

The legacy of polio: 2 cases of post-polio syndrome and review

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Abstract

Post-polio syndrome (PPS) is a rare neurological disorder that affects 20-40% of paralytic and non-paralytic polio survivors. It is estimated that about 15 million people worldwide are survivors of the polio infection that occurred during the 1940s and 1950s, until the vaccine was first introduced. Its main characteristic is the appearance of de novo muscle weakness or its increase and atrophy, accompanied by other symptoms such as fatigue, joint, bone or muscle pain, intolerance to cold, and bulbar symptoms (involvement of swallowing, speech and breathing). PPS usually affects performance in daily activities with a negative effect on patients' quality of life. We present two cases with a diagnosis of PPS, with a current review of the literature.

Keywords: Post-polio syndrome. New neuromuscular symptoms. Poliomyelitis. Polio. Electromyography.

El legado del polio: 2 casos de síndrome postpolio y revisión

Resumen

El síndrome post-polio (SPP) es un trastorno neurológico raro que afecta del 20 al 40% de los sobrevivientes del polio paralítico y no paralítico. Se estima que alrededor de 15 millones de personas en todo el mundo son sobrevivientes de la infección por poliomyelitis que ocurrió durante las décadas de 1940 y 1950, hasta que se introdujo por primera vez la vacuna. Su característica principal es la aparición de debilidad muscular de novo o su aumento y atrofia, acompañado de otros síntomas como fatiga, dolor articular, óseo o muscular, intolerancia al frío y síntomas bulbares (compromiso de la deglución, el habla y la respiración). El SPP generalmente afecta el rendimiento en las actividades diarias con un efecto negativo en la calidad de vida de los pacientes. Presentamos dos casos con diagnóstico de síndrome postpolio, con una revisión actual de la literatura.

Palabras clave: Síndrome post-polio. Nuevos síntomas neuromusculares. Poliomyelitis. Polio. Electromiografía.

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Introduction

Post-polio syndrome (PPS) is a neurological disorder affecting 20-40% of paralytic and nonparalytic polio survivors, characterized by a range of neuromuscular manifestations that occur years after initial infection with poliovirus¹⁻³. The interval between acute infection and PPS is approximately 35 years, with a range varying from 20 to 70 years^{4,5}.

Its main characteristic is the appearance of de novo muscle weakness or its increase and atrophy, accompanied by other symptoms such as fatigue, joint, bone or muscle pain, intolerance to cold, and bulbar symptoms (involvement of swallowing, speech, and breathing). PPS usually affects performance in daily activities with a negative effect on patients' quality of life³⁻⁵.

In this paper, we report two cases of PPS with different clinical manifestations and fatal outcomes. We consider of interest to our continent due to the large number of patients with a history of paralytic and non-paralytic polio, in addition to the wide spectrum of differential diagnoses.

Case report 1

A 69-year-old female, natural from Nocaima (COL), housewife, was referred with a 5 years of progressive, asymmetric weakness that begins in the right foot, and then progresses to compromise the entire limb with limitation for walking until prostration in a wheelchair within 3 years, associated with joint and muscle pain in general management with non-steroidal anti-inflammatory drugs. She had history of paralytic poliomyelitis at age 2 years with shrinking of lower left limb as sequelae and controlled arterial hypertension. During school she had participated in all activities without difficulty. Neurological examination shows normal mental status, loss of cephalic support, bilateral interosseous atrophy in both hands, predominantly in the right and both quadriceps, quadriplegia with distal predominance, and hypoactive reflexes in lower limbs. Sensory examination was normal.

