027

Chapter 4

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 4

Neurology

Features • headache chronic postural headache (suggested by its improvement as the day progresses) 10% of cases are free of headaches. • blurred vision, (Horizontal diplopia) Diplopia is common due to sixth nerve palsy. • papilloedema (usually present) • enlarged blind spot • Reduction in colour vision is common • sixth nerve palsy may be present • normal appearances of the magnetic resonance imaging (MRI). Normal ventricular size, anatomy and position. Normal CSF cell count and protein content. • plantars are flexor Extensor plantars suggest alternative diagnosis. • Absence of retinal venous pulsations Diagnosis • the diagnosis is confirmed by finding an elevated CSF opening pressure (more than 20 cm H2O). CSF protein, glucose and cell count will be normal. • CT and MRI scans are often normal CT brain is needed to exclude a space occupying lesion and obstructing hydrocephalus. MRI venogram is recommended afterwards to exclude cerebral sinus thrombosis. Management • weight loss • diuretics e.g. acetazolamide • topiramate (anticonvulsant) is also used, and has the added benefit of causing weight loss in most patients • repeated lumbar puncture • surgery: A lumboperitoneal or ventriculoperitoneal shunt may also be performed to reduce intracranial pressure optic nerve sheath decompression and fenestration may be needed to prevent damage to the optic nerve. In progressive visual loss Lumbo-peritoneal (LP) shunt is the treatment of choice. Optic nerve fenestration is an alternative. There are no comparative studies between the two interventions.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Complication • Progressive visual loss and optic atrophy Scenario A young, obese female presents with a progressive blurring in her vision over the last 12 months but denies any headache. on fundoscopy she has bilateral blurred and heaped up optic discs which are obviously pale. CT head scan was reported as normal. Which appropriate investigation for this patient? Brain MR venography The description of the pale but prominent optic discs goes with early secondary optic atrophy and hence should promote a search for a cause for a longstanding papilloedema. she is likely to have idiopathic intracranial hypertension; 10% of cases are free of headaches. The next most appropriate investigations would be assessment for any underlying causes and include magnetic resonance venography (MRV) (exclude cerebral sinus thrombosis) and

cerebrospinal fluid (CSF) analysis with assessment of the opening pressure and other CSF parameters as a confirmatory step. MRCPUK-part-1-September 2008 exam: Sudden loss of vision in left eye + headaches + bilateral papilloedema. Which drug is most likely to be responsible? Prednisolone →intracranial hypertension

---

Spontaneous intracranial hypotension (SIH) Strong postural relationship with the headache generally much worse when upright and easy with lying horizontal. Patients may therefore be bed-bound Definition • Low (CSF) pressure headache, (< 6 cm CSF) • The lower limit of the normal range for CSF pressure is 10 cm H2O Causes • The most common cause following lumbar puncture, The leak is typically from the thoracic nerve root sleeves. • Other possible causes: following an episode of possible minor trauma to meninges (eg sports injury to neck or back) without apparent cause (SIH). Mechanism and features • CSF leak leads to low CSF pressure orthostatic headache in association with one or more of the following symptoms: nausea, vomiting horizontal diplopia unsteadiness or vertigo altered hearing neck pain/stiffness interscapular pain visual field abnormalities

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 4

Neurology Diagnosis • CSF opening pressure at lumbar puncture: opening CSF pressure is low, (< 6 cm CSF), and often a 'dry' tap is encountered However, the pressure may be normal CSF fluid analysis is normal • MRI with gadolinium confirming the diagnosis demonstrates distinctive dural gadolinium enhancement and downward displacement of brain on sagittal views. typically reveal diffuse pachymeningeal enhancement, frequently in association with 'sagging' of the brain, tonsillar descent and posterior fossa crowding Treatment • usually conservative (first-line): bed rest, analgesia, increased fluid intake • if this fails an epidural blood patch may be tried

---

Medication overuse headache Medication overuse headache • Simple analgesia + triptans: stop abruptly • Opioid analgesia: withdraw gradually Definition • a headache occurs ≥ 15 days per month due to overuse of headache medication (e.g. opioid, paracetamol, triptans and NSAIDs) for ˃ 3 months. Epidemiology • Prevalence:1 to 2% and is higher in females than males. Features • A history of symptomatic medication use more than two to three days per week in association with chronic daily headache is suggestive. • Commonly occurs daily or nearly daily. • Butalbital-containing analgesics and opioids has the highest risk of medication overuse headache. Management • Simple analgesics and triptans should be withdrawn abruptly (may initially worsen headaches) • Opioid analgesics should be gradually withdrawn • Withdrawal symptoms are likely to occur, including worsening headache, nausea, agitation and sleep disturbance. These usually settle within seven days, and headaches should stop within approximately three weeks. • While discontinuing the overused medication, some patient may require bridge therapy such as long-acting NSAIDs; eg, naproxen or oral prednisone.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Parkinsonism Definition • Parkinsonism refers to clinical syndromes that mimic the symptoms of Parkinson's disease (PD) (e.g. tremor, bradykinesia, rigidity). Causes • Parkinson disease (PD): Idiopathic • Secondary parkinsonism Drug-induced e.g. antipsychotics, metoclopramide Progressive supra-nuclear palsy Multiple system atrophy Wilson's disease Post-encephalitis Dementia pugilistica (secondary to chronic head trauma e.g. boxing) Toxins: carbon monoxide, MPTP Drugs-induced Parkinsonism Phenothiazines: e.g. chlorpromazine, prochlorperazine Butyrophenones: haloperidol, droperidol Metoclopramide Domperidone does not cross the blood-brain barrier and therefore does not cause extra-pyramidal side-effects

