SUGGESTED ANSWER 1

B

EXPLANATION / COMMENTS

The symptoms are typical of ciguatera poisoning, resulting from ingestion of ciguatoxin in a contaminated reef predator fish. These fish concentrate ciguatoxin by consuming smaller reef fish, which in turn feed on toxic dinoflagellates (e.g. Gambierdiscus toxicus), which are bottom dwelling micro-organisms. Ciguatoxin is a family of potent lipophilic sodium channel activator toxins.

The patient had eaten tuna and red snapper which are potentially ciguatoxic fish. He displayed the characteristic temporal pattern of abdominal then neurological symptoms. The latter usually develop within 3 days of ingestion of the ciguatoxic fish and include reversal of thermal sensation (paradoxical dysaesthesias), which are considered to be virtually pathognomonic of the condition. In addition he had increased nociperception, even small changes of temperature provoking pain. The diagnosis is made on the history and there is no diagnostic test for this condition.

REFERENCES


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SUGGESTED ANSWER 2

A

EXPLANATION / COMMENTS

This lady presented in her teenage years with a bradykinetic parkinsonian syndrome accompanied by a change in mood and evidence of fronto-striatal cognitive dysfunction. Her family history is relevant in that both her father and paternal grandmother died at a relatively young age from progressive neurological problems with predominant psychiatric symptoms and dementia respectively, thus implying that this condition is dominantly inherited. Consequently Huntington’s disease is the most likely diagnosis.

If Huntington’s disease presents early in life below the age of 20 then it is said to have a juvenile onset and is characterised predominantly by a bradykinetic parkinsonian phenotype as opposed to the more typical adult presentation where chorea is the dominant movement disorder. The cognitive deficits are often targeted to the fronto-striatal network and volatile mood disturbance is a common presenting feature with behavioural problems being a dominant aspect of juvenile Huntington’s disease.

This case is unlikely to be Niemann-Pick type C because of the autosomal dominant inheritance pattern and the fact that the eye movements are abnormal in all directions rather than just a vertical gaze palsy. In addition the clinical phenotype and family history are slightly against a diagnosis of NBIA, which, like NPC, is inherited in an autosomal recessive pattern and tends to present with additional features such as spasticity, ataxia and bulbar symptoms. SLE is a distinct possibility if this were a sporadic case but given the family history this seems very unlikely. Similarly neuroacanthocytosis can present with a movement disorder and cognitive dysfunction but there was no evidence of a peripheral neuropathy or seizures which often accompany this condition and again the family history makes this unlikely.

REFERENCES


ACKNOWLEDGEMENTS

I would like to thank Alasdair Coles, Stephen Sawcer and Caroline Williams-Gray for their useful comments on this case.

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EXPLANATION / COMMENTS
Musical hallucinations are a disorder of complex sound processing in which the perception is formed by instrumental music, sounds or songs. They are less common than unformed acoustic hallucinations such as tinnitus. Typically, there is insight for the nature of the hallucination. Fukunishi et al. reported musical hallucinations in 0.16% of a large sample in a general hospital setting. However, in a sample of elderly subjects with audiological complaints, the prevalence of musical hallucinations was 2.5%.

Moderate or severe acquired hearing loss or deafness is broadly acknowledged to be the main aetiological factor; 61% of the case reports reviewed in by Evers and Ellger had a history of hearing impairment or deafness. This fact supports the hypothesis that a possible mechanism for hallucinations is perceptual release. According to this theory, a sustained level of sensory input is necessary to inhibit the unwanted emergence of memory traces to consciousness. Musical hallucinations can therefore be compared with visual hallucinations caused by focal lesions leading to visual deafferentation (Charles-Bonnet syndrome). However, the phenomenon of musical hallucinations remains a heterogeneous group with respect to clinical characteristics and aetiology as psychiatric disorders, epilepsy, focal brain lesions and intoxication have all been reported to induce musical hallucinations.

REFERENCES


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SUGGESTED ANSWER 4

D

EXPLANATION / COMMENTS
This description would fit best with the syndrome of paroxysmal dystonic choreoathetosis, often inherited as an autosomal dominant condition. Attacks may be triggered by caffeine or alcohol and may respond to clonazepam although conventional antiepileptic drugs are often unsuccessful. PKC is usually associated with more brief attacks (less than 5 minutes) typically triggered by sudden movement or startle, and usually respond to carbamazepine. Demyelination is usually associated with neurological signs. Familial frontal lobe seizures are usually brief and typically occur during sleep; they are likely to be associated with loss of consciousness and/or followed by a period of post-ictal confusion. Dopa-responsive dystonia may be paroxysmal and familial but typically affects both legs.

