

**CASE VIGNETTE**

A 24 years old young male is brought to the casualty with 2 days history of acute onset, progressive weakness of all four limbs. At presentation he is bed bound. On examination he has flaccid quadriplegia with swallowing difficulty. What should be the approach to such a patient?

**INTRODUCTION**

Acute flaccid paralysis (AFP) can be defined as a clinical syndrome characterized by rapid onset (usually hours to days), progressive weakness of at least one, usually two or more limbs. There may be bulbar and respiratory involvement.

Accurate diagnosis of the cause of AFP is important for therapy and prognosis. If untreated, AFP may not only persist but also lead to death due to failure of respiratory muscles. It can also cause complications like aspiration pneumonia, deep venous thrombosis, bed sores and contractures. AFP also is of great public health importance because of its use in surveillance for poliomyelitis in the context of the polio eradication initiative.

**NEUROANATOMICAL CORRELATE OF DIFFERENTIAL DIAGNOSIS**

Before approaching the given case it is useful to keep some common differential diagnoses in mind as per anatomical location starting from one end of the neuraxis.

**Muscle:**

- Inflammatory myopathy (polymyositis, dermatomyositis)
- Viral myositis
- Periodic paralyses (hypokalemic, hyperkalemic)
- Metabolic derangements (hypophosphatemia, hypokalemia, hypermagnesemia)

**Neuromuscular Junction**

- Myasthenia Gravis
- Animal toxins (snake bite especially cobra, krait; shellfish, crab etc)
- Botulism
- Tick paralysis
- Organophosphate toxicity (can also cause neuropathy)
- Lambert-Eaton Myasthenic Syndrome (LEMS)

**Nerve (acute neuropathies)**

- Diphtheria
- "Dumb" rabies
- Porphyria
- Drugs & Toxins (arsenic, thallium, lead, gold, chemotherapy - cisplatin / vincristine)
- Vasculitis (incl. lupus, polyarteritis)

**Nerve Roots (acute polyradiculopathies) and plexus lesions**

- Guillain-Barre Syndrome
- HIV
- Other viruses like CMV
- Cauda equina syndrome (lumbar disc, tumour, etc.)
- Sarcoidosis
- Lyme disease
- Plexus lesions (brachial plexitis, lumbosacral plexopathy)

**Anterior Horn Cell**

- Poliomyelitis
- Other viruses like HIV
- Paraneoplastic

**Spinal Cord**

- Inflammatory (Transverse myelitis)
- Other myelopathies (epidural abscess or hematoma)
- Anterior spinal artery syndrome

**CLINICAL CLUES**

History: Following points in the history must be enquired into so as to classify the presenting pattern of weakness (as given below). This helps not only finding the underlying etiology but also the prognosis and deciding the therapy:

- Onset & progression of weakness: sudden, acute (over hours), subacute (days to weeks)
- duration of weakness (hours to days to weeks)
- pattern of weakness (eg: proximal, distal)
- pattern of progression (eg: onset in arms, "ascending paralysis")
- sensory involvement (numbness, tingling, loss of balance esp. in dark, pain / burning)

- 424
- bulbar involvement (change in voice or swallowing)
  - facial weakness (trouble chewing, sucking with straw, blowing)
  - extraocular muscle weakness (diplopia) or ptosis
  - respiratory involvement (inability to complete sentences, dyspnea, orthopnea)
  - bladder or bowel involvement
  - autonomic involvement (diarrhea, orthostatic dizziness, urinary retention, palpitations)
  - systemic symptoms (fever, weight loss, rash, joint pain)
  - recent illness or immunization (diarrheal or respiratory tract infection, anti rabies vaccine, oral polio vaccine)
  - recent travel (out of country, to woods [tick bites])
  - recent h/o dog bite
  - precipitating factors (exertion, carbohydrate loading - with periodic paralyses)
  - fluctuation in weakness (eg. diurnal variation, fatigability in myasthenia)
  - drug or toxin exposure (canned or 'bad' food, pesticides, lead exposure)
  - family history (porphyria)

### PHYSICAL EXAMINATION

- Distribution and degree of weakness looking specially for extraocular muscles, facial muscles and bulbar involvement
- Assess for fatigability
- Sensory impairment: particular modality (vibration / proprioception vs. pain / temperature) - is there a sensory level?
- Reflexes: Are the deep tendon reflexes lost? (ie. areflexic), depressed, preserved, or brisk); Do diminished reflexes facilitate with repeated efforts? (LEMS)
- Autonomic features (postural fall, abnormal sweating, pupillary response, ileus)
- Skin: lines on nails with arsenic poisoning (Mee's lines), ticks, photosensitivity, Gottron's papules on extensor surfaces & heliotrope discoloration over eyelids (dermatomyositis), fang marks
- Spinal tenderness (with epidural abscess or hematoma, spinal tumour)
- Straight leg raise (radiculopathy)

### CLINICAL CLUES TO DIFFERENTIAL DIAGNOSIS

Step 1: Is it an upper motor neuron (UMN) or a lower motor neuron (LMN) lesion?

