Multiple Sclerosis (MS)

Disclaimer

Contents

Red Flags

- Rapidly progressive neurological symptoms leading to neurological disability

Background

About multiple sclerosis (MS)

- *MS is characterised by inflammation of the central nervous system (CNS) resulting in neurological deficits sometimes affecting the patient's functional ability.*
- *The disease presents as either:*
  - *Relapsing and remitting:*
    - *The most common presentation and with better prognosis than progressive deterioration.*
    - *Periods of symptomatic episodes followed by periods of remission.*
  - *Progressive – symptoms worsen over time without periods of remission.*

- *Peak onset is between the ages of 20 and 40 years and prevalence is 3 times greater in women.*
- *Pregnancy appears to be protective against relapses, but there can be an increased risk of relapses postpartum.*

Assessment

1. Take a history, assessing for ***focal neurological symptoms*** consistent with a demyelinating lesion.

Focal neurological symptoms

- Symptoms typically evolve, increasing in severity over days, then stabilise over days to weeks, followed by gradual improvement.
- Ask about:
  - ***Visual symptoms***
    - *Features of optic neuritis include:*
      - *Monocular decrease in visual acuity and colour vision*
      - *Usually with pain on eye movement*
    - *Diplopia*
- *Progressive weakness of limbs*
- *Sensory impairment over the face or limbs:*
  - *Typically a pattern of increasing symptoms over a course of days.*
  - *Sensory symptoms that last < 24 hours, particularly positive sensory symptoms such as tingling, are common in healthy adults and rarely represent demyelinating disease.*
- *Vertigo*
- *Progressive balance disturbance*
- *Bladder, bowel, and sexual dysfunction*
- *Cognitive symptoms (especially decreased memory and processing speed)*
- *Seizures*

2. Undertake a ***neurological examination.***

Neurological examination

- *Muscle tone, reflexes, power, and coordination*
- *Cerebellar signs – nystagmus, ataxia, dysdiadochokinesia (inability to perform rapidly alternating movements), dysarthria*
- *Brainstem signs – facial weakness, sensory impairment, hypo- or hyperacusis, eye movements to assess for convergence, weakness, diplopia and saccades*
- *Sensory impairment of limbs and trunk*
- *Features of optic neuritis:*
    - *Visual acuity*
    - *Eye movements to assess for pain on eye movement*
    - *Assessment for reduced colour vision*
- *Gait and stance for balance and coordination (including tandem gait)*

3. Assess stage of disease and separate MS disease activity from pseudo-relapses or symptoms from previous damage:

- ***Relapsing and remitting MS (RRMS)*** – the first episode is a ***clinically isolated syndrome (CIS).***

Relapsing and remitting MS (RRMS)

- *Neurological signs or symptoms (similar to a clinically isolated syndrome) lasting at least 24 hours.*
- *Characterised by a series of relapses which occur on average less than annually, and which tend to recover completely or almost completely. Mild residual deficits persist in approximately 40% of patients.*
- *The average rate of relapse is 0.65 per year.*
- *Isolated fatigue or fever-related exacerbations are not relapses.*

Clinically isolated syndrome (CIS)

A neurological disturbance developing over days or weeks e.g:

- *optic neuritis – pain on eye movement, loss of vision in one eye*
- *cerebellar – ataxia, vertigo, clumsiness, loss of balance, nystagmus*
- *brain stem – blurred or double vision, limb, sensory, or motor skills*
- *bowel or bladder disturbance e.g., urgency*

- ***Secondary progressive MS (SPMS)***

Secondary progressive MS (SPMS)

- *Phase of progressive accumulation of disability that was preceded by relapsing-remitting phase.*
- *May be accompanied by an occasional relapse or MRI activity.*
- *There is an 50 to 80% lifetime risk of RRMS transitioning to SPMS.*

- ***Primary progressive MS (PPMS)*** – PPMS does not respond to current treatments.

