**QUESTION 1**

A 50 year old man gave a twelve year history of progressive bilateral ptosis. There was no diurnal variation or fatigability. He had always been “quietly spoken” and recently noted difficulty swallowing tablets. He was a smoker and had intermittent claudication. He took aspirin, bendrofluamethazine and a statin.

His paternal grandmother, aunt and uncle all suffered from ptosis in their 60’s.

On examination he had bilateral non-fatiguable ptosis: Cogan’s lid twitch test was negative. He had an early left cataract with acuities of 6/9 L and 6/6 R. He had limitation of his upgaze bilaterally, but otherwise full eye movements. He had normal facial, neck and limb power. There was no myotonia, and no other abnormalities. A bedside swallow assessment was normal.

Which investigation is most likely to be helpful?

<table>
<thead>
<tr>
<th>ANSWERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Acetyl choline receptor antibodies</td>
</tr>
<tr>
<td>B DNA analysis (Dok-7 gene)</td>
</tr>
<tr>
<td>C DNA analysis (PABPN1 gene)</td>
</tr>
<tr>
<td>D Muscle biopsy</td>
</tr>
<tr>
<td>E Tensilon test</td>
</tr>
</tbody>
</table>

**SUGGESTED ANSWER**

C
EXPLANATION / COMMENTS

This gentleman’s presentation with a familial late-onset ptosis and dysphagia is suggestive of oculopharyngeal muscular dystrophy. The onset of this rare genetic disorder is usually in the fifth or sixth decade. It is inherited in an autosomal dominant manner and has near complete penetrance by the age of seventy, although the severity of symptoms varies, so this may not always be obvious form the family history. The condition is caused by GCG repeats on the PABPN1 gene. Mutation carriers have between 8 and 13 GCG repeats.

Familial myasthenia has rarely been reported but you would not expect the number of affected family members seen here. The lack of fatigability and normal Cogan’s lid twitch test also make myasthenia less likely.

Kearns Sayre syndrome can present with a chronic progressive ophthalmoplegia; increased serum and CSF lactate levels and muscle biopsy abnormalities may be seen. However, most patients will have an onset of symptoms before 40. Given that Kearns Sayre is a mitochondrial condition you would not expect it to be passed along the paternal line.

Dok-7 mutations are one of the causes of congenital myasthenia. The clinical onset of symptoms is normally before five years of age. These patients will normally have proximal limb weakness.

REFERENCES


ACKNOWLEDGEMENTS / CONSENT (if applicable)

Not applicable.

YOUR NAME, POSITION, ORGANISATION
Graham Mackay (Research registrar). National CJD Research and Surveillance unit, Edinburgh

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QUESTION 2

A 64 year old woman presented with a two year history of unsteadiness, and recently had started falling. She felt lightheaded walking upstairs, making her more unsteady. She thought her speech slurred, particularly on the telephone and occasionally choked on dry bread or biscuits. Her right arm felt weak and she had noticed loss of dexterity, with difficulty doing up buttons. She had a long history of stress incontinence and more recently urge incontinence. She was often tearful and felt her memory was poor. Although sleeping well, she was disturbed by vivid dreams and on two occasions had woken after falling out of bed.

On examination, she looked well, and scored 29/30 on the MMSE. She had hypometric saccades, with some limitation of upgaze. Jaw jerk was present, as were facial reflexes. Her speech was quiet and slurred. Cough was impaired, although palatal elevation normal. There was a mild postural tremor of both outstretched arms and fine myoclonic jerks of the fingers. There was axial rigidity and mild rigidity in the right upper limb. Fine finger movements were slowed. Reflexes were brisk throughout with downgoing plantars. She was slow to rise from the chair and had a broad based gait. Postural reflexes were impaired.

Which MRI feature would be most consistent with the clinical diagnosis?

