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(REVIEW ARTICLE)



## Acute flaccid paralysis

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### Abstract

Acute Flaccid Paralysis (AFP) is a syndrome characterized by a diffuse, acute muscular weakness that develops with hypotonia and deep or abolished hypoactive reflexes. Literature review of the last five years in the databases Pubmed, Scopus, Embase, and Web of Science. Data were collected from epidemiological studies using the keywords. AFP includes heterogeneous diseases, variable clinical presentation, and correlated with a specific etiology. The differential diagnosis of acute flaccid paralysis includes spinal cord diseases, acute polyneuropathies, myoneural plaque dysfunction, and muscle disease. PFAs represents a set of disorders used by the World Health Organization (WHO) as an indicator of polio eradication. Therefore, the knowledge and understanding of the respective etiologies are necessary to make their differential diagnosis and appropriate treatment.

**Keywords:** Paralysis; Acute inflammatory polyneuropathy; Acute autoimmune neuropathies; Acute infectious polyneuritis; Acute transverse myelitis; Myasthenic syndromes

### 1. Introduction

Acute Flaccid Paralysis (AFP) is a syndrome characterized by rapidly evolving diffuse muscle weakness (critical course), muscular hypotonia, and deep or abolished hypoactive reflexes [1-3]. It is a sudden disease that develops in hours to weeks, and the acute term refers to neurological disability in this range. The time of AFP evolution varies and depends on the etiology [4-7]. The incidence of AFP is used by the World Health Organization (WHO) as an indicator of polio eradication. From 1990-1996, the etiological characterization in 3,619 cases of AFP in children under 15 years old allowed us to establish that Guillain Barré Syndrome (GBS), the leading representative, occurred in 46%, and the other etiologies were: myelitis (3%), post-vaccine polio (2%), tumors (1%), trauma (1%), various causes (32%), undefined etiology (14%) [8-10]. In this sense, due to the severity of the disease, the present study aimed to evaluate the primary evidence and results found in scientific studies about the definition, risk factors, epidemiology, clinical manifestations, diagnosis and treatment of Acute Flaccid Paralysis (AFP).

### 2. Material and methods

A literature review was conducted in the last five years on Pubmed, Scopus, Embase, and Web of Science databases. Data were collected from cohort studies, systematic reviews, case reports, and literature reviews using the keywords: paralysis, acute inflammatory polyneuropathy, acute autoimmune neuropathies, acute infectious polyneuritis, acute

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transverse myelitis, myasthenic syndromes. The authors were based on the following guiding question: "What are the main evidence and findings identified in international research on the definition, risk factors, epidemiology, clinical manifestations, diagnosis and treatment of acute flaccid paralysis in the last five years?"

### 3. Results and discussion

AFP is heterogeneous, has a clinical picture that varies according to etiology and evolves with diffuse and acute muscle weakness, hypotonia, hypo, or areflexia [11-13]. Differential diagnosis includes bone marrow disease, acute polyneuropathies, myoneural plaque dysfunction, and muscle disease. Supraspinatus lesions do not fall into the group of AFP because they have localized paresis, hypertonia, hyperreflexia, and sometimes involvement of superior brain functions, such as strokes and other structural lesions in the pyramidal, extrapyramidal, or cerebellar system [14-16].