---

Parkinson's disease (PD) Definition • Progressive neurodegenerative condition caused by degeneration of dopaminergic neurons in the substantia nigra. Epidemiology • The second most common neurodegenerative disorder following Alzheimer disease • Prevalence is 1-2 per 1000 people • More common in men (2:1) • Mean age of diagnosis is 65 years Risk factors • Advanced age (>60 years) • Family history • Male sex • Environmental pesticides.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 4

Neurology Pathophysiology • In normal circumstances There are two pathways in the brain that promote motion, the direct (stimulatory) pathway and the indirect (inhibitory) pathway. In normal circumstances, the stimulatory pathway is activated while the inhibitory pathway is deactivated, allowing for smooth motion. Dopamine stimulate the Direct Pathway and inhibits the Indirect Pathway. The substantia nigra (part of the basal ganglia) produces dopamine, which binds the D1 receptors in the striatum, inhibiting the globus pallidus, leading to activation of the thalamus and allowing movement (activation of the direct stimulatory pathway) Also, dopamine binds the D2 receptor, inhibiting the inhibitory pathway (inhibition of the indirect pathway). • In Parkinson disease Aggregates of α-synuclein proteins → form Lewy bodies → loss of the dopamineproducing neurons in the substantia nigra. Decreased dopamine causes increased inhibitory output from the globus pallidus via both the direct and indirect pathways → ↓motion. ↓dopamine →↓activation of D1 receptor on striatum →↓excitatory (stimulatory) direct pathway →↑globus pallidus internus output →↓thalamic function → ↓motion. ↓dopamine →↓activation of D2 receptor on striatum →disinhibiting the inhibitory pathway The classical signs of bradykinesia, resting tremor and rigidity start to appear after approximately 50% of the dopamine neurons, and 75-80% of striatal dopamine is lost. Decreased dopamine impairs movement by which mechanisms? Decreased activation of the D1 and D2 receptors Which mechanism underlying the neurodegeneration seen in Parkinson's? Impaired protein degradation Mutations in either the parkin gene or UCHL1 lead to impaired protein degradation. Alpha-synuclein is a synaptic protein accumulates in Lewy body dementia and Parkinson's disease. What is the characteristic microscopic finding in Parkinson's disease? Lewy body

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Features • Bradykinesia poverty of movement also seen, sometimes referred to as hypokinesia short, shuffling steps with reduced arm swinging difficulty in initiating movement • Tremor

most marked at rest, 3-5 Hz worse when stressed or tired typically, 'pill-rolling', i.e. in the thumb and index finger The tremor of parkinsonism only disappears during REM sleep. • Rigidity lead pipe cogwheel: due to superimposed tremor • Other characteristic features mask-like facies flexed posture micrographia drooling of saliva psychiatric features: depression is the most common feature (affects about 40%); dementia, psychosis and sleep disturbances may also occur impaired olfaction REM sleep behaviour disorder The earliest feature (During REM sleep, the patient may be seen kicking, laughing, punching, or fighting invisible enemies.) Intestinal pseudo-obstruction a common feature of advanced Parkinson's results in symptoms of intermittent abdominal bloating and vomiting. Drug-induced parkinsonism differs from Parkinson's disease in: • motor symptoms are generally rapid onset and bilateral • rigidity and rest tremor are uncommon The classic triad of features: bradykinesia, tremor and rigidity The symptoms of Parkinson's disease are characteristically asymmetrical.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 4

Neurology A Lewy body (stained brown) in a brain cell of the substantia nigra in Parkinson's disease. The brown colour is positive immunohistochemistry staining for alpha-synuclein. Discoloration of the substantia nigra due to loss of pigmented nerve cells. Diagnosis: Diagnostic criteria for Parkinson's disease • Step 1. Diagnosis of a parkinsonian syndrome Bradykinesia and at least one of the following: Muscular rigidity Rest tremor (4-6 Hz) Postural instability unrelated to primary visual, cerebellar, vestibular, or proprioceptive dysfunction • Step 2. Exclusion criteria for Parkinson's disease History of: Repeated strokes with stepwise progression Repeated head injury Antipsychotic or dopamine-depleting drugs Definite encephalitis or oculogyric crises on no drug treatment More than one affected relative Sustained remission Negative response to large doses of levodopa (if malabsorption excluded) Strictly unilateral features after 3 years Other neurological features: supranuclear gaze palsy, cerebellar signs, early severe autonomic involvement, Babinski sign, early severe dementia with disturbances of language, memory, or praxis Exposure to known neurotoxin Presence of cerebral tumour or communicating hydrocephalus on neuroimaging

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

• Step 3. Supportive criteria for Parkinson's disease Three or more required for diagnosis of definite Parkinson's disease: Unilateral onset Excellent response to levodopa Rest tremor present Severe levodopa-induced chorea Progressive disorder Levodopa response for over 5 years Persistent asymmetry affecting the side of onset most Clinical course of over 10 years. Investigations • Single photon Emission Computed Tomography (SPECT) The investigation of choice for people with tremor if essential tremor cannot be clinically differentiated from parkinsonism. Management • First-line treatment If the motor symptoms are affecting the patient's quality of life →levodopa If the motor symptoms are not affecting the patient's quality of life →non-ergot dopamine agonist (e.g., ropinirole, apomorphine), levodopa or monoamine oxidase B (MAO-B) inhibitor (e.g., selegiline) Patients > 65 years or multimorbid patients of any age → levodopa PLUS decarboxylase inhibitor (carbidopa): due to inevitable motor complications that is associated with levodopa. Patients < 65 years with no significant comorbidities → Non-ergot

dopamine agonists (e.g., pramipexole, ropinirole, apomorphine) Feature most strongly suggest idiopathic Parkinson's disease →asymmetry of tremor
General rule of treatment: • Starting dopamine agonists such as ropinirole for younger patients under 65. • Saving L-dopa for later in the disease while reducing the long-term risk of motor complications.

