested answer

B

Explanation / Comments

He presents with a gradually progressive history of visual problems, alexia, picture agnosia and prosopagnosia. In contrast to his marked visual deficits, other cognitive domains remain intact. This is in keeping with a diagnosis of posterior cortical atrophy (PCA).

PCA commonly presents with an insidious onset of visuospatial and visuoperceptual impairments and alexia. Patients can have features of Gerstmann's syndrome (acalculia, agraphia, finger agnosia and left/right disorientation) and Balint's syndrome (simultagnosia, oculomotor apraxia, optic ataxia and environmental agnosia). As in this case, patients with PCA are often initially referred to ophthalmology, where examinations are unremarkable. Some patients with PCA are found to have a homonymous visual field defect, however visual field examination can be challenging and inconsistent.

The majority of cases of PCA are due to Alzheimer's disease (AD) pathology. Although AD usually presents with amnesia, roughly one third of cases of young-onset sporadic AD present with non-amnestic deficits. PCA is the most common of these non-amnestic presentations.

This question concerns the use of biomarkers in the diagnosis of dementia. As AD pathology usually underlies PCA, investigations are expected to show evidence of AD. In contrast to the temporal lobe structural changes found in amnestic AD however, there is a relative predominance of parietal and occipital atrophy. Expected biomarker changes in PCA therefore consist of:

- Posterior atrophy on MRI
- Posterior hypoperfusion/ hypometabolism on functional neuroimaging (SPECT & PET)
- CSF changes suggestive of AD, with an elevated tau/Aβ42 ratio

With regards to the other answers: the frontal hypoperfusion on SPECT would be more commonly seen in frontotemporal dementia, this is not a picture suggestive of paraneoplasia, and the EEG periodic sharp wave complexes are a feature of Creutzfeld-Jakob disease. Whereas a parietal stroke may account for some of the symptoms in this case, the history is too progressive for this to be a likely cause of his presentation.

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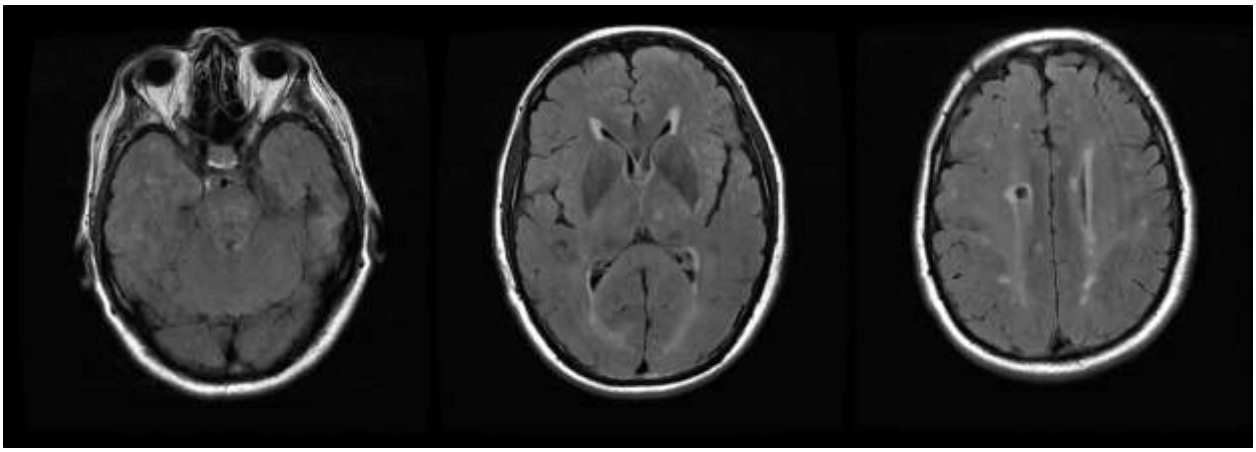
Question 8

A 48 year old man presented with a two day history of severe unilateral headache associated with vomiting, confusion and behavioural change.

He had a background of migraine, asthma, and had been treated for depression in the last 3 years. His mother had a stroke aged 44 and demented in her 60s, his father died aged 35 in car accident.

Neurological examination was normal other than mild photophobia. Blood pressure was 125/80. He was apyrexial.

FBC, U&E and CRP were normal; ESR was 38 mm in the first hour. His MR head (T2 FLAIR) was reported as consistent with microvascular change (below).



Which investigation is most likely to be diagnostic?

