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Case report

SARS-CoV-2 induced abducens nerve palsy: A case report and response to methylprednisolone

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ABSTRACT

Introduction: The abducens nerve (sixth cranial nerve) is a motor nerve that innervates the lateral rectus muscle, playing a key role in ocular abduction. Palsy of this nerve leads to convergent strabismus and diplopia. Common causes include strokes, trauma, inflammation, and infections, though in some cases, the etiology remains undetermined. With the emergence of COVID-19, neurological manifestations such as cranial neuropathies, including abducens nerve palsy, have been reported.
Case presentation: We present a case of a previously healthy 48-year-old male diagnosed with SARS-CoV-2 infection who developed abducens nerve palsy in the left eye. Following the resolution of respiratory symptoms, strabismus persisted. Treatment with methylprednisolone was initiated, resulting in partial recovery within one week and complete resolution after three months.
Conclusion: SARS-CoV-2-induced abducens nerve palsy can be reversible with conservative treatment using methylprednisolone. Early recognition and appropriate management are crucial for achieving a favorable prognosis.

Introduction

Since the onset of the COVID-19 pandemic caused by SARS-CoV-2, numerous studies have highlighted the virus's impact on various organ systems, including the central and peripheral nervous systems [1]. Among the neurological manifestations, neuro-ophthalmological complications, such as cranial nerve palsies, have garnered increasing attention due to their rarity and clinical complexity [2].

SARS-CoV-2 uses the angiotensin-converting enzyme 2 (ACE2) receptor to enter cells. Cells expressing ACE2, such as glial cells, neurons, and endothelial smooth muscle cells in the brain, are particularly vulnerable to SARS-CoV-2 infection, underscoring the virus's neurotropic potential [3]. Additionally, the virus can damage vascular endothelial cells, impair mitochondrial function, and disrupt endothelial nitric oxide synthesis. These effects lead to secondary cerebrovascular consequences, causing widespread endothelial dysfunction and systemic endotheliitis associated with apoptosis, culminating in neuronal cell death [4].

In addition to its neurotropic properties, multisystem inflammatory syndrome represents another mechanism of neuropathogenesis. It has been demonstrated that critically ill COVID-19 patients exhibit signs of severe systemic inflammation consistent with cytokine release syndrome, characterized by elevated inflammatory markers and pro-inflammatory cytokines [5]. This may explain the visual manifestations associated with current or past COVID-19 infections and their favorable response to corticosteroid therapy. Despite growing recognition of its neurological effects, only a few reports have documented this specific complication.

This case report describes a previously healthy patient who presented with abducens nerve palsy as a complication associated with SARS-CoV-2. Complete clinical recovery was achieved following conservative management with methylprednisolone, emphasizing the importance of early diagnosis and individualized treatment to improve prognosis. This case contributes to the emerging literature on SARS-CoV-2-related neurological complications, highlighting the potential benefits of early intervention with methylprednisolone in the context of

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inflammatory neuropathies.

Case presentation

Patient presentation

A 48-year-old male patient, originally from São Paulo and residing in Uricurituba, a municipality in the interior of the Amazonas state, Brazil. He is a former smoker, abstinent for 10 years, with a past smoking history of 9.75 pack-years. He denies alcohol consumption, regular physical activity, comorbidities, or chronic medication use.

The patient sought outpatient care at the Neurology service with a complaint of persistent diplopia for one month (Fig. 1), which began during an episode of severe acute respiratory syndrome and persisted after hospital discharge and resolution of respiratory symptoms.

Clinical history

The condition initially presented with respiratory symptoms, including odynophagia, fever (38–39 °C), myalgia, and dry cough. On the following day, the patient developed hyposmia associated with progressive dyspnea on moderate to intense exertion. He sought medical assistance and was initially treated symptomatically without significant improvement. Three days after symptom onset, he developed sudden-onset diplopia accompanied by convergent strabismus and vertigo, along with worsening dyspnea, which was now present even with minimal exertion, leading to a drop in peripheral oxygen saturation to 92 % on room air. Due to the worsening condition, hospitalization was indicated, and the patient was transferred to a higher-complexity center in Manaus.