Neurology • Second line Adjuvant treatment of motor symptoms (dyskinesia and/or motor fluctuations) if not responded despite optimal levodopa therapy →Add non-ergot-derived dopamine agonists, MAO-B inhibitors or catechol-O-methyl transferase (COMT) inhibitors (e.g., entacapone) • Third line If dyskinesia is not adequately managed by modifying existing therapy, consider amantadine • Fourth- line → deep brain stimulation For advanced Parkinson’s disease, whose symptoms are not adequately controlled by best medical therapy Targets: subthalamic nucleus or internal globus pallidus In the context of suicidal behaviour, the patient would not be a candidate for deep brain stimulation, which for unknown reasons, increases the risk of suicide. Comparison between anti-Parkinson drugs • Improvement in motor symptoms and activities of daily living. Levodopa → More improvement Other antiparkinsonian medicines (e.g. Dopamine agonists, MAO-B inhibitors & COMT inhibitors) → Less improvement Amantadine → No evidence of improvement • Off time (periods of the day between medication doses when the medication is not working well, causing worsening of Parkinsonian symptoms). Dopamine agonists → More off-time reduction Amantadine → No studies reporting this outcome • Adverse events Levodopa, MAO-B inhibitors & COMT inhibitors → Fewer adverse events Dopamine agonists →Intermediate risk of adverse events Amantadine → No studies reporting this outcome • Motor complications Levodopa →More motor complications Dopamine agonists & MAO-B inhibitors → Fewer motor complications • Hallucinations Levodopa, MAO-B inhibitors & COMT inhibitors →Lower risk Dopamine agonists →More risk Amantadine → No studies reporting this outcome Management of non-motor symptoms of Parkinson’s disease • Excessive daytime sleepiness → modafinil • Rapid eye movement sleep behaviour disorder → clonazepam or melatonin • Nocturnal akinesia → levodopa or oral dopamine agonists • Postural hypotension Review the possible pharmacological causes, e.g: antihypertensives (including diuretics), dopaminergics, anticholinergics, antidepressants. First line →midodrine (alpha agonist): monitor for supine hypertension. Second line →fludrocortisone (If midodrine is not tolerated or not effective).

• Psychotic symptoms (hallucinations and delusions) Do not treat if they are well tolerated. Reduce the dosage of any Parkinson's disease medicines Consider quetiapine (in people without cognitive impairment) or clozapine. Do not offer olanzapine • Dementia 1st line: cholinesterase inhibitor (rivastigmine, donepezil, or galantamine capsules or rivastigmine patches) 2nd line: if cholinesterase inhibitors are not tolerated or contraindicated → memantine • Drooling 1st line: glycopyrronium bromide (anticholinergic) → reduce excessive saliva (sialorrhea) & does not cross the blood–brain barrier →no central effects. 2nd line: If glycopyrronium bromide is not effective → referral for botulinum toxin Parkinson's medication withdrawal • Antiparkinsonian medicines should

not be withdrawn abruptly or allowed to fail suddenly due to poor absorption (for example, gastroenteritis, abdominal surgery) to avoid the potential for acute akinesia or neuroleptic malignant syndrome. • The practice of withdrawing people from their antiparkinsonian drugs (so called 'drug holidays') to reduce motor complications should not be undertaken because of the risk of neuroleptic malignant syndrome. • Parkinsonian malignant syndrome Triggered by abrupt withdrawal from anti-parkinsonian medication. The presentation is similar of neuroleptic malignant syndrome (pyrexia, rigidity, tachycardia) but without a history of neuroleptic drug use. Re-initiation of Parkinson's therapy is curative.

Anti-Parkinson drugs Levodopa (L-DOPA) • Mode of action Precursor to dopamine, can penetrate the blood brain barrier (peripherally administered dopamine cannot penetrate the blood brain barrier) Converted to dopamine by DOPA decarboxylase at the presynaptic neuron → direct dopaminergic effect • Indication First-line treatment for patients > 65 years of age or patients with comorbidities. Second-line treatment for patients < 65 years of age. • Administration Normally combined with a peripheral decarboxylase inhibitor (e.g. carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine (levodopa alone → peripheral conversion of levodopa to dopamine → significant GI side effects such as nausea and vomiting). • Advantages Most effective drug for reducing symptoms

