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Case Report

Headache, Loss of Smell, and Visual Disturbances: Symptoms of SARS-CoV-2 Infection? A Case Report

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Abstract

Objective. The purpose of this case report is to describe the main components of the history and physical examination that led to idiopathic intracranial hypertension differential diagnosis, which initially was investigated as COVID-19.
Methods (Case Description). A 28-year-old woman complaining of constant headache and loss of smell and taste was suspected as SARS-CoV-2 infection by her general practitioner. She underwent 3 molecular swab tests, all negative, then decided to seek her physical therapist for relieving headache.
Results. The full cranial nerve examination revealed impaired olfactory (CNI), abducens (CN VI), and facial (CN VII) nerves, leading the physical therapist to refer the patient to a neurosurgeon for a suspected central nervous system involvement. The neurosurgeon prescribed a detailed MRI and an ophthalmologic examination, which allowed for the final diagnosis of idiopathic intracranial hypertension.
Conclusion. An urgent lumbo-peritoneal shunting surgery resolved the patient's symptoms and saved her sight. Despite the ongoing COVID-19 pandemic, health care professionals must pay attention to properly investigating patients' signs and symptoms using comprehensive clinical reasoning, considering the screening for referral to specialist medical attention.
Impact. A thorough physical examination is required for every patient even if patients' signs and symptoms are in line with apparent common and widespread pathologies. Cranial nerve evaluation is an essential component of the physical therapist assessment and decision-making process. The ongoing pandemic highlighted the fundamental assistance of physical therapists toward physicians in the screening and management of musculoskeletal diseases.

Keywords: Cranial Nerves, Differential Diagnosis, Idiopathic Intracranial Hypertension With Papilledema, Physical Therapists, Pseudotumor Cerebri

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Background and Purpose

The ongoing pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has severely challenged health care systems worldwide.[1] As of December 2021, more than 290 million COVID-19 cases were confirmed globally.[1,2] The most common signs and symptoms associated are fatigue (76.6%), fever (62%), myalgia (50.4%), headache (43.6%), cough (43.5%), and loss of smell and taste (43.5%).[3–5] Indeed, early recognition and appropriate interpretation of these symptoms is challenging for health care professionals (HP) because these symptoms imitate many other common diseases such as flu, cold, or headache.[3,4] Given the high rate of contagion and the progressive spread of knowledge related to COVID-19 disease, several less common manifestations of SARS-CoV-2 infection are described in the literature; therefore, the array of symptoms is broad.[1–3] Usually, COVID-19 infection affects the respiratory system, involving lungs with severe respiratory distress syndrome.[1,3] However, the virus can invade other tissues as well as the gastrointestinal, cardiovascular, and musculoskeletal systems.[5] The nervous system also may be affected, and SARS-CoV-2 has been detected in the brain and cerebrospinal fluid (CSF).[6] The most common neurological clinical manifestations include headache, dizziness, or cognitive disorders; notably, all of them are benign, systemic, and nonspecific neurological symptoms.[6] However, the latter could also be early symptoms of more serious neurological syndromes, such as pseudotumor cerebri syndrome (PTCS) or adult idiopathic intracranial hypertension (IIH). Both conditions present migraine-like headache, cranial nerve palsy, visual loss or disturbance, pulsatile tinnitus, neck/back pain, and dizziness.[7–9]

The reported incidence of these 2 conditions in the general population is approximately 4.7 per 100,000.[8,9] Their etiology is still not completely understood, but it seems these frequently occur in young obese women during childbearing age, presenting with an increased intracranial pressure (ICP). Rarely, they have also been observed in older normal-weight men. To note, PTCS and IIH shared common onset and clinical presentation features, which make the differential diagnosis a challenge. The triage process can be made only after appropriate imaging investigation, which excludes any mass or structural lesion of the brain parenchyma. In Table 1 are provided further details of the characteristics, main differences, and diagnostic criteria of IIH and PTCS.[8–12] The management of PTCS and IIH usually consists of weight loss and acetazolamide medications, and surgery is only required to decrease the CSF pressure to avoid permanent visual damage or disabling headache.[9,11–13]

The purpose of our case report is to inform clinicians of a misleading serious intracranial pathology presenting with typical early symptoms of SARS-Cov-2 infection (eg, loss of taste and smell) and to describe the triage process that raises the index of suspicion of a patient outside the physical therapy scope.