REFERENCES


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SUGGESTED ANSWER 5

B

EXPLANATION / COMMENTS

In handling this real case, there is great potential for spinning out of diagnostic control down the infectious disease pathway. A key observation is that the patient is so well, despite five weeks of illness and widespread radiological abnormalities: this effectively excludes malaria, TB and typhoid.

The “typhoid blood test” is probably the Widal test, about one hundred years old now, which detects antibodies to the flagellar (H) and somatic (O) antigens in typhoid and paratyphoid organisms. Patients with previous exposure, or immunisation, may well give a false positive result. Typhoid fever can cause headaches which persist for four weeks or so, but the patient would be very unwell with fever, continued diarrhoea or constipation, anorexia, myalgia and the famous “Rose spots” rash. CSF contents would be normal.

Cerebral malaria may cause headache and have normal CSF contents (although the CSF pressure is usually high). But this is a devastating illness, which would have caused encephalopathy, seizures, coma and death by now if untreated. Meningeal enhancement is not usual.

People with tuberculosis meningitis are usually very unwell and, characteristically, have abnormal CSF constituents (and increased SCF pressure). Occasionally, the CSF may be nearly normal in people with concomitant HIV infection (Laguna F.AIDS 1992;6:1165). In such cases, a meningeal biopsy may be needed to make the diagnosis.

Sarcoidosis is possible, although the history is quite short for that diagnosis. It would certainly be reasonable, if nothing turned up on a diagnostic scout-around, to consider a meningeal biopsy.

In fact, none of these are correct and the patient can be saved from a meningeal biopsy.

The critical symptom is orthostatic headache: headache worse on sitting up or standing. This is a cardinal feature of the low CSF pressure syndrome, which would not occur with any of the above illnesses. Her other symptoms are usual with this syndrome. When the SHO was interrogated about the CSF pressure, he remembered it was 4cm H20. The radiological abnormalities described are characteristic, as is some degree of cerebellar tonsilar herniation, which was noted on review of the MRI. In this context, the likely cause is a spontaneous CSF leak, which most commonly comes from the cervical or thoracic cord meninges. Identifying the leak is often very difficult. Luckily, it is usually not necessary. A useful diagnostic test and therapy is an autologous epidural blood patch; resolution of the postural headache within
seven days (as was the case with this patient) makes the diagnosis. Recurrence is possible.

Unfortunately, there are many examples of people with this syndrome undergoing meningeal biopsies before the penny dropped.

REFERENCES


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SUGGESTED ANSWER 6

D

EXPLANATION / COMMENTS

Serum ammonia was elevated at 327μmol/L (normal range 10-35 μmol/L), confirming hyperammonaemic encephalopathy. Haemodialysis was commenced with a dramatic improvement in her conscious level, and she was discharged well 48 hours later.

Hyperammonaemic encephalopathy is a recognised but rare complication following ureterosigmoidostomy (1-3). Following this procedure, urine is drained into the sigmoid colon and then excreted at defecation. Increased production of ammonia occurs in the colon due to ureolysis due to urea splitting bacteria (e.g. Proteus mirabilis), and ammonia is subsequently rapidly absorbed via the permeable colonic mucosa. Ammonia is metabolized by the hepatic urea cycle, but this may be overwhelmed and coma ensues, akin to hepatic encephalopathy. The risk of hyperammonaemia is increased by constipation leading to prolonged colonic absorption of ammonia, and while coma can ensue in the presence of normal liver function (as in our patient), hepatic dysfunction may further increase the risk of the development of coma. Hyperammonaemic coma has also been reported in patients with an ileal conduit (4) but appears to be more common following ureterosigmoidostomy. This increased risk with ureterosigmoidostomy is presumably due to the longer segment of bowel mucosa exposed to urine.

In addition to supportive measures the treatment of hyperammonaemic coma should include removal of ammonia from the plasma by haemodialysis, reduction in ammonia production by colonic washout and broad spectrum antibiotics, and measures to prevent recurrence in the future.

REFERENCES

ACKNOWLEDGEMENTS

Case reported fully in: Mark PB et al, Scottish Medical Journal, 2006, 51 (3):50

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SUGGESTED ANSWER 7
D

EXPLANATION / COMMENTS

These case histories illustrate the critical differences in clinical presentation between disorders of glycogen (Gary) and fatty acid (Freddy) metabolism. During early (and particularly during intense) exercise, muscle is dependent upon the anaerobic breakdown of muscle-stored glycogen for ATP generation. During sustained exercise ATP generation is predominantly from the beta-oxidation of circulating free fatty acids.