Neurology • Disadvantages Increased risk of severe motor dysfunction: levodopa-induced dyskinesia (LID) → involuntary writhing movements: choreiform movements, dystonia, myoclonus, and ballism). Peak-dose dyskinesia is most common: Due to higher dose of levodopa. Usually involve upper limbs, trunk, and orofacial muscles. Treatment: reduction of levodopa dose (use frequent smaller dosage) Amantadine is an NMDA antagonist and considered the most effective drug used for LID. Reduced effectiveness with time (usually by 2 years) On/off effect (phenomena) due to long-standing chronic levodopa therapy and seen when the serum level of levodopa is least.
 usually manifest as abnormal spasm of body parts, which most commonly affect foot or leg and rarely present on the arm or trunk. Off-period dystonia usually occurs at night or early morning Treatment may be improved either by the addition of cabergoline (a dopamine agonist) or a subcutaneous infusion of apomorphine. Liquid forms of l-dopa may also be helpful as they allow closer titration of dose, and splitting meals into smaller snacks. • Side effects Nausea & vomiting , dry mouth, anorexia Cardiac arrhythmias, postural hypotension Drowsiness Reddish discolouration of urine upon standing Psychosis, hallucinations (usually visual) usually appear late (more than two years after initiation of treatment). The risk for developing psychiatric symptoms increases with age, other psychiatric conditions, long duration of levodopa treatment, and high doses. Levodopa can increase intraocular pressure, therefore it is not recommended in patients with glaucoma. • Not used in neuroleptic induced parkinsonism Dopamine receptor agonists • Agents Non-ergot dopamine agonists agents: Ropinirole, apomorphine, pramipexole, rotigotine Ergot-derived dopamine agonists: bromocriptine, cabergoline, pergolide (not recommended as first-line treatment for Parkinson's disease). • Action: Act directly at striatal dopamine receptors • Indication First-line treatment for patients < 65 years of age Adjunctive

treatment for patients of any age

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

• Advantage: Fewer motor side effects • Disadvantage: Less effective than L-DOPA • Side effects Nausea, orthostatic hypotension, daytime drowsiness (somnolence) Psychotic symptoms: Hallucinations, psychosis, impulse control disorders impulse control disorders (e.g. compulsive gambling, hypersexuality, binge eating and obsessive shopping). If modifying dopaminergic therapy is not effective →cognitive behavioural therapy Dopamine agonist withdrawal syndrome Ergot dopamine agonists: fibrosis (cardiac, pulmonary, retriperitoneal) retroperitoneal fibrosis →obstruction of both ureters →bilateral hydronephrosis →chronic kidney disease echocardiogram, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored MAO-B (Monoamine Oxidase-B) inhibitors • Agents: Selegiline, Rasagiline, Safinamide. • Action: inhibits the breakdown of dopamine secreted by the dopaminergic neurons Selective inhibition of MAO-B → ↓ metabolization of dopamine into DOPAC in the brain → prolonged dopamine availability and effect→ ↓ demand for L-DOPA • Indication Alternative to L-DOPA or dopamine agonists Can also be given in combination with L-DOPA → ↓ motor fluctuations • Side effects: Headache, dyskinesia, psychological disorders (e.g., hallucinations) NMDA antagonists (Amantadine) • Action Acts antagonistically at the glutamate N-methyl-D-aspartate (NMDA) receptor → dopaminergic effect ↑ Dopamine release and ↓ dopamine reuptake in central neurons • Indication Short-term treatment of mild symptoms Drug of choice during akinetic crisis Reduction of L-DOPA-induced dyskinesia • Side-effects ataxia, slurred speech, confusion, dizziness livedo reticularis peripheral edema (should be avoided in congestive heart failure) COMT (Catechol-O-Methyl Transferase) inhibitors • Agents: Entacapone, tolcapone • Action Inhibition of catechol-O-methyltransferase (COMT) → ↓ peripheral metabolization of L-DOPA to 3-O-methyldopa (3-OMD) → ↑ availability Tolcapone also prevents central COMT from breaking down dopamine to 3methoxytyramine (3-MT) by crossing the blood-brain barrier → ↑ dopamine effect → ↓ demand for L-DOPA and longer therapeutic effect for each dose • Indication: used in conjunction with levodopa. COMT inhibitor monotherapy is ineffective; therefore, it should always be combined with L-DOPA and carbidopa.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 4

Neurology Anticholinergic drugs (muscarinic antagonists) • Agents: Procyclidine, Benztropine, Trihexyphenidyl (benzhexol) , Biperiden • Action: Inhibition of excitatory cholinergic neurons → ↓ concentration of acetylcholine • Indication Useful as monotherapy in patients < 65 years of age with tremor as the main symptom Help tremor and rigidity but does not improve bradykinesia. Now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease Usually avoided in patients > 65 years because they are more prone to anticholinergic side effects (e.g., urinary retention, delirium, constipation) MRCPUK-part-1-January 2017 exam : H/O schizophrenia , developed parkinsonism secondary to his antipsychotic medication. Which drug is most useful in the management of tremor? Benzhexol MRCPUK-part-1-January 2018 exam: What is the mechanism of action of selegiline in Parkinson's disease? Monoamine Oxidase-B inhibitor

Progressive supranuclear palsy (PSP) Overview • aka Steele-Richardson-Olszewski syndrome • a 'Parkinson Plus syndrome Features • Impairment of vertical gaze (especially downward gaze - patients may complain of difficultly reading or descending stairs) • Parkinsonism • Postural instability leading to frequent falls (often first symptom); retropulsion (falling backward on a pull test) is characteristic • Slurring of speech (pseudobulbar palsy) • Cognitive impairment: frontal lobe abnormalities (apathy, disinhibition, impaired reasoning) • Dementia Diagnosis • MRI: “hummingbird sign” showing atrophy of midbrain structures with a relatively intact pons region Management: poor response to L-dopa Prognosis: usually fatal within 5–10 years Progressive supranuclear palsy: • the triad of parkinsonism, vertical gaze palsy and cognitive impairment

