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An Uncommon but Important Cause of Bilateral Lower Limb Paresis or Paralysis

Dr. Lee Tsun Sing

A 53-year-old woman presented to our emergency department for bilateral lower limb weakness for 1 day. She had a history of hypertension, hyperlipidemia, diabetes mellitus, obesity and goitre.

During her first attendance, the vital signs were stable with blood pressure 148/76mmHg, pulse rate 99/min, respiratory rate 18/min, oxygen saturation 99% on room air and body temperature 36.9°C. The Glasgow Coma Scale was full. Neurological examination showed no facial asymmetry and normal upper limb muscle power (according to MRC Muscle Power Scale). The power for the left lower limb was 4 out of 5, while the power for the right lower limb was full. The point-of-care glucose level was 7.7mmol/L. The point-of-care blood test showed unremarkable blood gas analysis and potassium level of 4.1 mmol/L. The X-ray of the lumbosacral spine and the computed tomography of the brain showed no gross abnormalities. She declined admission and was discharged with a referral to the medical outpatient clinic for further workup.

She returned 2 days later with a progression in her weakness resulting in an episode of fall. Her vital signs were stable with blood pressure 146/90mmHg, pulse rate 79/min, respiratory rate 18/min, oxygen saturation 98% on room air and body temperature 36.7°C. The Glasgow Coma Scale was full. Neurological examination showed intact cranial nerve functions. The power for the upper limbs was full while the power for bilateral lower limbs was 4 out of 5. There was no focal tenderness over the spine. Repeated computed tomography of the brain was unremarkable and she was admitted to the emergency medicine ward for further workup and management.

During the stay in the emergency medicine ward, the lower limb power further deteriorated. She also developed an acute retention of urine requiring Foley catheter placement. Neurological examination was repeated, and it showed power of 3 out of 5 in the right lower limb and power of 4 out of 5 in the left lower limb. There was a sensory level starting from T4 to below. Rectal examination showed a lax anal tone.

How to approach a patient presenting with weakness?

It is not uncommon for us to encounter patients presenting with weakness in the emergency department. The causes may

consist of a range of neurological and non-neurological conditions. Therefore, we need to have a systematic approach to look for pathologies affecting different anatomical sites with a careful history taking, a focused neurological examination and the arrangement of appropriate investigations. For example, a hemiplegic pattern would point more towards a central lesion and neuroimaging studies should be arranged, while a paraplegic pattern would point more towards a spinal cause and spinal imaging studies would be more appropriate. Monoplegia could be the initial symptoms for many conditions causing paraplegia or hemiplegia. Therefore, further evaluation of the associated symptoms would help guiding us to work up for the underlying etiology. A focused clinical examination of the neurological system should be performed to gather the bedside clues that can guide us to arrange the most appropriate investigations for our patient.

Differential diagnoses

The differential diagnosis would be based on the anatomical structures being affected. Any abnormalities affecting the brain, the spinal cord, the peripheral nerves or the muscles can cause weakness in the lower extremities.[1] Vascular causes including arterial occlusion and metabolic causes must also be considered. Table 1. summarizes the anatomical structures that can be affected and lists a few examples of diseases in each anatomical site.

Clinical assessment for lower limb weakness

The approach for assessing a patient with bilateral lower limb weakness in the emergency department always starts with "A, B, C". Any patients with compromise of the airway, breathing and circulation should be resuscitated appropriately before proceeding to further clinical assessment.

It is then important to clarify whether the patient has a genuine loss of strength. Like "dizziness", "weakness" can be nonspecific and can mean fatigue, malaise or anhedonia.

Anatomical structures affected	***Possible etiologies***
Brain	Vascular causes (ischaemia/ hemorrhage) Infection (brain abscess) Tumour
Spinal cord	Trauma Infection (spinal abscess) Tumour Inflammation (transverse myelitis) Haematoma
Peripheral nerve	Gullain-Barre Syndrome
Neuromuscular junctions	Myasthenia Gravis Lambert-Eaton Syndrome Toxicology causes (Botulism, Organophosphate poisoning)
Muscle	Myopathy (alcoholic myopathy) Myositis
Vascular	Acute limb ischaemia Peripheral vascular disease
Metabolic causes	Hypoglycaemia Hypokalaemia (e.g. hypokalemic periodic paralysis) Severe hyperkalaemia Hyper- or hypo-calcaemia

Table 1. Differential diagnoses of generalised weakness according to the structure involved

Etiologies such as anemia and hypoglycaemia can also present with "weakness" without a

true loss of motor strength. Inquiring about functionality by asking the patient what he or she can no longer do can be useful.

