COMMENTARY

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COVID-19 complications — new types of cardiovascular disease in 2021? A few comments on: COVID-19, post-COVID syndrome and the LONG COVID syndrome



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The study performed by the team led by Prof. Małgorzata Lelonek on the newly detected ventricular arrhythmia in coronavirus disease 2019 (COVID-19) convalescents fits well in the completely new field of interest in cardiology — evaluation of COVID-19 complications. This is a highly speculative field, as the disease has been in fact present in Europe since February 2020, and therefore one-year observation reports concerning first Italian patients will not be available until the first quarter of 2021. One-year observation reports concerning larger groups of Polish patients will most likely not arrive earlier than by the end of 2021, and our experience cannot be based solely on the registries maintained by the country

most affected by COVID-19, namely the United States of America (USA). In the USA, the African-American race has been determined as an important risk factor conducive to cardiovascular complications during and after COVID-19, thus any local statistics regarding the influence of the virus on the cardiovascular system must be interpreted and extrapolated with particular caution. As it was pointed out in the paper, there is a need to consider a long-term medical observation of non-hospitalised patients, even those after a mild course of SARS-CoV-2 (severe acute respiratory syndrome-related coronavirus 2) infection. I am afraid, however, that it is unrealistic in Poland. As on the day of this column – the end of 2020 – 1,300 000 of Poles have been infected with the virus. Given the scandalously low number of tests performed, some experts estimate that this number may be 4–5 times higher. Therefore, it is difficult to design a systemic follow-up of several million individuals to search for distant cardiovascular complications of SARS-CoV-2 infections. On the other hand, such follow-up could be included in a routine cardiac evaluation, together with other reasons for visiting a cardiologist, internal medicine specialist or a general practitioner, and that is perhaps what we ought to be focusing on.

At the present state of knowledge, it is probably necessary to distinguish at least three fields of interest for cardiologists with regard to SARS-CoV-2 infection:

- acute cardiac manifestations of SARS-CoV-2 infection (acute coronary syndrome, exacerbation of heart failure, myocarditis, cardiac arrhythmias and their exacerbation), known as COVID-19 disease, being the symptoms that we have relatively most extensive knowledge of, well-described in the literature on the subject [1]. Paradoxically, the more experience we gain, the fewer such cases we observe and report. As the leading diagnosis, they appear to concern only a few percent of COVID-19 hospitalised patients in the European population. More frequently, they are merely a derivative of a typical clinical sequence: infection → pneumonia → respiratory failure → cardiorespiratory failure v multiple organ failure. When this group of patients is excluded, the "cardiac manifestations" of COVID-19 affect merely 1–2% of patients, or maybe even less;
- post-COVID syndromes, in which the onset of cardiac symptoms occurs just a few weeks after the recovery (most often: abnormal heart rhythm, signs of myocarditis, vasculitis). That type of syndromes seems particularly interesting to paedia-tricians because it is in the population of children where multiple organ failure is most frequently described. It is often reversible but very dangerous in terms of clinical manifestation which occurs several weeks after recovery from COVID-19. It is also very often manifested by heart muscle damage, hence at the beginning of observations, it was sometimes identified as a variant of Kawasaki disease [2]. Currently, in the literature of the subject, the term "Kawasaki-like disease in children with COVID-19" is replaced with "multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19" [3];
- chronic organ damage associated with LONG COVID syndromes, which we have the least knowledge of, defined as complications that last for months after suffering from the disease and are associated with cardiac, pulmonary or neurological complications. Currently, there is an ongoing debate on how they should be defined [4]. There are different terms used in the literature of the subject, including "LONG-COVID" or "COVID Long-haulers" which refers to "long-term COVID patients" [5, 6]. There are also other expressions used, such as chronic COVID or long-lasting COVID, which makes it difficult to determine how the systematics of those syndromes will eventually be arranged [7, 8].

After this theoretical introduction, let us go back to the case described by the team of Prof. Małgorzata Lelonek. If my classification, suggested above, turns out to be more popular in the world, that case could be included in the second category: post-CO-VID syndromes. If the other concept wins, supported by some experts, to combine the second and the third category, all cases of "convalescents" will be classified as LONG COVID.