McArdle’s disease is an autosomal recessive disorder in which there is deficiency of myophosphorylase, the enzyme required to cleave glucose molecules from stored glycogen. There is thus an absence of substrate for glycolysis. During early/intense exercise (cycling up a hill) there is failure of energy (ATP) generation which causes myalgia, weakness and muscle contracture. If severe, rhabdomyolysis leads to myoglobinuria (accompanied by a massive rise in serum creatine kinase) and the threat of acute tubular necrosis. Typically, onset is in childhood with exercise-intolerance, but its significance is often missed by patients and physicians and the diagnosis is frequently not made until adulthood, often after an episode of myoglobinuria. Most patients, even when at rest and asymptomatic, have modest elevation of serum creatine kinase. The prevalence is estimated to be 1:100,000, suggesting that many cases are undiagnosed. Diagnosis is by histochemical demonstration on a muscle biopsy specimen of deficiency of the enzyme. The biopsy also shows glycogen accumulation.

Gary clearly noted the second-wind phenomenon – if a lower intensity of exercise is maintained, symptoms ease as circulating fatty acids, and to a lesser extent glucose, become available for energy generation.

Debranching enzyme deficiency may cause a proximal myopathy but exercise-intolerance is usually a relatively minor feature. Phosphofructokinase deficiency shows many similarities to McArdle’s disease but is vanishingly rare – it is also associated with evidence of red cell haemolysis.

Carnitine palmitoyltransferase (CPT) deficiency is also an autosomal recessive disorder and is the commonest disorder of fatty acid metabolism presenting with a myopathy. Like McArdle’s disease it is probably under-diagnosed. Symptoms (myalgia, rhabdomyolysis) develop during sustained exercise, as fatty acid metabolism (β-oxidation) becomes the major source of ATP generation. CPT is required for transporting fatty acids into muscle. The consequences of rhabdomyolysis are as for McArdle’s disease. Symptoms are particularly likely to develop if sustained exercise is combined with fasting, as in Freddy’s case. Between attacks, patients are usually asymptomatic and their serum creatine kinase is normal, unlike McArdle’s disease. Also, muscle biopsy between attacks is usually normal. The diagnosis is often strongly
suggested by a particular acylcarnitine profile shown by tandem mass spectrometry performed on a blood sample after an overnight fast. Confirmation is by enzyme studies on cultured fibroblasts.

Other disorders of fatty acid metabolism/β-oxidation can present in similar fashion, for example very-long-chain acyl-CoA dehydrogenase deficiency.

REFERENCES

The Metabolic Myopathies
Moxley RT, Chinnery P, Turnbull D.
In: Disorders of Voluntary Muscle, 7th ed.
Eds: Karpati G, Hilton-Jones D, Griggs R

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SUGGESTED ANSWER 8

C

EXPLANATION / COMMENTS

The clinical history suggested left-sided lateral medullary syndrome caused by vertebral artery dissection. The distribution of his severe headache (occipital and retro-orbital) was characteristic, supported by signs of Horner’s syndrome, partial VIth and palatal palsy, ataxia and crossed spinothalmic sensory loss.

The T2 weighted axial MRI scan shows subtly increased signal in the left dorsal medulla. The MR angiogram shows reduced flow and narrowing of the left vertebral artery.

Acute management consisted of intravenous heparin, due to the risk of thrombosis, given the previous history of two deep venous thromboses, with a known history of Factor V Leiden and now with the added risk of immobility in the acute weeks after infarction.

Unfortunately two weeks later his clinical condition deteriorated, with further severe headache, drowsiness and the new sign of a gaze palsy. A CT scan demonstrated acute subarachnoid haemorrhage anterior to the brainstem, as well as blood in the 4th ventricle and lateral ventricle occipital horns. There was also acute communicating hydrocephalus.

Given the nature of the initial presentation it is most likely that the secondary presentation occurred as a consequence of the first. Dissecting aneurysm is a well recognised cause of subarachnoid haemorrhage. A dissection represents the extension of arterial blood into the arterial wall disrupting the intima or media. Once subintimal haemorrhage occurs, blood can dissect through the media, or along the subadventitial plane. Subintimal haemorrhages typically result in luminal narrowing, whereas dissection through the media into the subadventitial plane results in dilatation of the outer wall of the vessel and the subsequent development of a pseudoaneurysm. The media of intracranial arteries is often very thin and intracranial arterial dissection may rupture through the adventitia and cause a subarachnoid haemorrhage.

