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Pathological Spectrum of the Lung in Cases of Violent Death: Part I. Lesion Classification

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ABSTRACT: The results are presented of the pathological study of the lungs in 66 cases of violent death observing the more frequent types of lesion and establishing 4 different groups of postlesioned pulmonary condition.

1. Inflammatory alveolar lesions without a diffused interstitial involvement (IAL) including contusions or direct aggressions, lobular pneumonias, or bronchopneumonias with a predominance of intra-alveolar inflammatory exudation.
2. Inflammatory alveolar lesions with a diffuse interstitial involvement (IALW) including generalized affectation of the parenchyma with lesions in the capillary structure of the wall.
3. Edemohemorrhagic lesions (EHL) presenting phenomena of capillary congestion with hematic extravasation and interstitial and intra-alveolar edema, without inflammatory involvement. This is the most numerous group and it can constitute the preliminary stage of any other.
4. Unspecific chronic lesions (UCL) not related to the cause of death, being chronically inflammatory and fibrotic alterations of limited interest in our study.

We emphasize the importance of the inflammatory involvement of the alveolar wall in the pathogenia of diffuse alveolar damage (DAD) and the aggravation of pulmonary lesions by capillary structure alteration, direct lesion of alveolar epithelium, presence of macrophages, and liberation of certain intracellular enzymes.

KEYWORDS: pathology and biology, death, lungs, lesions, diffuse alveolar damage

The behavior of lung parenchyma when subject to attack has been extensively studied in the last decades, particularly since the Asbaugh description in 1967 [*1*] of the Adult Respiratory Distress Syndrome (ARDS), including a group of clinical phenomena which are both physiologically and pathologically similar to the Infantile Respiratory Distress Syndrome, and which appear especially during the course of severe trauma.

This term has come to replace a long list of synonyms which had appeared in the literature since the end of the Second World War [*2*].

Clinically, the syndrome is characterized by acute respiratory failure with refractory hypoxemia caused by a diffuse lesion of the alveolocapillary membrane [*3*]. This lesion leads to the development of pulmonary edema by increasing its permeability [*4-6*]. The role of the defense cells of the alveolocapillary membrane [*7-12*] is being investigated in its origin. The histopathological substrate has been described by Katzenstein [*13*] as diffuse alveolar dam-

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age (DAD) which evolves in two phases: (1) acute or exudative, and (2) proliferative, leading to pulmonary fibrosis.

However, this is not the only way in which the lungs can react to attack by violent exogenous agents.

Acute posttraumatic respiratory failure, defined as hypoxemia of an acute nature and pulmonary origin, produced as a consequence of or in relation to traumas could, according to Trambaugh [*14*], be caused by a pulmonary contusion, atelectasis, aspiration, pulmonary embolism, pneumonia, pneumothorax, or ARDS.

We suggest that it is also possible to classify the above findings by reference to the type of attack, and thus to establish a correlation as set out in Table 1.

In this work, we present the results of a pathological study of the lung in 66 cases of violent death using as the basic criteria for classification the presence of inflammatory components and of diffused affectation of the interalveolar wall.

Material and Methods

We have studied 66 cases of violent death, the autopsies being performed in the Forensic Institute of Zaragoza (Spain). In 52 cases (78.80%) death was due to trauma, in 8 cases (12.10%) to mechanical asphyxia, and in 6 cases (9.10%) to intoxication.

At autopsy, after opening the thorax, a specimen measuring 3 by 3 by 3 cm was taken from each pulmonary lobule and prepared by conventional methods for microscopic examination. The following dye techniques were used: hematoxilin-eosin, periodic acid-Schiff (PAS), Masson trichromic, Weigert elastic, and Gomori argent.

The histological study was carried out by two pathologists who were not themselves present at the autopsy. They studied 40 parameters of pulmonary lesion (Tables 2 to 5) classified according to whether they were: (1) focal or diffuse and (2) of severe, moderate, or slight intensity, save for thrombus and aspiration, whose presence was simply noted rather than classified.

Results

Alteration Frequency in the Parameters Studied

In the alveolocapillary membrane the most frequent change noted was capillary congestion (96.96%), followed by thickening (80.30%), fibrosis (60.60%), interstitial hypercellularity (51.51%), and pneumocitary hyperplasia (72.72%). Except for cases of congestion and hyperplasia, which were predominantly diffused, the balance presents only a slight predominance of diffused over focal affectation.