For a patient with genuine loss of motor strength, careful history taking and physical examination would be essential for helping us to identify the location of the lesion. First, we need to evaluate the distribution of weakness, whether it is unilateral or bilateral, whether it affects only the lower limbs or with upper limbs or bulbar involvement, and whether it affects the proximal or distal parts of the extremities. The patient should also be asked if the weakness follows an ascending or a descending pattern which may indicate certain etiologies. The pattern of weakness and the possible etiologies are listed in Table 2.. Emergency physicians should be aware of both the upper and lower motor neuron lesions that may give rise to these weakness patterns and perform careful physical examinations and proper investigations for the evaluation of the underlying etiology.

Pattern	***Etiologies***
Paraplegia	Lesion at spinal cord or peripheral nerves
Hemiplegia	Lesion at contralateral cerebral hemisphere
Monoplegia	Lesion at the contralateral cerebral hemisphere, spinal cord or peripheral nerves
Quadriplegia	High spinal cord lesion or myopathy
Ascending	Guillain Barre syndrome, transverse myelitis, tick paralysis
Descending	Myasthenia gravis, botulism
Diffuse or sporadic	Dermatomyositis, polymyositis, hypokalemia, hyperkalemia, toxins

Table 2. Pattern of motor power loss

On the other hand, the onset and duration of the symptoms and any predisposing factors are also important. If the onset is abrupt, the likely cause is vascular such as stroke, until proven otherwise. If the onset is from minutes to hours, vascular, metabolic or toxin related causes are possible. If the onset is from hours to days, inflammatory causes or neuromuscular diseases are more common.

Associated symptoms and signs should also be evaluated carefully. The presence of vertigo, altered mental state, visual field deficits and bulbar involvement should raise the clinical suspicion for a lesion affecting the central nervous system, such as a brainstem stroke. The presence of bladder dysfunction points more towards a spinal cord lesion. The presence of a fatiguing pattern may point towards myasthenia gravis.

Clinical findings	***Location of lesion***
Dysarthria or dysphasia	Left cerebral hemisphere
Neglect	Right cerebral hemisphere
Diplopia, dysarthria, dysphagia, incoordination	Brainstem
Bladder dysfunction	Spinal cord
Sensory level	Spinal cord
Loss of reflexes, absence of Babinski sign	Lower motor neuron lesions (Peripheral nerve)

Table 3. Findings associated with weakness

Physical examinations aim for a systematic approach to identify the location of the lesion. The test of muscle strength and the pattern of muscle weakness helps to localize the level of the lesion. Reflex testing and sensory assessment are also essential for neurological assessment of patients with paraparesis.[2] For instance, a clearly defined sensory level is a hallmark of spinal cord diseases and loss of reflexes would indicate a

lower motor neuron type lesion. The associated symptoms and physical examination findings that may narrow the differential diagnoses have been listed below in Table 3.

In the emergency department, initial investigations usually consist of simple blood tests or point-of-care tests, neuroimaging and spinal imaging examinations. Point-of-care glucose level is essential to exclude hypoglycaemia as an easily reversible cause for weakness. Blood test is helpful to identify potential electrolyte disturbances causing the weakness, such as in the case of thyrotoxic periodic paralysis due to hypokalemia.

Neuroimaging examinations, such as plain computed tomography of the brain is useful in identifying any acute intracranial bleeding or space-occupying lesions when we suspect a central cause of the weakness. However, imaging of the spine would be more appropriate when the clinical assessment pointed more towards a spinal cord lesion as indicated by the presence of a sensory level and paraparesis. X-ray imaging of the spine can reveal potential causes of spinal cord lesions. Although magnetic resonance imaging (MRI) of the spine is the imaging modality of choice when we are examining a suspected spinal lesion, it is usually arranged after the patient is admitted for further workup.

Progress of our patient

The patient was transferred from the emergency medicine ward to the orthopaedic ward for a suspected spinal cord compression on the same day of admission.

Physical examinations by the orthopaedic surgeon showed that the limb power of the upper limbs and the left lower limb was full. The limb power of right lower limb ranged from 1 to 4 out of 5. The right plantar reflex was upgoing while the left plantar reflex was equivocal. There was a sensory level starting from T5 to below. The rectal examination showed a lax anal tone with weak grip. There was also reduction in the saddle sensation.