In this case the further consequential tearing and shearing forces caused formation of a pseudoaneurysm at the proximal end of the basilar artery.

This patient had a further CT angiogram, after a CT scan, which provided the structural evidence for a subarachnoid haemorrhage, a consequence of the left vertebral dissection. It demonstrated filling defects in the distal left vertebral artery and an irregular outline in the basilar artery. There was also a
fusiform pseudoaneurysm of the proximal basilar artery, which had a bleb on its lateral wall.

It seems unlikely that anticoagulation played a major role in the mechanism of this secondary presentation, although it may have made the outcome of aneurysmal rupture worse. The risks of omitting anticoagulation in the face of his previous history and factor V Leiden could have been fatal.

REFERENCES


ACKNOWLEDGEMENTS

I would like to thank Dr Shawn Halpin, Dr Tom Hughes and Dr Phil Smith for their comments in the preparation of this case.

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SUGGESTED ANSWER 9

C

EXPLANATION / COMMENTS

Most cases of chronic nitrous oxide have been reported in anaesthetists or dental surgeons (first series written up in 1978) although it is also reported in young adults in the USA who get hold of it though the cannisters used in cream whipping machines.

Nitrous oxide inactivates vitamin B12 by oxidising irreversibly the Cobalt at its heart from 1+ to 3+.

The presentation is essentially one of subacute combined degeneration of the cord. Roughly one half of the original case series had Lhermitte's phenomenon.

I have not put in the question the B12 level of 125 ng/L (160-800) or homocysteine level of 25 umol/L (5-15), because I thought this would make it too obvious that the problem was related to B12-deficiency. In our case, basic nerve conduction studies were normal as were SSEPs, although most in the literature had some deficit in at least one of these.

The answer is not ‘B’ because Pernicious Anaemia does not affect this age group.

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SUGGESTED ANSWER 10

E

EXPLANATION / COMMENTS

From the history, this woman had no muscle symptoms until she was aged 20. She then developed pain and swelling in first one and then the other posterior calf muscles. She has now become weak in predominantly her distal leg and proximal arm muscles.

This story and pattern of weakness is characteristic of a form of muscular dystrophy associated with a deficiency of the muscle cell protein dysferlin. This is an autosomal recessive condition also classified as one of the limb girdle muscular dystrophies. This is potentially confusing as the pattern of weakness may be exclusively distal, particularly in the early stages when it is termed Miyoshi myopathy, although often the weakness later becomes proximal too (1). Dysferlinopathy is one of the more common limb girdle muscular dystrophies in this country and it has become apparent that many cases were previously mistakenly assumed to have an inflammatory myopathy.

Until fairly recently, an inflammatory infiltrate seen in a muscle biopsy sample was thought to be a clear indicator of an inflammatory myopathy, most commonly polymyositis. However, review of case series suggests that polymyositis is a rare condition (2). Many of the previously-diagnosed cases have now been attributed to other conditions, most commonly inclusion body myositis.

Recognition that a condition is not polymyositis despite the inflammatory features on biopsy is important as it prevents the fruitless use of steroid treatment and its associated complications. Apart from inclusion body myositis, there are now several other conditions in which inflammatory cells appear in the biopsy. Dysferlinopathy has been recognised for a few years and there are other rare forms of limb girdle muscular dystrophy which share this feature as does, for example, facioscapulohumeral muscular dystrophy (3). In many cases there may be other abnormalities on the biopsy such as variation in fibre size, increased numbers of central nuclei and so on: these indicate that a dystrophic process is also occurring.

This patient’s muscle weakness will not respond to steroids so there is no indication to either increase the steroid dose or introduce a steroid-sparing agent, ruling out C and D. A steroid myopathy is a theoretical possibility given the duration of steroid treatment but is not really compatible with the pattern of weakness nor at all consistent with the history. Nor will it affect management. This rules out A. Repeating the biopsy to see if the inflammatory process has been suppressed is also a possibility but, again, the history and examination suggest that there is a different diagnosis from the original one and so, even if the inflammatory process continues, would not lead to an increase in the...
steroid dose. In other circumstances such as a clear previous diagnosis of polymyositis or dermatomyositis then B would be a contender.

