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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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SARS-COV-2 INFECTION AND INVOLVEMENT OF PERIPHERAL NERVOUS SYSTEM: A CASE SERIES OF CARPAL TUNNEL SYNDROME AGGRAVATION OR NEW ONSET WITH COVID-19 DISEASE AND A REVIEW OF LITERATURE

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Abstract.

Introduction: COVID-19 may be asymptomatic or have a typical presentation with fever, cough, anosmia, lymphocytopenia. In some cases, it occurs with a "chimeric" presentation, with more subtle and ambiguous symptoms which may be initially misdiagnosed and are referred to in long covid condition. A possible central and peripheral nervous system involvement has been recognized. We present our experience and review the literature about association between carpal tunnel syndrome (CTS) and hand's arthritis presenting a case series of patients who firmly state that their condition of CTS arised or got worse during a typical presentation of COVID-19. The outbreak of COVID-19 has resulted in significant global healthcare implications. While the respiratory manifestations of COVID-19 have been widely studied, there is emerging evidence suggesting potential associations between COVID-19 and various other health conditions. This review of the literature aims to investigate the potential relationship between COVID-19 and the development or exacerbation of CTS. By synthesizing the available literature on this topic, we aim to provide a comprehensive overview of the current knowledge and enhance our understanding of the potential implications of COVID-19 on CTS.

Case series: In this article we report 13 cases of typical presentations of COVID-19 with fever, myalgia, and respiratory system involvement, with a simultaneous aggravation of the median nerve pre-existing neuralgia and some cases that developed a median nerve neuralgia during COVID-19, which came to the attention of the hand surgeon. Some cases had stable symptomatic CTS and were on waiting list for surgical carpal tunnel release, some cases were previously asymptomatic and developed a median nerve neuralgia during COVID-19. All patients referred to a rapid worsening of acral paraesthesia and neuralgic pain of the same quality of CTS and in the median nerve topography. Some patients developed typical COVID-19 symptoms and died; the others were surgically treated.

Conclusion: CTS could be an atypical presentations of COVID-19 or a condition of long-covid disease and clinical and epidemiological significance needs to be fully studied. We presented cases of worsening of the median nerve neuralgia which presented among other symptoms of COVID infection. We conclude a causal relation may exist and needs to be further investigated.

Key words. Covid, Coronavirus, Carpal Tunnel Syndrome, neuralgia, peripheral nervous system, nerve, arthritis, elderly.

Introduction.

COVID-19 (SARS-Cov-2 disease) may have an asymptomatic course or a typical presentation with fever, cough, anosmia, lymphocytopenia [1,2].

Unusual findings have also been described [1]. Of these less typical presentations, those affecting the nervous system, either central or peripheral, are not uncommon [3,4].

Carpal tunnel syndrome (CTS) is a common peripheral nerve entrapment disorder characterized by compression of the median nerve at the wrist, leading to hand and wrist pain, numbness, and weakness. While CTS is typically associated with repetitive hand movements and occupational factors, emerging evidence suggests that viral infections may also play a role in its pathogenesis. Given the broad spectrum of systemic manifestations observed in COVID-19, investigating a potential link between COVID-19 and CTS is warranted.

In this article, we report some cases of typical presentations of COVID-19 with fever, myalgia, and respiratory system involvement, with a simultaneous aggravation of the median nerve pre-existing neuralgia, and some cases that developed a median nerve neuralgia during COVID-19, which came to the attention of the hand surgeon. The aim of this article is to describe this unusual symptom we recognized as possibly due to COVID-19, based on clinical observation and known considerations on pathophysiology of the coronavirus infection.

Materials and Methods.

We analyzed all patients who had come to the attention of our Hand Surgery Unit, from 2020 to the present day, complaining of symptoms referable to CTS and related by them to Covid-19 infection. We included patients who already had a known diagnosis and a reported worsening of symptoms as well as patients with new-onset symptoms. All the patients included underwent Electroneurography and Electromyography to confirm the diagnosis.

Results.