Case Description

A 28-year-old woman, a professional care assistant, visited her general practitioner (GP) during the first wave of the pandemic complaining of flu-like symptoms: mild fever and headache associated with loss of taste and smell. Given that symptoms were strongly suggestive for a SARS-Cov-2 infection, the GP immediately prescribed her an urgent reverse transcriptase polymerase chain reaction (RT-PCR)–based diagnostic testing (with both nasal and oropharyngeal swab) and a 10-day quarantine period. The RT-PCR swab test result was negative, and during the quarantine, the fever has completely resolved. Therefore, the GP prescribed a second RT-PCR at the end of the isolation period to certify the negative COVID-19 test, which was negative again. However, the headache and the loss of taste and smell did not change. Rather, the latter changed to an unusual headache pattern described as "dull, aching head pain that wraps overhead and pushes from the inside." Also, it was rapidly getting worse, together with dizziness and visual transient disturbances (flashes, flashing lights, scotomata) as associated symptoms. Taking into account the result of the second RT-PCR swab test, the GP allowed the patient to return to work, in accordance with the local covid restriction, notwithstanding he was still dubious about a possible hidden SARS-Cov-2 infection.[1,2] For this reason, a third RT-PCR test was performed after 1 week, which was still negative. For a detailed description of the timeline of the events, see Figure 1.

Because of the headache, the patient decided to consult her physical therapist because she was successfully treated for previous episodes of headache.[14] During the history taking, the patient reported having significantly gained weight over the last year, reaching a BMI > 30. Also, she reported to have kept under control her headache by taking ibuprofen 600 mg twice a day during the last week; she also noticed that coughing and sneezing aggravated her headache (ie, Valsalva maneuver). Furthermore, she experienced a few episodes of transient (1–2 seconds) blurring vision over the last 2 weeks. All the above symptoms (ie, acute onset described as "never complained before," rapid worsening, and a positive Valsalva sign)[14,15] in addition to the visual disturbances (ie, blurred vision and scotoma) and the loss of taste and smell[16] are concerning features and red flags that increased the level of concern for a potential serious headache.[15,17] For a best-informed judgment, all clues offered by the patient during the subjective examination led the physical therapist to a targeted physical examination and appropriate triage. Particularly, the raised ICP-like symptoms behaviors lead to a review of vitals.[18] Blood pressure (BP) and heart rate (HR) were 135/90 mmHg and 85 bpm, respectively; pulse oximetry saturation level was measured by an index finger oximeter, which indicated 98% saturation. Findings were suggestive for avascular risk profile (ie, high BP and HR > 80 bpm).[18] Notably, there are no standard rules or interview items able to show when it is indicated to perform a cranial nerve examination. In this case, loss of taste and smell were cues to consider testing the cranial nerves potentially due to more serious neurological syndrome.

The cranial nerve testing revealed loss of smell (CN I), impaired extra-ocular movements (CN VI), and loss of taste (CN VII) (Appendix 1 describes the full examination).[19,20] All the above led the physical therapist to recommend a referral to an appropriate medical colleague (ie, neurosurgeon) detailing the objective findings and offering a clearer referral, which offered anatomical clues to the potential pathology and was suggestive of urgency. Appendix 2 highlights the thorough assessment, findings, and reasoning during the triage process.