Clues to UMN lesion (mostly a spinal cord lesion) could be presence of either:

- Brisk reflexes
- Extensor plantar
- Definite sensory level
- Bladder or bowel involvement

A LMN lesion will have absent reflexes with mute plantar. Frequently, an acute onset spinal cord lesion may present with absent reflexes due to spinal shock. But the presence of other differentiating features (extensor plantar, definite sensory level and bladder involvement) help localize the lesion to spinal cord.

Step 2: If it is a LMN lesion what is the pattern of weakness? Is it proximal or distal?

Lesions localized to the following anatomical locations cause proximal, mostly symmetrical weakness in AFP:

- Muscle
- NMJ
- Polyradiculoneuropathies

Poly neuropathy will present with distal, mostly symmetrical weakness. Lesions localized to the anterior horn cells can present with symmetrical or asymmetrical, proximal, distal or a combination of both. The reflexes will be absent in both the conditions.

Step 3: Are the reflexes preserved?

Localization of lesions with proximal weakness and preserved reflexes include muscle or NMJ. Fatigability (appearance of weakness with repeated use) is a prominent feature in NMJ disorders especially myasthenia.

Reflexes would be absent in:

- Anterior horn cell disorders
- Polyradiculoneuropathies
- neuropathies

Step 4: Are sensations preserved?

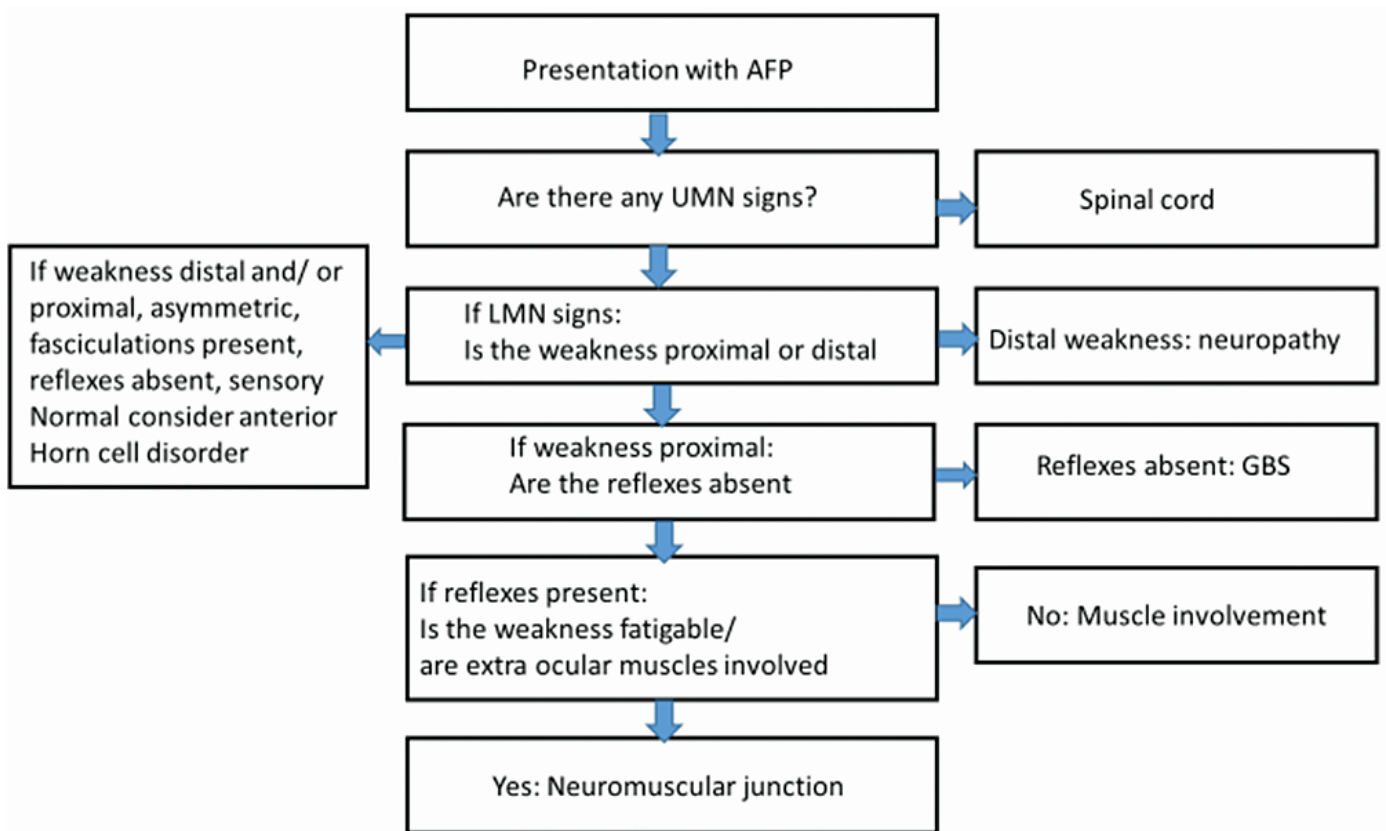
Neuropathies present with sensory involvement. Polyneuropathy presents with glove and stocking sensory involvement while mononeuritis multiplex would present with patchy sensory loss.