Hospitalization and clinical course

Initially admitted to a local hospital in Uricurituba, the patient received empirical treatment due to the absence of a definitive etiological diagnosis. He had a complete COVID-19 vaccination schedule, with two doses of AstraZeneca administered nine and six months before symptom onset, respectively. Due to the unavailability of RT-PCR testing for viral detection at the local facility, empirical treatment was initiated with ceftriaxone (1 g IV every 8 h), oseltamivir (75 mg orally every 12 h) and symptomatic therapy.

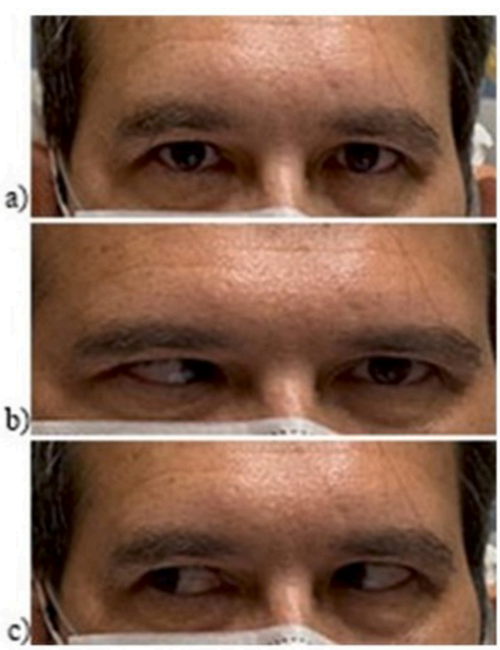

Fig. 1. Initial image of the patient during outpatient admission to the Neurology service with persistent diplopia.

Given the persistence of symptoms without significant improvement, the patient was transferred to a hospital with greater clinical support in Manaus. Upon admission, a rapid COVID-19 test was negative; however, he continued to present respiratory symptoms (asthenia, intermittent fever, myalgia, dry cough, and dyspnea with minimal exertion, with oxygen desaturation to 89–90 % on room air), necessitating supplemental oxygen therapy. Physical examination revealed mild tachypnea on exertion without accessory muscle use and evident convergent strabismus. Chest computed tomography (CT) showed extensive bilateral ground-glass opacities, predominantly in the peripheral regions. The findings were suggestive of viral lung involvement, consistent with a typical pattern observed in patients with COVID-19 (Fig. 2). Nasopharyngeal and oropharyngeal swabs were collected for real-time RT-PCR analysis, confirming SARS-CoV-2 infection.

Management and diagnostic investigation

Laboratory tests revealed a significant elevation in C-reactive protein (> 10 mg/L) and mild leukocytosis with neutrophil predominance. Corticosteroid therapy with dexamethasone (4 mg IV/day) was initiated. Follow-up imaging studies revealed diffuse ground-glass opacities predominantly in the lower lobes, consistent with viral pneumonia.

Given the persistence of convergent strabismus and diplopia, a cranial CT scan was performed. The analysis of the brain structures revealed symmetry and preservation of the sulci, gyri, and cerebral ventricles, with no signs of mass effect, midline shift or hypodense areas suggestive of acute ischemic injury. There were no intracranial hemorrhages, abnormal collections or apparent structural alterations (Fig. 3). Serological tests for VDRL, HIV, cytomegalovirus, and herpesvirus were requested. Results were negative for syphilis and HIV, while cytomegalovirus and herpesvirus serologies showed positive IgG but negative IgM. The patient received oral acyclovir with no satisfactory clinical response.

Clinical evolution and outcome

During hospitalization, the patient showed progressive clinical improvement in pulmonary symptoms, allowing for oxygen therapy weaning, with oxygen saturation maintained at 94–95 % on room air. Upon completing corticosteroid therapy and stabilizing laboratory parameters, he was discharged from the hospital, although persistent