**ANSWERS**

A Asymmetric frontoparietal atrophy  
B “Hot cross bun” sign  
C “Hummingbird” sign  
D Hydrocephalus  
E “Mickey Mouse” sign

**SUGGESTED ANSWER**

B
Clinically the patient presents a picture consistent with multiple system atrophy (MSA), with akinetic-rigid syndrome, autonomic and cerebellar dysfunction. The patient fulfils clinical diagnostic criteria as proposed by Gilman et al (Gilman et al., 2008). Eye movement abnormalities may be seen in MSA (mild compared to PSP) including hypometric saccades, square wave jerks, nystagmus and mild limitation of upgaze (Quinn, 2005). Patients with MSA may develop dysphagia, fine myoclonic jerks of the fingers, mild pyramidal dysfunction, emotional incontinence, REM sleep behavioural disorder and mild frontal dysexecutive syndrome (Kawai et al., 2008; Kollensperger et al., 2008; Quinn, 2005).

Currently the diagnosis of the parkinsonian disorders (MSA, PSP, PD and CBGD) remains clinical; however, certain MRI features may provide support for the diagnosis. In MSA, degeneration of transverse fibre tracts within the pons, with relative sparing of longitudinal tracts, leads to the “hot cross bun” sign on T2 weighted (and FLAIR) images (Schrag et al., 1998). In addition there may be pontocerebellar atrophy, T2 signal changes within the putamen and putaminal atrophy. The hummingbird (or penguin) signs and Mickey Mouse signs occur in PSP, due to selective atrophy within the midbrain (see article by J Schott below). In CBGD, there may be asymmetric frontoparietal atrophy (Schrag et al., 2000).

“Hot cross bun” sign in the pons of a patient with MSA.

REFERENCES


**ACKNOWLEDGEMENTS / CONSENT** (if applicable)

The patient whose scan is pictured kindly took part in my PhD study

**YOUR NAME, POSITION, ORGANISATION**

Dr Camilla Blain  
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A 66 year old lady presented with a six week history of progressive unsteadiness. She had a background of rheumatoid arthritis (quiescent) and was a smoker. Over the previous weeks she described a sensation of imbalance “as if on a boat” and occasional falls. She also described tingling in the feet. She had lost half a stone in weight. There were no other systemic features.

Examination revealed jerky visual pursuit with slowed horizontal and vertical saccades. She was dysmetric and her gait broad based. Light touch sensation was impaired in the right hallux; sensory examination otherwise normal. There were no other neurological findings.

Baseline bloods including inflammatory markers were normal. Her MR head (diffusion weighted) is below.

Which investigation is most likely to aid diagnosis?

**ANSWERS**

A anti Hu antibody  
B CSF examination  
C EEG  
D Serum carbon monoxide level  
E Tonsil biopsy

**SUGGESTED ANSWER**

B
EXPLANATION / COMMENTS

This lady presents with a cerebellar syndrome. The B1000 image from her diffusion weighted MRI scan demonstrates bilateral caudate and putamen high signal. In addition there is less marked bilateral thalamic high signal.

The MRI result in this context is suggestive of sporadic Creutzfeldt-Jakob Disease (CJD). This presentation and imaging is in keeping with one of the rarer sub-groups of sporadic CJD. Patients in the MV2 or VV2 sub-groups often present with a more gradual deterioration than more classical sporadic CJD cases. They often present with ataxic symptoms prior to deteriorating, often over one year.1 These patients will often have both basal ganglia and thalamic high signal on diffusion-weighted MRI sequences.2 However, unlike variant CJD cases, the thalamic high signal is less prominent than that shown in the basal ganglia. The pulvinar sign, seen in variant CJD requires that the signal in the thalamus is greater than that of the anterior putamen.3

Typical EEG abnormalities (i.e. periodic complexes) are rare in these sporadic CJD sub-groups. Indeed they were not seen in any of 23 patients within these groups in one recent study.2 In variant CJD prion proteins are found in the lymphoreticular tissues. Therefore, tonsil biopsies can be useful in variant CJD to confirm the presence of prion proteins.4 Abnormal prion proteins are predominantly found in the brain, retinal and corneal tissues in sporadic CJD; so tonsil biopsies will be negative.5 CSF biomarkers (14-3-3 and S100) are normally positive in patients with MV2 or VV2 sporadic CJD.2 This is therefore, a useful investigation in this context and will support the diagnosis.