Additional studies were carried out considering alternative diagnoses; immunological, infectious, and/or paraneoplastic etiologies were ruled out. Spinal magnetic resonance imaging (MRI) showed degenerative changes without medullary lesions. The neuro-conduction and electromyography (EMG) show signs of acute denervation with very large, long-duration, and polyphasic motor unit action potentials (MUAPs) (Figs. 1 and 2). She received 1 cycle of human Immunoglobulin G accompanied by a rehabilitation plan, with stabilization of symptoms for 1 year. Subsequently, she presented

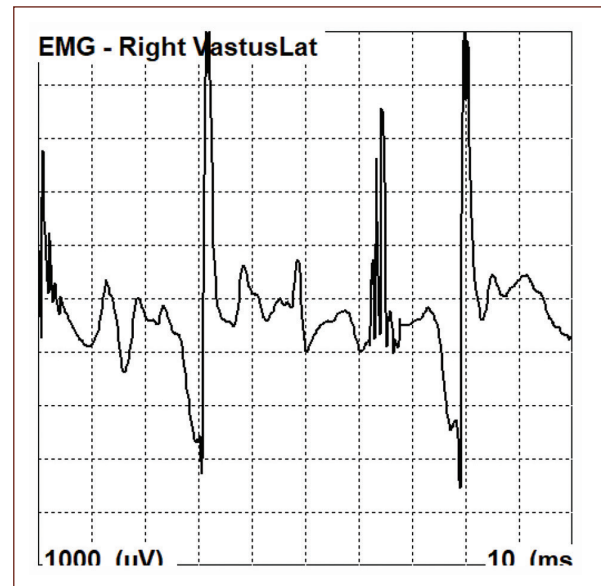


Figure 1. Neuropathic PUM in right lateral vastus.

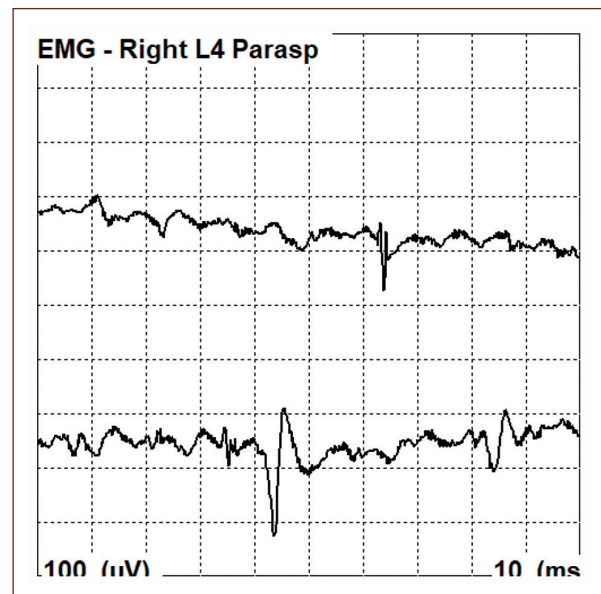


Figure 2. Positive wave in right L4 Paraspinalis.

increased weakness with greater axial, cephalic, and upper limb involvement. During the past 6 months dependent on supplemental oxygen per nasal cannula. Finally, she presented acute ventilatory deterioration and died of ventilatory failure.

Case report 2

A 54-year-old male patient, from Bogota (COL), mechanical engineer, currently retired, was referred with

5 years of evolution of progressive asymmetric weakness that begins in upper limbs, of distal predominance, and then progresses to lower limbs of ascending characteristics, until limited for standing and walking, with subsequent appearance of hypophonia and solids dysphagia. He had history of paralytic polio at 1 year old with shrinking of the lower right limb and foot drop as a sequel with surgical correction during childhood (Fig. 3), moderate sleep apnea/hypopnea syndrome, heart failure (Fev1 50%), atrial fibrillation, pulmonary hypertension with public-safety answering point 50 mmHg, recurrent deep vein thrombosis, and heavy ex-smoker. Physical examination with evidence of central obesity, grade II edema in lower limbs, and skin changes secondary to heart failure (Fig. 3). Neurological examination showed hypomimia, nasal voice, hypotrophy, and generalized hypotonia, quadriparesis of distal predominance, reflexes were absent and steppe gait. Studies were performed in search of alternative diagnoses ruling out immunological, infectious, and/or paraneoplastic etiologies. Additional screening for negative Pompe was done. Biopsy of gastrocnemius muscle was normal and neurophysiological studies with acute denervation signs, with very large, long-duration, polyphasic MUAPs, and the presence of pseudomyotonic discharges (Figs. 4 and 5). He received 5 cycles of human immunoglobulin G as a treatment, accompanied by a rehabilitation plan with clinical stabilization of symptoms. One year ago, he began with multifactorial respiratory insufficiency and subglottic stenosis with two tracheal dilation attempts plus stent placement, post-resuscitation state, and requirement of prolonged stay in intensive care unit for more than 4 months, with the need for tracheostomy and gastrostomy placement. Now, he remains hospitalized.

