(2) Observations on the Coagulation and Fibrinolysis in the Lungs

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Since the time of Virchow who performed ligation on artificial embolization in the pulmonary artery with an intention of producing pulmonary infarction experimentally, innumerable attempts have been made in order to clarify the question why embolization in the pulmonary vasculature does not necessarily result in the infarction. Our attempts were, therefore, made to clarify the mechanism with which the pulmonary infarction occurred and the pathophysiology in the pulmonary embolism and infarction, from coagulation-fibrinolytic point of view.

1) Mechanism of the production of pulmonary infarction

Experimental pulmonary infarction was produced in 50 or 56% of the rabbits by the pretreatment with minced thrombi and in 78 or 80% of the rabbits by the pretreatment with Lycopodium spores. On these differences of the incidence, it may be concluded that the differences in the diffusibility and size of microthrombi between Lycopodium spores and minced thrombi brought about the difference in cessation of the blood flow in the collateral vessels, in blood coagulation, and in fibrinolytic activity. Rabbits with the pulmonary infarction showed the tendency of hypercoaguability and hypofibrinolytic activity at the time of the infusion of blood clot after the injection of Lycopodium spores or minced thrombi, as compared to the animals without the pulmonary infarction. The mechanism of the production of pulmonary infarction may be characterized by the consumption of coagulation factors due to the microscopically-anatomically observed secondary production of thrombi around the embolus (clot) at 24 or 48 hours after the infusion of blood clot, and the hyperfibrinolysis due to the release of tissue activator from the tissue around the embolus (clot), coupled with the tendency for hemorrhage in the periphery from the embolus (clot). It has been assumed that a close relationship exists between the production of pulmonary infarction and the disorders of the coagulation-fibrinolytic system, especially the fibrinolytic factors in the blood and tissues.

2) Time lag between changes of coagulation-fibrinolysis and the appearance of clinical features in pulmonary thromboembolism

From the clinical studies in patients with pulmonary embolism and infarction, changes of coagulation-fibrinolytic system induced by the intravascular coagulation were seemed to be brought about before the appearance of clinical findings. Then, it must be important for clinical treatment that changes in coagulation-fibrinolytic system are examined before the appearance of clinical findings, if possible.

3) Clinical significance of hyperfibrinogenemia in pulmonary infarction

From the examination of coagulation-fibrinolytic activities in patients with pulmonary infarction, it appeared that the degree and the duration of the elevation of fibrinogen were dependent upon
the severity of the disease in those patients. Thereafter, it is assumed that fibrinogen is increased as a sign of chronic intravascular coagulation syndrome triggered by tissue thromboplastin. As a model experiment, 1% thromboplastin solution was injected intravenously 5 times a week for 3 successive weeks. Fibrinogen showed the significant increase, indicating the possibility that thromboplastin could act as a trigger.

4) Fibrinogen turnover in pulmonary thromboembolism

The disappearance curves of fibrinogen in normal rabbits and in rabbits injected with Lycopodium spores were individually analyzed into two exponential components. That is, the disappearance curve was composed of the first component with the exponential decay and the second component with parabolic pattern. From these compounded pattern of the disappearance curve, diagnosis of pulmonary embolism and infarction may be performed. A half time of labelled fibrinogen must be calculated from the disappearance curve of clottable part, because the similarity of the pattern was not always recognized between the disappearance curve of plasma (or heparinized haemolytic blood) and clottable part. A half time (27.4 hours) of the second slope in clottable part at the time of the elevation of fibrinogen induced by the injection of Lycopodium spores was shorter than that (50.2 hours) of the second slope in normal rabbits. However, there was no difference as to a half time of the first slope between them. On the basis of the above-mentioned results, it may be concluded that the elevation of fibrinogen originated from the overproduction.

5) Pulmonary microembolism

Our further attempts were made to clarify the mechanism by which the microthrombi occurred, from the injection of thromboplastin. Microemboli were seen histologically in small lung vessels at 5 or 15 minutes after the injection of thromboplastin. In addition, consumptions of coagulation-fibrinolytic factors was shown at 3 hours after the injection of it. It appeared from the immunological examination that the affinity to the thromboplastin existed in the endothelium of small vessels. On the basis of our results, the future advance in the investigation concerning the relationship between the production of microthrombi and the plasma membrane of the endothelium is expected.