Although a paraneoplastic process with anti Hu antibodies can cause a cerebellar syndrome, it would not result in the MRI changes. Carbon monoxide poisoning, whilst it may lead to similar MRI changes (high signal on T2 generally confined to the globus pallidus), does not correlate with the patient’s clinical presentation.

CSF examination would therefore be the diagnostic test of choice, since an elevated 14-3-3 protein level carries a sensitivity of 85-95% and when combined with an elevated s100b, the sensitivity is over 90%.

REFERENCES


ACKNOWLEDGEMENTS / CONSENT (if applicable)

YOUR NAME, POSITION, ORGANISATION
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QUESTION 4

A 32 year old woman presented to the ED with her first ever generalised tonic clonic seizure. She was 36 weeks into her first pregnancy. Other than a single episode of proteinuria, at 32 weeks, she has been well through pregnancy. She had received treatment for arthritis in the past but was not currently on any medication.

Examination: she was confused and disoriented (GCS 14), with a mild right hemiparesis and bilateral optic disc swelling. BP 146/82, urine dipstick clear.

Her CT head (non-contrast) is below.

What is the most appropriate treatment?

ANSWERS

A Immediate delivery via C section
B Intravenous aciclovir
C Intravenous magnesium
D Intravenous Methylprednisolone
E Low molecular weight heparin

SUGGESTED ANSWER

E
EXPLANATION / COMMENTS
There are many conditions that might cause the clinical picture (see Phil Smith’s excellent discussion in a CPC from 10 years ago in Practical neurology), but cerebral venous sinus thrombosis must be top of the list, as there is an increased risk in the last trimester and postpartum period. The symptoms are notoriously variable, ranging from nothing to death. In this case, the CT shows the so called “empty delta” sign and early infarction within the left hemisphere, but where available, MR imaging is now the preferred diagnostic method (the Lancet neurology review made no mention of CT!). Treatment in the first instance is anticoagulation with low molecular weight heparin, reserving more aggressive/invasive therapies (e.g. local intravenous thrombolysis or thrombectomy) for deteriorating clinical scenarios despite treatment.

REFERENCES


ACKNOWLEDGEMENTS / CONSENT (if applicable)
YOUR NAME, POSITION, ORGANISATION
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QUESTION 5

A 34 year-old female presented with a short history of recurrent sudden weakness affecting the arms and legs. This occurred several times per week, usually after exertion. They were not associated with disturbance of consciousness or incontinence, and the weakness typically lasted for one hour before complete resolution. She was normal between episodes, apart from intermittent involuntary cramp affecting her fingers. Her mother was said to have had similar symptoms which were felt to be “hysterical”.

Blood tests taken by her GP were normal (including FBC, sodium, potassium and liver function). MR whole spine/brain was normal.

What is the most likely diagnosis?

ANSWERS

A Acute porphyria
B Anterior spinal artery TIAs
C Functional/psychogenic “drop attacks”
D Hyperkalaemic periodic paralysis
E Hypokalaemic periodic paralysis

SUGGESTED ANSWER

D
Clearly it would have been important to establish in the history whether the blood tests were done during an attack or not, but given that they were part of the GP routine visit, it is unlikely that this coincided with an attack. Spinal TIAs are rare, and the episodes are far too frequent, in the wrong sort of patient, to allow this diagnosis. Functional drop attacks are common, but this is not the description here, and the symptoms are very specific, and unusual for functional symptoms. AIP does not cause these sort of brief recurrent attacks.

Having narrowed down the most likely differential to a channelopathy, the clue is in the history. Positive family history, episodes occurring during the day after exercise, and associated myotonia should allow the candidate to differentiate hyper- from hypokalaemic periodic paralysis. Th references below include helpful tables detailing the differences between hypo- and hyperkalaemic paralyses.

