Pulmonary Fat Embolism
-A Pathological Study of a Non-selected Autopsy Material-

by

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Abstract

A pathological study of a non-selected autopsy material was performed on fat embolism. Pulmonary fat embolism was found in 53 out of 102 consecutive autopsies.

Fat embolism seemed as closely associated with bone fracture and bone marrow embolism. Main source of the embolic fat should be the traumatized tissue, especially the marrow cavity of the fractured bone.

The incidence of the case numbers of pulmonary thrombosis had an intimate relationship with severity of pulmonary fat embolism. Intravascular fat droplets were sometimes trapped in fibrin clots.

It should be very reasonable to consider that fat embolism contributes to the formation of intravascular thrombi.

Introduction

Intravascular fat embolism of the lung was first described by Zenker, F. A. in 1862, and since then this pathologic condition has become well recognized.

However, there is no agreement on the etiology of intravascular embolic fat droplets. In the classic theory, it is chiefly caused by intravasation of fat from the site of injury, most often from the marrow cavity of fractured bone. On the contrary, one suggestion has been proposed that embolic fat droplets are formed by coalescence of plasma lipid particles, especially chylomicrons.

Moreover, the role of embolic fat droplets which are seemed as intimately related to the pathogenesis of 'fat embolism syndrome' has not yet been fully delineated. Presently, any explanation must consider the recognized association of intravascular coagulation of fat
embolism.

The present paper is based upon a pathological study of a non-selected consecutive autopsy material and it is attempted to throw light upon the source of embolic fat droplets and to clarify the relationship between fat embolism and intravascular coagulation.

Material and Method

Material consisted of clinical records, autopsy reports and autopsy specimens from 102 adult cases who died of various diseases and additional four cases suffered from acute decompression sickness (diver's disease).

For the histologic examination, more than two small pieces from both right and left lungs were taken. The frozen sections of them were prepared and then stained with Oil-red-O or Sudan-III for searching fat emboli. Besides, the paraffin sections were prepared and were stained with Hematoxyline & Eosin (H-E) and Phosphotungstic acid hematoxyline (PTAH) for searching bone marrow emboli and fibrin thrombi.

From the autopsy material of the cases which had pulmonary fat emboli in marked degree (more than five embolic fat droplets were existent in a 1 cm² section), frozen sections of the brain, kidney, etc. were prepared for subsequent Oil-red-O staining.

Results

Fracture and Fat Embolism

29 of the 102 cases revealed one or more fractures at the time of autopsy. The sites of the fractures were ribs and sternum in most cases. The costal and sternal fractures should have been caused by application of heart massage in the terminal stage of the patients. Three of the 29 cases ('fracture'-group) had fractures other than those of the ribs and the sternum.

There was no description about bone fracture in the autopsy records of the remaining 73 cases ('unknown'-group).

More or less pulmonary fat emboli were found by histologic examination in 27 out of the 29 cases of 'fracture'-group and in 26 out of the 73 cases of 'unknown'-group. Ratios between the numbers of cases which revealed fat embolism and the numbers of the cases of both 'fracture'- and 'unknown'-groups were 93.1% and 35.6%, respectively. And the ratio of the 'fracture'-group is significantly higher than that of the 'unknown'-group ($p<$

| Table 1. Comparison of Case Numbers between the Cases with and without Fat Embolism and Those with Bone Fracture ('Fracture'-Group) and Those without Description about Bone Fracture in the Autopsy Records ('Unknown'-Group) |
|---------------------------------|---------------------------------|---------------------------------|------------------|
|                                 | Cases with Pulmonary Fat Embolism | Cases without Pulmonary Fat Embolism | Total            |
| 'Fracture'-Group               | 27                               | 2                               | 29               |
| 'Unknown'-Group                | 26                               | 47                              | 73               |
| Total                          | 53                               | 49                              | 102              |

$X^2=25.5$  $p<0.001$
Fat Embolism and Bone Marrow Embolism

More or less embolic fragments of bone marrow tissue were existent in the blood vessels of 13 of the 27 cases which belonged to the 'fracture'-group and showed pulmonary fat embolism, and in the blood vessels of 11 of the 26 cases which belonged to the 'unknown'-group and showed fat embolism, respectively.

