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RECURRENT PAIN FROM CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY AFTER COVID-19 INFECTION – A CASE REPORT

Loc Lam, DO[1], Vishal Bansal, MD[2], Thomas Chai, MD[3], and Larry C. Driver, MD[3]

Background: Studies show that COVID-19 can cause neurological complications in both central and peripheral nervous systems. Plausible theories include virus-induced hyperinflammation and hypercoagulability, direct infection, and postinfectious immune processes. Our case report appears to be one of the first case reports highlighting COVID-19 infection, as a possible trigger for recurrent chemotherapy-induced peripheral neuropathy (rCIPN).

Case Report: We present a case report of a 59-year-old man with rectal adenocarcinoma and a history of CIPN who experienced rCIPN after contracting COVID-19. Prior to infection, he experienced burning pain and dysesthesias in a stocking-glove distribution due to chemotherapy, with resolution of symptoms shortly after discontinuation. Unfortunately, within one week of his COVID-19 diagnosis, he experienced a return in his previous CIPN pain in a similar distribution and quality.

Conclusion: This case report suggests a potential role of COVID-19 infection in triggering the recurrence of CIPN, emphasizing the need for further research.

Key words: COVID-19, recurrent chemotherapy-induced peripheral neuropathy, neuropathic pain, cancer pain, chemotherapy-induced peripheral neuropathy

BACKGROUND

Significant health care reform and technological advancements have facilitated earlier detection, more efficient and personalized treatment, and improved patient care, especially in the oncological field (1,2). As the population of cancer survivors continues to grow, pain physicians are faced with clinical challenges due to the substantial subset of patients experiencing pain stemming from their disease and its associated treatment, such as the use of chemotherapy (1,3). Although often curative, chemotherapy comes with its own side-effect profile that can significantly impact the patient's quality of life (4). Peripheral neuropathy is a common and often debilitating consequence of chemotherapy, affecting a considerable proportion of cancer survivors. Certain chemotherapy medication classes, such as platinum-based antineoplastics, taxanes, vinca alkaloids, epothilones, proteasome inhibitors, and immunomodulatory drugs, can lead to neuronal damage, resulting in chemotherapy-induced peripheral neuropathy (CIPN) (1,5).

From: [1]H. Ben Taub Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, TX; [2]Department of Physical Medicine and Rehabilitation, The University of Texas Health Science Center at Houston, Houston, TX; [3]Department of Pain Medicine, Division of Anesthesiology, Critical Care Medicine, & Pain Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

Corresponding Author: Loc Lam, DO, E-mail: locplamdo@gmail.com
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CIPN typically develops in a dose-dependent manner, but can also present as acute neurotoxicity. Each class of medication contributes to neuronal damage and death in a unique pathway but often with underlying similarities (5,6). It is also a multifactorial condition, as some preexisting conditions, such as diabetes, which results in nerve damage, can increase the risk of developing CIPN and its severity (5,6). Studies have also made efforts to analyze potential risk factors, including race, age, and obesity for the development of CIPN; however, these factors have not been validated. While some studies have investigated the association between CIPN and preexisting autoimmune conditions, there is currently no literature available on the connection between SARS-CoV-2 and CIPN or recurrent CIPN (rCIPN).

SARS-CoV-2, the agent of COVID-19, is a highly contagious virus that resulted in a consequential pandemic, affecting millions of people worldwide (7). SARS-CoV-2 mainly affects human respiratory symptoms leading to acute respiratory syndrome with fever, fatigue, dry cough, myalgia, and dyspnea. However, SARS-CoV-2 has been reported also to affect other organs, including the neurological system (8,9). SARS-CoV-2 is known to invade the central and peripheral nervous systems causing neurological complications, such as encephalopathy, encephalitis, stroke, anosmia/ageusia, peripheral neuropathy, new/recurrent Guillain-Barre syndrome (GBS), etc (9).

Our case report is one of the first cases, to our knowledge, showing COVID-19 infection as a possible trigger for rCIPN. Similar studies of COVID-19 causing recurrent peripheral neuropathy are cases involving recurrent GBS (rGBS) post-COVID-19 infection. Although our patient's neurological symptoms were similar to previous CIPN, the mechanism of rCIPN might be similar to that of COVID-19-induced rGBS, which is immune mediated.