**REFERENCES**


**ACKNOWLEDGEMENTS / CONSENT** (if applicable)

**YOUR NAME, POSITION, ORGANISATION**

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QUESTION 6

A 21 year old man presented with events arising during sleep, which had concerned his new partner. She reported that he would sit up, appear frightened, and sometimes his legs would kick out briefly. This happened about once per week. They would usually last for less than a minute. Sometimes he would have more than one episode a night; on one occasion he had 4. Usually they would occur soon after he had fallen asleep, and once it had happened after he had fallen asleep on the couch in the afternoon. He had never bitten his tongue or been incontinent.

He had little recollection of most of the episodes, although on one or two occasions remembered waking up feeling afraid and aware but unable to respond normally, and feeling as if he was choking.

He had a history of sleep-related events going back to childhood. Since early childhood he would talk in his sleep. From his early teenage years he would have frequent awakenings from sleep, sometimes with the unpleasant fearful ‘choking’ sensation; at other times he would awaken standing by the side of his bed. He had never sought medical attention for these, and he and his family had thought they were nightmares. The episodes had become less frequent as he had got older, and he had thought they had largely stopped until he had recently moved in with his partner.

He was generally well with no other medical history. On direct questioning he reported being a generally quite ‘sleepy’ person who would often fall asleep when relaxing or watching television. He scored 11 on the Epworth sleepiness scale. His partner said he snored when lying on his back but not loudly and she had not noticed him stop breathing. He was taking no medication. His father had a history of sleepwalking in childhood.

Neurological examination was normal. He was overweight with a BMI of 31. He had prominent tonsils but examination of the pharynx was otherwise unremarkable.

What is the most likely diagnosis?

ANSWERS

A Nocturnal frontal lobe epilepsy
B Obstructive sleep apnoea
C REM behaviour disorder
D Restless legs syndrome
E Sleep terrors/ sleepwalking

SUGGESTED ANSWER

A
The diagnosis of nocturnal events can be difficult, particularly as a clear description may be lacking. Often the most important consideration is whether the patient may be having epileptic seizures. While nocturnal tonic-clonic seizures are usually straightforward to diagnose (with a witness account), partial seizures can be much more difficult. In particular frontal lobe seizures, which have a propensity to arise from sleep, are associated with a variety of behaviours that can easily be confused with non-epileptic events, particularly NREM arousal parasomnias (such as sleepwalking and night terrors). In a proportion of patients with frontal lobe epilepsy, most or all seizures occur from sleep; if at least 90% of attacks occur from sleep the term nocturnal frontal lobe epilepsy (NFLE) is used.

Several key features in the history can be useful in this setting. Multiple events per night, clear recollection of some or all events, a subjective feeling of choking, and events very early in the sleep cycle (including during daytime naps) or just before the usual time of waking, are strongly suggestive of NFLE, as are clear descriptions of dystonic posturing.

Single events per night, with no recall (or only very vague dream-like recollections), extensive wandering out of the bedroom, apparent purposeful behaviours (such as eating or dressing), and with onset 1-2 hours after sleep onset, are much more suggestive of NREM arousal parasomnias.

Many individual behaviours such as sitting up, shouting (including coherent words), screaming and walking or running, are non-discriminatory and may occur in either condition. Likewise, some other clinical features including a family history, onset in childhood, and a reduction in severity with increasing age are common in both conditions.

In this patient, the multiple events, lucid recollection of some episodes with a ‘choking’ sensation, and their brief, stereotyped nature is highly suspicious for NFLE.