**Table 1** Etiologies of Acute Flaccid Paralysis

<b>Spinal cord injuries (acute phase)</b>
<ul style="list-style-type: none"> <li>• Infectious: Human immunodeficiency virus, syphilis, tuberculosis, bacterial, or viral infection</li> <li>• Inflammatory: transverse myelitis, multiple sclerosis</li> <li>• Compressive: tumor, hernias or disc protrusions, abscesses</li> <li>• Vascular: ischemia, syringomyelia, epidural or subdural spinal cord hemorrhage</li> </ul>
<b>Previous spinal cord injuries</b>
<ul style="list-style-type: none"> <li>• Poliovirus infection, coxsackievirus infection, West Nile virus infection</li> </ul>
<b>Root or peripheral nerve disorders</b>
<ul style="list-style-type: none"> <li>• Guillain-Barre Syndrome</li> <li>• Diphtheria Syndrome</li> <li>• Paralytic seafood poisoning</li> <li>• Tick Bite Paralysis</li> <li>• Porphyria</li> <li>• Heavy Metal Poisoning</li> <li>• Critical disease polyneuropathy</li> <li>• Acute Alcoholic Polyneuropathy</li> <li>• Acute toxic or needy polyneuropathy</li> </ul>
<b>Neuromuscular Junction Disorders</b>
<ul style="list-style-type: none"> <li>• Myasthenia gravis</li> <li>• Eaton-Lambert Myasthenic Syndrome</li> <li>• Botulism</li> <li>• Aminoglycoside Toxicity</li> </ul>
<b>Muscle disorders</b>
<ul style="list-style-type: none"> <li>• Necrotizing myopathies</li> <li>• Metabolic Myopathies</li> <li>• Acute Alcoholic Myopathy</li> <li>• Muscular Dystrophies</li> <li>• Hypo or severe hyperkalemia</li> <li>• Periodic paralysis</li> </ul>

#### 3.1. Myelopathies

Myelopathies are disorders that affect the spinal cord or part of it. The clinical picture varies with the etiology. Loss of muscle strength associated with bowel dysfunction, urinary or sexual bladder, and a defined sensory level suggest myelopathy [17]. In the acute phase, there may be hypotonia and reduced reflexes. In the later stage, the reverse occurs;

reflexes increase and spasticity (pyramidal syndrome) [3; 6, 18]. Progressive weakness in the legs or arms preceded or accompanied by pain in the spine, or lower limbs may suggest compressive myelopathy [3;6]. Lesions limited to the anterior horn of the spinal cord are not accompanied by changes in sensitivity but have muscle flaccidity and fasciculations [3, 6, 19]. Regarding the diagnosis, magnetic resonance imaging is useful in cases of acute myelopathy, since it demonstrates the site of the lesion [3, 6, 20].

### 3.2. Acute polyneuropathies

Peripheral nerve damage causes distal muscle weakness and sensory changes limited to nerve or root territory [17].

#### 3.2.1. Toxic neuropathies

Result from exposure to drugs (amiodarone), industrial agents, and environmental toxins [4]. Although rare, it is essential in the context of known or suspected toxic exposure, especially in the workplace, due to heavy metal poisoning, and is reversible when the toxic agent is identified and removed [2;4]. Arsenic poisoning can generate polyneuropathy that mimics Guillain Barré Syndrome in addition to the systemic effects that facilitate diagnosis [2-5].

#### 3.2.2. Tick bite paralysis

Caused by neurotoxins secreted by adult female ticks in North America and the east coast of Australia. The disease is common in children under eight years old. Paralysis affects isolated cranial nerves and may progress to quadriplegia and paralysis of the respiratory muscles [8]. Symptoms are influenza-like, irritability, drowsiness, anorexia, pain, and paresthesias that appear within 36 hours. After 4-7 days of the bite, neurological symptoms, ataxia, weakness, and muscle paralysis appear. When the tick is removed, symptoms disappear spontaneously [8].

#### 3.2.3. Metabolic neuropathies

Diabetes is the most common cause of duration-dependent symmetric polyneuropathy in the developed world. Polyneuropathy is related to disease duration, mean glycosylated hemoglobin, and early age [4]. In acute autosomal dominant porphyria, heme synthesis is abnormal. Heterozygous patients experience dangerous, life-threatening neurovisceral attacks following precipitating factors [9]. Symptoms are severe abdominal pain, vomiting, constipation, and bloating, sometimes followed by confusional state and psychiatric disorders. Tachycardia and hypertension may occur in addition to seizures by hyponatremia [9; 10]. Progressive muscle weakness accompanied by myalgia may be asymmetrical, starting in the upper limbs. The diagnosis is confirmed by the presence of heme metabolites in the urine [9,10].

