Sudden leg weakness

Where is the problem? What is the cause?

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Weakness in the legs of sudden onset requires urgent assessment and management. It is important to recognise that the actual onset of weakness may have preceded the patient's awareness or acknowledgement, for up to weeks at a time. Careful history-taking and examination will distinguish an apparent sudden weakness (over days or weeks) from an actual sudden weakness (over minutes to hours), requiring emergent referral and management. This article provides GPs with an approach to sudden leg weakness.

Neurological diagnoses are informed by identification of the precise location and aetiology of the underlying cause. GPs will have a working knowledge of the nervous system's gross anatomical structures and physiology, as well as familiarity with common patterns of disease and their presenting features. In many cases, taking a careful history and performing targeted physical examination are sufficient for formulating an accurate diagnosis and developing a management plan (Flowchart). Initial investigations should not delay an emergent neurological referral, if indicated, such as with acute spinal cord compression requiring prompt neurosurgical decompression (Box 1). Other causes of acute ascending paralysis, such as with postinfectious neuropathy or electrolyte disturbance (e.g. hypokalaemia), require cause-specific interventions.

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History

The presenting complaint

- What is the temporal profile of this weakness? Has it occurred over seconds to minutes, over hours to a day or two, or progressed over weeks? (Box 2)
- How and when has the weakness affected walking or running, going up and down stairs and getting up from a squatting position or chair?
- Has there been a previous episode of similar weakness?
- Is the weakness symmetrical? Did it begin in one or both legs?
- Is there any associated sensory disturbance or 'level'? Such information can provide clues as to the location of the lesion.
- Is there back or leg pain? Local back pain may indicate infection or compression; however, back pain can also occur with transverse myelitis, Guillain–Barré syndrome, and diabetic radiculopathy or plexopathy.

- Is there any associated bladder or bowel dysfunction?
- Does neck flexion cause weakness or tingling in the legs?
- Is the problem stable, progressing or improving?

Past medical history

Vaccinations and associated illnesses, such as recent infections, vascular disease, malignancy and collagen vascular disease, can be relevant. A comprehensive systems review can identify symptoms of such conditions.

Medication history

Previous use or misuse of neurotoxic medications (e.g. chloroquine, colchicine, cytotoxic agents), myotoxic substances (e.g. heroin, alcohol) or heparin may contribute to sudden leg weakness. Similarly, exposure to chemical toxins, such as arsenic, thallium and herbal cathartics containing podophyllin, may be relevant.

KEY POINTS

- 'Sudden' weakness can be interpreted to mean weakness that becomes obvious over seconds, hours, days or weeks.
- Important diagnostic clues, such as localised spinal tenderness or an extensor plantar response, can be revealed during a brief physical examination. A thorough neurological examination will also evaluate the appearance, tone, power and sensation of the face, neck, trunk and arms, as well as the legs.
- Indications for urgent referral include rapid progression of weakness that is ascending from the legs to the arms and face, or leg weakness with back pain and urinary retention.
- An acute lesion of the spinal cord may be accompanied by 'spinal shock' and may obscure the distinction between an upper and a lower motor neuron lesion.
- Common causes of sudden leg weakness include drop attacks, the Guillain–Barré syndrome and nontraumatic spinal cord compression due to metastatic tumour or an epidural abscess.

Family history

Although cases are not always familial, any family history of hypokalaemic periodic paralysis should be noted (Box 3).

Examination

General examination

An initial and brief general examination can yield important clues as to the diagnosis including:

- an irregular pulse, suggesting arrhythmia with associated risk of thromboembolism to the cerebral or spinal arteries
- stigmata of malignancy or collagen vascular disease
- localised spinal tenderness to percussion, suggesting an epidural abscess or local osteomyelitis
- a tick hidden in the posterior neck hairline.