After his consultation, the neurosurgeon confirmed the physical therapist's suspicion that the patient's symptoms were not related to SARS-Cov-2 infection, and a diagnostic hypothesis of PTCS was conducted needed to be confirmed

Table 1. Characteristics of Idiopathic Intracranial Hypertension and Pseudotumor Cerebri Syndrome

Idiopathic Intracranial Hypertension	Pseudotumor Cerebri
• Presence of papilloedema • Normal neuroimaging: absence of hydrocephalus, no mass or structural lesion, and no abnormal meningeal enhancement on MRI • Normal CSF composition • Increased lumbar puncture opening pressure [≥250 mmHg CSF in adults and ≥280 mmHg CSF in children (250 mm CSF, if child not sedated and not overweight)] in a properly performed lumbar puncture • No hypercoagulation • Elevated BMI	• Presence of papilloedema • If papilledema absent, diagnosis can be made if patient has unilateral or bilateral abducens nerve palsy; normal neurologic exam except for cranial nerve abnormalities; neuroimaging (see related section); normal CSF composition; elevated lumbar pressure • If papilledema and abducens nerve palsy absent, diagnosis can be suggested but not made if features described in second point are present; also, at least 3 of following neuroimaging criteria are satisfied = empty sella; flattening of posterior aspect of globe; distention of perioptic arachnoid space with or without tortuous optic nerve; transverse venous sinus stenosis • Cerebral venous abnormalities • Cerebral venous sinus thrombosis • Bilateral jugular vein thrombosis or surgical ligation • Increased right heart pressure • Superior vena cava syndrome • Arteriovenous fistulas • Middle ear or mastoid infection • Reduced CSF absorption from previous intracranial infection or subarachnoid hemorrhage • Hypercoagulation • Normal BMI

[a]BMI = body mass index; CSF = cerebrospinal fluid; MRI = magnetic resonance imaging.

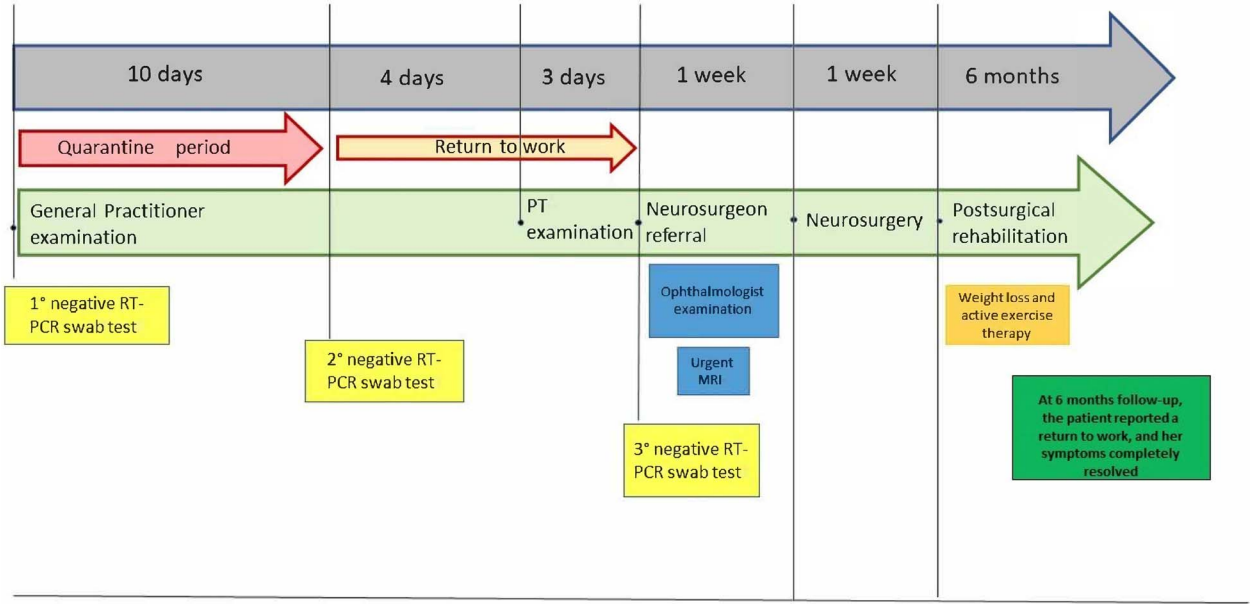

Figure 1. Timeline of case progression. MRI = magnetic resonance imaging; PT = physical therapist; RT-PCR = reverse transcriptase polymerase chain reaction.

with further investigation and an emergency secondary care referral.[10,12] At a following ophthalmologist consultation, a mild bilateral papilledema was detected; a computerized visual field test reported bilateral scotomata with upper-quadrantanopia, and the optical coherence tomography scan was unremarkable.[21] Finally, the following day, the magnetic resonance imaging (MRI) with venography findings allowed to discard the hypothesis of PTCS, shifting the diagnosis instead to IIH.[10,22–25] Figures 2 and 3 and Table 2 provide an in-depth description of the imaging findings that led to the final diagnosis.