---

Multiple system atrophy (MSA) Multiple system atrophy : a triad of • Parkinsonism • Autonomic disturbance (atonic bladder, postural hypotension) • Cerebellar signs (e.g., ataxia, tremor, dysarthria) Overview • Shy-Drager syndrome is a type of multiple system atrophy. • The average age of onset is 50 years (earlier than in Parkinson's disease) • The median survival six to nine years. • It runs a briefer course than Parkinson's disease. Pathology • Macroscopic: most commonly atrophy of olivopontocerebellar and striatonigral systems • Microscopic: glial cytoplasmic inclusions Features • Parkinsonism • Autonomic disturbance (urinary incontinence (atonic bladder), postural hypotension, erectile dysfunction) • Cerebellar signs (e.g., ataxia, tremor, dysarthria) • Myoclonus, dystonia, ocular motility disorders, pyramidal signs Treatment: Only symptomatic treatment MRCPUK-part-1-May 2019 exam: A 67-year-old increasing clumsiness + ataxic gait + ↑↑upper limb tone with cog-wheel rigidity. Blood pressure is 135/80 lying and 95/70 standing. What is the most likely diagnosis? □ Multiple system atrophy Corticobasal degeneration (a Parkinson-plus syndrome) characterised by: • Dementia • Asymmetric motor abnormalities, often initially affecting only one limb • Alien limb phenomenon: involuntary but purposeful movement of the limb PLUS feeling that the affected limb does not belong to the patient and acts on its own. Differential diagnoses of Parkinson-plus syndromes Multiple system atrophy Progressive supranuclear palsy • Autonomic dysfunction with urogenital problems • Vertical gaze palsy • Frontal lobe disturbances Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Corticobasal degeneration Dementia with Lewy bodies • Asymmetric motor symptoms • Alien limb phenomenon • Lewy bodies • Visual hallucinations

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 4

Neurology

Normal pressure hydrocephalus (NPH) Overview • Normal pressure hydrocephalus is a reversible cause of dementia seen in elderly patients. Mechanism • It is thought to be secondary to reduced CSF absorption at the arachnoid villi. • ↓ CSF absorption → CSF accumulation → enlargement of the ventricle Causes • Idiopathic (most common in adults > 60 years) • May be secondary to head injury, subarachnoid haemorrhage or meningitis Features: the triad of

1. urinary incontinence

2. dementia and bradyphrenia
3. gait abnormality (may be similar to Parkinson's disease) Diagnosis • Imaging: MRI (initial test), CT
   □ Ventriculomegaly without sulcal enlargement □ Hydrocephalus with an enlarged fourth ventricle • CSF tap test: confirmatory test □ Opening pressure is normal or slightly elevated. □ Improvement of symptoms after CSF removal via lumbar puncture or shunt confirms NPH. □ Lumbar puncture is both diagnostic and therapeutic. Management • the most likely helpful initial managements steps is CSF drainage via repeated lumbar puncture • ventriculo-peritoneal shunting What is the underlying cause of urinary incontinence in NPH? □ Inability to suppress voiding □ NPH → compression of the periventricular white matter tracts → functional frontal lobe impairment → loss of central inhibition of the detrusor muscle → strong voiding reflex that cannot be suppressed (urge incontinence). Normal pressure hydrocephalus □ Classic triad of urinary incontinence, dementia, and gait apraxia.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Delirium (Acute confusional state) Definition • Delirium: a syndrome of acute confusion characterized by fluctuations in awareness, cognition, and attention Risk factors • Age ≥ 65 years • Cognitive impairment (past or present) and/or dementia • Current hip fracture • Severe illness: affect up to 30% of all older patients admitted to hospital. Causes • DELIRIUM: Drugs, Electrolyte abnormalities, Lack of medication (withdrawal), Infection, Reduced sensorial input, Intracranial pathology, Urinary retention or fecal impaction, Myocardial and pulmonary disease • Delirium is frequently a complication of dementia. Features • Cognitive function: e.g., worsened concentration, slow responses, confusion, memory disturbances (loss of short term > long term). • Perception: e.g., visual or auditory hallucinations. • Physical function: e.g., reduced mobility, restlessness, agitation, sleep disturbance. • Social behaviour: e.g., lack of cooperation with reasonable requests, withdrawal, mood change Diagnosis • The Confusion Assessment Method (CAM) is the most effective tool in identifying delirium. • If there is difficulty distinguishing between the diagnoses of delirium, dementia or delirium superimposed on dementia, treat for delirium first. Management • Treatment of underlying cause • Agitation should initially be managed with nonpharmacologic strategies, verbal and nonverbal techniques to de-escalate the situation (e.g., modification of environment). • Medications should be reserved for refractory agitation. □ the 2019 NICE delirium guidelines recommend short-term haloperidol 0.5 mg (usually for ≤1 week). □ Avoid antipsychotic drugs in Parkinson's disease or dementia with Lewy bodies • If delirium does not resolve: Re-evaluate for underlying causes, assess for possible dementia MRCPUK-part-1-January 2011 exam: An elderly patient admitted for UTI, became agitated and aggressive. What is the most appropriate management? □ Haloperidol 0.5 mg orally