<table>
<thead>
<tr>
<th>Parasomnia (NREM arousal disorders e.g. sleepwalking, sleep terrors)</th>
<th>NFLE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at onset</strong></td>
<td>Usually &lt; 10 years</td>
</tr>
<tr>
<td>Positive family history</td>
<td>60-90%</td>
</tr>
<tr>
<td>Attacks per night (mean)</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Episode frequency/ month</td>
<td>&lt;1 to 4</td>
</tr>
<tr>
<td>Clinical course (over years)</td>
<td>Tends to disappear by adolescence</td>
</tr>
<tr>
<td>Disease duration (mean)</td>
<td>Approx 7 years</td>
</tr>
<tr>
<td>Episode duration</td>
<td>Seconds to 30 minutes</td>
</tr>
<tr>
<td>Semiology of movements</td>
<td>Variable complexity; not highly stereotyped (on video)</td>
</tr>
<tr>
<td>------------------------</td>
<td>--------------------------------------------------------</td>
</tr>
<tr>
<td>Trigger factors</td>
<td>Sleep deprivation, febrile illness, alcohol, stress</td>
</tr>
<tr>
<td>Associated conditions</td>
<td>Obstructive sleep apnoea</td>
</tr>
<tr>
<td>Ictal EEG</td>
<td>Slow waves, no epileptiform features</td>
</tr>
<tr>
<td>Time of episodes during sleep</td>
<td>First third of night, but usually after 90 minutes of sleep</td>
</tr>
<tr>
<td>PSG sleep stages when events occur</td>
<td>NREM stage 3 or 4</td>
</tr>
</tbody>
</table>

**REFERENCES**


**ACKNOWLEDGEMENTS / CONSENT** (if applicable)

**YOUR NAME, POSITION, ORGANISATION**

Chris Derry, Consultant Neurologist, DCN, Edinburgh

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**QUESTION 7**

A 48 year old retired accountant with established motor neurone disease (amyotrophic lateral sclerosis subtype) was referred because of possible cognitive impairment - possibly an early frontotemporal dementia - though he had previously resisted formal assessment. He used an electric wheelchair because of marked leg weakness. He lived alone with daily input of carers, but attended with his sister who knew him well.

In the last year he had experienced increasing dysphagia and weight loss, thought to be due to MND. A gastrostomy feeding tube had been discussed with him.

At consultation, he reasserted that he did not want a feeding tube, and that he has always been against “that kind of thing”. His sister questioned his ability to make this decision, indicating that he had never previously made his feelings clear to family on this issue. She also stated that he had been having increasing problems dealing with his financial affairs.

The waiting list for formal neuropsychology assessment is several months.

Which features should be considered in making the best possible assessment of his capacity?

<table>
<thead>
<tr>
<th>ANSWERS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong>: Ability to come to a decision in keeping with the opinions of a group of similarly placed peers.</td>
</tr>
<tr>
<td><strong>B</strong>: Ability to come to a decision which is in keeping both with the opinions of a group of similarly placed peers, and with current medical best evidence as understood by the patient.</td>
</tr>
<tr>
<td><strong>C</strong>: Ability to understand, retain and weigh in the balance information, and communicate decisions regarding a range of issues judged to be of a similar complexity.</td>
</tr>
<tr>
<td><strong>D</strong>: Ability to understand, retain and weigh in the balance information, and communicate decisions relating only to the decision in hand.</td>
</tr>
<tr>
<td><strong>E</strong>: Addenbrooke’s Cognitive Examination (ACE-R) score, and formal assessment for diagnosis of fronto-temporal dementia.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SUGGESTED ANSWER</th>
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<tr>
<td>D</td>
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</table>
EXPLANATION / COMMENTS

I suggest that “best” assessment of capacity in this context describes assessment in line with current laws and professional guidance governing doctors practising in the UK.

In the UK, judgements of a patient’s capacity are discussed by the Adults with Incapacity (Scotland) Act 2000 and the Mental Capacity Act 2005 (for England and Wales). They are also outlined by Good Medical Practice guidance issued by the General Medical Council. Judgements of this type may be important in a range of clinical situations.

Capacity is specific to the decision in hand, and may vary in regards to different decisions (particularly those of varying complexity). Capacity may also fluctuate over time, and any impairment may be temporary or permanent. Capacity can be optimised by careful attention to communication, and allowance of appropriate time. A formal diagnosis of dementia, or other disorder associated with cognitive problems, does not eliminate the need for a capacity assessment.