Outcomes

Because of the rapid worsening of the visual symptoms and the "high-pressure" headache symptoms, both suggestive of progression of the increase of the ICP, the neurosurgeon made the decision to perform a lumbar puncture to avoid major consequences (ie, rapid visual loss). The procedure partially relieved the headache, normalizing normal CSF composition by an estimated 10 mL of CSF draw, with a mild ICP of 235 mmH_20.[7] Then, in accordance with the modified Friedman diagnostic criteria, a final diagnosis of adult IIH was achieved.[26] Then, to maintain normal CSF

Figure 2. Brain magnetic resonance imaging without contrast axial fluid-attenuated inversion recovery (FLAIR) (A), sagittal T1-weighted (B) and coronal T2-weighted (C) images demonstrate mega cisterna magna (asterisk), an enlargement of the cerebrospinal fluid–filled subarachnoid space in the inferior and posterior portions of the posterior cranial fossa. B, Sagittal view showing an empty sella (circle).

Table 2. MRI Findings of Idiopathic Intracranial Hypertension[a]

Without Contrast Dye	With Contrast Dye
Mega cisterna magna with reduced communication toward fourth ventricle and hypoplasia of cerebellar vermis (so-called Dandy-Walker variant malformation) (see Fig. 2 asterisk in A–C; see Fig. 3A asterisk)	Adjunct of the contrast-dye did not improve imaging findings
Asymmetry in lateral ventricles with left side larger	
Empty sella (see Fig. 2B circle; Fig. 3 asterisk in A-B)	
Bilateral enhancement of prelaminar (intraocular) optic nerve	
Bilateral flattening of posterior sclera of optic nerve	
Neck and cervical spine were unremarkable	

[a]MRI = magnetic resonance imaging.

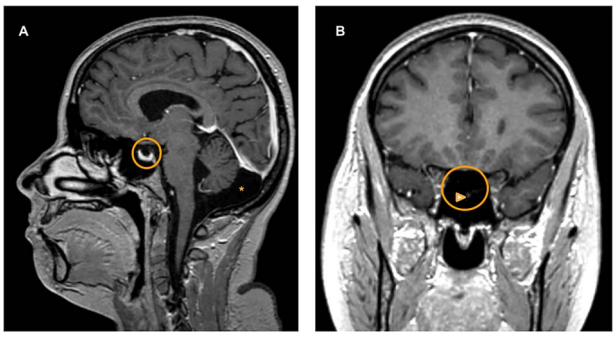

Figure 3. Brain magnetic resonance imaging T1-weighted images without contrast on sagittal (A) and coronal (B) plane demonstrate an empty sella (circle) filled with cerebrospinal fluid with no visualization of the pituitary gland. However, the pituitary stalk can be visualized (arrow in B). Sagittal image also shows mega cisterna magna (asterisk in A).

pressure, a permanent lumbo-peritoneal CSF shunting was surgically inserted (Valvola Integra OSV II Low Flow, INTEGRA NEUROSCIENCES IMPLANTS S.A., Sophia Antipolis cedex, France). After surgery the symptoms completely resolved, and the patient was discharged with the strong suggestion to reduce her weight by at least 10 kg. At 6 months follow-up, the patient was still completely pain free, and BMI has gradually been reduced to 25.