Discussion

Both patients meet the criteria for PPS. The patients present a chronic weakness of asymmetric onset that progresses to compromise mobility until prostration in a wheelchair and in case 2 associated with hypophonia and dysphagia for solids. Immunological, infectious, and/or paraneoplastic etiologies were ruled out with additional Pompe negative screening, and also normal muscle biopsy. EMG shows signs of acute denervation with neurogenic MUAPs and the presence of pseudomyotonic discharges. Despite the immunomodulatory therapy received, the weakness progressed to compromise respiratory function, and in the first case it ended with a fatal outcome.



Figure 3. Shrinking and atrophy of the lower right limb and foot drop as a sequel with surgical correction during childhood in patient with PPS and heart failure.

Natural history of disease in the world

It is estimated that about 15 million people worldwide are survivors of the Polio infection that occurred during the 1940s and 1950s, until the vaccine was first introduced^{6,7}. Since then, the number of people affected has dropped by nearly 99%⁸. However, polio remains endemic in two countries (Afghanistan and Pakistan) with 74 cases reported in 2015 and according to global polio surveillance data as of March 2016, five wild poliovirus cases were reported in Pakistan and one in Afghanistan^{8,9}.

The exact incidence and prevalence of PPS are unknown, for 2004 were estimated 250,000 patients with PPS in Europe and 20 million worldwide. Ragonese showed a prevalence of PPS of 31% in 2005 with predominance in women^{10,11}.

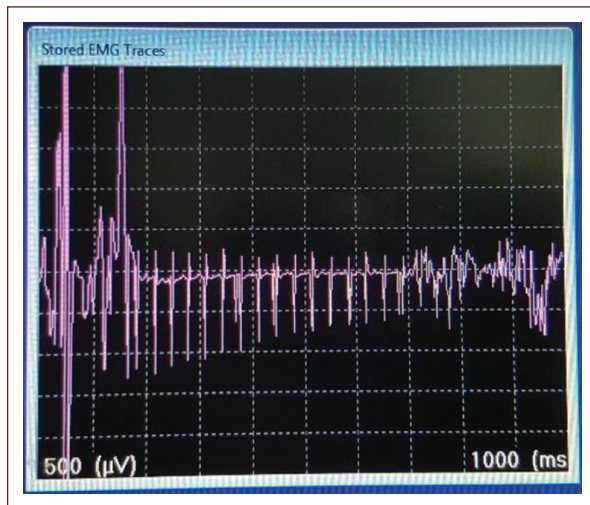


Figure 4. Pseudomyotonic discharge into right rectus femoris muscle.



Figure 5. Pseudomyotonic discharge into right rectus femoris muscle.

More than 80% of people who contracted polio as children develop new or increased disability decades after initial infection, considered late effects of polio¹².

Physiopathology

The etiology and pathogenesis of PPS is unknown. It has been hypothesized that the new weakness appears to be related to degeneration of individual nerve terminals in motor units. The overuse of these motor units for years generates an overload that eventually leads them to lose their ability to respond, producing a slow

deterioration which leads to a reduction in muscle strength^{13,14}.

