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Parsonage-Turner syndrome association with SARS-CoV-2 infection

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Parsonage-Turner syndrome (PTS), also known as idiopathic brachial plexopathy or neuralgic amyotrophy,[15] was first described by Julius Dreschfeld in 1887.[5] In 1943, Spillane[16] reported the first series of "localized shoulder girdle neuritis" cases, but Parsonage and Turner[10] more firmly established and detailed the clinical aspects of the disease, distinguishing that the pain was of sudden onset and was often severe without any "constitutional disturbance" present from the neck to the hand.[12] PTS is characterized by a single or multiple mononeuropathies at the level of the brachial plexus (not exclusive), acute and self-limited, associated with motor deficit, and muscle atrophy.[10,11,15,18] Electromyography shows severe axonal damage.[10,18] Recovery is usually between 6 months to 2 years, and it is not always complete.[10] Cases have been reported in patients as young as 3 months and as old as 81 years of age, but the highest incidence is between the third and seventh decades of life, and men are predominantly affected.[18]

In 1948, Parsonage and Turner[10] correlated infection, minor surgery, minor gunshot wounds, and minor trauma with the syndrome. The exact pathophysiology is still unknown. Of the many proposed causes, an infectious or immune-mediated process seems to be the most supported.[15] Suarez et al[17] showed the presence of T lymphocytes within the brachial plexus of patients with PTS. Furthermore, complement-fixing antibodies to peripheral nerve myelin have been reported as elevated in the acute phase of PTS.[24] In 20% to 52% of cases, infection precedes the development of PTS[22] (upper respiratory tract infection, flu-like syndrome, hepatitis, mononucleosis, malaria, pneumonia, abscess, typhus, smallpox, rheumatic fever, typhoid, poliomyelitis).[15] In fact, viral illness is the most common associated risk factor (25% to 55%).[6]

Currently, there are only three case reports in the literature on the relation of coronavirus disease 2019 (COVID-19) with PTS.[1,8,14] The COVID-19 neurologic involvement has been described mainly at the central nervous system, with Guillain-Barré syndrome being the most frequent at the peripheral nervous system.[2] In the context of a coronavirus pandemic, we should suspect this disease in patients with neuropathic pain in the shoulder region within the possible differential diagnoses. This publication is about a case of PTS in association with COVID-19 and a review of scientific literature available.

Case report

A 36-year-old man, left-handed, body mass index 30.1, without previous medical pathologies or recent surgical and vaccination history, was consulted for neuropathic pain in the right shoulder of 10 weeks of duration, mainly in the scapular region, without radicular distribution. Seven weeks after the onset of the symptoms, he developed progressive weakness in the right upper limb, which is why he sought medical attention because he limited his ability to perform activities of daily living. He denied the presence of trauma (Table I).

Two weeks before the development of this condition (during the peak of the pandemic in Chile), he presented symptoms of an upper respiratory infection, such as headache, ageusia, anosmia, fever, and asthenia suggestive of COVID-19. No polymerase chain reaction test was performed because it was cataloged as a positive case as per the protocol of the local authority.

No institutional review board approval was required for this case report. The patient provided informed consent before participation.

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Table 1
The differential diagnosis for neuralgic amyotrophy.[18]

Neurologic disc disease	Cervical root injury, multiple mononeuritis, vasculitis, tumor pathology, transverse myelitis, acute poliomyelitis, amyotrophic lateral sclerosis, hereditary neuropathies
Muscle-skeletal	Rotator cuff pathology, adhesive capsulitis, calcium tendinopathy, cervical spondylosis
Others	Myocardial infarction, pulmonary embolism, complex regional pain syndrome, diaphragmatic paralysis, Pancoast tumor