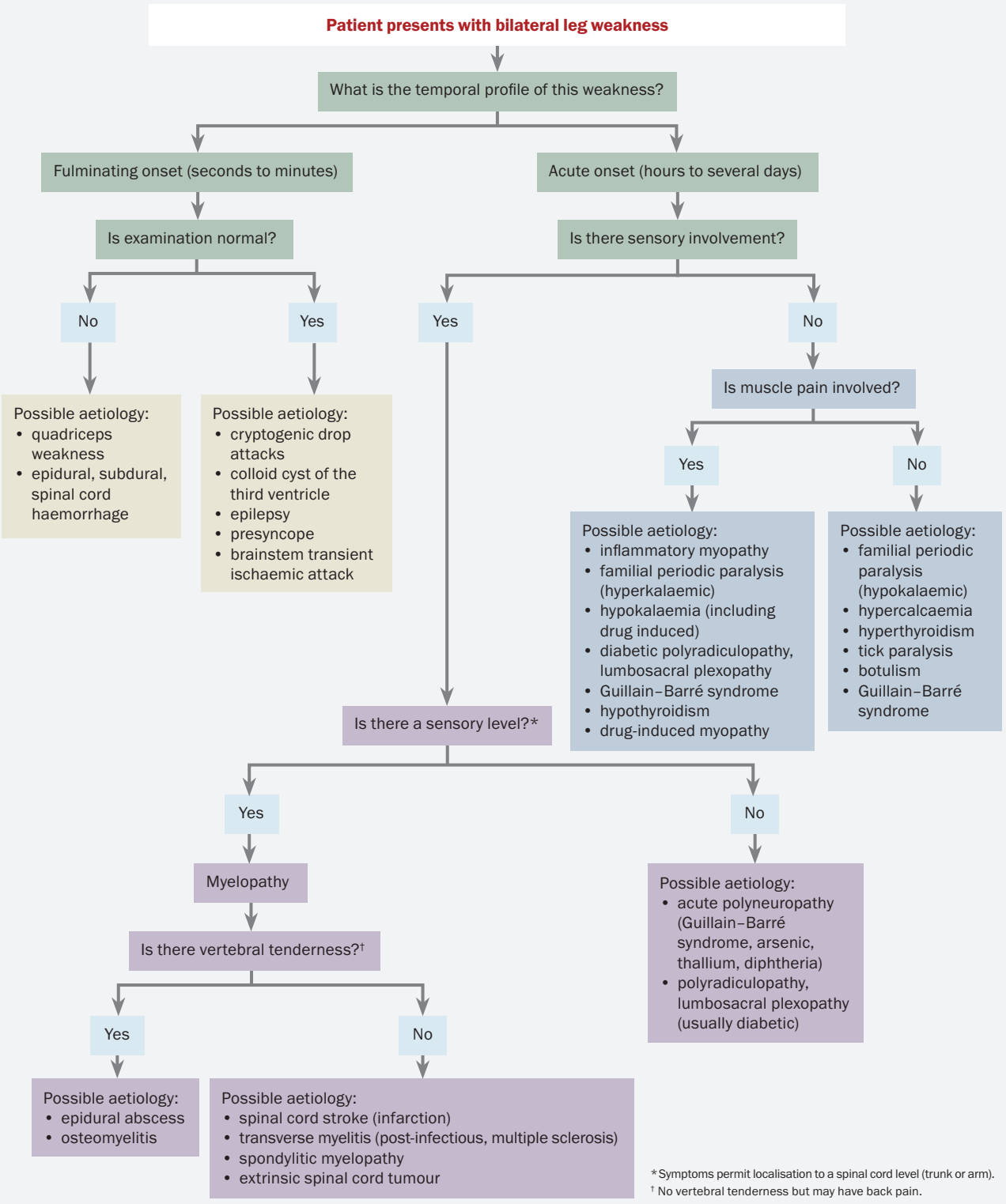
Neurological examination

Specific neurological examination is guided by hypotheses generated from history-taking, with an emphasis on early examination of the legs.