Q8 Answers

A Cerebral angiogram (DSA)
B CSF examination
C DNA analysis
D Temporal artery biopsy
E Voltage gated potassium channel antibodies

Suggested Answer

C

Explanation / Comments

He presents with migraine associated with confusion, with a history of migraine and depression. His family history includes a first degree relative with stroke and dementia. The MRI demonstrates periventricular white matter hyperintensities with involvement of the anterior temporal poles, external capsule and brainstem.

All these features should prompt consideration of Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), a rare inherited small vessel vasculopathy (although the most common of the hereditary small vessel diseases, Federico et al 2012). It is caused by mutations in the *NOTCH3* gene, and inherited in an autosomal dominant pattern (Joutel et al 1996). Whilst the abnormal receptor is found throughout the body, symptoms are confined to the brain with stroke, executive impairment, apathy, depression and migraine occurring, usually manifesting in early to mid-adulthood (Chabriat et al 2009). Increasingly a wider spectrum of disease is recognised, with older patients being diagnosed with minor symptoms. Family history in patients presenting in late middle age or older may be incompletely ascertained due to the assumption that it is not relevant in this age group.

Structural brain imaging in CADASIL identifies abnormalities some years before the clinical manifestations and consists of white matter hyperintensities, lacunes, microbleeds and brain atrophy. Localisation of white matter hyperintensities to anterior temporal poles and external capsule (as seen above) offers a high specificity for CADASIL, at least in European populations (O'Sullivan et al 2001). In this case, the MR changes are subtle for his age but the pattern is the clue.

Migraine is common in CADASIL, often with atypical aura, including prolonged or severe neurological disturbance. "CADASIL coma" has been described where patients experience a typical migraine followed by confusion, seizures, hallucinations and occasionally fever. Encephalitis may be suspected, but complete recovery is the norm (Schon et al., 2003).

DNA analysis, specifically *NOTCH3*, would therefore be the investigation most likely to confirm the diagnosis here; a negative result all but excludes the diagnosis. Whilst this could be a cerebral vasculitis, the history is much more suggestive of CADASIL, and thus angiography unlikely to help. He is too young for temporal arteritis, and the history is not one of a limbic encephalitis. Although many patients in this acute scenario undergo CSF examination, it is usually normal.

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Question 9

A 38 year old Nigerian man returned from a 2 week holiday in his home country. Whilst there he noticed mild symmetrical ankle swelling with bilateral calf pain, as if he had run too far. Two weeks after his return to the UK he noticed that he was able to walk less well on the flat, was becoming unsteady and had distal numbness in his feet. Three weeks later he presented to the ED as his hands had become numb as well.

On examination he had dry skin and mild pitting oedema to his knees. His cranial nerves were normal except for papilloedema with marked subretinal and peripapillary haemorrhages. Examination of the limbs revealed distal but marked weakness affecting hands and feet, areflexia, and a glove and stocking sensory loss to all modalities.

Routine blood tests demonstrated a normal Hb and WCC with platelets $479*10^{9}$, normal U&E, glucose, LFT, TFT, serum protein electrophoresis and immunofixation. An excess of lambda light chains was found in the urine.

Neurophysiology showed small CMAPs ($\leq$ 1mV) throughout the upper limbs and no lower limb CMAPs. Nerve conduction velocities were 20-23 ms^{-1} in the upper limbs and F waves 55ms where recordable. There was no conduction block or dispersion. SNAPs were all absent except radials of 5uV bilaterally. EMG demonstrated length dependent denervation changes in all four limbs.

Which test would most likely confirm the diagnosis?

Q9 Answers

A. 24hour urinary protein estimation
B. CSF examination
C. IgG anti-ganglioside antibodies
D. Serum VEGF
E. Whole body CT-PET

Suggested Answer

D

Explanation / Comments

POEMS syndrome is a rare paraneoplastic systemic disorder which usually presents with a neuropathy. This can be aggressive and rapid or more slowly progressive and 'treatment resistant' before often worsening suddenly. Muscle pain is not an infrequent feature at onset and a very distal pattern of weakness is usual. This is not Guillain-Barre syndrome as it is still getting worse beyond 4 weeks. Although it could be heading towards CIDP, it has not reached the critical diagnostic 8 week time point. Furthermore as there is no proximal weakness, it would not fit the criteria for typical CIDP [EFNS/PNS criteria 2012]; there are too many additional features to comfortably fit any of the atypical patterns .