In the present article we report 13 cases of patients who firmly state that their condition of CTS aroused or got worse during a typical presentation of COVID-19 (Table 1). Some cases, which had stable symptomatic CTS and were on waiting list for surgical carpal tunnel release, referred a typical presentations of COVID-19 with fever, myalgia, and respiratory system involvement, with a simultaneous aggravation of the median nerve pre-existing neuralgia. Some cases were previously

Table 1. *Case Series. *clinical improvement was obtained with open carpal tunnel release, after conservative treatment and an observational period of 2-3 months.*

Patient	Sex	Age	Side	New onset or disease worsening	Comorbidities	Covid-19 Symptoms					Outcome
						Fever	Myalgia	Respiratory	Gastro-intestinal	Other	
1	M	90	Both	New onset	high blood pressure, diabetes	Yes	Yes	Yes			Death
2	F	82	Left	Worsening	high blood pressure, glaucoma	Yes	Yes	Yes			Death
3	M	66	Both	Worsening		Yes	Yes	Yes			Clinical improvement*
4	F	41	Both	Worsening		Yes	Yes	Yes			Clinical improvement*
5	M	52	Both	Worsening	benign prostatic hypertrophy	Yes	Yes	Yes	Yes		Clinical improvement*
6	M	60	Both	Worsening		Yes	Yes	Yes			Clinical improvement*
7	M	80	Both	New onset	high blood pressure	Yes	Yes	Yes		Skin lesions	Clinical improvement*
8	M	54	Both	New onset	high blood pressure	Yes	Yes	Yes			Clinical improvement*
9	F	84	Both	New onset	high blood pressure	Yes	Yes	Yes			Clinical improvement*
	F	46	Both	Worsening		Yes	Yes	Yes			Clinical improvement*
10	F	58	Left	New onset		Yes	Yes	Yes			Clinical improvement*
11	F	72	Both	New onset	high blood pressure	Yes	Yes	Yes	Yes		Clinical improvement*
12	M	80	Left	Worsening	high blood pressure	Yes	Yes	Yes			Death
13	F	68	Right	New onset		Yes	Yes	Yes			Clinical improvement*

asymptomatic and developed a median nerve neuralgia during COVID-19. All patients referred to a rapid worsening of acral paraesthesia and neuralgic pain of the same quality of CTS and in the median nerve topography during or immediately after COVID-19. Three patients developed typical COVID-19 symptoms and died; the others were surgically treated.

After an observational period of 2-3 months and conservative treatment [5-7], clinical improvement was obtained with open carpal tunnel release in all patients. Surviving patients had a 12-month post-operative follow-up. All 10 patients treated surgically benefited from the surgical treatment.

Two further patients who suffered from a pre-existing median nerve neuralgia (due to a documented CTS) referred to us because of aggravation of the symptoms immediately before CD COVID-19 onset. These two patients were excluded from our case series, because we did not obtain any clinical follow-up, but we think that they may nevertheless be worthy of description and may enhance the very sparse literature on this subject.

Case One.

The first case is a 68-year-old male patient with a confirmed diagnosis of bilateral CTS (CTS), mild on the right and moderate on the left hand, according to Padua classification [8], who had been on waiting list for carpal tunnel release on left hand for two months. He was also hypertensive, treated with a sartan. In March 2020, he reported an abrupt worsening of symptoms and contacted by phone his referring surgeon. He referred to bilateral acral paraesthesia and neuralgic pain of the same quality of CTS and in the median nerve topography, rapidly worsening over the last two days. To confirm median nerve topography and exclude polineuropathy we asked explicitly for the presence of “pins and needles” on the fifth finger and on the back of the hand, which the patient denied. On the left-hand pain was greater than the contralateral side, with a Numerical Rating Scale (NRS) of 7/10 on the left vs 5.5/10 on the right, and its intensity was more persistent and fixed all day long without circadian oscillations, and sleep was impaired. At the first contact he referred slight evening fever (37.2°) and slight myalgia, without cough and dyspnea. He had not taken any new medication in the past month. We indicated prompt contact with the general practitioner for complete re-evaluation. Moreover, we offered our re-evaluation for the neuropathy.