It is probably an effect of motor neuron damage during acute poliovirus infection that leads to overloading and degeneration of the remaining motor neurons in the frontal horns of the spinal column^{15,16}.

More than 50% death must occur in the anterior horn neuron population before weakness can be detected clinically. EMG studies suggest that many of the clinically unaffected muscles were sub-clinically involved during the acute episode of the disease⁷. This hypothesis explains why PPS occurs after so many years and has a slow progressive course¹⁷.

Sharief et al. demonstrated the presence of immunoglobulin M antibodies against poliovirus and cells sensitized to poliovirus in the cerebrospinal fluid (CSF) of patients with PPS. However, no conclusive evidence of CSF poliovirus has been found in such patients¹⁸.

In addition, histopathological damage to the reticular activation system has been demonstrated in patients with PPS, which is probably related to cognitive performance impairment and chronic fatigue syndrome¹⁹.

Risk factors

No strong associations have been found between risk factors and PPS; however, some risk factors have been described such as age, genetics, time since acute polio, stress, and inactive lifestyle²⁰. Among those that stand out are the female gender and the severe course of the initial infection¹⁵.

Klingman et al. noted that patients who developed PPS had a history of greater generalized paralysis during acute illness or greater lower extremity involvement, but also those who had greater functional recovery. This indicated that the degree of functional recovery could be a predictor for skin perfusion pressure (SPP)^{7,21}.

Several viruses are known to cause chromosomal abnormalities in circulating lymphocytes during infections in humans (such as measles, chickenpox, mumps, and hepatitis viruses), such as chromosomal breakage. However, these chromosomal abnormalities due to direct or indirect effects as well as the immediate or delayed effects of the poliovirus have not been fully understood²². Bhattacharya et al. reported a significant increase in chromosomal aberrations in patients with PPS than in controls, showing a delayed effect of the poliovirus in humans²².

The poliovirus has a common receptor known as a poliovirus receptor (PVR) that belongs to the CD155

immunoglobulin superfamily, a poliovirus cell surface receptor found on chromosome 19q13²³.

Polymorphism of the PVR gene in patients with progressive muscle atrophy was reported by Saunderson et al. in 2004²⁴. Later, it was reported that Ala67Thr polymorphism in the PVR gene was a possible risk factor for the etiology of polio²⁵. Single nucleotide heterozygous polymorphism (Ala67Thr) in the CD155 gene has been reported in healthy populations (6.8-8.5%) and the incidence has been shown to be significantly higher in patients with polio paresis (13.3%) and progressive muscle atrophy (20%)^{24,25}.

Clinical course

PPS was described 15 years after the first polio outbreak, when new neuromuscular symptoms were reported. Affecting 20-75% of survivors of acute infection, 15 years or more after acute illness^{15,26-28}.

The new symptoms are characterized by muscle weakness, generalized atrophy and fatigue, pain at rest or during activities and intolerance to cold, and bulbar symptoms (compromised swallowing, speech, and breathing)^{3-5,29}.

Joint and muscle pain is present in 70% of patients with PPS. Muscle atrophy and intolerance to cold temperatures are rarer and about 50% are seen³⁰. Apnea and dysphagia are observed in 30% of patients³¹.

Symptoms may be seen in clinically affected and unaffected muscles during primary polio infection. Post-polio progressive muscle atrophy is the term designated to describe the clinical picture, and muscle weakness progression is usually slow and lasts for many years. About 90% of patients with PPS also complain of general fatigue, concentration problems, and mood swings^{32,33}.

There are two aspects of fatigue related to PPS, a central fatigue involving central nervous system involvement due to SRA involvement leading to mental fatigue related to difficulties in cognitive functions, such as planning and inhibition tasks, concentration problems, and mental sustainability. Moreover, the peripheral fatigue that mainly derives from the peripheral system, that is, the compromise of the motor units³⁴.

