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Letter to the Editor

## **Before a SARS-CoV-2 Infection is Held Responsible for Sinus Arrest, All Other Causes must be Ruled Out**

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We read with interest the article by Zhang *et al.* about a 79-year-old woman who was diagnosed with recurrent sinus arrest (SA) with a maximum pause of 7.2s on Holter monitoring 16 days after the onset of a second SARS-CoV-2 infection (SC2I), with the indication for implantation of a pacemaker <sup>[1]</sup>. Although the patient had a number of cardiovascular risk factors (arterial hypertension, diabetes, atrial fibrillation), the SA was also attributed to SC2I because it spontaneously regressed during hospitalization <sup>[1]</sup>. The study is impressive, but some points should be discussed.

The first point is that the causal relationship between SC2I and SA has not been proven <sup>[1]</sup>. Before attributing SA to recent onset SC2I, all different causes of SA must be thoroughly ruled out. In general, the causes of SA can be intrinsic or extrinsic. Intrinsic causes include hereditary diseases, degenerative fibrosis of the nodal tissue or unknown etiology. Common extrinsic factors include atherosclerosis (coronary artery disease) or vasculitis of the sinus node artery or upstream arteries, hyperkalemia, cardiotropic medications (e.g. diltiazem, verapamil, beta-blockers, digitalis, quinidine, procainamide), increased vagal tone, arterial hypertension, atrial fibrillation, myocarditis, cardiomyopathy, pulmonary embolism, hypoxemia, electrolyte disturbances, advanced age and Takotsubo syndrome <sup>[2]</sup>. Since the index patient had two risk factors for atherosclerosis (hypertension, diabetes), advanced age and atrial fibrillation, it should be discussed why the SC2I and not these other possible causes were responsible for the SA. In this context, coronary angiography, cardiac MRI with contrast, electrophysiologic stimulation of the cardiac conduction system, transesophageal echocardiography, and nerve conduction studies are lacking. Cardiac disease as the cause of SA is supported by the fact that the troponin was elevated between the 7th and 18th day of SC2I.

The second point is that the patient had paroxysmal atrial fibrillation (AF), but the cause was not stated <sup>[1]</sup>. We should know the cause of AF and how the authors ruled out that AF was the cause of SA, as has been repeatedly reported <sup>[3]</sup>. Myocarditis, endocarditis, pericarditis and autonomic neuropathy should be excluded. Since the patient had a history of ischemic stroke, it is also conceivable that the recurrent SA is due to microembolization of the sinus node artery. Incidentally, the pathophysiology of the ischemic stroke in the index patient was not reported <sup>[1]</sup>. Was it due to micro/macroangiopathy, coagulopathy, heart failure, hypovolemia, atrial fibrillation or hematologic disease?

The third point is that the vaccination status of the index patient was not reported <sup>[1]</sup>. Since SARS-CoV-2 vaccination (SC2V) can be complicated by myocarditis <sup>[4]</sup>, endocarditis and pericarditis, and since there are also reports that SC2V can be complicated by arrhythmias, including SA <sup>[5]</sup>, it would have been mandatory to report whether the index patient had received SC2V that was temporally associated with the occurrence of SA.

The fourth point is that it was not reported whether the patient had developed a critically ill neuropathy or myopathy <sup>[1]</sup>. As the patient was mechanically ventilated for a prolonged period of time, it is conceivable that she developed a critically ill neuropathy. Since critically ill neuropathy can also affect the autonomic nervous system <sup>[6]</sup>, it is conceivable that the SA was due to dysfunction of the cardiac autonomic innervation.

The fifth point is that there is no mention of what symptoms the patient had during SA. Was there a history of fainting or near fainting, palpitations, chest pain or chest discomfort, confusion, dizziness, lightheadedness, fatigue or exertional dyspnea?

The sixth point is that the patient was tetraplegic on admission to the rehabilitation unit, which was attributed to an ischemic stroke <sup>[1]</sup>. However, if the index patient was indeed tetraplegic due to the stroke, it must have been bilaterally localized either supra- or infratentorial. Where was the ischemic stroke actually located? Was the tetraplegia due to a severe critically ill neuropathy or Guillain-Barre syndrome?

In summary, the present study has limitations that should be addressed before final conclusions are drawn. Clarification of the weaknesses would strengthen the conclusions and could improve the study. Before attributing recurrent SA to SC2I, all other causes must be thoroughly excluded.

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