Progressive flaccid paralysis occurring over a period of hours or days is usually associated with the Landry-Guillain-Barré-Strohl syndrome. This symptom complex is often accompanied by a history of a previous flu-like illness, antecedent myalgias, and subjective sensory complaints of tingling or simply a “tight” sensation in hands and feet. The paralysis that ensues either ascends from the feet and legs or descends from the facial muscles to involve all or most of the voluntary skeletal musculature. Along with paralysis of the intercostal and diaphragmatic musculature, severe cases may also involve other cranial nerves as well as the autonomic nervous system. In all cases the deep tendon reflexes are markedly diminished or absent early in the course of the disease. Sensory abnormalities are usually mild or absent. Confirmatory diagnostic studies include examination of the cerebral spinal fluid (CSF) which shows no or few mononuclear cells and an elevated protein. Nerve conduction studies may show prolonged distal latencies, slowing of nerve conduction velocities, and prolonged F responses which measure the radicular segments of the nerve. Overall prognosis is difficult to predict, with recovery taking weeks to months. Fatalities can occur despite optimal care in an intensive care unit. Electromyographic evidence of denervation suggests a more prolonged course with a greater chance of residual weakness. Atypical forms of this syndrome are more difficult to diagnose as can be illustrated by the following case history:

The patient was a 15-year-old boy with a progressive flaccid paralysis which began with leg pains and a gait disturbance; he required tracheostomy 72 hours later. Two weeks prior to this he suffered a flu-like illness and the day before he became weak he had been mowing a field freshly sprayed with insecticide. Initial examination showed a flaccid paraplegia and absent deep tendon reflexes, but the CSF was normal with no cells and a protein less than 50 mg/100 ml. Nerve conduction studies done on arrival at the hospital and the next day showed normal distal latencies, nerve conduction velocities, and F wave latencies. In some of the severely weakened distal muscles no compound action potential could be elicited and in others these potentials were of low amplitude and not augmented by 30 Hz trains of supramaximal stimulation. During the second week of total paralysis, distal latencies were slightly prolonged and conduction velocities had decreased. The spinal fluid remained normal. After the third week, the patient began to recover, initiating movements in arms and legs. Nerve conduction studies now showed definite prolongation of distal latencies and prolonged F wave latencies. The spinal fluid now had an elevated protein and no cells. By the fifth week strength had returned and the patient was weaned from the respirator.

Discussion

The absence of the early electromyographic and spinal fluid changes usually associated with a post-infectious polyradiculopathy instigated a search for other disorders which may present in a similar fashion. In devising a systematic approach towards a differential diagnosis in this atypical case, it was help-
ful to consider the component parts of the motor unit, specifically the anterior horn cell, axon (peripheral nerve), neuromuscular junction, and the muscle fibers innervated by that anterior horn cell.

Anterior Horn Cell Disease

Most of the anterior horn cell diseases that are encountered today are chronic and progressive and are not likely to be confused with the clinical presentation under discussion. However, there remains the possibility of the emergence of a new neurotrophic virus or the occurrence of acute poliomyelitis in the uninoculated. Poliomyelitis presents as a biphasic illness beginning as a flu-like syndrome which remits within 48 hours. Headache, severe myalgias and meningismus mark the next phase, with the spinal fluid showing a pleocytosis of 50 to 250 cells, an elevated protein (100 to 250 mg/100 ml), and a normal glucose. Some cases may then progress with muscle fasciculations and paralysis. If mild, the paralysis can be quite asymmetrical, but if severe, it may appear symmetrically and involve bulbar musculature. Deep tendon reflexes may be exaggerated early, but these are lost in the paralytic stage of the disease.

Peripheral Nerve

Acute polyneuropathies or polyradiculoneuropathies most often fall within the symptom complex of the Guillain-Barré syndrome. A wide variety of infective agents are capable of producing a state likened to experimental allergic neuritis with monocytic infiltration, edema, and demyelination of the peripheral nerve as the common pathological reaction. Such agents appear to combine with cell membranes, triggering an aberrant immune response which is directed towards cell membrane and, consequently, myelin. Generalized inflammatory states as seen with systemic lupus erythematosus are capable of producing a syndrome indistinguishable from the postinfectious variety. Furthermore, this syndrome has also been caused by infiltrations of plasma cells in association with multiple myeloma.

In some patients there is a tendency to suffer from a chronic relapsing steroid-dependent form of a polyradiculoneuropathy. In these patients the onset is usually more gradual, over one to two weeks, and usually does not involve cranial nerves or respiratory muscles. With the use of steroid medication, the patients become asymptomatic, although nerve conduction studies still remain abnormal. In the event of steroid withdrawal there is an exacerbation of all symptoms with a progressive paralysis.

Diphtheria toxin, although rapidly fixing to peripheral nerve, has a delayed effect as it appears to block myelin production. Consequently, the turnover of new myelin is inhibited, resulting in progressive demyelination of the peripheral nerve weeks to months later. Despite the characteristic clinical features of diphtheria, long delays between the time of the initial infection and the subsequent neuropathic complications may make the association difficult. Paralysis begins and may be localized to cranial nerves involving, in particular, the palate and the pupil with a characteristic fatigue of accommodation. More rarely, facial and extraocular muscles are also involved. A certain number of patients then develop a generalized peripheral sensori-motor neuropathy with loss of reflexes, mild sensory loss, and peripheral weakness. A tachycardia is oftentimes associated with the peripheral neuropathy, as well as spinal fluid changes of elevated protein with or without pleocytosis. A similar onset and cause have also been described in the neuropathy associated with extrafacial diphtheria.