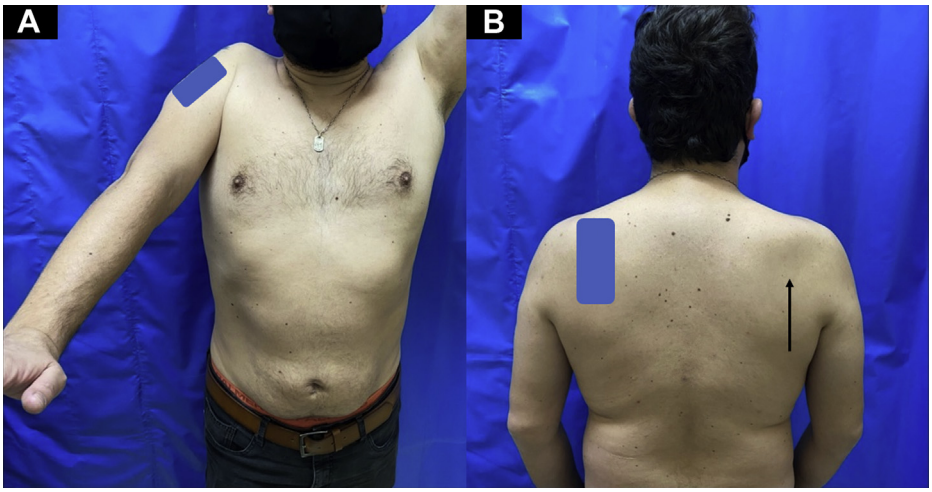

Figure 1 Inspection at initial presentation. (**A**) Severe active anterior elevation deficit. (**B**) Muscle atrophy at the level of the supraspinatus and infraspinatus fossa.

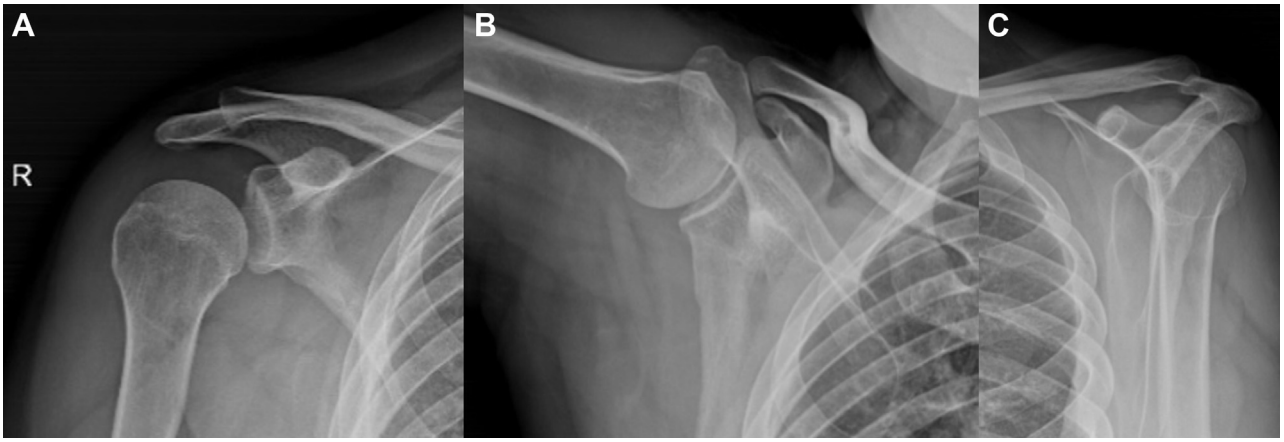

Figure 2 Radiographic study. The radiographic study shows no alterations. (**A**) True anteroposterior view. (**B**) Axillary view. (**C**) Scapular Y Lateral.

On initial presentation, he was afebrile. Physical examination revealed muscular atrophy of the supraspinatus and infraspinatus fossa, deltoids, and biceps; preserved passive mobility; and decreased force in anterior elevation (M2), abduction (M2), external rotation (M2), and internal rotation (M3), as per the Medical Score Council score (Fig. 1). No scapular dyskinesis was observed for static and dynamic evaluation. Scapular balance angle[3] was less than 5°. Upper limb deep tendon reflexes and sensitivity were normal. Provocative maneuvers were negative (Hawkins, Neer, O'Brien, speed, uppercut, and Spurling).

