POST-COVID-19 INTERSTITIAL LUNG DISEASE AS A MANIFESTATION OF THE POST-COVID-19 SYNDROME

O. K. Yakovenko, Y. O., Dziublyk, O. G. Khanin, L. Ya. Romaniv, L. M. Dzhumaniuk, E. M. Khodosh

Abstract

The aim was to study the clinical features of post-COVID-19 interstitial lung disease (ILD) and to determine the prospects for the use of the antifibrotic drug nintedanib in patients with moderate and severe COVID-19.

Material and methods. A prospective cohort study was conducted in 266 patients (≥ 18 years old) with moderate and severe COVID-19 who were hospitalized and discharged after treatment at the Volyn Regional Clinical Hospital between September and November 2021. The study design included telephone contact with patients one year after hospital discharge to collect the complaints and history data related to post-Covid syndrome. The patients with persistent respiratory symptoms were invited for an examination. A questionnaire, assessment of objective status, laboratory and functional tests were performed. The study included a group of patients (n = 25) with post-COVID-19 interstitial lung disease as a sequela of severe coronavirus infection. In all cases, interstitial pneumonia with a radiological pattern of chronic organizing pneumonia was established by computer tomography. All patients with post-COVID-19 ILD received glucocorticosteroid (GC) therapy with methylprednisolone 16 mg/day for 3–6 months with a gradual dose reduction until complete withdrawal. In addition, 9 patients with post-COVID-19 ILD received off-label antifibrotic therapy with the nintedanib 300 mg daily for 3 months. Statistical analysis was performed by means of SPSS Statistics 26 using the binomial test, the asymptotic T-test for the probability of success in two independent Bernoulli trial schemes, and the non-parametric Kolmogorov-Smirnov, Mann-Whitney U, and median tests.

Results and discussion. In 9.4 % (n = 25) of patients post-COVID-19 ILD was diagnosed: 76 % (n = 19) — COVID-19 associated ILD; 16 % (n = 4) — systemic connective tissue disease (SCTD) triggered by COVID-19; 8% (n = 2) misdiagnosed pre-COVID-19 ILD. Radiological pattern of fibrosis-like lesions was established in 64% (n = 16); true fibrotic radiological pattern of pulmonary fibrosis (PF) — in 36 % (SCTD — 4 cases, other ILD — 2 cases). It was found that CPAP respiratory support did not significantly correlated with the presence of a radiological pattern of PF ($p = 0.774$) and the progression of post-COVID-19 ILD ($p = 0.146$). No significant correlation was found between the presence of a radiological pattern of PF and the gender of patients ($p = 1.000$ and $p = 0.146$, respectively) or age ($p = 0.881$ or $p = 0.885$). Despite the presence of autoimmune markers in number of cases and the diagnosis of SCTD, there was no correlation between PF pattern and SCTD ILD ($p = 0.146$ and $p = 1.000$). The use of nintedanib (n = 9) for 3 months in the remote period of severe COVID-19 disease did not changed the radiological pattern of PF ($p = 1.000$) and the progression of post-COVID-19 ILD ($p = 0.180$), same as the blood oxygen saturation post 6-minute walking test ($p = 0.411$ according to the median test and $p = 0.329$ according to the Mann-Whitney U test). There was no effect on the dyspnea index as well ($p = 0.451$ or $p = 0.422$). In our opinion, anti-fibrotic therapy in post-COVID-19 ILD should only be prescribed on individual basis for more than 3 months in the presence

of a clinically significant PF radiological pattern. This recommendation requires further investigation.

Key words: post-COVID-19 interstitial lung disease, post-covid syndrome, pulmonary fibrosis, nintedanib.

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Oleg K. Yakovenko
Volyn Regional Clinical Hospital
Head of pulmonology department
MD, PhD
21, Grushevskogo av., Lutsk, 43005, Ukraine
volyn_pulmo@ukr.net