Formal definitions of capacity are outlined in the statutes, and General Medical Council (GMC) guidance, referred to below. To hold capacity the patient requires to be able to understand, retain and weigh up information, and to communicate their wishes.

Appropriateness or wisdom of the patient’s decision (in the opinion of the medical team or of others) is not a requirement for capacity. The process of decision making rather than the endpoint is of particular interest. Although several aids for capacity assessment exist (including the ACE – “Aid to Capacity Evaluation” rather than Addenbrookes Cognitive Examination – Sessums et al 2011) these are not intended to replace clinical judgement and should not be used in isolation. There is no gold standard test.

The GMC recommends that if an assessment leaves you in doubt about the patient’s capacity, it may be helpful to seek advice from nursing staff closely involved with the patient, or relevant colleagues including psychiatry, psychology or speech and language specialists. Disagreements among the healthcare team, or between the team and others involved, may be resolved by involving an independent advocate, consulting a more experienced colleague, using local mediation services, or holding a case conference. In particularly difficult cases recourse to legal advice may be required.

REFERENCES

General Medical Council guidance information includes:
http://www.gmc.uk.org/guidance/ethical_guidance/consent_guidance_maximising_patients_ability_to_make_decisions.asp

Adults with Incapacity (Scotland) Act 2000 information includes:
http://www.scotland.gov.uk/Publications/2008/03/25120154/1

Mental Capacity Act 2005 information includes:
http://www.direct.gov.uk/en/governmentcitizensandrights/mentalcapacityandthelaw/makingdecisionsforsomeoneelse/dg_186479

Other references:

ACKNOWLEDGEMENTS / CONSENT (if applicable)
<table>
<thead>
<tr>
<th><strong>YOUR NAME, POSITION, ORGANISATION</strong></th>
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</thead>
<tbody>
<tr>
<td>Peter Foley, Neurology Registrar, NHS Lothian</td>
</tr>
<tr>
<td>Simon Kerrigan, Solicitor and Neurology Registrar, NHS Lothian</td>
</tr>
</tbody>
</table>

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<tr>
<th><strong>CONTACT EMAIL</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><a href="mailto:peterfoley@nhs.net">peterfoley@nhs.net</a></td>
</tr>
</tbody>
</table>
**QUESTION 8**

A 66-year-old woman presented with reduced vision in the right eye. Her vision had deteriorated to almost complete blindness over six weeks. After assessment by the ophthalmologists, a central retinal vein occlusion was diagnosed and she was started on aspirin. Since then she noted increasing imbalance, with several falls. She reported a right sided headache and her arms were clumsy. There were no bulbar or cognitive symptoms, and no previous neurological symptoms.

Two years previously a pleural effusion had been identified; aspiration revealed malignant cells and subsequent investigations revealed bony metastases and a breast lump on mammography. She had received letrozole, and remained well until one year ago when her disease progressed. This had responded to single agent epirubicin. Her most recent investigations (three months previously) had shown stable disease.

On examination she was in a wheelchair. Her gait was shuffling, narrow-based and unsteady with impaired postural stability. Her speech was normal. She had unequal pupils with the right larger than the left. The right consensual pupillary reflex was normal, but the direct response absent. The right optic nerve was swollen and pale. The left disc was slightly swollen medially. There were no dilated vessels or retinal haemorrhages. Cranial nerves were otherwise normal. She had a coarse postural tremor and some finger-nose ataxia affecting the right arm. She had normal power, brisk reflexes and flexor plantars. Sensation was intact.

An MRI head scan showed subcortical white matter changes in the frontal and parietal lobes consistent with small vessel disease, but also periventricular white matter lesions more suggestive of demyelination. All ventricles were dilated with periventricular lucencies. There were patchy areas of abnormal meningeal enhancement within the post-contrast images but no brain metastases.