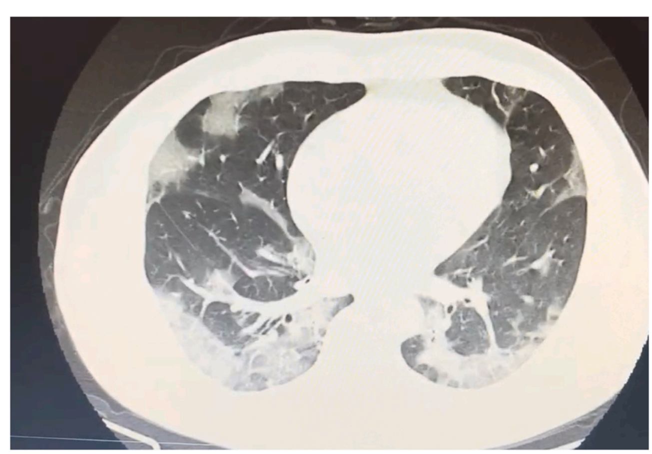

Fig. 2. The image shows an axial chest computed tomography scan, revealing extensive bilateral ground-glass opacities, predominantly in the peripheral regions. These findings are suggestive of viral lung involvement, consistent with a typical pattern observed in patients with COVID-19.

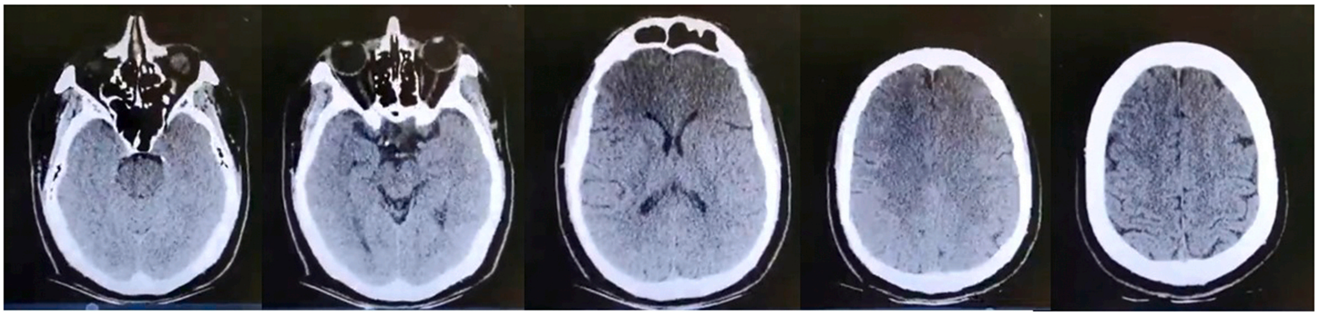

Fig. 3. The image showed a series of axial slices from a non-contrast cranial computed tomography scan. The analysis of the brain structures revealed symmetry and preservation of the sulci, gyri, and cerebral ventricles, with no signs of mass effect, midline shift, or hypodense areas suggestive of acute ischemic injury. There were no intracranial hemorrhages, abnormal collections, or apparent structural alterations that could explain the clinical presentation of persistent convergent strabismus and diplopia.

diplopia remained (Fig. 4).

Three days after discharge, the patient was evaluated at the Neurology Outpatient Clinic, where left abducens nerve palsy was diagnosed without contralateral ocular involvement. A diagnosis of abducens nerve neuritis secondary to SARS-CoV-2 infection was established, and pulse therapy with methylprednisolone (1 g IV/day for three days) was initiated, followed by outpatient follow-up. One week after completing immunomodulatory therapy, a slight improvement in ocular mobility was observed.

After three months of follow-up and four months after the initial infectious episode, the patient achieved complete resolution of left abducens nerve palsy, with full recovery of ocular abduction, remission of convergent strabismus, and resolution of diplopia (Fig. 5).

Discussion

Abducens nerve palsy, although rare, has been reported in patients with SARS-CoV-2 infection [6]. The mechanisms through which SARS-CoV-2 causes neuropathies are not yet fully understood. Several hypotheses have been proposed, including direct invasion of the central nervous system [7], immune-mediated dysfunction [8] and vascular compromise [9]. The case reported in this study supports the hypothesis that SARS-CoV-2 may be directly or indirectly associated with cranial neuropathies.