Discussion

The dramatic spread of the COVID-19 pandemic has changed care priority and stolen the attention of first-line HPs from other diseases.[1] As an example, health care systems were drastically affected by the pandemic, resulting in cancelled or postponed first-line and continuous health services in which early intervention is crucial, often resulting in delayed diagnoses.[27–29] However, it is the HP's responsibility to remain vigilant for other serious diseases, especially when they present as overlapping pathologies or when they share similar manifestation. Specifically, delay in diagnosis due to hypervigilance for prodromes of SARS-Cov-2, which might potentially be shared by more common neurological, cardiovascular, or gastrointestinal diseases, may lead to severe or fatal consequences.[17,18] It is well documented that the novel COVID-19 infection is commonly misdiagnosed instead of gastroenteritis, urinary tract infections, or heat stroke.[18,19] Also, neurological symptoms such impaired consciousness, encephalitis, and acute cerebrovascular events have been described as features of COVID-19 infection.[30–35] Taking into account the aforementioned symptoms, clinicians should increase their vigilance during their differential diagnosis: they should avoid an excessive focus on epidemiological probability and prevent superficial symptoms-pattern recognition reasoning (ie, availability bias).

In our case, the first-line HP was mainly focused on typical early symptoms of COVID-19 infection (ie, loss of taste or smell),[3–5,33–35] leading him to an initial proper care choice (ie, exclude the infection by performing RT-PCR testing).[36,37] RT-PCR testing is the more diffuse and cost-effective resource to screen COVID-19 infection, but its diagnostic accuracy and the level of sensitivity (ie, false negative) are still under research. Although an early triage of COVID-19 is a priority for patient safety and is advocated by local pandemic regulations,[36,37] solely relying on testing repetition based on few early symptoms cannot replace the patient history and the HP's clinical reasoning. That is, following an in-depth history by the physical therapist, the patient

presented warning symtoms and red flags that drastically changed the clinical presentation of COVID-19 infection. The acute onset described as "never complained of before," the rapid worsening of symptoms, which were aggravated by a Valsalva-like maneuver, and the antecedent transient neurological symptoms such as blurred vision episodes provided important cues for the hypothesis generation phase during the physical therapist consultation. Accordingly, the following physical examination drastically changed the patient's prognosis and confirmed the negative RT-PCR testing.

Headache is commonly encountered in daily practice; even though usually benign, it can be an important pretender of more severe pathologies.[15,38] It has been reported that 81% of patients with cervical arterial dissection events may report headache as a common early symptom. Also, more than 30% complain of visual disturbances.[15] Furthermore, the early stages of cervical arterial flow limitation may be also mistaken for other diseases, such as migraine,[10,22] iron deficiency anemia, or cerebral venous sinus thrombosis.[8,9,23] Therefore, first-contact physical therapists should be aware that headache, neck, and/or oro-facial pain could be potentially of viscero-somatic origin or a challenging manifestation of more serious pathologies.[14] In our case, sound reasoning allowed the physical therapist to recontextualize early symptoms, which were easily attributable to COVID-19 infection, within a more comprehensive and dispositional frame of reasoning, followed by an informed examination, and finally to an appropriate referral.[11,13–15,22,23] Thus, it is a professional responsibility to be trained for appropriate reasoning, examination (including CN examination and review-of-systems), and referral skills.[11,13–15,22,23]

In addition to the common early symptoms of COVID-19 infection, another challenging aspect of our case were the pathognomonic signs and symptoms of IIH (ie, uncommon headache pattern and the cranial nerves disfunctions) that are shared clinical presentations between IIH and PTCS. Indeed, both terms have been used for a neurologic syndrome consisting of elevated ICP, headache, vision loss, and cranial nerves palsy without mass lesion or underlying infection or malignancy.[8,9] Imaging and the level of CSF opening pressure allowed a final diagnosis of IIH secondary to rapid weight gain and a congenital Dandy–Walker malformation. Dandy–Walker malformation is a rare congenital brain malformation where the cerebral vermis (the part where the 2 hemispheres of the cerebellum join) does not fully form, causing an enlargement with CSF of the fourth ventricle and the posterior fossa that predispose to IIH.[39] Congenital craniovertebral anomalies are rare conditions but could be encountered in daily practice: their triage for direct-access physical therapists is a professional challenge.[40,41] The COVID-19 pandemic had a detrimental effect on global health care systems, particularly on GPs: because of their primary-line role, they have been overwhelmed by a wave of contagion. The challenges to a regular path of care due to the pandemic emergency highlight the importance of a dynamic teamwork diagnostic process and the advantages that skilled physical therapists could provide as a first-contact HP for both the patient and the health system.[15,20,21,42–44] Actually, serious pathology triage is a priority and requires a systematic approach and expertise in that field. Therefore, physical therapists must be schooled and skilled in a wide range of examination procedures required to screen all potential serious clinical presentations.

