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The Occurrence of Fibrin in the Lungs in an Autopsy Material*

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Das Vorkommen von Fibrin in den Lungen am Autopsiematerial

Zusammenfassung. Bei 301 fortlaufenden Fällen von gerichtsmedizinischen Obduktionen wurde das Vorkommen von Fibrin in Lungengefäßen und Alveolen histologisch untersucht (s. Tabelle). In 54 Fällen wurde Fibrin gefunden meist bei Pneumonie, Bronchitis oder Lungeninfarkt, selten bei Lungenblutungen. Die Anwesenheit oder das Fehlen von Fibrin in Blutungen bei Lungentraumen kann also keine Auskunft darüber geben, ob die Schädigung, welche zur Blutung geführt hat, vor oder nach dem Tode erfolgte. Fibrinablagerungen wurden in Lungengefäßen einer Gruppe von Fällen mit Trauma in der Anamnese beobachtet; man könnte an eine mögliche Verknüpfung des Vorkommens von Fibrin mit einer Fettembolie der Lungengefäße denken.

Summary. The occurrence of fibrin in pulmonary vessels and alveoli was studied histologically in an autopsy material consisting of 301 consecutive medicoforensic cases.

Fibrin was observed in a total of 54 cases, often in patients with pneumonia, bronchitis or pulmonary infarcts. Fibrin was seldom seen in the lungs in cases of pulmonary haemorrhage. The presence or absence of fibrin in haemorrhages occurring in traumatic lung injuries cannot thus provide information as to whether the damage associated with these haemorrhages had occurred before or after death.

Fibrin deposits were observed in pulmonary vessels in a group of cases with a history of trauma. The possibility of a relationship between the occurrence of fibrin in the pulmonary vessels and pulmonary fat embolism is discussed.

The migration of fat from a site of trauma (usually a fracture or fat tissue injury) to pulmonary or cerebral capillaries has long been considered to be the cause of the post-traumatic fat embolism syndrome and death occurring with it. In recent years, however, this theory has been disputed (for reviews, see Bergentz, 1961 and Sevitt, 1962). In discussions on this subject it has been suggested that intravascular coagulation in the lungs resulting from an ingression of material containing thromboplastin (fragments of connective and muscle tissue) from the site of trauma to the circulation could be responsible for the symptoms (Voigt, 1962).

If this latter theory is correct, fibrin should be visible in the pulmonary vessels in post-traumatic cases of death. No special attention appears to have been paid to this question hitherto. This may possibly be due to the fact that it has been generally accepted that in non-sudden cases of death fibrin clots formed post mortem are usually present in the heart and large pulmonary vessels. Since fibrin can be demonstrated in these clots by the conventional histological staining methods, it would seem reasonable to assume that fibrin deposited after death

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might also be observed in the smaller pulmonary vessels, which would then complicate considerably the identification of intravitally deposited fibrin in these vessels.

A preliminary study of a series of autopsies showed, however, surprisingly, that fibrin was relatively seldom found histologically in small or medium-sized pulmonary arteries. This observation prompted a systematic investigation of the occurrence of fibrin in the lungs in a larger series of autopsies. Attention was focused not only on the occurrence of fibrin in the blood vessels but also on its presence in the pulmonary alveoli. The series included numerous post-traumatic cases of death, but also cases where death had occurred after a fairly long period of illness, and where both the heart and the large pulmonary vessels exhibited clots containing fibrin at post mortem.

Material and Methods

The investigation was based on an analysis of a consecutive series of 301 forensic autopsies. In about half of these cases death had occurred suddenly. The majority of these autopsies were performed 1—3 days after death.

In each case formalin-fixed material from different parts of the lungs was stained with eosin-haematoxylin, elastica-van Gieson and fibrin stains. Several methods for demonstrating the presence of fibrin were used: Mallory PTAH (phosphotungstic acid haematoxylin), the Mallory method modified according to Ladewig, the picro-Mallory method as described by Lendrum and McFarlane (1940) and modified by Carstairs (1964), the Weigert method, and DAB nitrite-method according to Adams (1957).

