Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.nrl.2021.12.002.

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Parsonage-Turner syndrome associated with COVID-19: About 2 family cases

Síndrome de Parsonage Turner asociado a Covid-19: A propósito de 2 casos familiares

We would like to underscore the relevance of the case of Parsonage-Turner syndrome (PTS) secondary to SARS-CoV-2 infection reported by Alvarado et al.,[1] as this syndrome has an incidence of 1.6 cases per 100 000 population. PTS has been associated with viral infections triggering an immune-mediated response against the brachial plexus; however, this case associated with SARS-CoV-2 infection is particularly relevant as the syndrome may constitute a clinical manifestation or neurological complication of COVID-19, even after vaccination.[2,3] Familial aggregation has been observed in PTS, which suggests the involvement of genetic factors.[4] Cases have been reported of hereditary neuralgic amyotrophy, with a clinical phenotype similar to that of PTS, linked to mutations at a locus on chromosome 17q25 (*SEPT9* gene, between the markers D17S1301 [centromeric] and D17S784 [telomeric]). However, and unlike in PTS, hereditary neuralgic amyotrophy presents from the second decade of life, and a founder effect has been described in families from the United States.[4,5] Few candidate gene studies have been conducted for PTS. Previous studies helped us to establish the clinical diagnosis of familial neuralgic amyotrophy in a rural setting in 2 siblings with SARS-CoV-2 infection (beta variant, PANGO lineage B1.1.35, clade GH/501Y.V2 [clade-specific TaqMan RT-qPCR]), a man and a woman aged 44 and 45 years, respectively. Both patients presented severe pain in the left shoulder associated with a tingling sensation; the physical examination detected atrophy of the deltoid, supraspinatus, and scapular muscles. They also presented odynophagia, fever of 40°, and palatopharyngeal vesicular enanthem (an early finding of COVID-19)[6]; anteroposterior chest radiography revealed ground-glass opacification. Electromyoneurography revealed abnormal postganglionic sensory nerve action potentials in the left brachial plexus at the level of the trunk and cervical vertebrae, from the C2 to the C5 nerve roots, suggestive of acute brachial plexopathy. Both patients were intolerant to corticosteroids. They gave informed consent to treatment. They were treated on an outpatient basis, receiving ciclosporin A dosed at 5 mg/kg/day for 3 days (this drug may inhibit viral replication, blocking 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, which prevents mitochondrial dysfunction associated with COVID-19 and blocks the cytokine storm, inhibiting the calcineurin inflammatory pathway and NF-kB[7]), ivermectin 6 mg/12 h for 7 days, azithromycin 500 mg/day for 5 days, lopinavir/ritonavir 2 tablets/12 h for 14 days, subcutaneous interferon-

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beta 0.25 mg every 24 h for 14 days, hydroxychloroquine 200 mg/12 h for 14 days, and OM85 one capsule/day for 30 days (Broncho-Vaxom, an immunostimulant and immunoregulator promoting opsonisation and mediating immune response via β-defensins and interferons), and subcutaneous enoxaparin 60 mg/day for 30 days. Brachial amyotrophic neuralgia was initially managed with non-steroidal anti-inflammatory drugs, opioids, and neuromodulators such as gabapentin, due to the patients' intolerance to corticosteroids. During the first 22 days of infection, COVID-19 symptoms and brachial neuralgia did not respond to treatment in either patient; RT-qPCR yielded positive results for the SARS-CoV-2 E-gene, and non-steroidal anti-inflammatory drugs, opioids, and neuromodulators were withdrawn. We added prolonged-release pirfenidone (600 mg/12 h) given the drug's strong anti-inflammatory, antioxidant, antiviral, and antifibrogenic properties and its ability to stabilise oxygen saturation; this drug was used as an adjuvant to control viraemia, neuralgia, and perineurial oedema associated with SARS-CoV-2 infection.[8] At day 30 after COVID-19 symptom onset, both patients were asymptomatic and RT-qPCR yielded negative results, and they presented oxygen saturation levels of 96% and 98%, respectively. However, left brachial plexus neuralgia persisted and the patients continued to test positive for SARS-CoV-2 IgG antibodies; therefore, pirfenidone was not discontinued. Symptoms of brachial plexus neuralgia resolved on day 21 post-infection in the woman and on day 26 in the man. Both patients tested negative for SARS-CoV-2 IgG antibodies; pirfenidone was withdrawn. In the rural setting of Sierra Sur de Oaxaca, in Mexico, the management of neuropathy is extremely challenging due to the scarcity of resources and tools for neurophysiological and imaging diagnosis; in this respect, the study by Alvarado et al.[1] was very helpful for clinical diagnosis. Neither of our patients received corticosteroids to inhibit the cytokine storm and manage neuralgia, as they both were intolerant to this drug group; instead, they received the first-line drugs ciclosporin A and pirfenidone, which, in addition to their anti-inflammatory properties, also have an antiviral effect against SARS-CoV-2. In conclusion, we present 2 familial cases of PTS associated with SARS-CoV-2 (beta variant, PANGO lineage B1.1.35, clade GH/501Y.V2) in whom the viral infection was successfully managed. Pirfenidone should be regarded as a new adjuvant drug for the treatment of PTS, as resolution of neuralgia may be linked to the reduction in viral load.

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Conflicts of interest

None.

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