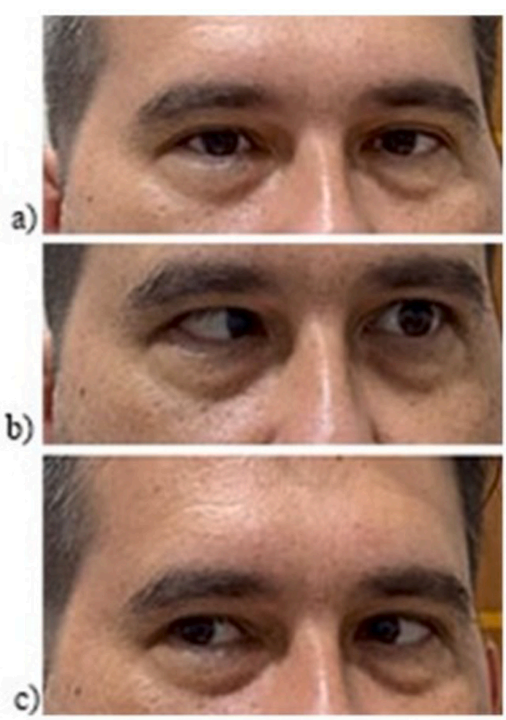

Fig. 4. Patient during hospital discharge, after completing corticosteroid therapy and stabilizing laboratory parameters, with persistent diplopia.

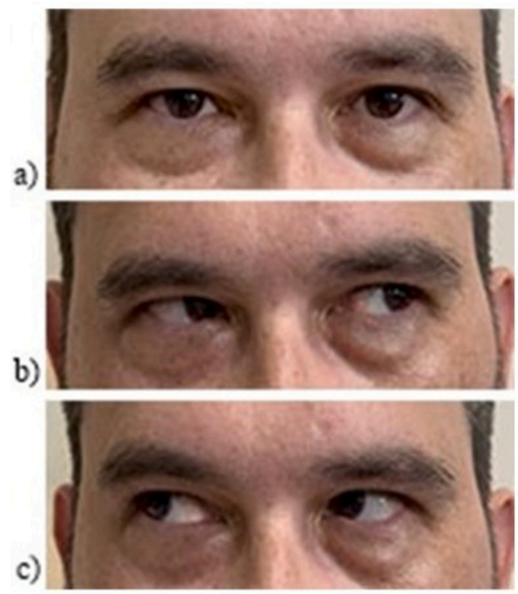

Fig. 5. Complete resolution of left abducens nerve palsy, with full recovery of ocular abduction, remission of convergent strabismus, and resolution of diplopia, after three months of follow-up and four months after the initial infectious episode.

To establish a link between abducens nerve palsy and COVID-19, it is essential to exclude other etiologies, such as diabetes mellitus, hypertension, intracranial tumors, and infections caused by other viral agents, including herpesvirus and Epstein-Barr virus [10].

The literature indicates that, in many cases, ophthalmologic symptoms related to abducens nerve palsy are managed conservatively without specific interventions. While spontaneous resolution has been documented in numerous cases, corticosteroid therapy, particularly pulse therapy, has demonstrated promising results in patients with significant or persistent inflammation [11]. Pulse therapy with methylprednisolone, commonly used in inflammatory neuropathies, has proven effective in reducing inflammation and accelerating functional recovery [12].

In the case presented, the administration of methylprednisolone at a dose of 1 g per day for three days resulted in progressive improvement in ocular mobility, culminating in complete recovery within three months.

This outcome aligns with the findings of Srijon et al. [13], who reported partial improvement in diplopia following pulse therapy, although long-term follow-up was lacking. In contrast, Medeiros et al. [14] described full recovery from a similar case only after eight months without specific intervention. The differences in recovery times suggest that pulse therapy may significantly accelerate rehabilitation in patients with SARS-CoV-2-associated abducens nerve palsy.

The use of corticosteroids, such as methylprednisolone, for managing neuropathies related to SARS-CoV-2 is based on their immunomodulatory properties. These agents suppress the exaggerated inflammatory response characteristic of immune-mediated manifestations in COVID-19, reducing immune damage to neural tissue and promoting functional recovery [15].