The radiographic study was normal (Fig. 2), and the right shoulder magnetic resonance imaging (MRI) (Fig. 3) showed supraspinatus and infraspinatus intramuscular hyperintensity in T2-weighted sequence and global atrophy of the periscapular musculature associated with initial fatty infiltration, without lesions in the tendinous portion of the rotator cuff.

Electrodiagnostic evaluation (nerve conduction study and needle electromyography, Table II) showed signs suggestive of a subacute and severe degree of right brachial plexopathy (upper trunk), with elements of active denervation and initial reinnervation, compatible with PTS.

MRI diffusion neurography of the brachial plexus was performed (Fig. 4). Adequate visualization of the three main trunks on each side, with greater signal intensity on the right in T2-weighted and short tau inversion recovery images, distinguishes part of the suprascapular nerve, in its retro and infraclavicular path, especially of the medial and posterior fascicles. The measurements of anisotropic fractions and apparent diffusion coefficient, compared with the healthy side (left), showed a tendency to isotropy (structural disorganization of the nervous elements), compatible with PTS. With the administration of contrast medium, no abnormal reinforcement foci are observed. This signal asymmetry is of probable inflammatory etiology.

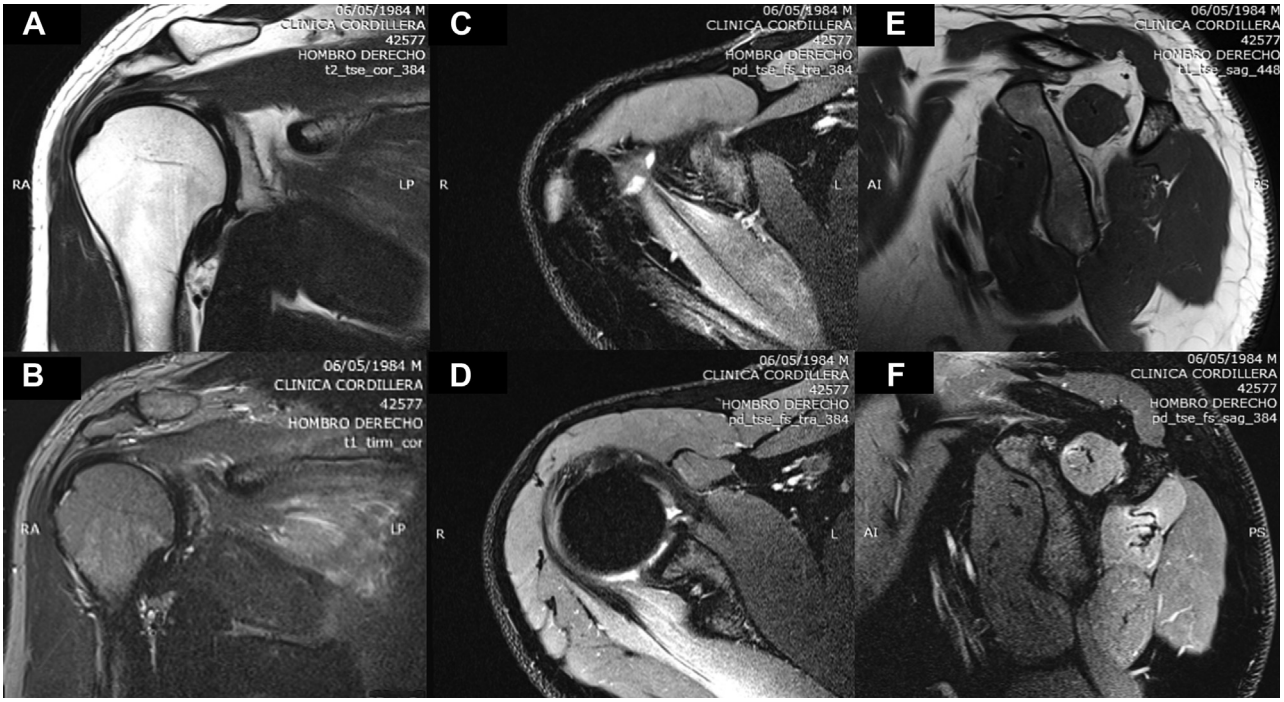

Figure 3 Magnetic resonance imaging (MRI). MRI showed supraspinatus and infraspinatus intramuscular hyperintensity in T2-weighted sequence (**C-D**), global atrophy of the periscapular musculature associated with initial fatty infiltration (**E-F**), without lesions in the tendinous portion of the rotator cuff (**A-B**).