A lumbar puncture was acellular and CSF cytology negative. CSF protein was raised at 1.3 g/l and CSF glucose was 2.6 mmol/l (plasma glucose 5.8 mmol/l). Oligoclonal bands were negative. A CT scan of her chest, abdomen and pelvis indicated no change in her metastatic disease. A transthoracic echocardiogram was normal.

Which next investigation is most likely to provide a diagnosis?

**ANSWER S**

A Anti-neuronal antibodies  
B Bronchoscopy with washings for TB culture  
C Repeat CSF analysis  
D Transoesophageal echocardiography  
E Visual evoked responses

**SUGGESTED ANSWER**

C
Although the MRI scan is suggestive of demyelinating disease, the subacute onset of visual loss without recovery and the absence of oligoclonal bands in the CSF would argue against this. The high CSF protein and low CSF glucose are non-specific but are more typical of a malignant or infectious process than an inflammatory CNS disorder. Her age and the absence of a previous neurological history would be against MS. The appearance of the discs and the meningeal enhancement seen on the MRI scan is more typical of malignant meningitis. The gait disturbance was apraxic rather than ataxic due to communicating hydrocephalus.

Malignant meningitis (MM) is rare in comparison to brain and spinal cord metastases but increasing in incidence as the survival from solid tumours continues to increase. The commonest associated cancers are breast, SCLC, lymphoma and melanoma. MM presents with a multitude of symptoms and signs reflecting the potential for multifocal distribution of tumour cells. These include cranial neuropathies particularly second, sixth and eighth cranial nerve palsies, multiple radiculopathies, patchy sensory loss (beware the ‘numb chin’), raised intracranial pressure symptoms and meningism. The diagnosis should be suspected if there is clinical involvement of more than one anatomical area or cranial nerve/root lesions in the absence of any obvious mass on standard imaging, particularly in a patient with a previous history of metastatic cancer. Cytological examination of the CSF is the most valuable diagnostic test but only 50% of patients with MM will have malignant cells in their first LP. A minimum of 10 ml should be collected and immediately taken to the laboratory to minimise the time for autolysis of malignant cells to occur. At least three samples should be taken if necessary to increase sensitivity. Other characteristic abnormalities, in the absence of malignant cells, include a raised opening pressure, raised CSF white cell count and protein concentration, and reduced glucose concentration. Imaging is helpful and is useful to exclude intraparenchymal mass lesions. Gadolinium enhanced MRI is the preferred imaging modality and may show nodular or linear ‘tramline’ meningeal enhancement in the basal cisterns, around the brainstem or along the spinal cord. However the false negative rate is still about 30% when compared to CSF cytology. Treatment is dependent on the clinical presentation and status of the patient. As a general rule, focal radiotherapy is used in patients with bulky nodular disease, whole brain radiotherapy for diffuse brain disease and intrathecal chemotherapy reserved for high performance patients to treat the entire subarachnoid space.

In this patient’s case, a second lumbar puncture showed malignant cells typical of metastatic breast cancer and the patient was treated with intraventricular chemotherapy via an Ommaya reservoir, given the diffuse nature of her disease and her reasonably performance status. Unfortunately she didn’t improve on this and died four months later.

REFERENCES


ACKNOWLEDGEMENTS / CONSENT (if applicable)

YOUR NAME, POSITION, ORGANISATION
Dr J H Rees, Consultant Neurologist, National Hospital for Neurology and Neurosurgery. Queen Square

CONTACT EMAIL
A 70 year old man presented with speech problems; investigations confirmed the cause of this was an ischaemic left hemisphere stroke. His speech was difficult to understand with multiple phonemic errors affecting almost every word; his speech sounds were distorted and jumbled up (incorrectly ordered). His writing, by contrast, was much better preserved. Comprehension was normal. The most likely clinical syndrome is:

**ANSWERS**
A Broca’s aphasia  
B Bulbar dysarthria  
C Global aphasia  
D Speech apraxia  
E Wernicke’s aphasia

**SUGGESTED ANSWER**
D

**EXPLANATION / COMMENTS**
Aphasia is a central language disorder, meaning that more than one modality of language reception or production is affected. E.g.: if patients have a problem with speech output, this is usually mirrored in their written output. However, patients can present with very disordered speech output without having aphasia, rather there is a problem with the speech output machinery. At the 'lowest' level this could be due to a dysphonia or a dysarthria but at a 'higher' level this can be due to speech apraxia.