1. INDICATIONS FOR URGENT REFERRAL

- Rapidly progressive weakness
- Ascending weakness from the legs to the arms and face. Guillain–Barré syndrome is the most likely cause and patients may require ventilatory support
- Leg weakness associated with unusual back pain and urinary retention. An acute spinal cord compression may progress to complete paraplegia if not urgently diagnosed and surgically decompressed

CLINICAL PATHWAY TO DIAGNOSING SUDDEN BILATERAL LEG WEAKNESS



2. DIFFERENTIAL DIAGNOSES ACCORDING TO ONSET OF LEG WEAKNESS

Fulminating (seconds to minutes)

- Drop attacks
- Haemorrhage (epidural or intraspinal)

Acute (hours to several days)

- Inflammatory transverse myelitis (post-infection, post-vaccination)
- Demyelinating transverse myelitis (multiple sclerosis)
- Compressive myelopathy
- Polyneuropathies (Guillain–Barré syndrome, tick paralysis, botulism, diphtheria)
- Spinal cord stroke (rarely brainstem or bilateral cortical stroke)
- Familial periodic paralysis (usually hypokalaemic, rarely hyperkalaemic)
- Metabolic myopathy (hypercalcaemia, hypokalaemia, drug induced)
- Hysterical conversion disorder

Subacute (days to several weeks)

- Compressive myelopathy
- Intrinsic spinal cord lesion
- Meningeal carcinomatosis (multiple nerve roots)
- Myopathies (inflammatory, metabolic – hypercalcaemia, hypokalaemia, hypothyroid, hyperthyroid, and drug induced)
- Chronic inflammatory demyelinating polyneuropathy
- Neuromuscular junction diseases (myasthenia gravis, myasthenic syndrome)

TABLE. EXAMINATION FINDINGS OF UPPER VERSUS LOWER MOTOR NEURON WEAKNESS

Feature	Lower motor neuron	Upper motor neuron
Atrophy	Marked	None or mild
Fasciculations	Yes	No
Tone	Reduced	Increased
Weakness	Yes	Yes (pyramidal distribution)*
Tendon reflexes	Reduced	Increased
Plantar reflexes	Flexor response	Extensor response

* Leg muscle flexors and abductors affected more than extensors.

Head and neck

- Leg paraesthesia or weakness on neck flexion can indicate cervical cord demyelination or canal stenosis (and spinal cord compression).
- Weakness of the face is present in 50% of Guillain–Barré syndrome patients during the disease course and may be evident on presentation, so test carefully for facial muscle. weakness (especially eye and lip closure power).
- Abnormal eye movement or evolving ophthalmoplegia may point to Guillain–Barré syndrome or a multifocal central nervous system process, such as multiple sclerosis.
- Tongue movement and power may be weak in Guillain–Barré syndrome.

Trunk and upper limbs

- In examining the trunk, note whether superficial abdominal reflexes are present or absent, and test for abdominal muscle weakness on attempting to sit from lying in the supine position. A change to light touch or pinprick sensation may localise pathology to a thoracic spinal cord level.
- Signs of increased muscle tone, weakness, reflex or sensory abnormality in the arms can point to a cervical level or suggest a more generalised neuropathy.

Lower limbs

- Examine light touch, pinprick, position and vibration sensation. Include examination of the buttocks and perianal area, as well as the trunk. If abnormal, determine a sensory level, where possible.
- Identify any pattern to the weakness, such as with a proximal myopathy with graded distal to proximal weakness; flexor more than extensor muscle weakness of an upper motor neuron disorder; the reduced reflexes of a polyneuropathy; or the fatiguable weakness of a neuromuscular junction disease. In a patient with variable weakness against resistance and normal reflexes, consider hysterical conversion disorder.
- Examine for upper or lower motor neuron signs (Table).
- Consider spinal shock (see below).

Investigations

Imaging

Plain x-rays

Plain x-rays of the spine may reveal a destructive bony lesion or severe degenerative spinal disease, but otherwise have little benefit in the investigation of sudden leg weakness.

Computed tomography

In clinical practice, CT is easier to access than MRI in investigating patients with a suspected spinal cord lesion. Figure 1 shows a colloid cyst of the third ventricle, which can be associated with sudden bilateral leg weakness.

Magnetic resonance imaging

MRI has superior resolution to CT scans and can display the spinal cord in both transverse and sagittal planes. MRI can also detect parenchymal spinal cord disease and extramedullary infection or haemorrhage. Figures 2a and b show demyelination of the thoracic spinal cord in the transverse and sagittal section, respectively.

