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HIF-1A/VEGF AXIS IN THE DYNAMICS OF THE DEVELOPMENT OF HEMORRHAGIC PNEUMONIA WITH FIBROSIS (EXPERIMENTAL STUDY)

Ziablitsev D. S.
Candidate of Medical Sciences, Docent,
Associate Professor at the Department of Immunology and Allergology
Bogomolets National Medical University
Kyiv, Ukraine

Mykhailovska V. V.
Postgraduate Student at the Department of Immunology and Allergology
Bogomolets National Medical University
Kyiv, Ukraine

Babenko M. S.
Postgraduate Student at the Department of Immunology and Allergology
Bogomolets National Medical University
Kyiv, Ukraine

Background. Hemorrhagic pneumonia with fibrosis is characterized by progressive damage to the lung parenchyma with the development of critical hypoxia and pathological vascular remodeling, which causes high mortality and disability of patients [1, p. 17074]. The key regulators of the adaptive response to hypoxia and the processes of reparative angiogenesis are hypoxia-inducible factor-1α (HIF-1α) and vascular endothelial growth factor (VEGF), the imbalance of which can determine the transition from compensatory mechanisms to pathological fibrogenesis [2, p. 1269]. The study of the temporal dynamics of HIF-1α and VEGF in lung tissue during the development of hemorrhagic pneumonia will allow identifying critical points of pathogenesis and justifying new targets for pathogenetically oriented therapy.

Aim: to determine the dynamics of HIF-1α and VEGF content in lung tissue in experimental hemorrhagic pneumonia with fibrosis and to establish their role in the pathophysiological mechanisms of damage and repair.

Materials and methods. In male Wistar rats weighing 190-220 g (n=60), hemorrhagic pneumonia with fibrosis was simulated by intratracheal injection of a nylon thread (length 2.5 cm, thickness 0.2 mm), animals were withdrawn from the experiment on days 1, 3, 5, 7, 14 and 21 (5 animals each), a histological

study of lung tissue was performed and the content of HIF-1α and VEGF was determined by immunoblotting using monoclonal antibodies (Invitrogen, Sigma Aldrich, USA) with densitometric analysis in the TotalLab program.

Results. In rats with experimental hemorrhagic pneumonia with fibrosis, a progression of morphological changes in the lungs was observed from pronounced edema, microthrombosis, and serous-hemorrhagic exudate (days 3–5) to productive inflammation with fibrosis formation (days 14–21). According to immunoblotting, the content of HIF-1α increased, reaching a maximum on day 5 (1.9-fold; $p<0.05$) and remained elevated on days 7 and 14, with a further decrease in the fibrosis phase. The dynamics of VEGF generally corresponded to the changes in HIF-1α, but was more pronounced, with a peak on day 7 (3.4-fold; $p<0.05$) and the increase persisting until day 21. The recorded increase in the monomeric form of VEGF from the 5th day (by 2.3–3.5 times) indicates the activation of its cellular synthesis during the period of intensive angiogenesis.

Conclusion. The development of hemorrhagic pneumonia with fibrosis is accompanied by coordinated activation of HIF-1α and VEGF in the lung tissue with a maximum in the phase of exudative-hemorrhagic inflammation, which indicates the key role of hypoxic adaptation mechanisms. During the transition to fibrosis, HIF-1α normalizes, while VEGF remains elevated, confirming its leading role in the processes of neoangiogenesis and tissue remodeling. The revealed patterns reveal the pathophysiological mechanisms of the HIF-1α/VEGF system in pulmonary fibrosis and substantiate the prospects for the development of targeted therapeutic approaches.

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