Speech apraxia (also known as Apraxia of Speech - AOS) has been variously defined but is perhaps best thought of as a disorder affecting the motor programming system for speech production. Individuals with AOS demonstrate difficulty in speech production specifically with the sequencing and forming of sounds. Clinically, in cases of pure speech apraxia, written output should be normal or at least markedly better than speech output, thus differentiating it from aphasia.

That said, aphasia and AOS can co-occur, but even in this scenario, AOS can be confidently diagnosed (Ogar et al. 2005). AOS is often the presenting symptom of primary progressive aphasia and cortico basal degeneration.

Anatomical localization of the lesion responsible is controversial. An influential article in 1996 placed it in the left anterior insula (Dronkers 1996 - see below). This has since been questioned and other lesion sites have been proposed (superior longitudinal fasciculus, cerebellar connections).
REFERENCES


ACKNOWLEDGEMENTS / CONSENT (if applicable)

YOUR NAME, POSITION, ORGANISATION
Alex Leff

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QUESTION 10
A 67 year old retired sales representative gave a 4 year history of bilateral arm pain and parasthesiae, with a 3 month history of left sided foot drop. She had previously been well apart from blackouts and palpitations two years previously; these had been investigated, no cause had been identified, and they had resolved spontaneously. She was on no medication. There was no family history of neurological disease.

Examination revealed wasting of both quadriceps and the first dorsal interrossei bilaterally. She was areflexic with a stocking sensory loss.

Nerve conduction studies showed absent sural sensory action potentials and small leg motor action potentials. Conduction velocities were normal.

Investigations included normal FBC, ESR and ANCA, Glucose and electrolytes, Chest X ray, B12, Bence Jones protein and serum protein electrophoresis.

Her CSF contained 0.66 g/l of protein and no cells. Oligoclonal bands were negative.

Which of the following tests would be most helpful?

ANSWERS

A. Abdominal fat biopsy
B. Bone marrow
C. Kappa Lambda ratio
D. Serum free light chains
E. Sural nerve biopsy

SUGGESTED ANSWER

D
EXPLANATION / COMMENTS
There are a number of possible answers to this question each with their own advantages and depending a little on local expertise.

She has a mixed motor sensory axonal neuropathy which has been present for a few years but with a recent subacute motor deterioration. This would be unusual for a genetic neuropathy especially with the positive sensory symptoms. There is a suggestion of possible autonomic involvement from the cardiac history. The differential would be between a peripheral nerve vasculitis and amyloid. A paraneoplastic neuropathy would be unusual with the long history.

A normal Bence Jones protein and normal protein electrophoresis does not exclude AL amyloid. Immunoelectrophoresis is better but still misses many cases of AL amyloid especially if excess of a single light chain is being produced. Detection of free light chains picks up 86% of patients with amyloid negative on immunoelectrophoresis. The combination of immunofixation in serum and urine with measurement of serum free light chains appears to give a sensitivity of 96% and is probably the best answer.

A bone marrow may show plasma cells but these may be a relatively low frequency and this test frequently fails to detect those patients that have peripheral nerve amyloid.

The gold standard test for amyloid is a peripheral nerve biopsy but detection of amyloid requires diligent examination of perfectly processed and preserved biopsy specimens often supplemented with electron microscopy. Such a peripheral nerve histology service is rare. In addition nerve biopsy is associated with significant local discomfort and morbidity.

Abdominal fat biopsy can also be used for detection of amyloid and has the advantage of low morbidity. Sensitivity of 86% is claimed but some recent reports give values as low as 19% in practice. Such biopsies are of course easily repeated and if positive are highly specific.

Reference


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