Peer Review File

Article Information: https://dx.doi.org/10.21037/tau-22-587

Reviewer A:

Comment #1: results line 107: time range of 588 to 380. I suspect these are either out of order or 1 number is incorrect. please review. This entire section in fact needs to be reviewed and framed in a written form that is more easily digestible. right now it is just a handful of numbers drawn from figure 1.

Reply #1: We agree that this was a bit confusing, and redundant with the data from the figure. We simplified this paragraph, emphasizing analysis rather than raw numbers.

Changes in the text: See lines 107-111

Comment #2: The authors assert that the patient has central sleep apnea but do not provide strong evidence of this. in fact, "To assess central apnea..... all were normal".

Reply #2: Indeed, this was a bit unclear to readers who are not sleep physicians. Actually, the diagnosis of central apnea is made on the basis of polysomnography, with a cessation of airflow for 10 seconds or longer without an identifiable respiratory effort. The work up described afterwards (brain MRI, echocardiography, blood gases, opioid intake) is only etiological, with the aim of identifying the cause of the central apnea. This was clarified in the manuscript.

Changes in text: see lines 97, 98

Comment #3: I would add that this patient did not have leptin levels reported.

Reply #3: Indeed it was not measured. This is now clarified in the manuscript.

Changes in text: see line 140

Comment #4: With the disordered sleep section with melatonin. the authors write well and clearly. The temperature discussion is also quite good. It just seems like a stretch to attribute to this patient. It would be helpful also, and further cement the goal of the authors, if they could provide at least some comment on whether initiation with CPAP therapy was subjectively or objectively helpful to this patient. It would close out this case report nicely.

Reply #4: Indeed, there is not much available data about peripheral temperature as analyzed by wearables. We have an ongoing much larger study, in which we study peripheral temperature in a large number of Klinefelter subjects, as well as controls. Reports about the CPAP and melatonin therapy initiation were added at the end of the case description.

Changes in text: see lines 117-120

Reviewer B:

Comment #1: The authors did not present a strong argument on how this case report brings new information. The authors cited a number of papers on sleep of men with KS (with a larger sample size). I think the authors should describe how the current case report is unique, and presents new knowledge.

Reply #1: Admittedly there are other papers on sleep and KS. However, what we believe is unique and prompted publication in our manuscript is that we show that sleep disturbances in

those patients are multifactorial (obstructive apnea, central apnea, and melatonin secretion deficiency), and those causes are intertwined. Indeed, this is only a case report, with a therefore modest scientific strength, but we have an ongoing larger study, with more KS cases and controls. This was clarified in the manuscript.
Changes in text: see lines 214-215

Comment #2: There are many typos (e.g., spacing, spelling, etc).
Reply #2: fixed.
Changes in text: changes throughout the manuscript. For those revisions we received help from one additional colleague.