Six days after, the patient's wife contacted us by phone reporting that later, the day after the first contact, the patient developed typical presentation of COVID-19 with fever (39.0°C) and dyspnea. He immediately accessed the nearest emergency department, where a throat swab was performed for a nucleic acid SARS-Cov-2 identification test (or PCR test), which was positive. He was hospitalized and died two days later of respiratory failure; autopsy was not performed.

Case Two.

The second patient is a 69 year old male, with obesity, diabetes, hypertension in treatment with metformin, ace-inhibitor and a beta blocker. He was in follow-up for secondary post traumatic right ankle osteoarthritis and confirmed diagnosis of bilateral CTS, minimal on the left and moderate on the right hand, according to Padua classification.[8] He had been on waiting list for carpal tunnel release on right hand for three months. In March 2020 he reported a quick worsening of pain and contacted us by phone. He reported acral paraesthesia and neuralgic pain in the median nerve topography on both hands, with a NRS of 6/10 on the left-hand vs 4.5/10 on the right, worsening over the preceding three days. He denied pain or paresthesia on the fifth finger and on the back of the hand. Pain was present for the whole day. We offered our re-evaluation for the worsening of pain. The day after the first contact, neuralgic pain of the median nerve territory attributable to CTS slightly decreased on both sides (NRS of 5/10 on the left-hand vs 4/10 on the right), while fever until 37,5°C and a worsening diffuse musculoskeletal pain started (visual analogue scale 7/10), with a highest intensity on the right ankle (visual analogue scale 7/10). Over the following three days, body temperature raised until 39.5°C and he presented cough. He accessed the emergency department, where a throat swab was positive for SARS-Cov-2 (PCR test). Furthermore, he presented Leucopenia (3.44, min 4), Lymphocytopenia (19.7%, normal >20%), thrombocytopenia (86 × 109/L, normal >120), high transaminase (61 UI/L, normal range 7 - 45), high LDH (254 UI/L, normal <250), high C-reactive protein (13.4 mg/L, normal <5) normal coagulation screening (INR, aPTT, D-Dimer, fibrinogen), blood glucose: 147 mg/dL. Patient died of unspecified causes related to COVID-19 few months later.

Review of Literature.

The review of the literature reported in the present article was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive search of electronic databases, including PubMed/MEDLINE, Embase, and Scopus, was conducted. Keywords and MeSH terms related to COVID-19, CTS, and neuropathy were used. Studies published between January 2020 and July 2023 were included. Studies reporting on patients diagnosed with COVID-19 and presenting with new-onset CTS or exacerbation of pre-existing CTS were considered for analysis. The review of the literature was performed according to the flow chart in figure 1.

Review questions

The review questions were formulated following the PICO scheme (population, intervention, comparison, and outcome) as follows:

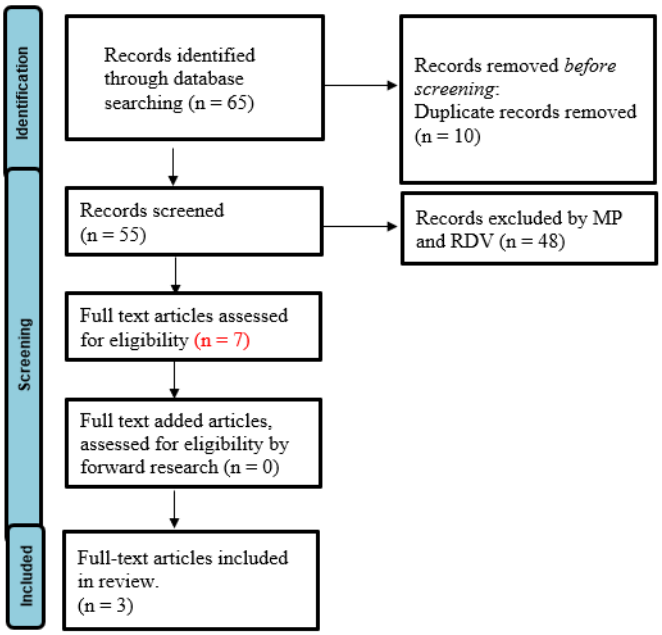

Figure 1. *Study flow chart.*

Did patients who suffered from COVID-19 contagion (P) have a new onset rather than worsening of already known CTS (C)? Did they need carpal tunnel release surgery (I)? What clinical evolution should we expect (O)? Can be the clinical outcome (O) be influenced by comorbidities (P)?