Author Contributions

Concept/idea/research design: F. Maselli, L. Storari, V. Barbari, F. Mourad
Writing: F. Maselli, L. Storari, F. Mourad, V. Barbari, M. Signorini, F. Signorelli
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Data analysis: F. Maselli, M. Signorini, and F. Signorelli
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Providing participant: F. Maselli
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Consultation (including review of manuscript before submitting): F. Maselli, L. Storari, F. Mourad, F. Signorelli

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Ethics Approval

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent was made available for review by the editors of this journal.

Data Availability

The authors confirm that the data supporting the findings of this study are available within the article.

Disclosures

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

References

1. Rauf A, Abu-Izneid T, Olatunde A, et al. COVID-19 pandemic: epidemiology, etiology, conventional and non-conventional therapies. *Int J Environ Res Public Health*. 2020;17:1–32. https://doi.org/10.3390/ijerph17218155.
2. World Health Organization coronavirus (COVID-19) dashboard | WHO coronavirus (COVID-19) dashboard with vaccination data. n.d. Accessed December 15, 2021. https://covid19.who.int/.
3. Guan W, Ni Z, Hu Y, et al. China Medical Treatment Expert Group for Covid-19 clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382:1708–1720. https://doi.org/10.1056/NEJMoa2002032.
4. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*. 2020;382:727–733. https://doi.org/10.1056/nejmoa2001017.
5. Murat S, Dogruoz Karatekin B, Icagasioglu A, Ulasoglu C, İçten S, Incealtin O. Clinical presentations of pain in patients with COVID-19 infection. *Ir J Med Sci*. 2021;190:913–917. https://doi.org/10.1007/s11845-020-02433-x.
6. Wu Y, Xu X, Chen Z, et al. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav Immun*. 2020;87:18–22. https://doi.org/10.1016/j.bbi.2020.03.031.
7. Burkett JG, Ailani J. An up to date review of Pseudotumor Cerebri syndrome. *Curr Neurol Neurosci Rep*. 2018;18:33. https://doi.org/10.1007/s11910-018-0839-1.
8. Markey KA, Mollan SP, Jensen RH, Sinclair AJ. Understanding idiopathic intracranial hypertension: mechanisms, management, and future directions. *Lancet Neurol*. 2016;15:78–91. https://doi.org/10.1016/S1474-4422(15)00298-7.
9. Wakerley BR, Mollan SP, Sinclair AJ. Idiopathic intracranial hypertension: update on diagnosis and management. Clinical medicine. *J R Coll Physicians Lond*. 2020;20:384–388. https://doi.org/10.7861/CLINMED.2020-0232.