Polyradiculoneuropathies may or may not have a sensory loss. Some GBS variants may have sensory loss. Cauda equina may present with a sensory loss in a radicular distribution.

### CATEGORIZATION AS PER PATTERN OF INVOLVEMENT

It is useful to classifying the pattern of involvement into any one of the following given below. This approach narrows the differential diagnosis further (Figure 1).

1. Flaccid symmetric quadriparesis ( $\pm$  bulbar and respiratory involvement) with areflexia and minimal to profound sensory loss (but often



**Fig. 1: Flow diagram of approach to acute flaccid paralysis (AFP)**

- sensory symptoms) - Acute neuropathy or polyradiculopathy (eg GBS)
- Symmetric proximal muscle weakness without sensory symptoms or signs and with preserved reflexes: Acute myopathy (eg. polymyositis); periodic paralysis
  - Fatiguable muscle weakness with diplopia, ptosis and bulbar dysfunction (eg myasthenia and other neuromuscular disorders)
  - Flaccid Paraparesis with sensory level (often with reduced lower limb reflexes & bladder dysfunction) - Cauda equina syndrome (painful), thoracic spinal cord lesions (eg. transverse myelitis, spinal cord infarct)
  - Bulbar predominant involvement:
    - Botulism
    - Myasthenia gravis
    - GBS
    - Snake bite
  - Ophthalmoplegia with motor weakness:
    - Miller-Fischer variant of GBS (areflexia)
    - Botulism & Tick paralysis
    - Snake Bite
  - Prominent autonomic dysfunction:
    - GBS
    - Paraneoplastic syndromes
    - Organophosphate toxicity (muscarinic cholinergic overstimulation)
    - Botulism

### FURTHER INVESTIGATIONS

It is imperative to have a clinical approach as outlined above rather than relying only on electrophysiology, lab parameters or imaging to aid in the diagnosis. After the differential diagnosis is narrowed then tests can be done to confirm diagnosis. Further management strategies will depend on the most probable diagnosis.

### MANAGEMENT OUTLINE IN SOME SPECIFIC AFP

#### Guillain- Barre Syndrome

Specific Measures:

- IVIg or plasmapheresis are equally effective in reversing the conditions. However the side effect profile of IVIg is better.
- IVIg is given in dose of 400 mg/kg /day for 5 days while plasmapheresis can be done on alternate day for 5-6 sessions depending on the response.
- Indications include
  1. Rapidly progressive weakness
  2. Presence of respiratory or bulbar involvement
- Not indicated if the degree of weakness is non progressive and has been present for more than 2 weeks.

## 426 Supportive Measures:

- Air way protection
- Cardiovascular monitoring for autonomic dysfunction
- Enteral feeding if oropharyngeal dysfunction present
- Nutrition and daily fluid balance in ICU patients
- Correction of electrolyte imbalance and conditions like SIADH
- Heparin/ LMWH for prevention of DVT
- Prevention of bed sores
- Early rehabilitation

### MYASTHENIA GRAVIS

- Steroids are the main stay. However should start at low dose and then gradually build up
- Immunosuppressants like azathioprine may be added subsequently as steroid sparing agents. Other drugs like mycophenolate also are a good option
- Acetyl Choline esterase inhibitors like pyridostigmine (60 mg tablet) or neostigmine (15 mg tablet) are started along with steroids and titrated as per requirement.
- IVIg (400 mg/kg / day X 5 days) or plasmapheresis is indicated if patient presents in crisis or impending crisis. Presence of respiratory distress defines the presence of crisis
- Patient may be referred for thymectomy if they have generalized disease and

1. Thymic mass is demonstrated on a CT chest
2. If no thymic mass then if age is between 10 to 55 years

### POLYMYOSITIS

- Steroids are started as soon as the diagnosis is confirmed.
- On follow up once improvement starts steroid sparing immune suppressants like azathioprine or mycophenolate etc are added.
- Early rehabilitation is needed

### HYPOKALEMIC PERIODIC PARALYSIS

- Correction should start with oral therapy of 15 ml solution of KCl (diluted) and can be given as frequent as 30 minutes till improvement starts.
- IV replacement is usually not necessary and indicated if there is swallowing difficulty or vomiting.
- Long term therapy consists of acetazolamide in doses from 250 mg-1000 mg/day.

### REFERENCES

1. Kasper DL, Fauci AS, Hauser SL, Longo DL, Jameson JL, Loscalzo J (editors). *Harrisons Principles Of Internal Medicine*. 19th Ed. New Delhi: Mc Graw Hill; 2015.
2. Campell WW. *DeJong's The Neurologic Examination*. 7<sup>th</sup> Ed. Lippincot Williams Wilkins; 2012.
3. Daroff RB, Jankovic J, Mazziotta JC, Pomeroy SL (editors). *Bradley's Neurology in Clinical Practice*. 7<sup>th</sup> Ed. Elsevier; 2016.