Urgent MRI of the spine was arranged by the orthopedic surgeon. There was a long segmental T2 hyperintense cord signal in association with cord swelling extending from lower C2 to T7 levels as shown in Fig.1. The post-contrast T1 weighted images also showed a rim enhancement pattern from C5/6 to T4 levels as shown in Fig.2. With a high suspicion of transverse myelitis, the medical team was consulted and the patient was taken over to the medical ward for further care.

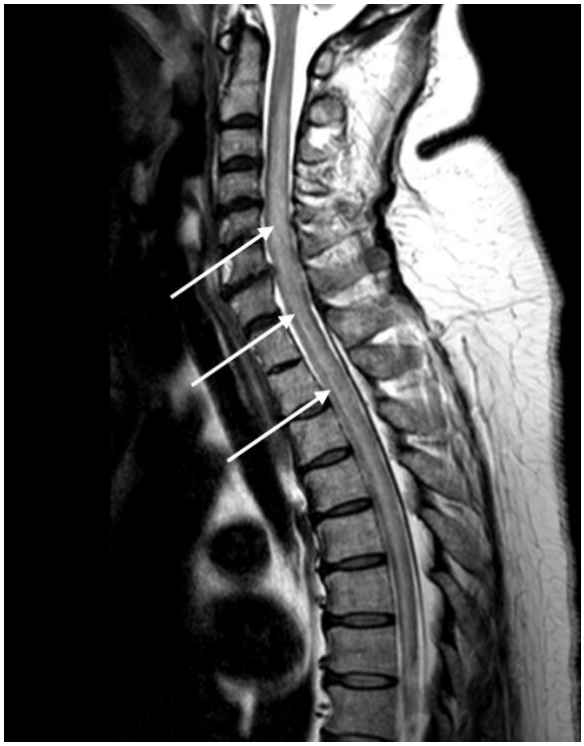

Fig.1 T2-weighted image of MRI spine showing a hyperintense spinal cord signal from C2 to T7 levels (long white arrows)

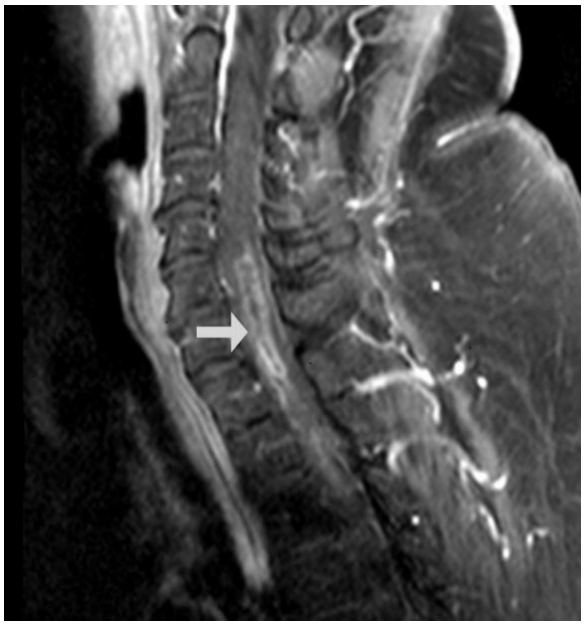

Fig.2 Post-contrast T1-weighted image of the MRI spine showing a patchy rim like enhancement of the cord lesion (short grey arrow)

After assessment by the neurologist, pulse steroid was started. There was some clinical improvement in the lower limb power. However, the ankle control and the ambulatory function were still suboptimal.

Therefore, plasma exchange was arranged after liaison with the intensive care team. She was later transferred to the rehabilitation ward for rehabilitation. There was an improvement in the lower limb power. The patient was later discharged home after home screening and carer training done.

More about transverse myelitis

Clinical features

Transverse myelitis is a rare immune-mediated disorder affecting the spinal cord. Common clinical features include a rapid onset of weakness, sensory deficits and autonomic dysfunction affecting the urinary bladder function or bowel opening.[3] Besides being a manifestation of some autoimmune disorders like multiple sclerosis or neuromyelitis optica, many cases of transverse myelitis are considered idiopathic as the cause is not identified. A large proportion of these cases presented after a respiratory or systemic infection. It is suspected that the spinal cord injury is due to a systemic response to infection rather than a direct infection to the cord by pathogens. Some researchers believed that the insult could be a result of molecular mimicry and microbial superantigens, which causes autoimmune responses damaging different spinal cord structures.[4]