The cases which did not show pulmonary fat embolism had no embolic fragment of bone marrow tissue in the lungs.

The statistic calculation disclosed that the close relationship lays between fat embolism and bone marrow embolism (p<0.001) (Table 2).

<table>
<thead>
<tr>
<th>Table 2. Comparison of Case Numbers between the Cases with and without pulmonary Fat Embolism and Those with and without Pulmonary Bone Marrow Embolism</th>
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<tr>
<td>Cases with Pulmonary Fat Embolism</td>
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<tr>
<td>Cases with Pulmonary Bone Marrow Embolism</td>
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<tr>
<td>Cases without Pulmonary Bone Marrow Embolism</td>
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<td>Total</td>
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$X^2=25.8 \quad p<0.001$

Fat Embolism and Thrombosis

From the examined 102 cases, 52 cases (51.0%) had more or less numbers of thrombi in the small vessels or the capillaries. On the other hand, 34 of the 53 cases which showed pulmonary fat embolism had more than five embolic fat droplets in a 1 cm² lung section (cases with marked pulmonary fat embolism), and 25 out of the 34 cases (73.5%) showed pulmonary thrombosis. From the 19 cases which had fat emboli in lesser degree (cases with slight pulmonary fat embolism), 9 cases (47.4%) showed pulmonary thrombosis. 18 of the 49 cases (30.6%) which had no fat emboli (cases without pulmonary fat embolism) showed pulmonary thrombosis. The ratios between the degrees of fat embolism and the incidence of thrombosis were statistically significant (p<0.001) (Table 3).

<table>
<thead>
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<th>Table 3. Comparison of Case Numbers between the Cases with Pulmonary Fat Embolism and Those with Pulmonary Thrombosis</th>
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<td>Cases with Marked Pulmonary Fat Embolism</td>
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<tr>
<td>Cases with Pulmonary Thrombosis</td>
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<tr>
<td>Cases without Pulmonary Thrombosis</td>
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<tr>
<td>Total</td>
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$X^2=11.8 \quad p<0.001$
**Histologic Findings**

Embolic fat droplets were existent in the small branches of the pulmonary arteries or the alveolar capillaries of the cases with pulmonary fat embolism. They were seldom found in the pulmonary veins. In some cases, fat droplets were trapped in the thrombi which were formed within calibers of the pulmonary artery (Photo. 1).

![Photo. 1 Intravascular fat droplets trapped in a fibrin clot. Lung. Oil-red-O, × 150.](image)

Bone marrow emboli were always found in the branches of the pulmonary arteries, but not in the capillaries and the veins, and they sometimes attached to fibrin clots (Photo. 2).

![Photo. 2 A bone marrow embolus with attachment of fibrin material (arrows). Lung. H-E., × 150.](image)

There was only one case of which the capillaries in the cortex of the brain possessed small amounts of embolic fat. This case had pulmonary fat emboli in marked degree and had suffered from a fracture of the right femoral neck two days before death.

**Cases of Acute Decompression Sickness**

Three of the four cases who died of acute decompression sickness (diver's disease) revealed pulmonary fat embolism in more or less degree. A 28-year-old case expired 10 hours after the onset of the disease showed maintenance of large or small air bubbles in

![Photo. 3 Bone marrow necrosis accompanied with tissue bubbling. Femoral shaft. H-E, × 60. (Acute decompression sickness)](image)

![Photo. 4 An intrasinusoidal air bubble lined by membranous fat material (arrow). Femoral head. Oil-red-O, × 150. (Acute decompression sickness)](image)
the bone marrow cavity of the femoral shaft resulting in acute necrosis of the bone mar-
row tissue, i. c. marked karyorrhexis and karyolysis of the cellular components and tissue
destruction (Photo. 3). In the sinuses of the femoral head, a number of small air bub-
bles were existent and lined by membraneous fat substance (Photo. 4). Thrombus forma-
tion was also observed around some of the intrasinusoidal air bubbles.

Discussion

Although, it was generally accepted that large numbers of cases of fat embolism were
superimposed in traumas, especially in bone fractures, the etiology of fat embolism had still
been a subject of controversy. According to the classic and the most conventional theory,
it is chiefly caused by intravasation of fat from the site of injury, most often from the
marrow cavity of fractured bone.