Table II
Electrodiagnostic evaluation.

Nerve conduction study	Needle electromyography
Sensory conduction of both medial, ulnar, superficial radial, and lateral antebrachial cutaneous shows potentials within normality. The motor driving of both medians recording in *abductor pollicis brevis* and both radials recording in *extensor digiti minimi* shows potentials within normality. The motor conduction of the right axilla shows severely diminished amplitude; to the left, it is normal.	Electromyography shows positive sharp waves and fibrillation in deltoids, biceps, supraspinatus, and rhomboids; the rest show electrical silence at rest. When exerting effort, impoverished traces are shown in deltoids, biceps, and supraspinatus. Does not achieve adequate activation of rhomboids.

Given the symptoms suggestive of prior COVID-19 disease, antibodies were requested to confirm the relationship with the findings found (Table III) (Laboratorio Barnafi Krause, semi-quantitative, ELISA, Santiago, Chile). The results suggest prior infection/exposure to SARS-CoV-2 (elevated IgG, normal IgM).

Based on the triad of clinical, imaging, and laboratory history, the clinical picture was interpreted as PTS in a COVID-19 context.

Medical treatment was performed using neuromodulator drugs (pregabalin 75 mg bid for 4 months) and kinesiological treatment with the aim of recovering the functionality of the right upper limb. For this, assisted passive and active mobility exercises of the entire right limb were performed to maintain and increase ranges of motion. Subsequently, mobility exercises and isometric activation of the stabilizing muscles of the right scapula, as well as isometric activation of the rotator cuff and the middle and anterior deltoids, were performed. Next, exercises were performed to strengthen the elbow and shoulder flexors and the right shoulder abductors, achieving the 1-kg active free and resisted active anterior shoulder elevation with 1 kg up to 160°. Throughout the kinesiology therapy, he presented a good response and tolerance to the exercises.

At 2 months of evolution, despite maintaining a decreased muscle trophism of supraspinatus and infraspinatus on physical examination, active joint ranges are preserved, with recovered muscle strength: deltoid (M5), subscapularis (M5), supraspinatus (M4), and infraspinatus (M4).

At 4 months, he completed eight physiotherapy sessions, regained his active range of motion and muscle strength in all affected muscle groups, and continued with home physical therapy[4] (Fig. 5). Finally, at 6 months, he was discharged without symptoms, complete mobility, recovered strength, and carrying out life and work without complications. Currently, he can perform all his basic and instrumental activities independently and without difficulty.

Discussion

In shoulder surgery, the history and physical examination are essential,[9] particularly in the diagnosis of PTS. A thorough medical history, physical examination, and electrodiagnosis are necessary for proper diagnosis. The pathophysiology of PTS remains unclear. However, it has been associated with infections, vaccines, or systemic disease.[21]

The clinical picture consists of sudden neuropathic-type shoulder pain, of greater intensity at night associated with progressive muscle weakness. Ten to thirty percent of patients can develop symmetrical symptoms. However, the most common is