The onset of transverse myelitis is usually acute or subacute. Most common initial symptom is sensory change, followed by weakness and pain. Motor symptoms depend on the spinal cord levels involved. Upper cervical lesions may affect all four extremities or even the phrenic nerve, leading to diaphragmatic dysfunction and respiratory failure. Lesions in the lower cervical spine may lead to upper and lower motor neuron signs in the upper limbs, and exclusive upper motor neuron signs in the lower limbs. Lesions in the thoracic region, which is most common, may lead to upper motor neuron signs in the lower limbs. It is essential to note that in upper motor neuron injury, the initial presentation would be flaccid paralysis rather than spasticity. Due to spinal shock, there would be an initial period of hypotonicity before spasticity develops.

The presence of a sensory level is common in patients with transverse myelitis. Sensory symptoms may include pain, dysesthesia and parathesia. Autonomic symptoms including

urinary, bowel and sexual dysfunction can also be seen. Therefore, it is important for us to identify for any sensory level which can prompt us towards a spinal pathology causing the symptoms.

Investigation approach

It is clinically difficult, if not impossible, to differentiate whether the symptoms are caused by the autoimmune mediated neuropathy or a spinal lesion causing a true cord compression. Therefore, an urgent spinal imaging would be essential to differentiate the underlying etiology.[5] A spinal MRI scan would be the preferred choice of investigation. Common MRI features include a contrast-enhancing signal abnormality. The lesion usually gives a poorly delineated hyperintense signal in T2-weighted images and variable (none, diffuse, patchy or rim) enhancement on post-contrast T1-weighted images. The lesion typically extends over several spinal segments. The affected cord usually becomes swollen.[6]

If transverse myelitis is suspected, lumbar puncture for cerebrospinal fluid analysis may also be required for further evaluation of the underlying inflammatory condition or infectious etiology.

Blood tests such as various autoantibodies, inflammatory markers, vitamin B12 level, HIV and syphilis serology as well as other viral studies would also be warranted to determine the underlying etiology if the cause of myelitis is not obvious. Sometimes, MRI brain may also be required to evaluate brain lesions, for example, in the case of multiple sclerosis or other systemic inflammatory disorders that can involve the brain.

Treatment

The treatment of transverse myelitis is aligned with many other autoimmune conditions. High-dose intravenous glucocorticoid therapy is considered as the first-line and standard treatment for patients with acute transverse myelitis.[7] The initial treatment regime usually lasts for three to five days. An extended course of therapy may be needed depending on the clinical response.

The clinical response to the initial therapy is difficult to predict. However, some researchers believe that an early initiation of treatment would be associated with a better clinical responsiveness to the treatment.

For patients with poor response to high dose steroid therapy, plasma exchange can also be considered. It is an extracorporeal treatment to remove the abnormal autoantibodies which causes the damage to the spinal cord.[8]

Some clinical studies also showed a good outcome of using cyclophosphamide for patients with aggressive transverse myelitis.

For patients with recurrent diseases, long-term immunomodulatory therapies have to be considered.

Prognosis

Most patients would have a partial recovery within the first few months of treatment. However, the rehabilitation process takes years, and it is not uncommon to have residual disabilities in these groups of patients.[9] Therefore, a multidisciplinary group of healthcare professionals supporting these patients in their rehabilitation would be essential.

Comments on the case

The two doctors who attended to the patient in the A&E did not enquire about sensory symptoms or sphincter dysfunction in detail. They also did not perform a rectal examination. The weakness of the patient was mild initially and probably the doctors did not suspect an acute spinal cord lesion. Emergency physicians should be alert that some serious neurological conditions may initially present with mild weakness only, but may progress to complete paralysis within a few days. It is especially important to maintain a high index of suspicion of the potentially deadly conditions for patients presenting with limb weakness, and at the same time keep a broad list of differential diagnoses in mind when evaluating those patients. Adequate clinical examination of the neurological system, not only on the motor system, but also the assessment of the reflexes and sensory level, would be essential to guide us to identify the level of the lesion and help us to choose the most appropriate investigation for our patient.

Lessons to learn from the case:

- **Understand the differential diagnoses for a patient who presents with limb weakness**
- **Know the approach of clinical assessment for evaluation of the cause of weakness**
- **Do not underestimate the severity of the condition even if the initial symptoms are mild when the cause of weakness is uncertain**
- **Understand how the pattern of weakness and the associated symptoms may help to identify the potential underlying lesion**
- **Learn about transverse myelitis, including the clinical presentation, investigations, and treatments**

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