Primary progressive MS (PPMS)

- *Progressive disease from the outset, rather than relapsing and remitting course.*
- *The most common presentation is slowly progressive spastic paresis, bladder and bowel symptoms, sensory symptoms, cognitive impairment, or cerebellar symptoms.*

4. Consider ***differential diagnosis.***

Differential diagnosis for multiple sclerosis

Psychiatric or functional, and various neurological disorders combined with incidental non-specific white matter changes is the commonest differential diagnosis.

- *Migraine*
- *CNS neoplasms*
- *Nutritional deficiencies (e.g., vitamin B12)*
- *Compression of spinal cord*
- *Infections (e.g., HIV, syphilis)*
- *Motor neurone disease*
- *CVAs or TIAs*
- *Emboli*
- *Neuroimmunological diseases (neuromyelitis optica spectrum disorder, anti-MOG syndrome, Behcet's disease, Susac syndrome, anti-GFAP, Balo's concentric sclerosis, acute haemorrhagic encephalitis)*
- *Paraneoplastic syndromes (including syndromes mediated by antineuronal antibodies)*
- *Systemic autoimmune diseases of connective tissue (systemic lupus erythematosus (SLE), Sjogren's syndrome)*
- *Primary cerebral vasculitis or systemic vasculitis*

5. Arrange ***investigations.*** MRI brain is the most sensitive investigation but if ordered by general practitioners is not Medicare-subsidised. A CT scan is not helpful for diagnosis.

Investigations

Consider:

- *Urine dipstick*
- *FBE*
- *Urea and electrolytes*
- *CRP*
- *TSH*
- *Creatinine*
- *B12*
- *LFTs*
- *MRI brain (if available)*

Management

General management

1. If rapidly progressive neurological symptoms causing weakness and/or imbalance, arrange immediate neurology referral or admission.
2. For patients presenting with optic neuritis or diplopia only, arrange an immediate ophthalmology assessment.
3. Request urgent or routine neurology referral to:
    - confirm the diagnosis and discuss treatment.
    - offer an opinion on persistent and unexplained sensory symptoms.

Include results of MRI brain (if available).

4. Provide details of ***community support services*** to the patient and carers. Only discuss disease specific services where the diagnosis is confirmed.

Community support services

MS Australia – provides support to patients with neurological conditions, carers, and clinicians, including:

- *peer support*
- *self-management programs.*

5. Discuss the importance of:
    - exercising regularly.
    - maintaining a healthy diet and weight.
    - stopping smoking, if a smoker.
    - reporting any new symptoms.

6. If a new neurological episode, determine if this is a:
    - ***relapse.***

Relapse

Suspect a relapse if new neurological signs or symptoms, or worsening of previous symptoms:

- *last longer than 24 hours.*
- *are in the absence of fever or other infective symptoms*
- *with urinary tract infection excluded.*

    - ***pseudo-relapse.***

Pseudo-relapse

- *Not caused by new demyelinating lesions but is a common cause of neurological worsening in MS.*
- *Can be related to damage from previous demyelinating lesions.*
- *Triggered by:*
    - *Increased **body temperature***

Body temperature

Increased by:

- *Fever*
- *Over-exercising*
- *Hot bath or spa*
- *Sun exposure*

  - *Infection even in the absence of fever*
  - *Trauma*
  - *Surgery*
  - *New medications*
  - *Other medical conditions, e.g. hyperglycaemia*
  - *Psychological stress*
  - *Fatigue*

- *Suspect a pseudo-relapse when:*
  - *there are fluctuating symptoms, especially if they completely resolve and then return.*
  - *old symptoms return.*
  - *the localisation pattern of symptoms is inconsistent with a lesion in the brain or spinal cord.*

- ***complication of treatment.***

Complication of treatment

Patients with MS treated with natalizumab are at risk of ***progressive multifocal leukoencephalopathy (PML),*** *a rare brain infection.*

Progressive multifocal leukoencephalopathy (PML)

- *PML is a rare but serious demyelinating disease of the brain, characterised by progressive demyelination damage or inflammation of the brain.*
- *It may result in severe disability or death.*
- *JC polyomavirus (JCV) causes PML.*
- *It is associated with some immunosuppressive or immunomodulatory therapies including natalizumab, and less commonly fingolimod, dimethyl fumarate, rituximab, and ocrelizumab.*

If new neurological symptoms lasting > 48 hours in patient on natalizumab contact their treating neurologist for review.