The hepatic porphyrias, especially the acute intermittent and variegated forms, can cause paralysis following the abdominal and psychic manifestations. Oftentimes, pain precedes the weakness in affected muscles, which usually involves the upper limbs first and especially proximal muscles and wrist extensors. Progression may be stepwise over one to four weeks and involves limbs, trunk, cranial, and autonomic nerves. The spinal fluid protein is slightly increased and there are few monocytes. Nerve conduction studies are frequently normal since it is the axons which suffered a primary insult and not the myelin. Other abnormal metabolic states, such as hepatic and renal failure, as well as diabetes, are more likely to cause chronic neuropathies and do not present as acute paralytic states.

Exposure to toxic substances, either during their manufacture or use, can be the cause of progressive, flaccid paralysis. Cases are usually sporadic and in some this reaction seems to be determined by individual susceptibility. Cases can appear so typical that without a history of exposure to endrin, aldrin, dichloro-diphenyl-trichloroethane (DDT), or dichloro-diphenyl-dichloroethane (DDE), a diagnosis of acute, infective polynérritis may be made. The ingestion of thallium salts found in rodenticides and insecticides can cause an acute polyneuropathy in addition to gastrointestinal disturbances. The neuropathy is mostly sensory, affecting the lower extremities, and is associated with migratory arthralgias. In some pa-
tients paralysis may be generalized, involving respira-
tion and associated with circulatory difficulty as the
autonomic system is involved as well. Usually, with
massive doses, central nervous system symptoms pre-
dominate with hallucinations, convulsions, and
death. Several weeks after the ingestion of thallium,
alopoeia occurs and this is what implicates thallium
poisoning.

It would be an oversimplification to state that
there are a wide variety of agents capable of produc-
ing polyneuropathy—heavy metals, drugs, and toxic
chemicals—but for the most part these do not present
as acute neuropathic polyneuropathies. New sub-
stances are found capable of producing the syndrome
and isolated case reports continue to appear in the
literature. Examples of this are the ascending poly-
radiculopathies associated with the ingestion of the
fruit from poisonous shrubs as well as reports of
this syndrome as a complication of hyperalimenta-
tion.

Neuromuscular Junction

Neuromuscular blockade can occur either pre-
synaptically or postsynaptically and cause a rapidly
progressive, generalized, or selective paralysis. Pre-
synaptic blockade is thought to be the mechanism of
action in tick paralysis. Five to six days after the
attachment of certain female gravid ticks, usually
located on the scalp, there is a rapid ascending paral-
ysis which may begin with a gait disturbance and
myalgia. If the tick is not removed, this may proceed
to respiratory embarrassment. Spinal fluid is usually
normal. The substance which the tick secretes must
be quite potent, but it would also seem to have a
rather short half-life since symptoms improve within
hours of removing the tick.

Presynaptic neuromuscular blockade appears to
be the mechanism of action of botulinus toxin. Twenty-four to 48 hours after the ingestion of the
toxin, ocular motor weakness, pupillary paralysis,
and respiratory paralysis occur, usually preceded by a
gastrointestinal disturbance. Progression to general-
ized paralysis can also occur. Nerve conduction stud-
ies are usually normal, neuromuscular blockade
being demonstrated by high frequency stimulation
with subsequent augmentation in the compound ac-
tion potential.

Postsynaptic neuromuscular blockade can occur
due to the inability of the postsynaptic membrane to
respond to acetylcholine as it would in the myas-
thenic crisis. Occasionally myasthenia gravis may
begin with an acute, generalized severe form of
muscular weakness which involves cranial nerves.
Deep tendon reflexes are usually preserved and there
is no sensory loss. Myasthenics may develop acute
paralysis due to under-medication, or as a result of
exposure to drugs which have mild presynaptic
blocking properties and do not ordinarily affect non-
susceptible individuals. Postsynaptic blockade can
also occur as in cholinergic crises when acetylcholine
is not degraded at the receptor site. Such blocks can
occur in the myasthenic secondary to overmedication
with anticholinesterase-type drugs or in indi-
viduals who have been exposed to organophos-
phates such as tri-orthocresyl phosphate. Organophosphate compounds are not only capable of
producing an acute cholinergic crisis but also cause
severe demyelinating types of polyneuropathies usu-
ally after a latent period of one to three weeks after
exposure.

Muscle Fibers

Primary and secondary periodic paralyses are
classified as hypokalemic, hyperkalemic, and nor-
mokalemic depending upon the serum potassium at
the time of the paralysis. The onset is rapid and
progressive and usually follows exercise, exposure to
cold, or the ingestion of a heavy meal. During a
severe attack, deep tendon reflexes are depressed and
there is an inability to initiate muscle contraction by
electrical stimulation. Motor nerve conduction veloc-
ity may thereby be unobtainable. Spinal fluid is nor-
mal. The diagnosis may be suspected in the heredi-
tary forms which are recurrent and by the potassium
levels during the attack. The hyperkalemic and norm-
kalemic forms may be associated with the onset
of myotonia after exposure to cold between attacks.
The secondary periodic paralyses are usually spo-
radic. Hypokalemic periodic paralysis may be seen as
the presenting complaint or as a complication of
thyrotoxicosis in certain individuals. Hypokalemic
periodic paralysis is also seen in association with
hyperaldosteronism as well as a complication of
thiazides and spironolactone. Hyperkalemic forms
occur in association with renal and adrenal failure. It
would be extremely unusual for other myopathies to
present as rapidly progressive paralysis. With fulmi-
nant forms of polymyositis or in rhabdomyolysis
with associated myoglobinuria, patients are ex-
tremely ill, muscles are quite painful and the serum
creatinine phosphokinese levels should be very
high.

As with many conditions involving the nervous
system, the ability to localize the site of a particular
abnormality provides a logical means for considering a differential diagnosis in terms of what can happen at that particular site. In viewing the motor unit and its component parts a similar process is useful when considering progressive paralysis.

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