10. Hoffmann J, Mollan SP, Paemeleire K, Lampl C, Jensen RH, Sinclair AJ. European Headache Federation guideline on idiopathic intracranial hypertension. *J Headache Pain*. 2018;19:93. https://doi.org/10.1186/s10194-018-0919-2.
11. Curone M, Tullo V, Bussone G. Headache attributed to IIH: clinical evolution in IHS criteria through the years. *Neurol Sci*. 2019;40:55–58. https://doi.org/10.1007/s10072-019-03795-6.
12. Mollan SP, Ali F, Hassan-Smith G, Botfield H, Friedman DI, Sinclair AJ. Evolving evidence in adult idiopathic intracranial hypertension: pathophysiology and management. *J Neurol Neurosurg Psychiatry*. 2016;87:982–992. https://doi.org/10.1136/jnnp-2015-311302.
13. Mollan SP, Davies B, Silver NC, et al. Idiopathic intracranial hypertension: consensus guidelines on management. *J Neurol Neurosurg Psychiatry*. 2018;89:1088–1100. https://doi.org/10.1136/jnnp-2017-317440.
14. Olesen J, Bes A, Kunkel R, et al. *The International Classification of Headache Disorders*, 3rd edition (beta version). Cephalalgia 2013;33:629–808. https://doi.org/10.1177/0333102413485658.
15. Rushton A, Rivett D, Carlesso LC, Flynn T, Hing W, Kerry R. International framework for examination of the cervical region for potential of vascular pathologies of the neck prior to orthopaedic manual therapy intervention. *Man Ther*. 2014;19:222–228.
16. George SZ, Beneciuk JM, Lentz TA, Wu SS. The optimal screening for prediction of referral and outcome (OSPRO) in patients with musculoskeletal pain conditions: a longitudinal validation cohort from the USA. *BMJ Open*. 2017;7:e015188. https://doi.org/10.1136/bmjopen-2016-015188.
17. Finucane LM, Downie A, Mercer C, et al. International framework for red flags for potential serious spinal pathologies. *J Orthop Sports Phys Ther*. 2020;50:350–372. https://doi.org/10.2519/jospt.2020.9971.
18. Faletra A, Bellin G, Dunning J, et al. Assessing cardiovascular parameters and risk factors in physical therapy practice: findings from a cross-sectional national survey and implication for clinical practice. *BMC Musculoskelet Disord*. 2022;23:749. https://doi.org/10.1186/s12891-022-05696-w.
19. Mourad F, Lopez G, Cataldi F, et al. Assessing cranial nerves in physical therapy practice: findings from a cross-sectional survey and implication for clinical practice. *Healthcare (Switzerland)*. 2021;9:1–20. https://doi.org/10.3390/healthcare9101262.
20. Taylor A, Mourad F, Kerry R, Hutting N. A guide to cranial nerve testing for musculoskeletal clinicians. *J Man Manip Ther*. 2021;29:376–390. https://doi.org/10.1080/10669817.2021.1937813.
21. Mollan SP, Virdee JS, Bilton EJ, Thaller M, Krishan A, Sinclair AJ. Headache for ophthalmologists: current advances in headache understanding and management. *Eye (Basingstoke)*. 2021;35:1574–1586. https://doi.org/10.1038/s41433-021-01421-4.
22. Markey KA, Mollan SP, Jensen RH, Sinclair AJ. Understanding idiopathic intracranial hypertension: mechanisms, management, and future directions. *Lancet Neurol*. 2016;15:78–91. https://doi.org/10.1016/S1474-4422(15)00298-7.
23. Mollan SP, Hornby C, Mitchell J, Sinclair AJ. Evaluation and management of adult idiopathic intracranial hypertension. *Pract Neurol*. 2018;18:485–488. https://doi.org/10.1136/practneurol-2018-002009.
24. Wakerley BR, Mollan SP, Sinclair AJ. Idiopathic intracranial hypertension: update on diagnosis and management. Clinical medicine. *J R Coll Physicians Lond*. 2020;20:384–388. https://doi.org/10.7861/CLINMED.2020-0232.
25. Mollan SP, Grech O, Sinclair AJ. Headache attributed to idiopathic intracranial hypertension and persistent post-idiopathic intracranial hypertension headache: a narrative review. *Headache*. 2021;61:808–816. https://doi.org/10.1111/head.14125.
26. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology*. 2013;81:1159–1165. https://doi.org/10.1212/WNL.0b013e3182a55f17.