None of these methods are completely specific for fibrin. Attempts were also made to use fluorescein-labelled antibodies against fibrin, but up to now this method has given no encouraging results with regard to the identification of intravascular fibrin.

Only fibrous material stained deep blue in Mallory's PTAH was regarded as fibrin. An attempt was also made to distinguish between fibrin which had been deposited during life and that which had occurred after death. Intravitally deposited fibrin fibres are often numerous, regularly arranged, and parallel with each other and with the vessel wall, to which they not infrequently adhere, while those occurring post mortem are very sparse and irregularly arranged. In many cases, however, it was impossible to determine with certainty whether observed fibrin had been deposited before or after death.

The PTAH method was found to be best as a screening method, but the picro-Mallory method was also of great value in this investigation.

The occurrence of fibrin was only recorded qualitatively.

As a rule three sections from each case were studied.

Results

As seen in Table, fibrin was observed in 54 of the cases studied. It was remarkable that positive findings were made in only two of the approximately 150 cases of sudden death.

The cases in which fibrin was observed could be divided into three groups:

1. Inflammatory pulmonary changes and pulmonary infarction,
2. Lung haemorrhages,
3. Other cases.

1. Inflammatory Changes and Pulmonary Infarction

Most of the 54 cases in which fibrin was found in the lungs belonged to this group. Twenty-seven had pneumonia, 8 bronchitis and 3 pulmonary infarction. In 10 of the pneumonia cases, however, no fibrin was found in the sections

Table. *Survey of causes of death and occurrence of fibrin in the lungs. Figures in brackets indicate number of cases without fibrin. A = alveoli, V = vessels*

	Number of cases	*Fibrin*				
		Pneumonia	Bronchitis	Lung infarct	Lung haemorrhage	Other cases[a]
Blunt injury						
Cause of death[b] morphologically confirmed	105	11 (1)	—	2	(24)	2
Cause of death[c] not quite morphologically confirmed	44	—	3	—	2 (24)	9
Poisoning						
Ethyl alcohol	8	—	—	—	(2)	—
Barbituric acid	22	—	—	—	(5)	—
Miscellaneous	16	1 (2)	—	—	(6)	—
Bullet wounds	3	—	—	—	(1)	—
Burns, cold, electric current	8	—	—	—	(1)	—
Hanging	3	—	—	—	(2)	—
Drowning	5	—	—	—	(1)	—
Natural death						
Heart disease	29	1 (1)	—	—	1 (10)	—
Respiratory tract infl.	28	13 (5)	5 (3)	—	—	—
Miscellaneous	30	1 (1)	—	1	(4)	2
Total	301	27 (10)	8 (3)	3	3 (80)	13
Site of fibrin		A+V	V	A+V	A	V+(A)

[a] Fibrin in pulmonary vessels but without signs of pulmonary inflammatory changes or infarct.

[b] e.g. Aspiration of blood, haemorrhagia pontis, fatal bleeding, aortic rupture, cardiac rupture, massive rupture of cerebral vessels, pneumonia, pulmonary thromboembolism, laceration of the spinal cord, massive cerebral fat embolism.

[c] e.g. Pulmonary fat embolism, slight cerebral contusion, slight pulmonary contusion and slight cerebral fat embolism as well as shock after fractures.

examined, while in the remaining 27 fibrin was seen both in the blood vessels and, especially in the alveoli. In 8 of the bronchitis cases small quantities of fibrin were observed in the blood vessels, but none in the alveoli. In the remaining 3 bronchitis cases no fibrin was found in the pulmonary vessels. In all 3 cases of pulmonary infarction studied, fibrin was seen both in the vessels and in the alveoli.

In 11 of the pneumonia cases the inflammation of the lung was an additional complication following previous injury. In several of these cases an especial abundance of fibrin was found in the small pulmonary arterial brances. In these cases the intravascular fibrin was seen not only in the vicinity of the inflammatory changes but often in parts of the lungs with no such changes.