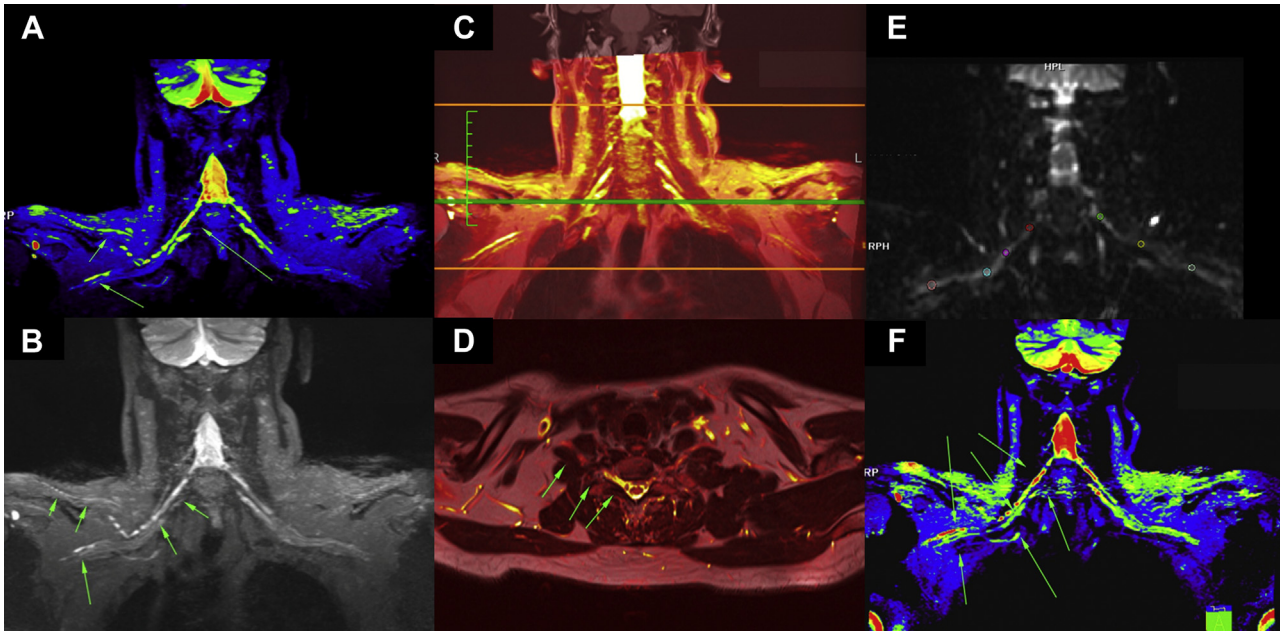

Figure 4 Magnetic resonance imaging diffusion neurography. Adequate visualization of the three main trunks on each side (**A-B**), with greater signal intensity on the *Right* in T2-weighted and STIR images (**C-D**), distinguishing part of the suprascapular nerve, in its retro and infraclavicular path, especially of the medial and posterior fascicles (thin arrows). The measurements of anisotropic fractions and apparent diffusion coefficient, compared with the healthy side (*Left*), showed a tendency to isotropy (structural disorganization of the nervous elements), compatible with PTS (**E**). With the administration of contrast medium, no abnormal reinforcement foci are observed (**F**). This signal asymmetry is of probable inflammatory etiology. *PTS*, Parsonage-Turner syndrome; *STIR*, short tau inversion recovery.

Table III
SARS-CoV-2–specific immunoglobulins.

Coronavirus anti SARS-CoV-2 IgG	Coronavirus anti SARS-CoV-2 IgM
2.1 ratio Reference: Inconclusive (0.8-1.1), positive (> 1.1)	0.4 ratio Reference: Inconclusive (0.8-1.1), positive (> 1.1)

that it is unilateral.[7] Muscle weakness in a separate peripheral nerve distribution rather than a root distribution is a key element of diagnosis.[12]

Understanding the chronology of symptoms is essential in the diagnosis as it allows identifying the triggering factor. In the reported case, there is a correlation with COVID-19 infection. The tests of choice in this pathology are radiography (essential to rule out differential diagnoses), MRI, and electromyography. The MRI findings are related to the severe axonal degeneration that it causes, with hyperintensity in T2 being the earliest intramuscular finding, affecting mainly the supraspinatus and infraspinatus.[13] The electromyography shows severe axonal denervation with positive sharp waves and fibrillation in the affected nerves.[15,18] Brachial plexus MRI was performed to verify categorical findings of brachial plexitis to ensure the diagnosis owing to the infrequency of the case.[20] There is no specific management for this disease, having a self-limited character with the recovery of strength and muscle trophism. There is no evidence from randomized trials to support any form of treatment. Evidence from one open-label retrospective series suggests that oral prednisone given in the first month after onset can shorten the duration of the initial pain and leads to earlier recovery in some patients.[23] In this case, we prefer using neuromodulator drugs for pain management. However, motor physiotherapy is the mainstay of treatment described in the literature.[12,15,18,23] The prognosis of the disease is good. Tsairis et al[19] demonstrated excellent recovery in 36% of patients at 1 year of follow-up, 75% at 2 years, and 89% at 3 years.