On the contrary, another opinion was proposed by some investigators7). They thou-
that fat emboli were formed by coalescence or agglutination of lipid particles which
were physiologically existent in the blood plasma (chylomicrons or others).

The results of the present study pointed out that the incidence of the cases which
showed pulmonary fat embolism was very significantly high among the cases which suffered
from bone fractures. Moreover, it became apparent that bone marrow embolism was sta-
tistically-highly superimposing in fat embolism.

Bone marrow embolism was considered as closely associated with bone injury, a fact
which apparently is an agreement with the concept that traumatic disruption of bone
marrow is a prerequisite for production of bone marrow embolism10,14). Yamaguchi (1956)
described that almost all the experimental rabbits had more or less embolic fat in the
blood vessels of the lungs, after the bone marrow injuries by surgical procedures. Some of
the animals had bone marrow emboli in the lungs, simultaneously.

Hallgren, et al. (1966) showed that emboli recovered from the lungs of dogs with frac-
tured legs had a triglyceride composition similar to that of bone marrow and deposit-fat,
but unlike that of chylomicrons. Most other experimental works also support the view
that the bone marrow is the source of the fat emboli3).

In this study, a case of acute decompression sickness revealed marked necrotic changes
in association with bubbling of the tissue were found in the bone marrow of the femoral
shaft. And large amounts of fat were found in the sinuses of the femoral head and also
in the pulmonary vasculature. These findings easily lead us to conclude that fat entered
the vasculature from the injured bone marrow.

So, it seems very appropriate and reasonable to consider that embolic fat should have
been chiefly originated from the traumatized tissue, especially from the marrow cavity of
fractured bone, although this study could not clarify whether the plasma lipid particles par-
ticipate in the development of fat embolism or not.

The results of this study also support the fact that fat embolism should associate with
blood changes of intravascular coagulation from the pathological-anatomical view point.
The incidence of case numbers of pulmonary thrombosis became higher according to the
increase in degree of fat embolism. Histology disclosed that the presence of fat droplets
in the blood vessels sometimes trapped in fibrin clots.

The aggregation of platelets on the surface of embolic fat droplets and the formation of fibrin have received scant attention in previous studies on fat embolism. Thompson, et al. (1969) first attempted an in-vivo study on fat embolism and they found that platelets aggregated in association with occasional formation of fibrin-thrombi on the surface of fat droplets in the blood vessels of the experimental rabbits. Then they considered that thrombus formation was one of the most fundamental and important events in fat embolism.

Recently, fat embolism has been reported to be associated with the blood changes of disseminated intravascular coagulation. Saldeen (1969), studying experimental fat embolism in rats, reported transient intravascular coagulation in the lungs and a reduction of fibrinogen and the platelet count in the circulating blood. Bradford, et al. (1970) reported that patients who developed the pictures of fat embolism syndrome after the fractures had a depression of the platelet count and some of those patients had an increase in fibrin degradation products (FDP). Rennie, et al. (1974) reported that the changes of the plasminogen level and the platelet count were great in the traumatized patients. Jacobs (1976) found some evidences for intravascular coagulation in experimental dogs.

In the blood vessels, the fat droplets began to exert direct mechanical effects, obstruction of the vascular lumina and then fat-blood interaction tends to alter the secondary and tertiary configuration of blood proteins. The fat droplets have a capacity to accelerate some hematological reaction by the activation of a plasma factor, presumably Hageman (XII)

Release of thromboplastic substances from the traumatized tissue may be more important for intravascular coagulation in fat embolism. When the fat enter the circulation, other products of cellular and tissue disintegration, such as tissue thromboplastin (III) or thromboplastin-like substances must enter together with fat. The adipose tissue is said to possess much thromboplastin.

Conclusively, fat embolism should contributes to the promotion of intravascular coagulation. And the significance of this investigation to the pathogenesis of fat embolism should never be recognized in the role of the intravascular fat droplets as a simple mediator of vascular occlusion.

References

7) Lehman, E. P. et al.: Fat embolism including experimental production without trauma.