Weakness may mean different things when a patient says he or she is weak. Some things to check on your history and physical:

- **Laterality:** Is the weakness unilateral, bilateral, or diffuse?
- **Isolation:** Does the weakness show up with isolating muscle groups, or only when the patient is forced to coordinate muscle groups?
- **Time course:** Are the symptoms acute in onset, or more prolonged? Are they constant or intermittent?
- **Progression:** Are the symptoms getting worse? Are they spreading to adjacent muscle groups or locations on the motor cortex, or are they skipping around?
- **Concurrent symptoms:** Is the weakness due to pain or decreased sensation, or is it true weakness? Is the weakness related to an underlying disease that may be exacerbated by another problem?

**Localizing the lesion** will help determine your workup. From distal to proximal, weakness can present from lesions in the following regions:

- **Muscle:** Often accompanied by pain at the site, and frequently bilateral; no sensory loss
  - Look for: pain at the site of weakness
  - *Ex:* steroid myopathy, muscular dystrophy, polymyositis, dermatomyositis
  - **Can’t miss:** rhabdomyolysis
- **Neuromuscular junction:** Often (but not always) fluctuating in time course, and exacerbated by either activity or rest; no sensory loss
  - Look for: historical clues (fluctuating course, exacerbating/alleviating factors, toxin exposure, etc.)
  - *Ex:* myasthenia gravis, Lambert-Eaton syndrome, botulism, cholinergic toxins
  - **Can’t miss:** myasthenic crisis, botulism, toxicologic causes
- **Peripheral nerve:** Often accompanied by pain; all lesions at and proximal to this site may also include sensory loss
  - Look for: symptoms following regions of nerve distribution, presence of concomitant diseases (e.g. DM or autoimmune disease can cause polyneuropathy)
  - *Ex:* DM neuropathy, Guillain-Barre, Bell’s palsy
  - **Can’t miss:** Guillain-Barre syndrome
- **Nerve root:** More often causes subjective weakness due to pain rather than true weakness
  - Look for: radicular pain along dermatomes, presence of red flags (e.g. urinary retention, bowel/bladder incontinence, saddle anesthesia)
  - *Ex:* disk herniation, cauda equina syndrome
  - **Can’t miss:** cauda equina syndrome
- **Spinal cord:** May be painful at the site of the lesion, uncommonly causes radicular pain
  - Look for: history of trauma, IV drug use, recent spinal surgery, anticoagulation

https://foundationsem.com/
- **Ex:** transverse myelitis, MS, trauma, mass lesion, neurosyphilis
- **Can’t miss:** any spinal cord pathology

  - **Brainstem:** Lesions here produce cranial nerve findings, and may include “crossed signs” (weakness/sensory loss on one side of the face and contralateral side of the body)
    - Look for: crossed signs, altered mental status (esp. level of alertness)
    - **Ex:** stroke, mass lesion, MS, vertebral artery dissection
    - **Can’t miss:** any brainstem pathology

  - **Cerebellum:** Lesions here don’t usually cause true weakness, but rather dyscoordination (hence importance of examining gait and coordinated motor tasks)
    - Look for: concurrent vertigo or ataxia, neck pain
    - **Ex:** stroke, EtOH cerebellar degeneration, vertebral artery dissection
    - **Can’t miss:** most cerebellar pathology, possibly excluding acute EtOH intoxication

  - **Cortical/subcortical cerebral hemisphere:** There are minutiae that can differentiate these, but these lesions are treated identically in the ER. These lesions may cause a headache (e.g. ICH) but rarely cause pain at the site of weakness.
    - Look for: symptoms following a “cortical homunculus” distribution, AMS
    - **Ex:** stroke, cortical degenerative process (e.g. Alzheimer’s, Parkinson’s)
    - **Can’t miss:** stroke/ICH, cerebral mass lesions

Note that any causes of weakness localizable to the central nervous system usually require imaging, whereas lesions at the nerve root or more distally usually do not, with trauma being a major exception.

Remember that metabolic derangements can cause weakness in patients with underlying disease, e.g., patients with Alzheimer’s may develop diffuse weakness in the setting of a UTI, or a patient with a history of stroke may have recrudescence of their symptoms in the setting of infection.

References:
Riebau, Derek: “Localizing Neurological Lesions.”

https://foundationsem.com/