In our case, his recovery was optimal with kinetic therapy. Its association with the current pandemic and its possible proinflammatory pathophysiological mechanism are intriguing.

The reported case presents similar clinical characteristics to the first reported case of a possible association between COVID-19 and PTS.[8] However, we believe that an electrodiagnostic study will be key to being able to increase the diagnostic precision in relation to this pathology.[8] The second case reported[14] is a severe mononeuropathy manifestation of neuralgic amyotrophy with compromise of the median nerve, without shoulder girdle symptoms. The third case is different because a pure sensory neuralgic amyotrophy diagnosis was made. Six weeks after the onset, hypoesthesia and dysesthesias persisted, without weakness.[1]

The cases reported in the literature are still scarce to be able to identify a distinctive pattern of PTS associated with COVID-19, but differences such as a pure sensory compromise or a fairly rapid recovery of patients can already be glimpsed.

The number of cases of SARS-CoV-2 (COVID-19) continues to rise worldwide, and this postinfectious syndrome is an increasingly significant possible etiology of shoulder pain.

Conclusion

Shoulder pain has multiple causes, and PTS is an infrequent cause. This clinical case reveals its association with COVID-19 infection, generating a diagnostic and therapeutic challenge that we must bear in mind in our differential diagnosis.

Our management was based in the current literature, drugs for pain relief, early physical therapy and progressive analysis of natural history of the disease.

Disclaimers

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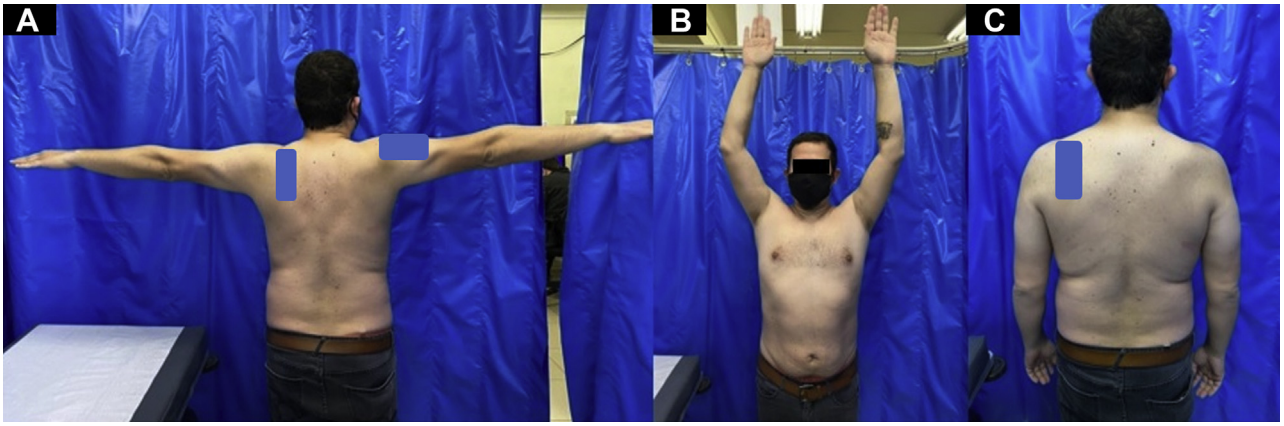

Figure 5 Inspection at 4 months. At 6 months, the patient was discharged without symptoms, complete mobility (**A-C**), recovered strength, and carrying out life and work without complications.

Conflicts of interest: The authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

Patient consent: Obtained.

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