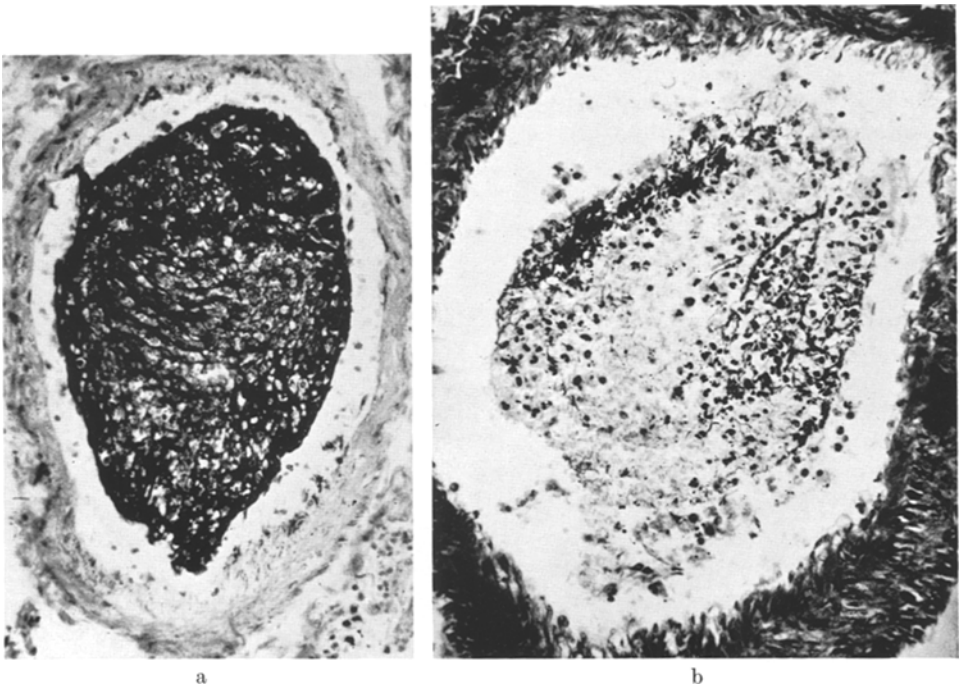
2. Lung Haemorrhages

In only three of the 83 cases with pulmonary haemorrhages was fibrin observed in the alveoli. In two of these cases the cause of the pulmonary haemorrhages was probably fat embolism. In both cases pneumonia was suspected at autopsy but

no pneumonic changes were found in the microscopic sections. The third case (sudden death) was a 42-year old man with a cardiac infarct and pulmonary oedema with numerous iron-containing macrophages in the alveoli. Negligible quantities of fibrin were seen in the alveoli in this case.

3. Other Cases

Fibrin was observed in the lungs in 13 other cases without coexisting inflammatory pulmonary changes or pulmonary infarction. In these cases the fibrin was found mainly in the vessels. Three of these cases had pulmonary emboli



a b

Fig. 1a and b. Fibrin in arteries. Varying degrees of fibrin in the deposits. As a rule there was predominance of fibrin and only few red blood cells or leucocytes. (PTAH)

which had originated from femoral vein thromoses. *All of the remaining 10 cases had a history of trauma with fractures.*

It was sometimes impossible to determine whether observed fibrin had been deposited intravitally or after death. In several cases, however, fibrin clots were found which undoubtedly must have formed during life. As a rule fibrin was observed more often in the arteries than in the veins (Fig. 1).

In 8 of these cases fat was observed in the pulmonary vessels.

The duration of survival varied between 0 and 14 days, and with one exception it was 3 days or more.

One 39-year old man died suddenly at an accident where he sustained laceration of the aorta and of the lungs, liver and spleen, and also a skull fracture. The day before death he had had a tooth extracted, and at autopsy his right cheek was found to be swollen. It is obviously difficult to determine whether this dental extraction was of any significance for the occurrence of fibrin in the pulmonary vessels.