#### 3.2.4. Diphtheria neuropathy

Historically, diphtheria has been a significant cause of morbidity and mortality in the pre-vaccination era, currently with reduced cases due to the DTP vaccine [11, 12]. The disease occurs from toxigenic strains of *C. diphtheriae* whose free toxin leads to the formation of a pseudomembrane in the pharynx - the so-called pharyngeal diphtheria. After 2-6 days, there may be palate paralysis, nasal voice, numbness of the tongue and face, dysphonia, associated with other affected nerves. Following this, sensory-motor polyneuropathy (5-8 weeks later) and proximal quadriparesis associated with paresthesia appear in about 60-90% of patients. Electroneuromyography demonstrates a demyelinating process [8, 11].

### 3.3. Neuromuscular Junction Disorders

It is the disorders of the myoneural (motor) plaque that present acute muscle weakness and absence of sensory signs or symptoms.

#### 3.3.1. Myasthenia gravis

One of the most common pathologies, results from immune-mediated aggression to acetylcholine receptors on the postsynaptic motor plate membrane and alters neuromuscular transmission [12]. It occurs at any age and is common in women. The onset may be acute, affecting striated muscles of the lower and upper limbs and/or related to the cranial nerves, having as a favorite target the extraocular muscles. Skeletal muscle weakness is fatiguing and fluctuating throughout the day [13]. The triggering factors of the acute phase are fever, infections, intense emotions, excessive exercise, extreme heat, hormonal changes, pregnancy or menstruation, with spontaneous remissions. The diagnosis is made by clinical history, positive edrophonium test, and electroneuromyography with a response to a decreased muscle action potential. The presence of acetylcholine anti-receptor (86%) and striated anti-muscle antibodies (8%) are used as diagnostic methods [13]. Eaton Lambert Myasthenic Syndrome: a disorder due to immune-mediated aggression to presynaptic membrane calcium channels in the myoneural plaque. Up to 60% of cases simulate paraneoplastic

manifestation associated with small cell lung cancer, while the remaining cases are related to underlying autoimmune disease [14; 15]. It resembles myasthenia gravis, evolves with progressive proximal muscle weakness, fatigue, flexion, and autonomic symptoms, so that the specific electroneuromyographic pattern and autoantibody search may help in the differential diagnosis [14;15]. Aminoglycosides, tetracyclines, penicillamine, diphenylhydantoin can cause presynaptic neuromuscular blockade, triggering signs and symptoms similar to myasthenia [11, 17].

### 3.3.2. Botulism

Caused by toxins from *Clostridium botulinum* or other neurotoxic clostridia, it is a rare disease but can kill. Food botulism due to poisoning is the most common worldwide, rarely occurring after injury, injecting drug use, iatrogenic after toxin injection or of unknown etiology [7, 16]. After about 12-48h of contaminated food intake, gastrointestinal symptoms are preceded and, soon after, neurological signs with symmetrical impairment of cranial nerves and autonomic disturbance, which develop into balanced, descending flaccid paralysis of voluntary muscles, maybe compromised the breath [18]. Diagnosis is made by measuring serum toxin, and electroneuromyography reveals an increased pattern of myoneural plaque dysfunction [15, 18].

## 3.4. Muscle disorders

### 3.4.1. Hypo and hyperkalemia

K<sup>+</sup> values above 7mEq/L or below 3mEq/L may be associated with confusion and affective disorders as well as muscle necrosis and rhabdomyolysis if K<sup>+</sup> <2.5mEq / L. In the case of hyperkalemia, paresthesias, and fasciculations are observed in the muscles of the upper and lower limbs, generally sparing the trunk, head, and respiratory tract muscles. Besides, patients have weakness associated with ascending paralysis and flaccid quadriplegia. Serum K<sup>+</sup> level should be corrected, and the underlying cause of the change should be investigated and treated [19,21]. Other electrolyte disorders such as hypophosphatemia and hypermagnesemia may lead to AFP.

