Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

American Journal of Emergency Medicine 61 (2022) 208–209

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Post-COVID-19 diabetes in the context of long COVID

Post COVID-19 diabetes [1] is a long-term complication of SARS-CoV-2 infection arguably belonging to the category designated as "long" COVID [2]. In the specific instance of post viral diabetes, animal studies suggest that damage to the Beta cells is mediated by inflammatory cytokines, namely, gamma interferon(IFN-gamma), in synergy with other cytokines [3]. It has also been shown that Coxsackie B viral infection of engrafted human islet cells can lead to diabetes [4], presumably by a direct cytolytic effect, independent of activation of the cytokine cascade. In the latter experiment immunodeficient mice initially underwent ablation of their native islet Beta cells. Subsequently, Beta islet cells from human donors were transplanted into those mice in order to maintain glucose homeostasis. Thereafter, it was shown that Coxsackie B infection(artificially induced by intraperitoneal injection) could lead to the development of diabetes in infected mice, an outcome not seen in control mice intraperitoneally injected with uninfected normal saline [4]. This experimental observation has its human counterpart in the association of Type 1 diabetes and the presence of low-grade enteroviral infection of the islets of Langerhans [5].

A more recent development is the documentation of infection of the islets of Langerhans by the SARS-CoV-2 virus [6]. Furthermore, a retrospective cohort study which evaluated risk of any new diabetes(Type 1, Type 2, or other diabetes) > 30 days after acute COVID-19 infection showed an association between COVID-19 infection and subsequent development of diabetes. That study covered the period March 1, 2020 through February 26, 2021. That study compared patients aged <18 who had been diagnosed with COVID-19 with counterparts who did not have previous COVID-19. The two groups were matched for age and sex. It was shown that diabetes risk was 166% higher in the COVID-19 group than in the non-COVID group(Hazard Ratio = 1.31, 95% Confidence Interval = 1.20–1.44) [7].

Post-COVID diabetes might, arguably, belong to the category of disorders which now have the diagnostic label of Long COVID [2]. Long COVID, in turn might be attributable to persistence of residual COVID-19 infection in various internal organs [8] including the gastrointestinal tract [9]. In the latter study persistence of gastrointestinal infection was documented by intestinal biopsy in subjects who had subsequently become asymptomatic following a clinically overt episode of COVID-19 infection [9]. Due to the intimate anatomical and physiological relationship between the upper small bowel and the pancreas it is possible that persistent colonisation of the small intestine by the SARS-CoV-2 virus could play a role in the etiopathogenesis of COVID-19-related diabetes.

The hypothesis of long COVID as the outcome of persistent residual infection was put to the test by Swank et al. [10]. In support of this hypothesis they performed a longitudinal comparison between 36 patients with long COVID symptoms and 27 counterparts who had fully recovered from COVID-19 infection without subsequently experiencing any long COVID symptoms. Over a period of up to 12 months multiple positive SARS-CoV-2 antigen tests were documented in the long COVID subgroup versus none in counterparts who had not experienced long COVID as a complication of SARS-CoV-2 infection. Most significantly, in the words of the authors, patterns of full spike antigen levels were observed over the course of several months in many patients. In others there were fluctuations between antigen being detected and not detected. By contrast, among 6 patients who had fully recovered without any post COVID sequelae, temporal antigen profiles showed high antigen levels soon after diagnosis of COVID-19, quickly dropping below the limit of detection thereafter [10].

Whether or not persistent infection causes diabetes or any other post-COVID manifestation might depend on whether or not viral infection causes direct cellular damage to the affected organ. It might also depend on the immunological profile of the patient [11], and presence or absence of molecular mimicry, the latter an entity which encompasses cross-reactive immunity against epitopes shared between viruses and Beta cells [12]. The documentation of higher prevalence of long COVID-19 in females also suggests a role for hormonal status in the etiopathogenesis of this syndrome [13].

Credit authorship contribution statement

Oscar M.P. Jolobe: Writing – review & editing, Writing – original draft, Validation, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

I have no conflict of interest or funding with regard to the manuscript with the above title.

Acknowledgment

I have no funding and no conflict of interest.

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30 June 2022