In four of the cases the cardinal final symptoms were dyspnoea and cyanosis, while in four others respiratory distress was one of the terminal symptoms. In five of the patients the cause of death was considered to be fat embolism, which in two of them was believed to be cerebral. In four cases the lungs showed haemorrhages macroscopically, while two other cases showed microscopic haemorrhages. In two cases it could not be excluded that inflammatory changes may have been present in other lung regions than those studied microscopically.

Discussion

As is generally known, blood clots formed post mortem are often found in the cavities of the heart and in large branches of the pulmonary artery at autopsy. Histological examination of such clots by conventional methods always reveals the presence of fibrin. It might be assumed, therefore, that histological examination of lung sections in these cases would reveal fibrin deposited post mortem in the medium-sized and small vessels also, and that the presence of fibrin in these vessels would thus be of no great interest from a diagnostic point of view.

The present investigation has shown, however, that fibrin is only relatively seldom found in the small pulmonary vessels. Only in 54 of the 301 investigated cases was fibrin found in pulmonary vessels or alveoli, and the occurrence of fibrin appeared to be associated with special diseases. Thus it was often observed in cases of pneumonia, bronchitis or pulmonary infarction. However, fibrin was not seen in all cases with these lung diseases; it was absent in three cases with bronchitis and in ten with pneumonia. Conceivably this may be due either to the fact that no fibrin had been formed in the lung in these cases, or to the dissolution of intravitally formed fibrin by, for example, the strong fibrinolytic activity in lung tissue (ALBRECHTSEN, 1957; WARREN, 1963), or again to the general fibrinolysis which accompanies the stress reaction (MCFARLANE and BIGGS, 1948). A local fibrinolysis in the lung appears to be the more likely explanation in view of the fact that in some cases clots were present in other organs, e.g. the heart. Yet another possibility that cannot be entirely excluded is that the lung sections studied in these cases were not representative, and that fibrin may thus have been present in other unstudied parts of the lungs.

If the fibrinolytic activity is responsible for the absence of fibrin, it would seem conceivable that fibrin in the lungs may be broken down at the time of or after death. If this is so, the value of seeking fibrin as a criterion of intravital intravascular coagulation, or as a criterion of whether observed lung damage associated with haemorrhage had occurred intravitally, is reduced.

The present investigation has in fact shown that the question of whether lung damage associated with intraalveolar haemorrhage has occurred intravitally or after death cannot be answered by means of histological methods for the demonstration of fibrin, since fibrin is very seldom found even in cases where it is certain that haemorrhages in the lung parencyma have occurred during life.

With regard to the presence of fibrin as a criterion of intravital intravascular coagulation in the lungs, the situation seems to be partly different. In addition to the cases mentioned previously fibrin was shown in pulmonary vessels in 10 cases without the co-existence of inflammatory changes in the lungs, pulmonary infarction or pulmonary emboli (thrombo-emboli).

It was of considerable interest in this connection that in all 10 cases death had occurred as a result of injuries with fractures, and usually several days after the trauma. In 5 of these fatal cases the cause of death was assumed to be fat embolism, and in 8 of the cases fat was observed in the pulmonary vessels.

To judge by the present investigation, the depostion of fibrin in the pulmonary vessels after death thus seems to be correlated not only to inflammatory conditions and pulmonary infarction but also to trauma and fat embolism. In most of the posttraumatic cases with fibrin in the pulmonary vessels, no lesions were present which could be assumed with certainty to have caused death, and it cannot be excluded, therefore, that the occurrence of fibrin in these cases may have been significant for the deaths.

In several cases where the cause of death had been assumed to be fat embolism, however, no fibrin was observed in the pulmonary vessels. This may appear to contradict the theory that intravascular coagulation may be of importance for these deaths. In the light of the previously mentioned possibility of fibrinolysis, however, this absence of fibrin at autopsy is not sufficient to exclude intravascular coagulation as a possible cause of the symptoms or of death, or to exclude the possibility that fibrin may have been deposited in these vessels at the time of death.

The possibility that the occurrence of fibrin in the pulmonary vessels may be due to an inhibition of the fibrinolytic system must, instead, be considered. A study concerning this question, together with further investigations on fat embolism and intravascular coagulation will be reported in a further communication.

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