Why would I personally prefer to classify that case as a typical example of the second category – cardiac post-COVID syndrome? Perhaps it is also due to the fact that there are more and more similar cases found in the literature. Attention should be given

to one of the case studies that has been recently published in the "European Heart Journal". It describes the case of a 71-yearold man who, several weeks after suffering from COVID-19 — which lasted 2 weeks and ended with full recovery, experienced unusual symptoms: weight loss, feelings of fatigue and tiredness, and chest pain radiating from the left shoulder blade [9]. A CT scan of the chest, abdomen and pelvis showed acute aortic inflammation, starting from the subclavian arteries and proceeding as far as the iliac arteries, without aortic dissection or aneurysm. Additional studies revealed an increased level of C-reactive protein and interleukin 6. Other common causes of aortic inflammation were ruled out, and no antibodies typical for vasculitis were found. Following oral steroid treatment, within just two weeks, inflammatory parameters declined and the image of "florid aortitis" kept returning to normal on subsequent computed tomography scans. According to the authors of this report, although such inflammatory post-COVID-19 complications have already been described in children (as part of the aforementioned MIS-C symptoms), this is the first such description of a late complication of COVID-19 in the form of aortic inflammation in adults, and it has never been published until late November 2020.

What is the conclusion for physicians, cardiologists, internists and general practitioners? We should be prepared — in view of the current epidemic situation - to face the increasing need to diagnose possible post-COVID and LONG COVID syndromes. In the case of post-COVID syndromes, which are usually diagnosed within a few weeks from often asymptomatic or mildly symptomatic infection, imaging tests will play a significant role. However, I would suggest extreme caution in their interpretation. It should be noted that the basis for the diagnosis of post-COVID syndromes, in the case described by the team of Prof. Lelonek, is clinical inference and indirect evidence in the description of cardiac magnetic resonance imaging. This is the "Achilles' heel" when it comes to recognising post-COVID syndromes.

I am not sure whether you recall the discussion in the world of cardiology following the publication of a German-Italian academic work of magnetic resonance imaging (MRI) specialists who, based on the analysis of a group of patients who had recovered from COVID-19, tried to determine what percentage of COVID-19 convalescents shows the signs of past or ongoing myocarditis [10]. The study I refer to was the one conducted by Puntmann et al., performed on a group of 100 subjects, which was also quoted in the above-mentioned case study. The authors concluded that the analysis of the cardiac MRI made it possible to confirm that inflammation was present in heart muscle in 78% of the cases, and there were signs of an ongoing inflammation found in 60% of patients, 2-3 months after recovery from COVID-19 on average. This study has provoked a sharp polemic, also with a Polish accent, of an outstanding expert in cardiac MRI and sports cardiology - Prof. Łukasz Małek (I encourage you to visit his Instagram account: kardiolog_sportowy, where you can find a discussion on this particular study). Łukasz Małek indicates that the study contained numerous methodological errors which led to the diagnosis of such a high percentage of myocarditis signs among the examined individuals [11]. Łukasz Małek, whose expertise I value immensely, provided direct commentary about this study in social media: "(...) the study hit the daily press and social media, arousing a fair amount of terror, since it showed that signs of myocarditis were observed in 78% of tested individuals, 2-3 months after infection (...). If this was really the case, then it would be necessary to consider performing in-depth cardiac evaluation in each person with a history of COVID-19 (...). The study from JAMA Cardiology contained a methodological error - the standards of parameters, based on which the heart failure was assessed, were derived from tests performed on a different type of NMR machine (manufactured by another company) than the one used in the current analysis (...) [as a result] the cut-off point was set very low, in a way that has not appeared in other articles using the sequences applied, hence the high number of positive – probably false-positive – results (...)". And this is what I am afraid of – overdiagnosis of myocarditis signs based on MRI imaging in patients with a history of COVID-19. If we recognise the signs of myocarditis based on the MRI description, and at the same time we are dealing with one of several million COVID-19 convalescents, it will be tempting - after excluding other causes - to diagnose the post-COVID syndrome in the form of newly diagnosed arrhythmia, heart failure, atrial fibrillation attack, or aortitis. And yet, not every newly diagnosed ventricular arrhythmia or other pathology will have a causal connection with the history of COVID-19. I would rather you did not regard my column as a polemical voice related to the case described by the team led by Prof. Lelonek. This is only a plea to remain particularly cautious and critical, and to refrain from overly impulsive diagnoses, to avoid overdiagnosis of post-COVID syndromes. On the other hand, it is necessary to be aware of their existence, even though we still do not know how common these syndromes are in practice. Therefore, due to the latter, the case published in "Folia Cardiologica" is particularly worth reading.

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