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 4

Neurology

Dementia Overview • Dementia affect over 700,000 people in the UKT • DP43 is a protein that has recently been found to be involved in a multitude of neurodegenerative diseases including dementia and motor neuron disease. Common causes of dementia • Alzheimer's disease (> 50% of dementia cases) • Multi-infarct dementia due to cerebrovascular disease (20% of dementia cases) • Lewy body dementia (c. 10-20%) Rarer causes (5% of cases) • Huntington's • CJD • Pick's disease (atrophy of frontal and temporal lobes) • HIV (50% of AIDS patients) Features • Mini-mental state examination. A score of 24 or less out of 30 suggests dementia • Short term memory impairment is the commonest clinical presentation of Alzheimer's disease. • The best way to test short term memory is to ask the patient to recall new information in the next few minutes. • Long term memory is usually intact. • Usually patients are fully orientated in time, person and place. Distinguishing between normal aging and dementia • Memory impairment, occasional difficulties in word finding, and slower cognitive processing are normal effects of aging. • An important distinguishing factor between normal aging and forms of dementia is the degree to which independence with everyday activities is impaired. In normal aging, independence in daily activities is preserved. • cognitive exams are within normal limits in aging. • Alzheimer's disease is often accompanied by behavioral changes (such as aggression, depression, insomnia) Investigations • Exclude reversible secondary causes e.g., hypothyroidism, FBC, U&E, LFTs, calcium, glucose, TFTs, vitamin B12 and folate levels. • Neuroimaging to exclude other cerebral pathologies (e.g. Subdural haematoma, normal pressure hydrocephalus) and to help establish the subtype diagnosis.(CT could be used, but MRI is better)

• Single-photon emission computed tomography (SPECT) should be used to differentiate Alzheimer's disease, vascular dementia and frontotemporal dementia if the diagnosis is in doubt. • Cerebrospinal fluid examination should be used if Creutzfeldt–Jakob disease or other forms of rapidly progressive dementia are suspected. Presence of the e4 allele of apo-lipoprotein E →Alzheimer's disease Loss of GABA is seen in →Parkinson's disease. Peri-vascular mononuclear inflammation is seen in →multiple sclerosis. Loss of Betz cells is seen in →motor neurone disease. Alzheimer's disease (AD) Overview • Alzheimer's disease is a progressive degenerative disease of the brain and it is the common cause of dementia. • Typically, first affects the temporal and parietal lobes Temporal lobe degeneration results in memory loss (misplaced keys, leaving the stove on) and language deficits (word-finding difficulties), whereas parietal lobe degeneration results in spatial navigation problems (getting lost during walks outside) • The primary anatomical target of Alzheimer’s disease is → the cerebral cortex Alzheimer's disease is a form of "cortical" type of dementia The “sub-cortical type” of dementia occurs in Huntington's disease, advanced Wilson's disease, and advanced multiple sclerosis Genetics • Most cases are sporadic • Early-onset (before the age of 65) familial AD represents ~10% of all AD cases • Mutations in presenilin 1 (PSEN1) Linked to ~50% of familial AD cases earlier onset compared to AD due to mutations of other genes (median is ~43 years) • Amyloid precursor protein (APP) gene Linked to 10–15% of early-onset familial AD cases Since the APP gene is located on chromosome 21, individuals with trisomy 21 have an increased risk of early-onset AD (around age 50) due to APP overexpression Vascular dementia • Typically occurs in those with widespread vascular disease. A history of strokes or the presence of focal neurological signs are very suggestive. • CT or MRI will show → multiple lacunar infarcts • Does not respond to acetylcholinesterase inhibitors such as donepezil. •

Vascular dementia caused by lipohyalinosis or microatheroma formation and NOT thromboemboli. Therefore, anticoagulation is not indicated. • Memory therapy is the best next step in management for patient's confirmed vascular dementia.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 4

Neurology Pathological changes • Macroscopic: widespread cerebral atrophy, particularly involving the cortex and hippocampus • Microscopic: cortical plaques due to deposition of type A-Beta-amyloid protein and intraneuronal neurofibrillary tangles caused by abnormal aggregation of the tau protein • Biochemical: there is a deficit of acetylcholine from damage to an ascending forebrain projection ↓production of choline acetyl transferase →↓acetylcholine synthesis →↓cortical cholinergic functioning Features • Short-term memory impairment (the most common presentation) of AD dementia (insidious onset, slow progression, episodic memory affected first) • Language impairment • Temporal and spatial disorientation (patients are usually not oriented to person, place, time, or events) • Impairment of executive functions and judgment • Behavioral changes (apathy, agitation, aggression, irritability) • Mood disorders (e.g., symptoms of depression) Investigations • Screening for B12 deficiency and hypothyroidism • MRI or CT to rule out reversible causes of cognitive decline MRI scan in Alzheimer →symmetrically increased size of the lateral ventricles along with cerebral cortical atrophy in a mainly frontal and parietal distribution. Do not rule out Alzheimer's disease based solely on the results of CT or MRI scans. • FDG-PET (fluorodeoxyglucose-positron emission tomography-CT), or perfusion SPECT (single-photon emission CT) if FDG-PET is unavailable • Examining cerebrospinal fluid for: total tau or total tau and phosphorylated-tau 181 amyloid beta 1–42 or amyloid beta 1–42 and amyloid beta 1–40. Management • Non-pharmacological: should always be attempted prior to resorting to pharmacologic treatment. Memory therapy for all dementias: involves improving cognitive abilities through image recognition, solving math problems, and past memory recall. Behavioral and environmental regulation, such as: adhering to a regular sleep schedule Maintaining a consistent environment will help orient the patient. Frequent travel has been shown to worsen the symptoms of Alzheimer's disease. • Mild to moderate Alzheimer's disease: acetylcholinesterase inhibitors (donepezil, galantamine and rivastigmine) A well-known side effect of rivastigmine is AV block NICE guidelines recommend discontinuation of cholinesterase inhibitors once the mini mental state examination has fallen below 12. There is no role for cholinesterase inhibitors in advanced Alzheimer's disease. NICE guidelines recommend discontinuation of cholinesterase inhibitors once the mini mental state examination has fallen below 12.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

