Review of: "Stellate ganglion block for anosmia and taste disturbance due to Long-COVID"

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In general, this is a well-written and straightforward case report by G Chauhan, and I encourage this author to take the time to write up case reports. The case presentation is clear. The introduction is generally good. However, the discussion section has several problems.

First, Chauhan makes the statement “ACE2-viral interaction theory also explains an increased incidence of anosmia in patients of European descent with an increased expression of ACE2 compared to Asians [22]." The citation given for this statement is a letter to the editor of *Clinical Infectious Diseases*, Volume 71, Issue 11, 1 December 2020 by Y Gourtsoyannis, which was written in response to an unidentified article by “Leurs and colleagues.” I STRONGLY caution Chauhan against citing letters to the editor as supportive evidence. Gourtsoyannis mistakenly cites Cao et al. (DOI: 10.1038/s41421-020-0147-1) to support a “hypothesis that there are differences in angiotensin-converting enzyme 2 (ACE2) receptor expression in the nasopharynx of East Asians as compared to European populations” and goes on to state “Increased expression of ACE2 in European populations may contribute to a higher risk of olfactory and gustatory symptoms.” In fact, Cao et al. only measured the allele frequencies of quantitative trait loci (QTLs) associated with higher expression of ACE2, which are in fact higher in East Asian sample sets than European sample sets. Thus, the actual source data that should support the statement made by the Chauan (that increased anosmia in Europeans correlates with increased expression of ACE2 compared to Asians), in fact contradicts Chauhan's statement.

Second, Chauhan states “The female gender, with overexpression of ACE2 as compared to males, has an increased propensity for olfactory issues due to COVID-19 infection [24].” While citation 24 (Lechien et al. doi: 10.1007/s00405-020-05965-1) does show that females in their study had more olfactory issues than males, Lechien et al attribute this difference to “gender-related differences in the inflammatory reaction process” and do not mention ACE2 expression levels. While estrogen can upregulate expression of ACE2 in animal models, nasal epithelial expression of ACE2 has been demonstrated to be independent of sex in a recent human study (Bunyavanich et al. doi:10.1001/jama.2020.8707). This does not support Chauhan's statement that olfactory issues are related to ACE2 expression levels.

Instead of trying to tie COVID-related anosmia to ACE2 expression levels, a stronger argument would have been to continue the discussion of inflammation associated with AngII/AT1R and ACE2 autoantibodies, since propensity for inflammation and autoimmunity strongly correlate with female gender. Also, “ATII molecule” should be replaced with “Ang II” for consistency.

The remainder of the discussion is solid. It would have been nice for this author to acknowledge my prior (and seminal) case series, which demonstrated resolution of anosmia (and provided the impetus for the current use of stellate ganglion block treatment of Long COVID). At any rate, I am glad to have a confirmatory case report in the record and thank the author for his efforts.