The criteria for the diagnosis of POEMS are published [Dispenzieri 2007]. Patients must have a neuropathy (typically a mixed axonal and demyelinating picture), and a paraprotein. A serum protein electrophoresis is only 20-60% sensitive to detect a paraprotein where there is no immunoparesis as in myeloma and therefore a serum immunofixation is a necessity. However there are some patients where the only evidence for the monoclonal plasma cell disorder comes from a Bence Jones protein, or occasionally from a monoclonal plasmacytoma identified from biopsy of a sclerotic bone lesion or a 'hot' abnormality on PET. The Lambda light chain here gives you enough preliminary evidence of the monoclonal plasma cell disorder, awaiting confirmation of its source. The CT-PET will help with this but adds nothing additional to your diagnosis at this point. Patients must also fulfil one of the other major criteria (Castelmann's disease, osteosclerotic bone lesions or a raised VEGF) and at least one minor criterion. CT PET can be very useful in detecting sclerotic bone lesions, where these are not found by skeletal survey, solitary extraosseous masses, Castleman's disease and organomegaly.

A raised VEGF is almost 100% sensitive and specific when interpreted in the correct clinical context (presence of an appropriate peripheral neuropathy as here and a monoclonal plasma cell disorder). TFT and glucose abnormalities are excluded from the diagnostic criteria as they are too prevalent in the community to be of diagnostic use. The subretinal haemorrhages associated with the papilloedema of POEMS is typical and due to the capillary leak resulting from the VEGF driven cytokine excess.

Treatment is complex and depends upon the age and performance status of the presenting patient [Kuwabara et al 2012 Cochrane Review]. Solitary lesions can be treated effectively with radiotherapy and this can provide a sustained response. More widespread disease can be treated with chemotherapy, but myelosuppressive regimens (such as those containing melphalan) are not favoured where peripheral blood stem cell transplantation might be considered. PBSCT can result in a sustained and effective remission with long term outcome results unknown so far.

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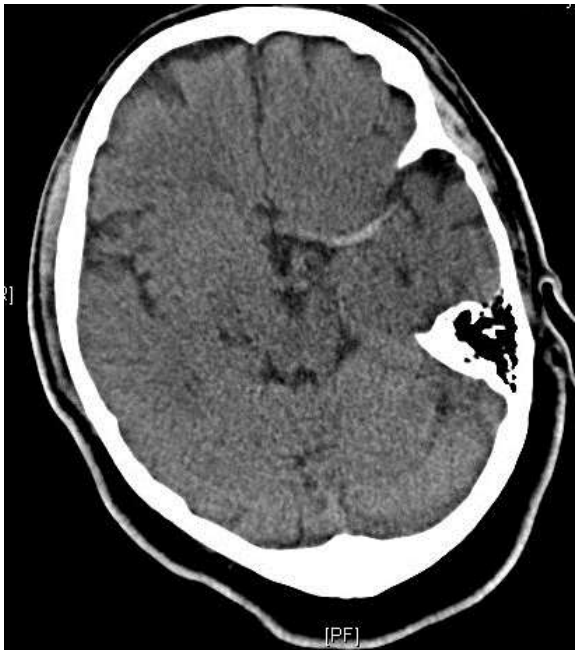
Question 10

A 49 years old man was admitted to the emergency department with right sided weakness, speech and walking difficulties. He was seen 90 minutes after symptom onset. On examination he had moderate expressive dysphasia; partial hemianopia, mild right facial weakness, right arm (3/5) and right leg (4/5) weakness, and reduced light touch sensation on the right side. His NIHSS score was 9.

His initial non contrast CT head is shown:



He had perfusion imaging and core was calculated at 10ml.

Which would be the best treatment option here (assuming all options available on site):

Q10 Answer

A. Alteplase IV immediately.
B. Alteplase IV immediately followed by stent clot retrieval.
C. Aspirin 300 mg and admission to the stroke unit.
D. Direct intra-arterial thrombolysis immediately.
E. Neurosurgical referral to consider urgent hemicraniectomy.

Suggested Answer

B

Explanation / Comments

Several recent studies have shown that patients having thrombectomy with stent retrieval following IV thrombolysis in eligible candidates had favourable outcome compared to standard treatment. Eligible patients had proximal artery occlusion and small core; and most studies performed thrombectomy within 6 hours of onset and rapidly after thrombolysis. In this case there is clearly a hyperdense left MCA sign suggesting proximal MCA occlusion and the core was reported to be 10ml which is very small. With such a proximal occlusion one would expect a large penumbra. The best treatment option here is IV thrombolysis with alteplase and, unless very rapid recovery, then thrombectomy with stent retrieval.

IV alteplase alone is suboptimal as the percentage of recanalization in patients with MCA hyperdense sign is low. Direct treatment with intra-arterial thrombolysis is no more effective than IV treatment. Hemicraniectomy is not relevant at this stage; if recanalization is achieved then the patient may not develop a large infarct requiring hemicraniectomy.

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