CASE PRESENTATION

A 59-year-old man with an oncologic history of rectal adenocarcinoma was initially treated by radiation therapy (3780 cGy in 21 fractions), followed by capecitabine chemotherapy. He then underwent abdominal perineal resection with lymph node resection, followed by additional chemotherapy with oxaliplatin and 5-fluorouracil. The patient was initially referred to the pain service for management of abdominal pain following his abdominal perineal resection.

His abdominal pain was initially described as constant, aching sensations with intermittent sharp pain in the bilateral epigastric region without radiation. Pain intensity was rated on a Numeric Rating Scale as 7/10. He was advised to start oxycodone extended release 9 mg twice daily and gabapentin 300 mg 3 times a day. On follow-up one month later, he reported improvement in postsurgical abdominal pain, weaned himself off of oxycodone, and continued on gabapentin. His gabapentin continued to provide relief for his persistent neuropathic pain, for which he reported average pain scores of 1-2/10 in severity.

After this visit, the patient started his second chemotherapy regimen with oxaliplatin and 5-fluorouracil and reported worsening of his neuropathy in his hands/feet, and abdominal pain. This was associated with tingling and numbness. At his own discretion, he tried gabapentin 600 mg doses at home, with improvement in his symptoms. The patient was able to tolerate titration of gabapentin with no accompanying side effects and with adequate pain control. He was advised to continue with this dose through completion of chemotherapy. Shortly after completing chemotherapy, he noticed an improvement in the pain and eventually tapered off of gabapentin.

Several months later, however, the patient was diagnosed with COVID-19 infection, and within one week of infection, he experienced the return of peripheral neuropathic pain in his hands and feet. His pain complaints were similar to his previous symptoms from his CIPN. The patient was restarted on gabapentin; however, despite dose escalation, there was no relief in pain and the side-effect profile was too burdensome. He was then changed to pregabalin, which was effective, resulting in near-resolution of his rCIPN pain.

DISCUSSION

CIPN is a significant and dose-limiting side effect of several chemotherapy agents, notably platinum drugs, vinca alkaloids, taxanes, and bortezomib (11). A systematic review demonstrated the prevalence of CIPN, with incidence rates of 68.1% after one month of treatment, 60.0% at 3 months, and 30.0% at 6 months or beyond (10). The pathogenesis of CIPN is multifaceted and not completely understood, though it has been proposed to involve a combination of DNA damage, oxidative stress, mitochondrial dysfunction, and inflammation, amongst others (5).

The rCIPN following COVID-19 infection, as observed in our case, provides a unique insight into a potential interplay between the 2 disease processes.

The SARS-CoV-2 virus has been postulated to impact the nervous system through direct mechanisms (e.g., viral invasion) and indirect mechanisms (e.g., immune mediated) (8,9,12). The invasion of peripheral nerve cells by SARS-CoV-2 might lead to neuropathic symptoms by exacerbating damage to peripheral nerves already susceptible due to chemotherapy (13). Alternatively, a potent immune response, driven by viral infection, might contribute to the recurrence or worsening of CIPN, given that inflammation is known to be involved in its pathogenesis (5).

To the best of our understanding, our case report appears to be among the initial instances indicating a potential role of COVID-19 infection in triggering the recurrence of CIPN. The most similar research involving COVID-19 leading to repeated instances of peripheral neuropathy focuses on cases of rGBS after a COVID-19 infection (14,15,16). Despite the neurological symptoms in our patient bearing a greater resemblance to earlier CIPN, the processes underlying rCIPN may align with those of the immune-mediated COVID-19-induced rGBS. In this context, it is plausible that an infection with SARS-CoV-2 could act as a triggering event, precipitating rCIPN in patients who have previously received chemotherapy. However, this hypothesis will require further validation through experimental and clinical studies.

This case serves to highlight the possible interaction between COVID-19 and preexisting neurological conditions, emphasizing the importance of considering COVID-19 as a potential triggering or exacerbating factor in patients with a history of CIPN who present with worsening or recurrent neuropathic symptoms. It is important that clinicians maintain vigilance in monitoring and managing these patients, as the recurrence of CIPN may significantly impact their quality of life and ability to receive future chemotherapy treatments.

CONCLUSIONS

Management of rCIPN in cancer patients can be challenging. This case report highlights rCIPN in the setting of a COVID-19 infection and emphasizes the need for more research into this phenomenon.

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