 The best option would be to withdraw donepezil and possibly consider memantine, which is licensed for use in moderate to severe dementia. Side-effects of cholinesterase inhibitors Bradycardia and, rarely, AV block Bladder outflow obstruction • Moderate to severe Alzheimer's: memantine (a NMDA receptor antagonist) • Management of aggression in dementia 1st line: non-pharmacological: identify and avoid triggers + behavioural techniques. 2nd line: pharmacological: Olanzapine or quetiapine for short-term Risperidone has been tested in this setting and is licensed for 6 weeks treatment of persistent aggression in those with moderate to

severe Alzheimer's disease For patients with dementia with Lewy bodies (DLB), only very low doses of certain atypical neuroleptics (eg, quetiapine or clozapine) should be used due to high risk of severe side effects with neuroleptic medications.

Lewy body dementia (LBD) Epidemiology • Second most common form of neurodegenerative dementia (10–20% of dementia cases) Pathology • Macroscopic: Cerebral atrophy, particularly of the frontal lobe. Relative sparing of the hippocampi • Microscopic: Lewy bodies: alpha-synuclein-positive, hyaline cytoplasmic inclusions in neurons (mostly cortical) that cause neuronal degeneration The characteristic pathological feature is alpha-synuclein cytoplasmic inclusions (Lewy bodies) in the substantia nigra, paralimbic and neocortical areas Features • Progressive cognitive impairment • Parkinsonism • Visual hallucinations • Intermittent confusion • Myoclonus • Marked sensitivity to neuroleptic treatment. Diagnosis • usually clinical • Single-photon emission computed tomography (SPECT) is increasingly used. The sensitivity of SPECT in diagnosing Lewy body dementia is around 90% with a specificity of 100% Lewy body dementia: a triad of: Dementia, parkinsonism, and visual hallucinations

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 4

Neurology Differential diagnosis: Parkinson's disease with dementia VS Lewy body dementia • Lewy body dementia presents with signs similar to Parkinson's Disease, but cognitive symptoms precede the motor symptoms. Lewy body dementia if the onset of both cognitive and motor symptoms is within 1 year Dementia secondary to Parkinson disease if cognitive symptoms occur > 1 year after the onset of motor symptoms Treatment • The treatment of choice is rivastigmine, which improves both the visual hallucinations, and cognitive impairment. • Neuroleptics should be avoided in Lewy body dementia, as patients are extremely sensitive and may develop irreversible parkinsonism. Questions may give a history of a patient who has deteriorated following the introduction of an antipsychotic agent The most appropriate therapeutic strategy with respect to maintaining his mobility is →Stop dopamine-blocking drugs (causing significant parkinsonism) eg: quetiapine MRCPUK-part-1-September 2018 exam: A 78-year-old man with memory impairment, hallucinations,
resting tremor, festinating gait and an expressionless face. He scores 12 / 30 on the mini-mental state examination (MMSE). which test is most likely to confirm the diagnosis? SPECT scan (Lewy body dementia) MRCPUK-part-1-September 2017 exam: H/O parkinsonian symptoms + agitation. deteriorated after prescribing haloperidol. What is the most likely underlying diagnosis? Lewy body dementia

---

Frontotemporal lobar degeneration (FTLD) Overview • Heterogeneous group of syndromes that involve degeneration of the frontal, insular, and/or temporal cortices • FTD is sometimes still referred to as Pick disease • The third most common type of cortical dementia after Alzheimer's and Lewy body dementia. • Age of onset: typically younger than in Alzheimer disease Pathology • Generally associated with pathological intracellular inclusion bodies (Pick bodies) that are caused by mutations in tau (main protein component of Pick bodies) or progranulin (precursor of granulin, which regulates cell growth) proteins. Haloperidol is contra-indicated in Lewy body dementia The inclusions found histologically in frontotemporal dementia, or Pick's disease are

hyperphosphorylated tau proteins.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Features • Onset before 65 • Insidious onset • Personality change and social conduct problems (apathy, disinhibited behavior) • Relatively preserved memory and visuospatial skills • Changes in cognitive functioning: Aphasia • CT/MRI: atrophy of the frontal and/or temporal lobes Types: There are three recognised types of FTLD • Frontotemporal dementia (Pick's disease) This is the most common type of frontotemporal dementia characterised by personality change and impaired social conduct. • Progressive non-fluent aphasia (chronic progressive aphasia, CPA) Here the chief factor is non-fluent speech. They make short utterances that are agrammatic. Comprehension is relatively preserved. • Semantic dementia Here the patient has a fluent progressive aphasia. The speech is fluent but empty and conveys little meaning. Unlike in Alzheimer's memory is better for recent rather than remote events. Treatment • No curative treatment. • Dementia: Cholinesterase inhibitors and memantine are usually not effective • Agitation, hallucinations, insomnia: Atypical antipsychotics