27. Yousefzai R, Bhimaraj A. Misdiagnosis in the COVID-19 era. *JACC Case Rep*. 2020;2:1614–1619. https://doi.org/10.1016/j.jaccas.2020.04.018.
28. Sud A, Jones ME, Broggio J, et al. Collateral damage: the impact on outcomes from cancer surgery of the COVID-19 pandemic. *Ann Oncol*. 2020;31:1065–1074. https://doi.org/10.1016/j.annonc.2020.05.009.
29. Kansagra AP, Goyal MS, Hamilton S, Albers GW. Collateral effect of Covid-19 on stroke evaluation in the United States. *N Engl J Med*. 2020;383:400–401. https://doi.org/10.1056/nejmc2014816.
30. Coleman JJ, Manavi K, Marson EJ, Botkai AH, Sapey E. COVID-19: to be or not to be; that is the diagnostic question. *Postgrad Med J*. 2020;96:392–398. https://doi.org/10.1136/postgradmedj-2020-137979.
31. Kurihara S, Nakajima M, Kaszynski RH, et al. Prevalence of COVID-19 mimics in the emergency department. *Intern Med*. 2021;60:3087–3092. https://doi.org/10.2169/internalmedicine.6434-20.
32. Wu Y, Xu X, Chen Z, et al. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav Immun*. 2020;87:18–22. https://doi.org/10.1016/j.bbi.2020.03.031.
33. Bancos S, Bernard MP, Topham DJ, Phipps RP. Ibuprofen and other widely used non-steroidal anti-inflammatory drugs inhibit antibody production in human cells. *Cell Immunol*. 2009;258:18–28. https://doi.org/10.1016/j.cellimm.2009.03.007.
34. Reese JT, Coleman B, Chan L, et al. NSAID use and clinical outcomes in COVID-19 patients: a 38-center retrospective cohort study. *Virol J*. 2022;19:84. https://doi.org/10.1186/s12985-022-01813-2.
35. Heming M, Li X, Räuber S, et al. Neurological manifestations of COVID-19 feature T cell exhaustion and dedifferentiated monocytes in cerebrospinal fluid. *Immunity*. 2021;54:164–175.e6. https://doi.org/10.1016/j.immuni.2020.12.011.
36. Mahendiratta S, Batra G, Sarma P, et al. Molecular diagnosis of COVID-19 in different biologic matrix, their diagnostic validity and clinical relevance: a systematic review. *Life Sci*. 2020;258:118207. https://doi.org/10.1016/J.LFS.2020.118207.
37. Test diagnostici e tracciamento Dei contatti n.d. Accessed March 12, 2022. https://www.salute.gov.it/portale/nuovocoronavirus/dettaglioFaqNuovoCoronavirus.jsp?lingua=italiano&id=244#7.
38. Rizzoli P, Mullally WJ. Headache. *Am J Med*. 2018;131:17–24. https://doi.org/10.1016/j.amjmed.2017.09.005.
39. Hutting N, Kerry R, Kranenburg R, Mourad F, Taylor A. Assessing vascular function in patients with neck pain, headache, and/or orofacial pain: part of the job description of all physical therapists. *J Orthop Sports Phys Ther*. 2021;51:418–421. https://doi.org/10.2519/jospt.2021.10408.
40. Spennato P, Mirone G, Nastro A, et al. Hydrocephalus in Dandy-Walker malformation. *Childs Nerv Syst*. 2011;27:1665–1681. https://doi.org/10.1007/s00381-011-1544-4.
41. Mourad F, Giovannico G, Maselli F, et al. Basilar impression presenting as intermittent mechanical neck pain: a rare case report rehabilitation, physical therapy and occupational health. *BMC Musculoskelet Disord*. 2016;17:7. https://doi.org/10.1186/s12891-015-0847-0.
42. Ojha HA, Snyder RS, Davenport TE. Direct access compared with referred physical therapy episodes of care: a systematic review. *Phys Ther*. 2014;94:14–30. https://doi.org/10.2522/ptj.20130096.
43. Hon S, Ritter R, Allen DD. Cost-effectiveness and outcomes of direct access to physical therapy for musculoskeletal disorders compared to physician-first access in the United States: systematic review and meta-analysis. *Phys Ther*. 2021;101:pzaa201. https://doi.org/10.1093/ptj/pzaa201.
44. Maselli F, Palladino M, Barbari V, Storari L, Rossettini G, Testa M. The diagnostic value of red flags in thoracolumbar pain: a systematic review. *Disabil Rehabil*. 2022;44:1190–1206. https://doi.org/10.1080/09638288.2020.1804626.