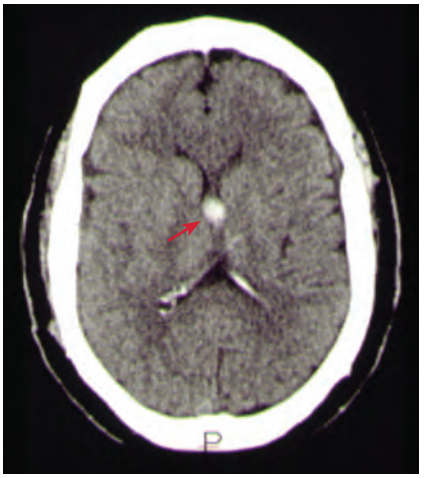
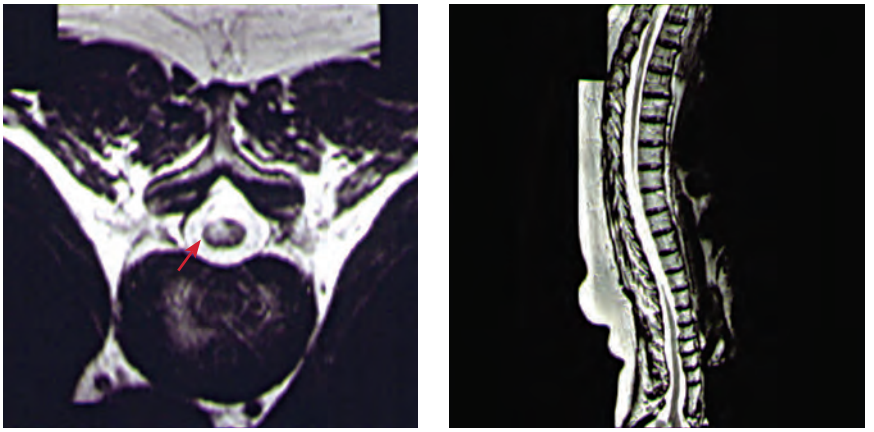


Figure 1. A CT scan of the brain showing a colloid cyst of the third ventricle (arrow). Bilateral ventriculoperitoneal shunts in the lateral ventricles allow for decompression of the ventricular system.



Figures 2a and b. An MRI of the spinal cord in a patient diagnosed with asymmetric transverse myelitis, showing demyelination at the midthoracic level (arrow). a (left). Transverse section. b (right). Sagittal section.

Neurophysiology

Nerve conduction studies

Nerve conduction studies may be urgently arranged to assist in the diagnosis of Guillain–Barré syndrome. The usual findings are significant slowing of conduction velocity and conduction block.

Electromyography

Electromyography may aid in the anatomical localisation of causative pathology to the level of the nerve root, plexus, peripheral nerve, neuromuscular junction or muscle.

Lumbar puncture

Cerebrospinal fluid analysis is required if acute spinal subarachnoid haemorrhage or infection is suspected. Lumbar puncture is desirable, but not necessary, for the diagnosis of Guillain–Barré syndrome, and the characteristic rise in protein levels may not be seen early in the disease.

Common diagnoses

Drop attacks

A drop attack is an unexpected fall with no obvious loss of consciousness (Box 4). The affected patient can usually rise immediately afterwards, but there is always a possibility of injury. The associations and causes of drop attack include epilepsy, vertebrobasilar insufficiency, quadriceps weakness, presyncope, multiple sclerosis, whiplash and midline cerebral lesions with acute intermittent hydrocephalus, such as a colloid cyst of the third ventricle (Figure 1). In clinical practice, most cases of drop attack occur in women who are otherwise healthy and have no apparent cause ('cryptogenic drop attacks'). The pathophysiology may relate to differences in postural control mechanisms between women and men.