TABLE 1—*Pulmonary pathology attributed to violent exogenous agents.*

Direct Lesions
contusion
wound
collapse
Direct or indirect lesion
DAD = ARDS
Most frequent complications
pneumonia
pulmonary embolism
atelectasis

TABLE 2—*Alterations of the alveolocapillary membrane.*

Interstitial	Epithelium
thickening	hyperplesia
fibrosis	Alveolar duct
hypercellularity	edema
acute inflammation	hemorrhage
chronic inflammation	fibrosis
fibroblasts	hyaline membranes
edema	macrophages
Capillaries	acute inflammation
congestion	chronic inflammation
microthrombus	fibroblasts
	aspiration

TABLE 3—*Alterations of the airways.*

Wall
denuded epithelial
acute inflammation
chronic inflammation
fibrosis
Duct
edema
mucus
hemorrhage
acute inflammation
chronic inflammation
aspiration

TABLE 4—*Alterations of the blood vessels.*

Congestion
Fibrosis
Inflammation
Thromboembolisms

TABLE 5—*Alterations of the pleura.*

Congestion
Edema
Fibrosis
Acute inflammation
Chronic inflammation
Hyperplasia-mesothelial
Hemorrhage

The alveolar lumen was occupied predominantly by macrophages (96.96%), but we consider both their focal or slightly diffused presence as a nonpathological feature; they were followed in frequency by hemorrhage (83.36%), edema (74.24%), chronic inflammation (51.51%), and acute inflammation (36.36%). Less frequent was the appearance of fibrosis (16.66%), fibroblasts (12.12%), and hyaline membrane (10.60%).

In the bronchioli, the changes were mainly diffused with a predominance of chronic pa-

thology: chronic inflammation on the wall accompanied by fibrosis (90.90%). Severe acute lesions were associated with parenchymal lesions and were of great importance in cases of aspiration.

In the larger caliber blood vessels, as in capillaries, congestion predominated (83.33%) followed by fibrosis of the wall (37.87%), being subendothelial, medial, or peripheral. The majority of those changes can be attributed to a chronic pathology.

The pleura is less affected. Acute phenomena, congestion, edema, inflammation, and hemorrhage can be found in the pleura in similar cases that produce it in the alveolar instance. Mesothelial hyperplasia, found in five cases, is related to an involvement of the pleural space.

Among the changes studied in a qualitative way, it was possible to demonstrate capillary microthrombus in 8 cases, and arteriolar thrombus (13 hematic and 7 bone marrow thrombus) in 20 cases. In 2 cases we found aspiration material in the bronchioli and in 1 case in the alveoli.

Classification by Lesion

These changes have been divided into four groups, according to the postlesioned condition of the lung.

1. Inflammatory alveolar lesions (IAL) without a diffused interstitial involvement. They include twelve cases divided into three subgroups.

(1.1) Slight and focal inflammatory lesions in the wall and the alveolar lumen including four cases corresponding to direct traumatic lesions in the thorax, being of short evolution. They are accompanied by capillary congestion and focal edema (Fig. 1).

(1.2) Lobar pneumonias found in four cases in which we observed numerous polimorphonuclear neutrophils, lymphocites, macrophages, and isolated plasma cells in the alveolar lumen with a focal pneumocitary hyperplasia, edema, and hemorrhage in the inflamed areas.