7. If the patient has a relapse, and it is impacting on their quality of life, consider treatment with corticosteroids:
   - Treatment hastens recovery and if administered early, may limit the magnitude of symptoms, but does not affect:
     - the likelihood of recovery.
     - degree of residual disability.

- future relapse rate.

- Treatment
  - high-dose corticosteroids – methylprednisolone 1 g a day for 3 to 5 days (administered IV or orally)
  - low-dose corticosteroids – prednisolone oral taper starting at 50 mg a day over 2 weeks.

- Exclude urinary tract infection (UTI) or other infection before treatment.
- Be aware of adverse drug reactions e.g., mood changes, psychosis, insomnia, avascular necrosis, and hyperglycaemia.
- Long-term exposure to corticosteroids is associated with reduced bone mineral density, especially in patients with limited mobility.

8. Give seasonal influenza ***vaccination.***

Vaccination

- *Give seasonal influenza vaccination.*
- *Vaccine-associated fever may exacerbate MS symptoms and cause a pseudo-relapse. Relapses after vaccination have rarely been reported.*
- ***Live vaccines** are contraindicated with all MS immunotherapies except for interferon beta and glatiramer acetate.*

Live vaccines

Live attenuated parenteral vaccines		Live attenuated oral vaccines	
Viral	***Bacterial***	***Viral***	***Bacterial***
• *Japanese encephalitis (lmojev)* • *Measles-mumps-rubella (MMR)* • *Measles-mumps-rubella-varicella (MMRV)* • *Varicella* • *Yellow fever* • *Zoster*	*Bacillus Calmette-Guérin (BCG)*	*Oral rotavirus vaccine*	*Oral typhoid vaccine*

- *Seek advice for travel vaccinations from travel vaccination clinics or neurology.*

9. If ***pregnant or considering pregnancy,*** request urgent or routine neurology referral.

Pregnant or considering pregnancy

- *Pregnancy is safe in patients with MS and may provide some disease protection from relapses.*
- *Some disease modifying drugs (DMDs) are contraindicated in pregnancy, e.g. fingolimod (D), teriflunomide (X). Other therapies are relatively contraindicated in*

pregnancy. Glatiramer acetate and dimethyl fumarate are deemed relatively safe in pregnancy (B).

- *Neurologist advice is required before any change in medication.*
- *If a patient becomes pregnant while on DMDs, immediately contact the treating neurologist or MS nurse.*
- *Request urgent or routine neurology referral for specialist pre-conception advice, particularly in a patient on DMDs.*
- *Risk of disease activity (clinical and MRI) is higher after childbirth. Women need to plan recommencement of DMDs after pregnancy (both timing and DMD).*

10. Offer advice regarding advance care planning.

11. Provide ***driving and transport advice.***

Driving and transport

- *Discuss the possibility that, at times, MS may affect the ability to drive safely because of relapses or disease progression.*
- *Consider eligibility for:*
  - *disability parking permits.*
  - *travel assistance.*

For more information, see Austroads – Assessing Fitness to Drive.

12. Encourage patient to seek early employment advice and support. If patient is working, consider a referral to MS Austalia and an occupational therapist for strategies to enable optimal function at work.

Symptom management

1. Manage ***fatigue.***

Fatigue

- *Fatigue often worsens as the day progresses, may be aggravated by heat, and is often seen with a relapse. Look for causes:*
  - *Sleep disturbances*
  - *Sleep apnoea*
  - *Depression*
  - *Medications*
  - *Pain*
- *Assist patient to manage fatigue with:*
  - *non-pharmacologic treatments, i.e. exercise programs, active cooling strategies, and energy conservation techniques.*
  - *medications – if required, these can be prescribed by a neurologist.*

2. Manage other symptoms:
   - ***Balance and coordination***

Balance and coordination

Assess falls risk and request physiotherapy assessment.