Guillain–Barré syndrome

Guillain–Barré syndrome is the most common form of acute polyneuropathy. Early diagnosis is important because of the potential for rapid deterioration and need for ventilatory support. For most patients, the initial symptoms are muscle weakness (up to 99%), paraesthesia (70%) and myalgia (30%). Weakness is noticed first in the legs (85%), arms (10%) or face (5%), and a bacterial or viral infection may precede symptom onset (Box 5). The differential diagnoses of Guillain–Barré syndrome include botulism,

3. CASE STUDY: A WOMAN WITH A GOITRE AND EPISODIC WEAKNESS

A 44-year-old woman of Chinese descent presented to an emergency department with bilateral leg weakness. The weakness had occurred over one to two hours while sitting and watching TV, to the extent that she was unable to appropriately weight-bear. Further questioning elicited a two-year history of recurrent episodes of similar weakness associated with myalgia, occurring after completing heavy meals or excessive exercise.

On examination, the patient was found to be thin, with a fine resting tremor of the outstretched hands. She was tachycardic (resting pulse 100 beats per minute) and had a palpable diffuse goitre. Cranial nerve examination was normal. On examination of the limbs, the patient had normal tone, with a moderate symmetrical generalised weakness of the legs and milder involvement of the trunk and arms. Sensation was found to be normal. The patient had global reduction in tendon reflexes, with flexor plantar responses.

A provisional diagnosis of hypokalaemic periodic paralysis associated with thyrotoxicosis was proposed, based on syndrome recognition, and was confirmed with a low serum potassium level (2.1 mmol/L; reference range [RR], 3.8 to 4.9) and thyroid function tests (free thyroxine, 76 pmol/L; RR, 9 to 23; thyroid-stimulating hormone, 0.06 mIU/L; RR, 0.40 to 4.00).

The patient recovered following administration of oral potassium chloride and was later treated for Graves' disease, with amelioration of further episodes of periodic paralysis. The association between Graves' disease and hypokalaemic periodic paralysis is a well-recognised entity presenting almost exclusively in people of Asian origin.

4. CASE STUDY: A WOMAN WITH SUDDEN FALLS

A 69-year-old woman presented with a three-year history of 'drop attacks', which had been occurring every three to four months. The episodes occurred without warning. On walking down the street, she would develop a sense of falling forwards without dizziness or vertigo. She would then fall and hit the ground, but was able to get up immediately, without having developed confusion or lost consciousness. Six years earlier, she had experienced an episode of right otitis media, complicated by labyrinthitis and mastoiditis, resulting in a period of disequilibrium and persistent deafness in the right ear.

Cardiovascular examination was normal. The patient had profound right sensorineural deafness, but the rest of the cranial nerve examination was normal. Upper and lower limbs were normal. Cranial CT, electroencephalography and 24-hour ambulatory Holter monitoring were normal. The patient's symptoms were felt to represent drop attacks, probably secondary to vestibular dysfunction.

5. CASE STUDY: A YOUNG MAN WITH LEGS ABOUT TO 'GIVE WAY'

A 28-year-old man publicist presented to an emergency department complaining of lethargy and leg weakness. He had a diarrhoeal illness one week earlier, from which he had apparently recovered. However, a few days later, he noticed he was becoming easily tired, and his legs felt like they would 'give way'. On initial assessment, he demonstrated mild (grade 4 to 5) leg weakness, with no other specific features identified. He was admitted under the care of a general medical unit for observation.

The following day, the patient's leg weakness progressed such that he became unable to weight-bear. He became aware of some arm involvement, especially noticeable when using his cutlery. He described his face as feeling 'flat' and he complained of intermittent diplopia.

A repeat physical examination found mild bifacial weakness, bilateral external ophthalmoplegia with dilated pupils, and mild upper extremity and moderate lower extremity weakness with areflexia and flexor plantar responses. The results of sensory testing were normal. Spirometry revealed a mildly reduced vital capacity.

A diagnosis of Guillain–Barré syndrome was made, and the patient was commenced on a course of intravenous immunoglobulin. Later electromyography and cerebrospinal fluid examination supported the clinical assessment. The patient made a good functional recovery and was discharged home three weeks after admission.

tick paralysis (in eastern Australia), severe acute hypokalaemia, meningeal carcinomatosis and acute transverse myelitis with ascending weakness and sensory disturbance.