---

Creutzfeldt-Jakob disease (CJD) Definition • Creutzfeldt-Jakob disease (CJD) is rapidly progressive neurological condition caused by prions that are resistant to degradation by proteases due to misfolding into beta-pleated sheets. prion is an incorrectly folded protein that causes misfolding of other proteins. Epidemiology • CJD is the most common prion disease in humans. Causes and types • Sporadic (~85%): no identifiable cause • Familial (~10–15%): various mutations in the PRNP gene • Acquired (< 1%) Iatrogenic CJD: transmission during medical procedures (e.g., via organ transplantation, blood transfusion) Rapidly progressive dementia and myoclonic jerks are the hallmarks of CreutzfeldtJakob disease. Patients with FTD display changes of personality and social behavior, but their memory generally remains intact.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 4

Neurology Variant CJD (vCJD): by ingestion of beef infected with bovine spongiform encephalopathy (BSE) BSE is a transmissible prion disease occurring in cattle. Infection leads to vCJD in humans.) Pathophysiology • Conversion of normal cellular prion proteins with alpha-helical structure (PrPc) to prions that demonstrate an increase in beta-pleated sheet structure (PrPSc) (insoluble, misfolded prions resistant to proteases)→ PrPSc accumulation→ plaque formation → neuronal cell death → progression to spongiform encephalopathy What is the agent responsible for variant Creutzfeldt-Jakob disease (CJD)? Proteinaceous infectious particle (prion protein) Features • Rapidly progressing dementia (weeks to months) • Myoclonus • Cerebellar disturbances (e.g., gait instability, ataxia) • Pyramidal weakness • Behavioural abnormality • Akinetic mutism. Investigation • CSF analysis : ↑ 14-3-3 protein →useful in confirming a diagnosis of sporadic CJD. • MRI: shows high-signal abnormalities (hyperintense signals) in caudate nucleus and putamen or at least 2 cortical regions (temporal-parietal-occipital) • EEG: biphasic, high amplitude sharp waves (only in sporadic CJD) EEG is usually normal in new variant CJD. • Brain biopsy Diagnosis can only be confirmed by biopsy/autopsy Microscopic findings include spongiform degeneration ,

amyloid plaques (vCJD)

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Types Form Features Sporadic caused by (Unknown cause) • Account for 85% of cases • Occur at middle-age (mean age of onset is 65 years) • Median duration of disease is 5 months Genetic caused by (Mutation in PRNP gene) • Can occur at younger ages • Family history can be negative • Dementia usually occur late in the course of the disease • Often no detectable 14-3-3 protein in CSF • Median duration of disease is several years Iatrogenic caused by (Transmission of prion protein by invasive medical treatment) • Similar as sporadic form Variant caused by (Ingestion of contaminated products with bovine spongiform encephalopathy) • Occurs at a young age (median age 25 years) • Psychological symptoms such as anxiety, withdrawal and dysphonia are the most common initial presenting features • Ataxia, myoclonus appear late (6 months after psychological symptoms) • EEG is usually normal • MRI brain typically shows bilateral pulvinar (posterior thalamic nuclei) high signals. • Median duration of disease is 13 months The rapidly progressive neurological impairment, with myoclonus and hyper-reflexia coupled with EEG abnormality and MRI changes in the caudate and putamen, is most consistent with sporadic CJD. Treatment • No curative therapy available • Symptomatic treatment and eventually palliative care Prognosis

---

Transient global amnesia Definition • Transient loss of memory function Pathophysiology • Aetiology is unknown, thought to be due to transient ischaemia to the thalamus (in particular the amygdala and hippocampus) Risk factors • Usually affects people over the age of 50 • Psychological and physical stress Following disease manifestation, most individuals with sporadic CJD die within 12 months, usually from complications such as pneumonia.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 4

Neurology

Diagnostic criteria • Abrupt onset of amnesia (anterograde or partial retrograde) • Patients may appear anxious and repeatedly ask the same question • Episodes last between 1–24 h, but never > 24 h • Patients are usually disoriented in time and place, but not usually person. • Normal perception, preserved personal identity • Absence of other cognitive or neurological impairments. • Patients have no recall of events after the attack Investigations • If the diagnosis is clear, further diagnostic procedures are not necessary. • If the diagnosis is uncertain: MRI: evidence of typical focal, hyperintense lesions in the hippocampus EEG: exclude differential diagnoses (e.g., epileptic amnesic attacks) Differential diagnosis • Epilepsy can present with discreet episodes of amnesia. This syndrome is called transient epileptic amnesia. Features that suggest epilepsy are: shorter duration (should be less than 1 hour) multiple attacks onset on waking from sleep accompanying epileptic features - e.g. motor automatism, stereotyped behaviour, limb shaking. Management • No treatment is needed except observation until recovery. • Most patients recover within 24 hours and do not get further such episodes. • Imaging is considered if amnesia does not resolve after 24 hours. Prognosis • Resolves spontaneously within 24 h • Recurrence is unusual.

Restless legs syndrome (RLS) Definition • Restless legs syndrome (RLS) is a syndrome of spontaneous, continuous lower limb movements that may be associated with paraesthesia. Epidemiology • It is extremely common, affecting between 2-10% of the general population. Transient global amnesia • The best line of management → Admit for observation

---

Revision #1
Created 2026-01-06 17:51:31 UTC by Omar Ayman
Updated 2026-01-06 17:51:31 UTC by Omar Ayman