The new symptomatology may further limit the ability to perform daily activities, especially those related to standing, walking, and climbing stairs, which increases the risk of falls³⁵. This, in turn, can negatively impact the quality of life of patients with PPS³⁶. In addition, psychological factors such as feelings of shame or discomfort, fear of injury, lack of motivation, and energy,

along with environmental factors are perceived as barriers to physical activity and participation^{12,37,38}.

Respiratory involvement

The leading cause of death during acute polio is respiratory disorder. Although respiratory failure is often caused by weak breathing muscles or bulbar dysfunction, it is also related to the high incidence of secondary complications such as scoliosis, obesity, and sleep breathing disorders (sleep apnea) in individuals with PPS³⁹⁻⁴¹.

According to pathophysiology, polio survivors suffer mainly from restrictive respiratory deterioration. At present, approximately 27-36% of patients with PPS suffer from respiratory failure⁴². The main respiratory conditions have been described as dyspnea, fatigue, or sleep-related respiratory disorders, increasing the risk of morbidity and mortality⁴³.

The restrictive defect in ventilatory function is secondary to the weakness of the respiratory muscles, which are unable to generate the intrathoracic vacuum necessary for complete inspiration or the positive pressure necessary for complete exhalation. Generating reductions in Total Lung Capacity below the 5th percentile of predicted value, vital capacity, and maximum voluntary ventilation⁴⁴. In an 11-year prospective study of 31 patients with PPS, more than half of patients with cardiovascular < 50% developed the need for ventilation or suffered a death related to respiratory failure⁴⁵.

Halstead and Rossi⁴⁶ observed that in patients with PPS, altered lung function was associated with age of onset (progression of 10 years or more), need for mechanical ventilation during the acute phase of the disease, quadriplegia, and time of exposure to the disease. In another study, Lane et al.⁴⁷ described an association between respiratory dysfunction and the presence of kyphoscoliosis or diaphragmatic paralysis.

Sleep disturbances

Sleep disorders are common in patients with PPS⁴⁸. Their insidious nature can make it difficult for patients, family members, and caregivers to recognize these disorders⁴⁹⁻⁵¹.

Among the sleep disorders associated with PPS, periodic leg movements (PLM), hypopnea, and especially obstructive sleep apnea (OSA) are the most common⁵².

A prospective study of 60 patients with PPS showed a prevalence of sleep disturbance of 78.3%, with sleep efficiency decreasing from 67.4% (patients with OSA, using non-invasive ventilation) to 69.5% (patients not

using non-invasive ventilation). This inefficiency was related to more than 10 awakenings per hour, disordered breathing, PLM, changes in the different stages of sleep and muscle and/or joint pain^{51,53}.

Diagnostic

Electrodiagnostic studies play an important role in the diagnostic process of PPS. Although they cannot differentiate patients with PPS from those with asymptomatic post-polio, they are important for excluding other neuromuscular diseases such as amyotrophic lateral sclerosis, radiculopathy, polyneuropathy, myasthenia gravis, radiculopathies, neuropathies, and myopathies^{54,55}.

Blood test results are generally normal, except for elevated serum creatine kinase (CPK) levels in some patients, which may suggest overuse and damage to muscle fibers^{56,57}.

Imaging studies (e.g., computed tomography scan and MRI) may be needed to exclude spinal conditions such as spondylosis, spinal stenosis, and neoplasms⁷.

Diagnostic criteria

The current diagnostic criteria for PPS were first described by Mulder et al. in 1972⁵⁸. These criteria are:

1. Previous episode of polio with residual loss of motor neurons.
2. A period of at least 15 years of neurological and functional stability after recovery from acute illness.
3. The gradual or, rarely, abrupt onset of new weakness or abnormal muscle fatigue and generalized fatigue.
4. The exclusion of other conditions that could cause similar manifestations.