Inclusion and exclusion criteria

Full-text articles were analyzed evaluating the correlation between CTS and COVID-19 contagion/disease. Articles written in English were only included. No publication date limits were set. Exclusion criteria were studies on animals, unpublished reports, cadaver or in vitro investigations, review of the literature, abstracts from scientific meetings, and book chapters.

Search strategy and study selection

MEDLINE via PubMed and Scopus were searched using the keywords: "SARS-CoV-2", "Covid 19", "Carpal tunnel", "Carpal tunnel syndrome", and heir MeSH terms in any possible combination. Forward research was performed onto the reference list of the selected studies, in order to identify the study of interest. The search was reiterated until July 23, 2023.

Data extraction and analysis

Two independent reviewers (M.P. and R.D.V.) extracted the data from the studies included. Any discordances were solved by consensus with a third author (V.C.). For each study, the following data were collected: demographic features (sex, age), involved side, new onset CTS or worsening of an already known CTS, diagnostics, associated lesions/symptoms, comorbidities, clinical outcome, and follow-up. Numbers software (Apple Inc., Cupertino, CA, USA) was used to tabulate the collected data. Categorical variables are presented as frequency and percentages. Continuous variables are presented as means and standard deviation. Only one decimal digit was reported and was rounded up.

Results from review of the literature

After the screening of 65 articles by title and abstract, 9 studies were considered eligible for the full-text analysis [9-17]. After reading the full text, only 3 studies that met inclusion criteria were included in the present review. Among the included studies, one had a level of evidence I [11], while two had a level of evidence IV [14,15].

Fleischer et al. concludes that objectifiable affection of the nervous system is rare in post-COVID-19 syndrome, thus psychosomatic factors can explain peripheral nervous system symptoms [11].

Tullie et al. described a case of CTS post their second dose of AZD1222 (ChAdOx1 nCoV-19) vaccination [15]. In our opinion, the clinical history of this specific case is heterogeneous with respect to the objective of our research.

Only Roncati et al. have currently described cases similar to the cases we report in this article [14].

1. A 51-year-old man (with low level of vitamin D in anamnesis) who developed a left side (monolateral) carpal and cubital nerve syndrome. He underwent decompressive surgery.
2. A 47-year-old man who developed a right side (monolateral) carpal and cubital nerve syndrome. He underwent decompressive surgery. He developed a LADA (latent autoimmune diabetes in adults) in the post Covid-19 disease.

As a conclusion, literature is currently extremely scarce in relation to the association between CTS and COVID-19 disease; the data we have obtained from our search do not allow us to answer our questions.

Discussion.

Our clinical practice has highlighted the possible relationship between COVID-19 and CTS, however the literature that analyzes the relationship between CTS and COVID-19 is sparse. However, a correlation between the two diseases has already been reported [14].

The literature produced on this subject is scarce, and there is no evidence to confirm the pathophysiological mechanism that determines peripheral neuropathy of the median nerve. Based on the present literature we cannot come to any evidence-based conclusions on this issue.

However, the involvement of the peripheral nervous system has been described in COVID-19, both in motor and in sensory form and has been attributed to various possible causes: the "cytokinic storm", hypoxic state, acute and chronic inflammatory state, immune mechanisms [18].

CTS is a high prevalence disease [19]. The clinical picture is linked to a chronic compression of the nerve at the wrist that firstly results in endoneural connective tissue thickening and goes on with the demyelination of the fibers and an axonal degeneration [6,7,19,20].

Good clinical compensation can occur in some cases, thus patients only refer to the physician when CTS is severe, when the nerve injury is permanent, the sensory impairment is persistent and muscular denervation is clinically relevant. On the other hand, there are some patients with slightly positive electromyography/electroneurography and with mainly very intense sensory impairment [20].