Corticosteroids inhibit the production of pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), while reducing vascular permeability, which may contribute to neural edema and injury [16]. Studies suggest that methylprednisolone, due to its high potency and rapid action, is particularly effective in acute inflammatory conditions such as cranial neuropathies associated with SARS-CoV-2 and has been linked to reduced mortality in patients [17]. Furthermore, several reports indicate that high-dose intravenous methylprednisolone has led to a rapid improvement in diplopia among COVID-19 patients, reinforcing its potential therapeutic role in managing virus-induced neurological complications [18].

The evidence supporting pulse therapy with corticosteroids, in comparison to other methods of administration in patients with COVID-19 and diplopia, remains limited, primarily relying on case reports and small case series. While specific studies on the use of methylprednisolone in patients with COVID-19 and diplopia are lacking, numerous articles have been published documenting the efficacy and associated risks of pulse therapy in severe COVID-19 cases, including those with neurological manifestations [19]. The optimal prescription of methylprednisolone for the treatment of COVID-19 patients remains inconclusive. Reported dosages in the literature have varied from 40 mg/day to 1 g/day, with positive outcomes observed in hospitalized patients. Studies have been demonstrating that methylprednisolone therapy within one week may benefit COVID-19 patients [20]. Given the potentially beneficial effects of pulse therapy in acute inflammatory neuropathies, randomized controlled trials are warranted to determine whether this approach is more effective than the standard corticosteroid regimens currently used in the treatment of COVID-19.

In the present case, pulse therapy with methylprednisolone resulted in complete recovery of abducens nerve function. This outcome reinforces the hypothesis that abducens nerve palsy may stem from a reversible inflammatory process responsive to immunosuppressive treatment. The favorable response in this case was likely influenced by early intervention, with rapid identification of the neuropathy and immediate initiation of treatment being key factors in achieving complete recovery.

While corticosteroids provide clear benefits in many cases of inflammatory neuropathy, it is important to consider the risks associated with their use, including immunosuppression, alterations in glucose levels, hypertension, and the potential for rebound inflammatory effects if treatment is discontinued improperly [21]. Thus, management should be individualized, taking into account each patient's specific risk factors and conducted under strict clinical and laboratory monitoring.

Managing neurological complications associated with SARS-CoV-2 remains a clinical challenge. Further studies are essential to determine the efficacy and safety of pulse therapy in cranial neuropathies related to COVID-19. Although this case demonstrates a favorable outcome with the use of pulse therapy in treating these clinical conditions, the lack of specific biomarker measurements is a limitation. According to the literature, biomarkers can help identify inflammatory processes, neuronal damage, and immune dysfunction, aiding in treatment personalization and improving clinical outcomes [22].

This case report contributes to the emerging literature by highlighting the potential benefits of early intervention with methylprednisolone in the context of SARS-CoV-2-induced inflammatory neuropathies. Our findings underscore that pulse therapy should be considered for patients with significant inflammation, given its potential to accelerate recovery and improve clinical outcomes.

Abbreviations

AVCs: Cerebrovascular Accidents
COVID-19: Coronavirus Disease 2019
SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2
g: Gram
IV: Intravenous
mg: Milligram
CT: Chest computed tomography
l: liter
ACE2: Angiotensin-Converting Enzyme 2
VTM: Viral Transport Medium
RT-PCR: Reverse Transcriptase Polymerase Chain Reaction
HIV: Human Immunodeficiency Virus
VDRL: Venereal Disease Research Laboratory
IL: Interleukin
IgG: Immunoglobulin G
IgM: Immunoglobulin M
TNF-α: Tumor Necrosis Factor Alpha

Ethical approval

The study was submitted and approved by the Human Research Ethics Committee (CEP-UEA) with CAAE: 31186920.5.0000.5016, in accordance with the procedures set out in the Plataforma Brasil.

CRediT authorship contribution statement

SIERPINSKIA CLEITIENE DE SOUZA: Validation, Investigation, Data curation. **PORTO CAMILA FELDBERG:** Investigation, Formal analysis, Data curation. **Abdalla Ligia Fernandes:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Formal analysis, Conceptualization. **Santos João Hugo Abdalla:** Validation, Supervision, Methodology, Data curation. **Naveca Felipe Gomes:** Validation, Supervision, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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