In the differential diagnosis, it is important to exclude orthopedic and neurological diseases similar to PPS such as amyotrophic lateral sclerosis, cervical spondylosis, tumors of the cervical and thoracic spine, and other causes of chronic fatigue syndrome, myasthenia gravis, myopathies and cardiac diseases, hematological, endocrine, cancer, chronic systemic infections, among others^{59,60}.

Electromyography findings

Symptoms of PPS should be evaluated by EMG, Single Fiber EMG (SFEMG), and macro-EMG. Muscle fatigue can be caused by neuromuscular junction transmission defects⁵⁸. Muscle weakness and atrophy may be associated with distal degeneration of motor units,

resulting in irreversible denervation of muscle fiber⁵⁸. The most characteristic finding of EMG in SPP is the presence of potential giants; these units are greater than 8 mV and occur as a result of chronic denervation and reinnervation by shoots of the same motor unit, generating motor units of great amplitude and area⁶¹.

In Chang's study, 31 patients with PPS were diagnosed with the use of EMG. In 41 (78.8%) of the 52 muscles, the duration of the motor unit increased. Amplitudes of larger motor units were observed in 43 (82.7%) of the 52 muscles. Polyphasia of more than 20% of the affected muscles was found and spontaneous activities such as fibrillation and positive acute waves were observed in approximately 30% of the muscles examined in this study. Fasciculations occurred in 26.9% of patients with PPS⁶².

At present, surface EMG is considered as a potential alternative to needle EMG or nerve conduction studies when neuromuscular disorders are investigated⁶³. It has an advantage in the detection of large non-invasive signals, it provides additional information in the study of fatigue in patients with PPS⁶⁴.

SFEMG has become the most sensitive method for diagnosing neuromuscular transmission disorders, even subclinical alterations in transmission can be detected with the use of this method⁶⁵. The SFEMG can provide information on the reorganization of the motor unit with fiber density, and increased instability is related to mild to severe disturbances recognized by impulse blockages^{64,65}.

These findings in the SFEMG confirm the theory that PPS is the result of degradation of nerve endings that influence the condition of neuromuscular unions⁶¹.

Neuroconduction findings

Electroneurography is usually normal in patients with PPS. Hachisuka studied 43 polio survivors and 20 healthy controls with studies of motor nerve conduction of the median and tibial nerves. They found a significant increase in abnormally stereotyped F-waves and a reduction in F-wave persistence in both nerves in polio patients compared to the control group. They conclude that the F wave reveals the electrophysiological characteristics of the anterior horn cells in polio survivors and reflects the loss of their motor units⁵⁸.

Treatment

There is no cure for PPS. The main objective of treatment is to improve the quality of life of patients through rehabilitation and intervention by the orthopedic group

of the affected limb. Attempts have been made to treat with pyridostigmine and amantadine, but their efficacy in this disease has not been demonstrated⁶⁶⁻⁶⁸.

Attempts are also made with intravenous immunoglobulins to achieve stabilization of symptoms, with no studies reporting confirmatory results yet. Assisted ventilation may be necessary in patients with respiratory symptoms³².

Finally, L-citrulline is known to modify the synthesis of muscle metabolism by increasing nitric oxide levels and increasing protein synthesis. Schmidt et al. are conducting a randomized, placebo-controlled, and double-blind trial aimed at demonstrating that L-citrulline positively influences muscle function and increases muscle energy production in patients with SPP⁶⁹.

Conclusion

PPS is a rare and disabling chronic neurological condition that affects millions of people around the world with unknown pathophysiology and no evidence of specific treatment to date. Controversial treatments such as immunomodulatory therapy are described, where the main objective is to improve patients' quality of life. Weakness associated with history of paralytic and no paralytic polio now is seen most often in the EMG laboratory. The neuro-conduction and EMG test are mandatory to exclude a superimposed process, related to entrapment neuropathy, radiculopathy, myopathy, and or motor neuron disease.

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Conflicts of interest

None of the authors has any conflicts of interest to disclose.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the

patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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