In cases where COVID-19 also presents with symptoms similar to the CTS, COVID-19 represents a "storm" that hangs over the median nerve that is probably already at the limit of its functioning due to a more or less compensated chronic inflammation.

This would also explain why surgical decompression is effective to relieve symptoms, according to the literature and as observed in our clinical practice [14]. What the chances of post-surgery recovery are in these patients are still to be assessed, as the long-term evolution of this disorder remains unknown.

Typical presentations of COVID-19 include cough or more serious respiratory impairment, or a completely asymptomatic course, but more subtle presentations, such as isolated anosmia, have been recently described [1,2].

COVID-19 should be recognized in the very first onset, to avoid, with adequate isolation, exposure of household contacts and clinical personnel [21]. We suggest that in some cases COVID-19 occurs with a “chimeric” clinical presentation, with more subtle and ambiguous symptoms which may be easily misdiagnosed at first evaluation [1,3,22-25].

We suggest that, in the cases described, a correlation between the Sars-Cov-2 and sudden neuralgic pain worsening in patients affected by CTS exists and recognizing it can lead to quicker recognition of the patient’s illness and a better management. We support the hypothesis of a causal relation between worsening of neuralgic pain and Sars-Cov-2 infection considering in our cases:

1. The temporal correlation of the symptoms.
2. Exclusion of other obvious causes of sudden aggravation of CTS.
3. Pathophysiology of human coronaviruses infections. Myalgia, fever, and limb pain, indeed, may be explicated by a “cytokine avalanche” effect, which in some cases may reach the threshold to provoke a Cytokines Release Syndrome (CRS) [22,26,27].

The role of interleukins has been documented as precipitating and aggravating factors in peripheral nerve suffering [28-31]. A direct infusion of IL-2, furthermore, has being recognized as a provoking factor of CTS [28], and very recent studies have highlighted its role in COVID-19 pathogenesis [32]. In the same way, other molecules as CCL5 have a recognized role in both CTS and COVID-19 [23,33]. Peripheral nervous system findings in COVID-19 have been already described and should not be underestimated [3,24].

The lack of objective evaluation and exams such as electromyography and patient-reported outcomes measures in our report is an obvious limitation [34]. Further analyses on our two non-objectifiable cases are not possible at the moment [35]. Long-term implications for the neuralgic symptom need to be studied at follow. In the second patient, after the overt respiratory system involvement, median nerve pain lessened, but whether the neuralgic pain and motor symptoms are only transient or persistently worsened after acute illness resolution needs to be investigated. According to our hypothesis, a restitution to previous pain and impairment would be more likely after resolution of infection. A further concern on COVID-19 potential to cause peripheral nervous system damage has been

raised from Zhao et al., who reported a case of Guillain-Barré syndrome with a concomitant Sars-Cov-2 infection [4].

The available evidence suggests a potential association between COVID-19 infection and the development or exacerbation of CTS. However, the current literature is limited in terms of sample size, study design, and lack of control groups. Additional robust studies are needed to further investigate this relationship and understand the mechanisms involved. Healthcare providers should be aware of the potential association between COVID-19 and CTS and consider this possibility in patients presenting with hand and wrist symptoms during or after a Sars-Cov-2 infection.

Conclusion.

Reviewing the literature, although limited, the available evidence suggests a potential link between COVID-19 and CTS. Healthcare providers should be vigilant in recognizing and managing CTS symptoms in COVID-19 patients. Further well-designed studies are required to validate and elucidate the underlying mechanisms of this association. Understanding the potential implications of COVID-19 on CTS can aid in early diagnosis, management, and appropriate referral of affected individuals [12,36].

We also presented a case series of worsening of the median nerve neuralgia, which presented among other symptoms of COVID-19 and a review of the literature on association between CTS and Sars-Cov-2. We conclude a causal relation may be relevant and needs to be further investigated and that the common external neurolysis performed for CTS not COVID-related could be an effective treatment for CTS Covid-related.

Conflicts of Interest.

The authors report no conflicts of interest.

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