This leaves E which is the best option at this stage. It is possible that there may be some frozen muscle tissue left in the muscle pathology laboratory and this could be used for immunostaining to detect muscle protein deficiencies. The panel of antibodies used continues to grow and the patterns of staining more complex. However, it should be possible to demonstrate deficiency of dysferlin compared with control specimens; this is highly suggestive of the diagnosis.

REFERENCES


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SUGGESTED ANSWER 11

D

EXPLANATION / COMMENTS

He has HSAN 1 due to a C133W mutation in SPTLC1. The history strongly suggests a hereditary neuropathy because of the slow progression and the suggestion of a neuropathy in the mother. The initial symptom of injuring himself without noticing it combined with the history of neuropathic pain and the finding of an ulcer are typical for HSAN1 due to SPTLC1 mutations. Historically these patients were thought to have a mainly axonal neuropathy with no significant motor involvement but since the gene has been identified it is recognised that there can be significant motor involvement. All UK patients described to date with HSAN1 have the C133W mutation. The UK patients (especially males for unknown reasons) can have motor nerve conduction velocities clearly in the demyelinating range although many patients (especially females) have an axonal neuropathy which is mainly sensory initially. It is also common for the pin prick loss to be much more severe than the vibration loss unlike other forms of CMT. In this patient the severe sensory neuropathy with pain and recurrent injuries in a patient with a suspicion of a hereditary neuropathy makes HSAN1 most likely and the demyelinating nerve conduction velocities would not put one off the diagnosis especially in an English male.

The pain and degree of pin prick loss would be unusual for CMT1 due to the chromosome 17 duplication despite the demyelinating nerve conduction studies.

Similarly although x-linked CMT due to a CX32 mutation could give nerve conduction studies similar to this the pain and degree of sensory involvement would be unusual.

Although CIDP can present with a slowly progressive history the suggestive family history and again the degree of neuropathic pain would be atypical.

CMT complicated by CIDP is a possibility but again this degree of pain would be unusual for CIDP.

REFERENCES


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Summary: 55 year old female with a 5 year history of systemic and neurological symptoms and signs most prominently; papilloedema and raised CSF protein, peripheral neuropathy, splenomegaly, hypothyroidism, sclerodermatous skin changes, renal impairment, slight bone chemistry derangement, B symptoms, raised IgA and mild thrombocytosis.

A number of differential diagnoses were initially considered including a systemic vasculitis, lymphoma, infections including HIV or granulomatous conditions. However it was felt that despite the absence of a monoclonal band a POEMS-like syndrome was the best fit (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy, Skin changes). Bone marrow biopsy demonstrated increased fibrosis, several lymphoid follicles, with morphology showing increased plasma cells with some clustering. Immunophenotyping confirmed clonality consistent with a plasma cell dyscrasia.

The peak incidence of POEMS syndrome is in the 5th-6th decade of life. The neuropathy is usually a symmetrical, distal, motor and sensory demyelinating neuropathy and autonomic involvement said to be rare. The diagnosis of POEMS syndrome requires the presence of the 2 major criteria of polyneuropathy and monoclonal plasma cell-proliferative disorder (thus not necessarily a detectable monoclonal paraprotein band) with at least one or more minor criteria: Sclerotic bone lesions, Castleman disease, Organomegaly (splenomegaly, hepatomegaly, or lymphadenopathy), Edema (edema, pleural effusion, or ascites), Endocrinopathy (adrenal, thyroid, pituitary, gonadal, parathyroid, pancreatic), Skin changes (hyperpigmentation, hypertrichosis, plethora, hemangiomata, white nails) and Papilledema. There are also some known associations including Clubbing, Weight loss, Thrombocytosis, Polycythemia, Hyperhidrosis and other possible associations with, Pulmonary hypertension, Restrictive lung disease, Thrombotic diatheses, Arthralgias, Cardiomyopathy (systolic dysfunction), Fever, Low vitamin B12 and Diarrhoea.

The pathophysiology of POEMS syndrome and the mechanism of some of the manifestations including papilloedema and neuropathy are not clear. It is thought to be a paraneoplastic phenomenon driven by the products of the plasma cell dyscrasia including possibly cytokines (such as TNF and IL6) and growth factors (vascular endothelial growth factor vEGF) as well as the light chains themselves.

REFERENCES

ACKNOWLEDGEMENTS

I would like to thank Dr Jeremy Isaacs for his help in the preparation of this case.

