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PERSPECTIVES

Headache during COVID-19: Lessons for all, implications for the International Classification of Headache Disorders

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The year 2020 will forever be remembered as the year characterized by a new global pandemic, COVID-19, caused by the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). In every scientific field, this new pathogen has represented the opportunity for either describing unknown disease presentations or re-assessing others from a new perspective.

So, what have we learned about headache, and, how should these lessons help redefine our comprehension and definition of *9.2.2 Headache attributed to systemic viral infection* in the International Classification of Headache Disorders (ICHD)?[1]

Headache is one of the most common[2] and disabling neurological symptoms of COVID-19, underlying a direct attack of SARS-CoV-2 on the trigeminovascular system, via transynaptic or bloodstream dissemination,[3] and/or immuno-mediated inflammatory responses[4] that act as well on the central nervous system. Other viruses, when sharing these characteristics, may cause headache as a predominant symptom; however, detailed studies are lacking in the field and should be implemented.

Headache associated with COVID-19 has multiple phenotypes. In almost 25% of patients, headache is severe with migraine-like features while the rest has a less intense pain probably more similar to the characteristics of tension-type headache.[5] Interestingly, this migraine-like phenotype is observed in other studies;[6,7] however, there is no significant association between its presence and prior migraine history.[5,6] So, potentially, anyone could experience headache similar to a migraine attack in the context of the pandemic, reflecting an activation of the trigeminovascular system.

Our experience with COVID-19 reinforces several important concepts of headache pathophysiology:

(A) Headache is the result of complex mechanisms involving (a) genetic predisposition, (b) the activation of the trigeminovascular system, (c) individual clinical characteristics (age, gender, comorbidities, etc.), and (d) the pathogen itself, its neuro-invasive potential, and ability to produce inflammation at a systemic or a more localized level;

(B) Primary and secondary headache disorders share common pathophysiological mechanisms. It is interesting to notice that this is also observed in other secondary headaches caused by completely different *noxae*, such as, post-traumatic headache.

The ICHD not only guides clinicians in the diagnosis of headache but also offers researchers a more systematic approach to study different headache types. In this regard, we believe that the next ICHD should try to provide a more pathophysiological-driven classification based on clinical characteristics. This would be a relevant conceptual change, considering that each phenotype probably reflects different pathophysiological mechanisms which might be correlated with different treatment responses. *9.2.2 Headache attributed to systemic viral infection* in the ICHD, for example, could include these different phenotypes as an alternative for criterion *C.4* and when coding this diagnosis specify if it is migraine-like or tension-type-like.

In the near future, we hope COVID-19 will also serve as an opportunity to regain interest in elucidating not only "headache attributed to systemic viral infection" pathophysiologically but also secondary headache in general.

CONFLICT OF INTEREST

The authors report no relevant conflict of interest relevant to this paper.

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REFERENCES

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. *Cephalalgia*. 2018;38(1):1-211. https://doi.org/10.1177/0333102417738202.
2. Poncet-Megemont L, Paris P, Tronchere A, et al. High prevalence of headaches during covid-19 infection: a retrospective cohort study. *Headache*. 2020;60(10):2578-2582. https://doi.org/10.1111/head.13923.
3. Desforges M, Le Coupanec A, Dubeau P, et al. Human coronaviruses and other respiratory viruses: underestimated opportunistic pathogens of the central nervous system? *Viruses*. 2019;12(1):14. https://doi.org/10.3390/v12010014.
4. Tay MZ, Poh CM, Rénia L, MacAry PA, Ng LFP. The trinity of COVID-19: immunity, inflammation and intervention. *Nat Rev Immunol*. 2020;20(6):363-374. https://doi.org/10.1038/s41577-020-0311-8.
5. Caronna E, Ballvé A, Llauradó A, et al. Headache: a striking prodromal and persistent symptom, predictive of COVID-19 clinical evolution. *Cephalalgia*. 2020;40:1410-1421. https://doi.org/10.1177/0333102420965157.
6. Trigo López J, García-Azorín D, Planchuelo-Gómez Á, et al. Phenotypic characterization of acute headache attributed to SARS-CoV-2: an ICHD-3 validation study on 106 hospitalized patients. *Cephalalgia*. 2020;40:1432-1442. https://doi.org/10.1177/0333102420965146.
7. Porta-Etessam J, Matías-Guiu JA, González-García N, et al. Spectrum of headaches associated with SARS-CoV-2 infection: study of healthcare professionals. *Headache*. 2020;60(8):1697-1704. https://doi.org/10.1111/head.13902.

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