### 3.4.2. Channelopathies

Rare neuromuscular disorders of genetic etiology related to mutations in the sodium, calcium, and potassium channel genes in skeletal muscle. Formerly known as familial periodic paralysis, the hypokalemic form is the most frequent and is associated with changes in Ca<sup>++</sup> channels, muscle weakness after exercise or ingestion of large amounts of carbohydrates. Within the channelopathies, we have, besides hypokalemic paralysis, hyperkalemic paralysis, and Andersen-Tawil Syndrome, for example. It resolves spontaneously within hours to days. Periodic paralysis (PP) are rare neuromuscular disorders caused by mutations in the skeletal muscle sodium, calcium, and potassium channel genes [1].

## 3.5. Myopathies

These are muscle disorders of any etiology that can lead to acute flaccid paralysis. The main ones are inflammatory and metabolic.

### 3.5.1. Inflammatory myopathies

Polymyositis and dermatomyositis are rare autoimmune diseases that affect women aged 20-40 years, and have a second peak after 65 years of age, and may be associated with other diseases such as carcinomas, lymphomas and autoimmune diseases [20,21]. The onset of symptoms is subacute, proximal weakness, and may affect cranial nerves. The diagnosis is made by the presence of two of the following characteristics, being definitive if three are present: clinical manifestations, creatine kinase elevation (CPK), electrophysiological examination and muscle biopsy. The treatment is based on corticosteroids. Inflammatory myopathies also include infectious myopathies, which may be caused by viruses (Influenza A and B, HIV, Epstein-Barr, Herpes Virus), bacteria (*S. aureus*, *C. perfringens*), fungi (*C. albicans*) or parasites. (toxoplasmosis, trichinosis, cysticercosis) [21-23].

### 3.5.2. Metabolic myopathies

Thyroid dysfunction can lead to myopathy in 30-80% of hypothyroidism cases, with proximal weakness, muscle stiffness and cramps, rhabdomyolysis associated with muscle weakness, myalgia, elevated creatine kinase (CK) and myoglobinuria [23-25]. In hyperthyroidism, there may be generalized muscle weakness, bulbar, myasthenia gravis, periodic toxic paralysis, and thyroid ophthalmopathy. The acute manifestation of muscle weakness is most commonly seen in thyroid storm, where symptoms are critical [24-26]. There is also toxic myopathy, which can be caused by affecting the myoneural junction or the muscle itself. Some substances related to this type of myopathy are statins, barbiturates, chlorpromazine, lithium, amphetamines, salicylates, corticosteroids, zidovudine, etc. [25] Alcohol can cause myopathy due to the toxic effect of its consumption or associated malnutrition, either acutely or chronic. The

acute form affects 5% of alcoholics, with muscle weakness, pain, elevated CPK and myoglobinuria, and possible rhabdomyolysis [25, 26]. Genetic myopathies are clinically heterogeneous and progressive muscle disorders with autosomal changes recessive or dominant inheritance. Despite the different etiologies and clinical presentations, all are characterized by muscular pathology. Examples: myotonic dystrophy, X-linked dystrophy, and mitochondrial myopathies that may appear in the emergency department due to clinical deterioration, generalized muscle weakness, and respiratory failure [7].

### 3.6. Critical patient muscle weakness

The critically ill patient has a severe general condition and is usually admitted to the ICU. High doses of intravenous corticosteroids, neuromuscular blockers, sepsis, and multiple organ failure are thought to play an essential role in the development of AFP of these patients, but the pathophysiology is not well understood. They may have diffuse polyneuropathy, dysfunction of the myoneural junction, and/or muscle. Throughout the pathological process, we can observe long-term sustained muscle loss and dysfunction, which causes physical disability [20]. To differentiate from Guillain Barré Syndrome, subsidiary tests are required, such as CSF collection [26].

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## 4. Conclusion

In conclusion, AFP's are multifactorial and require knowledge and understanding of their etiologies, so that diagnosis can be rapid and effective treatment, as the clinical picture may be reversible. In this sense, the study of acute flaccid paralysis enriches patient care based on new evidence from the literature. However, because it is a high morbidity entity, it deserves attention from health professionals for its early identification and proper management.

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## Compliance with ethical standards

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### *Disclosure of conflict of interest*

There are no conflicts of interest to declare by any of the authors of this study.

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