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SUGGESTED ANSWER 13

B

EXPLANATION / COMMENTS

The patient is at very high risk of stroke. ABCD score is a useful way of deciding the urgency of investigation. Age > 60 = 1 point, BP > 140 = 1 point, deficit = unilateral weakness = 2 points, Duration > 1 hour = 2 points, total = 6. In Rothwell’s OXVASC study, all strokes occurred in patients with a score > 3, suggesting this patient has a high early risk of stroke.1

On the risk prediction charts published in the Lancet, for a man of 75 with a cerebral TIA within the past two weeks, his 5 year risk of stroke without surgery is about 45%.2

The Cochrane systematic review of interventional treatment versus surgery for carotid stenosis concluded that there was no clear advantage of stenting over surgery, and that there was therefore no indication for a shift away from carotid endarterectomy as the standard treatment for severe symptomatic stenosis.3 The recent EVA 3S4 and SPACE5 trials, have again failed to provide clear evidence of the superiority of stenting over endarterectomy, in the short term. There is insufficient long-term follow-up data to compare the durability of carotid stenting with the proven long-term benefit of carotid endarterectomy.

Hence stenting is not the preferred option over early endarterectomy. The risks of performing intra-arterial angiography introduces extra delay, and a procedure-related risk of stroke, and hence is not justified, since the results of Doppler and another non-invasive test are concordant.6

There is no evidence to support the use of heparin in this setting (though it is often used!!)

REFERENCES

1. A simple score (ABCD) to identify individuals at high early risk of stroke after transient ischaemic attack Rothwell et al. Lancet 2005; 366: 29-36
2. Treating individuals 3: from subgroups to individuals: general principles and the example of carotid endarterectomy. Lancet 2005; 365; 256-65
5. The SPACE collaborative group; 30 day results form the SPACE trial of stent-protected angioplasty versus endarterectomy in symptomatic patients; a non-inferiority trial. Lancet 2006; 368: 1239–47

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B

EXPLANATION / COMMENTS

This patient has bilateral (peripheral) vestibular failure as suggested by his head movement induced oscillopsia. Unilateral vestibular loss does not generally cause significant head movement induced oscillopsia, at least chronically, due to compensation by central vestibular mechanisms. Vestibular compensation is not possible with bilateral vestibular failure.

This is not benign paroxysmal positional vertigo (BPPV). The duration of vertiginous attacks in this patient are too long. BPPV-associated vertigo lasts 10-20 seconds although patients may report feeling unwell and/or unsteady for several hours afterwards. In this condition, the question to ask is “do you ever get a spinning dizziness when you turn over in bed?” since this will eliminate postural conditions, e.g. postural hypotension. The Hallpike test may confirm BPPV.

Vestibular ocular reflex suppression is abnormal in patients with impaired smooth pursuit function (e.g. cerebellar dysfunction). Importantly, in patients with absent vestibular function, this test will be ‘normal’ since there is no vestibular ocular reflex to suppress. Therefore, before testing vestibular ocular reflex suppression, the examiner must always make sure that the patient does indeed possess a vestibular ocular reflex (see head thrust reference below - Cremer et al., 1998).

Tandem walking may well be impaired in patients with vestibular failure, especially if the vestibular loss is of relatively recent onset. Vestibular loss patients rely upon vision to stabilise their gait and with time, usually develop a normal gait in the light. These patients complain bitterly of an inability to walk in the dark or on uneven ground. In contrast, cerebellar patients’ gait tends to be the same with or without vision.

An MRI will not give the diagnosis although it may show contrast enhancement of the labyrinths in patients in whom there is underlying inflammatory condition, e.g. Cogan’s syndrome.

Idiopathic bilateral vestibular failure is included in the common causes of bilateral vestibular failure with up to 50% in some series. This diagnosis is easily missed since there are often few abnormalities on conventional neurological examination. Eye movements are usually normal except for those tests that specifically test the vestibular ocular reflex such as the head impulse (or head thrust) test. Laboratory confirmation of bilateral vestibular failure is with bithermal caloric irrigation. Other common causes of bilateral vestibular failure include meningitis and ototoxic drugs (gentamicin). Less common causes/associations include: cerebellar degeneration, cranial neuropathies and connective tissue disorders.
The head impulse test is an easy and quick way of assessing the integrity of peripheral vestibular function. The test relies upon the principle that rotating the head towards and within the plane of a functioning semicircular canal will cause activation of the motion detectors in that canal. This head-motion induced canal stimulation generates a signal (the vestibular ocular reflex) to move the eyes rapidly (latency < 10ms) in the opposite direction to head movement. The net result in the healthy state is that the eyes remain fixated on a viewed object despite head movement.