Most cases of Guillain–Barré syndrome will improve with intravenous immunoglobulin or plasma exchange. Supportive management includes prevention of the complications of immobility and, in the event of respiratory impairment or failure, admission to an intensive care unit. About 15 to 25% of patients with Guillain–Barré syndrome experience persistent functional deficit and the mortality rate is 5 to 10%.

Nontraumatic spinal cord compression

The clinical features of spinal cord compression depend on its location and the speed of its onset. In acute lesions, the rapid loss of motor power is associated with reduced muscle tone, variable weakness and sensory loss. Bladder dysfunction tends to occur later, except in acute cauda equina compression where it is an early feature. Spinal pain mostly predates or accompanies the onset of neurological symptoms in spinal cord compression.

The two most common aetiologies for acute nontraumatic spinal cord compression are metastatic tumour and infection (epidural abscess). Their main differential diagnoses are transverse myelitis and spinal stroke. Other rare causes of acute cord compression include epidural and subdural haemorrhage.

Imaging and surgical treatment must be carried out urgently if neurological function is to be preserved. Spinal MRI is the definitive investigation of choice, giving morphological information regarding the site of compression and the presence of tumour or infection (Box 6). If MRI is not available, myelography combined with CT scanning provides similar information, but carries a small risk of neurological deterioration. The timeliness of investigation and management can significantly reduce morbidity in patients with acute spinal cord compression.

Spinal shock

An acute lesion of the spinal cord may be accompanied by 'spinal shock', which may obscure the signs distinguishing upper and lower motor neuron lesions (Table). When the spinal cord is suddenly and severely damaged (such as by infarction, haemorrhage, sudden compression or inflammation), cord function and reflexes below the affected level become depressed or lost. Recovery occurs gradually over weeks; first, of reflexive function with extensor plantar responses (Babinski's sign), and then of muscle tone and tendon reflexes. Care must be taken not to misinterpret flaccid paraplegia as being due to a hysterical conversion disorder.

6. CASE STUDY: A TEENAGER WITH A 'FOOT SLAPPING'-TYPE GAIT

An 18-year-old female student was transferred from a rural hospital to a tertiary centre for urgent assessment. For four weeks, she had been aware of low thoracic back pain and progressive difficulty with walking. Initially, her legs felt stiff; later, she developed a 'foot-slapping'-type gait. She was unable to recall any significant trauma. By the time of review, she was unable to walk on uneven ground or negotiate steps. She had also noticed patchy numbness of both legs, at times to the level of the thighs.

Findings of physical examination of the cranial nerves and arms were normal. Flexion and extension of the lumbar and thoracic spine were limited by pain. The patient had increased tone in the legs with clonus at the ankles. There was moderate weakness in a 'pyramidal' pattern. There was also patchy sensory loss to all modalities to the level of the ankles bilaterally. All tendon reflexes were increased with extensor plantar responses. All cutaneous abdominal reflexes were absent.

A spinal cord lesion, most probably at the low thoracic level, was considered the most likely diagnosis. MRI of the thoracic spine demonstrated an extensive tumour surrounding the spinal cord at the T8 to T10 levels with compression and distortion of the cord as well as adjacent bony destruction.

The patient underwent urgent decompression surgery two hours later. Postoperatively, she retained good muscle strength in the legs. Histology reported a poorly differentiated small cell carcinoma and the patient was referred for radiotherapy.

Conclusion

Sudden weakness of the legs may develop over seconds, hours, days or weeks, and urgent assessment is always required. History-taking should acquire information regarding the patient's presenting complaint, past medical conditions, current medications and familial illnesses. General examination can yield important diagnostic clues, and focused neurological assessment should be guided by factors in the patient's history, with an emphasis on early examination of the patient's legs. Rapidly evolving weakness of the legs, unusual back pain and bladder dysfunction requires exclusion of acute spinal cord compression, and should indicate emergent referral for accurate diagnosis, early investigation and prompt neurosurgical decompression to significantly reduce adverse health outcomes. MT

Further reading

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COMPETING INTERESTS: None.

ONLINE CPD JOURNAL PROGRAM

True or false? Lumbar puncture for protein level analysis is required for the diagnosis of Guillain–Barré syndrome.

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