- ***Bladder problems***

Bladder problems

- *Bladder dysfunction is common in MS with up to 75% of patients affected.[2] Neurogenic bladder dysfunction leads to one or more of the following:*
  - *Failure of the bladder to store urine causing urgency, frequency, and urge incontinence.*
  - *Failure of the bladder to empty, causing interrupted stream, incomplete voiding, residual urine, and frequency.*
  - *Abnormal sensation causing urine retention, interrupted stream, and incomplete bladder emptying.*
- *Check for UTI.*
- *Provide continence aids if needed.*
- *Consider requesting physiotherapy assessment.*
- *In bladder urgency with or without incontinence and no symptoms of retention, consider mirabegron or oxybutynin.*
- *When other treatment for bladder spasm is not effective, request urgent or routine urology referral without delay as untreated neurogenic bladder can have significant consequences.*

- ***Bowel dysfunction***

Bowel dysfunction

Bowel dysfunction can include constipation, difficulty initiating a bowel motion, and faecal incontinence.

First, consider changes to diet, fluid intake, physical activity. If not effective, consider pharmacological approach.

Management:

- *If difficulty initiating a bowel motion, try:*
  - *bisacodyl.*
  - *glycerol suppositories.*
  - *digital stimulation.*
- *If faecal incontinence, consider:*
  - *whether this is part of normal bowel habit and manage with loperamide hydrochloride.*
  - *constipation with overflow incontinence:*
    - *If patient history unobtainable, consider X-ray abdomen.*

- *If confirmed, treat with rectal sodium citrate (Microlax or Micolette enemas) to manage impaction, and oral laxatives.*

- ***Cognitive impairment***

Cognitive impairment

- *While dementia is uncommon in patients with MS, cognitive impairment is common, affecting memory, reaction speed, planning and organising tasks, focus, and concentration.*
- *Consider depression and poor quality as a cause of, or contributing to, cognitive impairment.*

- ***Coughing and choking***

Coughing and choking

- *Poor cough can lead to the inability to clear secretions.*
- *Retention of oral secretions and silent aspiration can cause cough.*
- *Consider speech pathology assessment.*

- ***Dysphagia***

Dysphagia

See:

- *Dysphagia*
- *Adult Speech Pathology Referral*

- ***Pain and other sensory symptoms***

Pain and other sensory symptoms

- *Sensory symptoms are very common in MS and can include numbness, paraesthesia, tightness or cold sensation, itch, and pain.*
- *Pain may be:*
  - *musculoskeletal pain arising from immobility or spasticity.*
  - *neuropathic pain. See Peripheral Neuropathy pathway.*
- *Advise the patient to:*
  - *avoid triggers such as heat, wind, tight clothing, fatigue.*
  - *use pressure garments (hosiery or gloves) to convert painful sensations to pressure sensations.*
  - *exercise for core strength and to maintain flexibility and balance, e.g. yoga or Pilates.*
- *Consider pharmacotherapy with spasmolytics, tricyclic antidepressants, or other pharmacotherapy for neuropathic pain, as appropriate.*
- *Consider a referral for:*
  - *Cognitive behavioural therapy (CBT) or hypnosis*

- *Occupational therapy*
- *Physiotherapy*

- ***Sexual dysfunction***

Sexual dysfunction

- *Sexual dysfunction is common in patients with MS.*
  - *In men with MS, reduced libido, erectile dysfunction, loss of early morning erection, premature ejaculation, orgasmic dysfunction, and reduced penile sensation can occur.*
  - *In women with MS, sexual dysfunction includes reduced libido, difficulties achieving orgasm, decreased vaginal lubrication, decreased vaginal sensation, and dysparenunia.*
- *Body image can be affected by disease related changes, e.g. catheterisation.*
- *Relationship dynamics may be altered with the need for the spouse to be a caregiver.*
- *General management includes:*
  - *addressing pain, spasticity, bladder and bowel dysfunction.*
  - *treating depression adequately.*
- *Ensure adequate lubrication.*
- *Consider the adverse effects of medications. If selective serotonin reuptake inhibitors (SSRIs) are contributing to sexual dysfunction, consider the addition of a daytime dose of bupropion hydrochloride to counteract this effect.*
- *Consider phosphodiesterase type-5 inhibitors (e.g., sildenafil), which can be effective for the management of erectile dysfunction in men with MS.*
- *Consider referral to a psychologist.*