To illustrate the head impulse test, consider the example of testing right horizontal canal function. The examiner asks the patient to fixate on a straight ahead object. The examiner holds the patient's head and rapidly rotates the patient's head horizontally towards the patient's right. The head rotation should be of high acceleration (circa. 2,000 deg/s/s) but of small amplitude (circa. 15 deg). In the normal situation, the vestibular ocular reflex keeps the eyes fixated upon the original target. In a patient with impaired right peripheral labyrinthine function, the eyes get carried with the head when the head is thrust by the examiner and visual fixation of the straight ahead visual target is momentarily lost. The subject makes a re-fixation saccade toward the original target following the head thrust. THIS RE-FIXATION SACCADE IS THE ABNORMAL SIGN THAT THE EXAMINER LOOKS FOR. The examiner should repeat the test a number of times in both directions (right versus left) with the direction and timing of the thrusts randomised. This avoids a potential pitfall in which some subjects make predictive saccades in synchrony with the head thrust, and may thus obscure an abnormal test. Whilst in expert hands individual canals can be tested, in the acute setting, it is sufficient to perform the head thrust test in the horizontal plane. This test is also described in Halmagyi and Curthoys, 1988.

REFERENCES


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A

EXPLANATION / COMMENTS

Foix-Chavany-Marie syndrome is characterised by facioglossopharyngomasticatory weakness with loss of voluntary movements but the preservation of involuntary and emotional movements (Foix and Marie, 1926). Speech may be dysarthric or apraxic but there is typically no aphasia. The most common cause in adults are bilateral strokes that produce lesions in the anterior operculum (Frontera and Palestrant, 2006). These may be sequential and the syndrome only becomes evident following the second stroke which produces bilateral opercular damage. Occasional case reports of subacute and chronic progression have been reported with viral infections including herpes simplex encephalitis (Sasaguri et al., 2002).

A developmental form of the syndrome has been described (Kuzniecky et al., 1993). This is associated with cognitive impairment and epilepsy and is thought to result from neuronal migration disorders producing bilateral abnormalities in the anterior operculum.

REFERENCES


None

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C

EXPLANATION / COMMENTS

This question is designed to highlight the detection of depression in neurological patients and some common misconceptions. Around 30% of all neurological patients have co-morbid major depressive disorder and about 10% of all new neurology outpatients have active suicidal ideation. Depression can respond to treatment regardless of the neurological problem.

These are the DSM-IV criteria for major depression (admittedly not perfect but a reasonable starting point):

Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning:

At least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure (anhedonia).
(1) depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad) or observation made by others (e.g., appears tearful).
(2) markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)
(3) significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day.
(4) insomnia or hypersomnia nearly every day
(5) psychomotor agitation or retardation nearly every day
(6) fatigue or loss of energy nearly every day
(7) feelings of worthlessness or excessive or inappropriate guilt nearly every day
(8) diminished ability to think or concentrate, or indecisiveness, nearly every day
(9) recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

Therefore in this case, you can make a diagnosis of depression based on anhedonia, fatigue, insomnia, poor concentration and suicidal ideation. Despite his back pain and probable functional disorder, depression can still be usefully commented on and potentially treated (although it may require a more circumspect approach in someone hostile to the diagnosis). In patients with a personality disorder, although detection of depression may be harder they’re actually at higher risk of developing it. In patients with neurological disease, it can be harder to decide whether somatic symptoms such as fatigue relate to depression or their physical state. We suggest particular attention is paid to
anhedonia, particularly relating to experiences within their physical capacity, and to cognitive symptoms. Questions about loss of interest in children or grandchildren can be pertinent. In patients who appear unwilling to discuss psychological symptoms asking them whether their symptoms make them feel depressed may be more revealing than asking them if they are depressed.

REFERENCES


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SUGGESTED ANSWER 17

A

EXPLANATION / COMMENTS

The likeliest diagnosis is hypoglycaemia. In favour of this are waking with symptoms each morning and diabetes treated with a long acting agent. The fact that her blood glucose is normal at presentation to the emergency department does not rule out the diagnosis – the sulphonylurea has worn off by this time, as her symptoms resolved. The autonomic features of hypoglycaemia are usually absent. Focal neurological symptoms due to hypoglycaemia are an important, treatable differential diagnosis of stroke.