- ***Sleep***

Sleep

- *Recommend good sleep hygiene.*
- *Common sleep disorders in MS include:*
  - *Insomnia*
  - *Restless legs syndrome*
  - *Sleep-related breathing disorders*

- ***Spasticity and spasms***

Spasticity and spasms

- *Recommend:*
  - *Exercises and muscle strengthening, e.g. yoga, Pilates, or physiotherapy assessment.*
  - *Occupational therapy assessment:*
    - *Pressure injury assessment, management, and advice.*
    - *Assessment of patient's ability to carry out daily living tasks.*

- *Consider if skeletal muscle relaxant medications may be beneficial e.g.:*
    - ***Baclofen***
        - *If nocturnal only – baclofen 10 to 25 mg at night.*
        - *If continuous symptoms – baclofen 5 to 25 mg 3 times a day.*
        - *Withdraw slowly if medication ceased.*
        - *Adverse drug reactions include sedation, confusion, dizziness.*
    - ***Dantrolene***
        - *Dantrolene sodium 25 mg once or twice a day, mainly for bed-bound patients*
        - *Frequent adverse effects*
- *Consider discussing cannabis-based products (CBPs) with the treating specialist. CBPs may be an option for moderate to severe spasticity in MS patients who have not responded adequately to other anti-spasticity medication. Cannabis-based products are presently not PBS-listed and patients need to refrain from driving while on cannabinoids.*

- ***Thermoregulatory dysfunction***

Thermoregulatory dysfunction

- *Advise patient that overheating can exacerbate the signs and symptoms of MS. Limit strenuous exercise and exposure to the heat, e.g. hot weather, spas, baths or showers.*
- *Advise patient to use body cooling (cool showers, cooling vest, air conditioning).*

3. Address psychosocial issues, i.e.:

- ***Depression and anxiety***

Depression and anxiety

- *Antidepressant medications including SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs) can be effective, but CNS adverse effects are more common.*
- *If antidepressant medications are prescribed, start with lower doses and titrate dose slowly.*
- *See Depression in Adults and Anxiety in Adults.*
- *Consider referring patient to psychotherapist.*

- ***Grief reaction***

Grief reaction

Grief is the normal response to any loss and, in the setting of MS diagnosis and disease progression, is part of re-evaluating life and making changes.

- ***Behavioural changes***

Behavioural changes

Mood changes, personality, and impulsiveness can occur in relation to disease location, living with MS, or related to medication side-effects.

Referral

- If rapidly progressive neurological symptoms causing weakness and/or imbalance, arrange immediate neurology referral or admission.
- For patients presenting with optic neuritis or diplopia only, arrange an immediate ophthalmology assessment.
- Request urgent or routine neurology referral for:
    - investigation and confirmation of diagnosis.
    - persistent, unexplained sensory symptoms.
    - any new neurological symptoms.
    - patients who relapse.
    - specialist pre-conception advice, particularly in a patient on DMDs or planning IVF.
    - pregnant women.
    - Consider community support services via MS Austalia.
- If sexual dysfunction, consider referral to a psychologist.
- If depression or anxiety, consider referral to a psychotherapist.

Information

For health professionals

Further information

- Austroads – Assessing Fitness to Drive
- RACGP:
    - Clinical Guidance for MRI Referral
    - Multiple Sclerosis: Diagnosis, Management and Prognosis

For patients

MS Australia – What is MS?

References

1. Brown et al. Association of Initial Disease-Modifying Therapy With Later Conversion to Secondary Progressive Multiple Sclerosis. JAMA. 2019 Jan 15;321(2):175-187.
2. DasGupta R, Fowler CJ. Bladder, bowel and sexual dysfunction in multiple sclerosis: management strategies. Drugs. 2003;63(2):153-66.

Last Reviewed: December 2019

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