It would be unusual to have such stereotyped transient ischaemic attacks (though her diabetes, hypertension and age clearly put her at high risk of stroke), and TIAs are not common on waking from sleep. A normal CT scan makes subdural unlikely, and there is no evidence of a brain metastasis to cause a focal seizure.

In this case, after admission early morning blood sugars were very low. Her glimepiride was stopped and she had no recurrence of symptoms.

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SUGGESTED ANSWER 18

E

EXPLANATION / COMMENTS

Although the clinical stroke syndrome is lacunar (face, arm and leg only), his CT brain showed evidence of a dense left middle cerebral artery and some cortical low density. There is no evidence to support the assertion that ‘large vessel’ stroke responds better to intravenous rtPA – in fact in the famous NINDS trial of intravenous rtPA for ischaemic stroke, clinical lacunar strokes did rather better. Whilst we are cautioned about the risk of using rtPA in patient with diabetic retinopathy, the absolute risk of intraocular haemorrhage is probably very small and in this case outweighed by the benefit of treatment. The upper limit of blood pressure for rtPA treatment in the European licence is systolic BP of 185 mmHg and a diastolic BP of 110 mmHg, though whether we could treat patients with a wider range of blood pressures is currently being addressed in the multinational Third International Stroke Trial (IST-3). We have no evidence from randomised controlled trials that the benefits of intravenous heparin outweigh the risks in the early stages of ischaemic stroke in patients with atrial fibrillation.

In summary, this patient should be treated with intravenous rtPA.

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SUGGESTED ANSWER 19

B

EXPLANATION / COMMENTS

The patient had osteomyelitis of the base of skull associated with a chronic otitis externa – so called “Malignant Otitis Externa. The imaging studies (1a &b) show enhancement of the clivus and other bony structures with the suggestion of an abscess in the body of the clivus.

Ultimately Pseudomonas was cultured from operative samples obtained from the base of skull, and from the polyp removed from the left ear shortly before the clinical deterioration. Pseudomonas is the commonest causal organism detected is this condition, which often follows instrumentation (e.g. polypectomy from the left ear).

The CSF findings suggestive of an infectious process, but persistently culture negative, are characteristic of a perimeningeal infective process as was the case here.

Ultimately the patient died of this illness

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C

EXPLANATION / COMMENTS

Transient Global Amnesia (TGA) typically causes dense anterograde amnesia lasting for several hours, usually 4-6, with a more variable retrograde amnesia, extending from a few hours to many years. Attacks can recur, at a rate of around 3%/year, but rarely do so more than once or twice. Precipitation by emotional or physical stress is common, but episodes are not usually present on waking. Several features of the episodes described (brevity, frequent recurrence, lack of precipitants, attacks on waking) are therefore out of keeping with TGA.

TIAs, usually in the posterior circulation, can cause transient amnesia, and rarely this can be the only feature. More often, however, there are other features suggestive of ischaemia in this territory with visual disturbance, limb weakness, sensory disturbance, or other cranial nerve symptoms.

Transient epileptic amnesia (TEA) is a predominantly amnesic presentation of temporal lobe epilepsy (TLE). It usually presents in middle-aged or elderly patients, and causes brief (circa 30 minute) episodes of transient amnesia, often occurring on waking. The mix of anterograde and retrograde amnesia is variable, but patients can often ‘remember not being able to remember’. Other more familiar features of TLE, such as a blank stare, simple automatisms or olfactory hallucinations, may accompany episodes of TEA. Many patients with TEA report two associated problems with memory: i) a patchy but persistent ‘autobiographical amnesia’ for salient past events occurring up to several decades before; ii) ‘accelerated forgetting’, excessively rapid loss of recently acquired memories. The case described is therefore typical.

Psychogenic amnesia (PA) usually involves severe retrograde amnesia in the absence of anterograde amnesia. Loss of personal identity in amnesic ‘fugue’ is the extreme expression of such retrograde amnesia. PA usually occurs on a background of current life stress and past psychiatric difficulty – though this may not be apparent at the patient’s presentation, emerging only after some detective work. There is little or nothing in the case described to suggest PA – except, perhaps, for the autobiographical amnesia. This is, however, now recognised to occur in some types of ‘neurogenic’ amnesia.

Migraine is a risk factor for TGA, and it has been suggested that the pathophysiology of TGA has features in common with that of the migraineous aura. However, in the absence of a past history of migraine, or other more familiar manifestations of migraine, this diagnosis would be speculative here.

REFERENCES


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