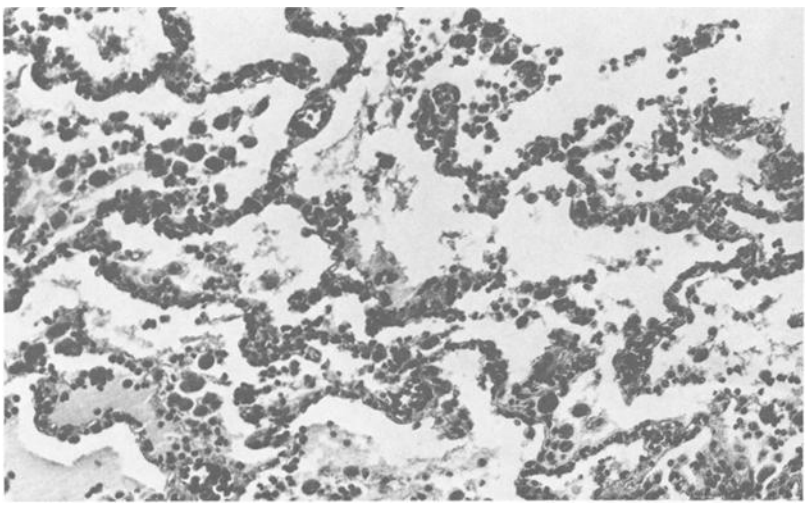

FIG. 1—*Inflammatory lesion in the alveolar wall with capillary congestion and slight focal edema (hematoxilin and eosin, ×125).*

(1.3) Multilobar bronchopneumonias: in the remaining four cases there was a massive inflammation of the parenchyma and airways with a marked predominance of alveolar lesions.

2. Inflammatory alveolar lesions with a diffuse interstitial involvement. They can be compared with different phases of diffuse alveolar damage (DAD). They included 20 cases divided into 3 subgroups.

(2.1) Lesions of the wall preceding diffuse alveolar damage: there were four cases having in common a dominant affectation of the wall in a slight, diffuse way with widening as a result of the presence of inflammatory cells in the interstice (Fig. 2). The death has been caused by a traumatic hemorrhagic shock of a short evolution. In three of them there were bone marrow thrombus in the arterioles.

(2.2) Diffuse alveolar damage in the acute phase: we found eight cases with inflammatory and edemohemorrhagic lesions in the wall and alveolar lumen of a diffused character. In all of them we could observe a thickening of the wall by capillary ingurgitation caused by leucocitary stasis, an invasion of the interstice by inflammatory cells, mainly polymorphonuclear neutrofils and an occupation of the alveolar lumen by inflammatory exudation with a fibrinoid framework, accompanied by variable hemorrhage, slight in some cases and massive in others (Fig. 3). The pneumocitary hyperplasia is constant, adopting a morphology in the form of cuboid strings with hyperchromatic nuclei and frequent mitosis (Fig. 4).

We could also observe hematic thrombus in the arterioles.

In only one case would we find hyaline membranes covering the surface of the alveoli which had been denuded of cells.

From the etiological point of view, four cases were traumatic in nature, two were the result of asphyxia by immersion and aspiration, and in another two cases death was related to the self-administration of endovenous drugs. Six of the above had been admitted to an intensive care unit.

(2.3) Diffuse alveolar damage in proliferative stage: the last eight cases presented, together with features described in 2.2, were a diffuse fibrosis of the alveolar lumen with young fibroblasts producing collagen and reticulin. The wall and alveoli inflammation persisted with a predominance of monocitic cells (Fig. 5).

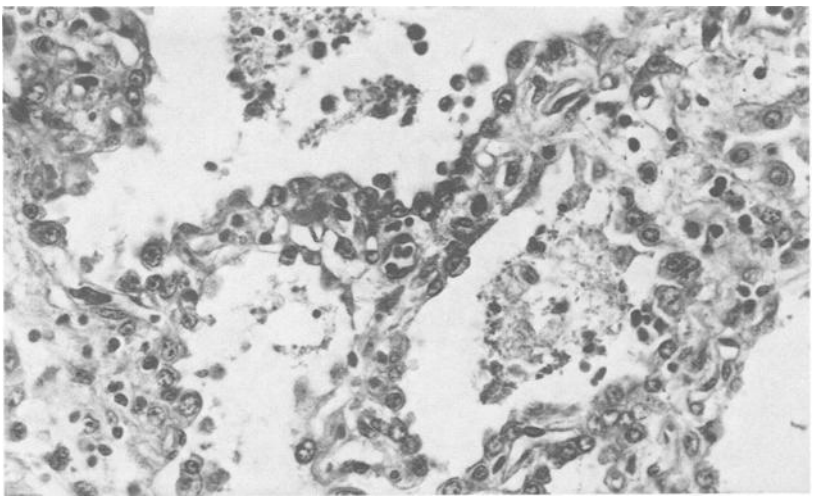

FIG. 2—*Alveolar wall widening as a result of the presence of inflammatory cells in a diffuse shape (hematoxilin and eosin, ×500).*

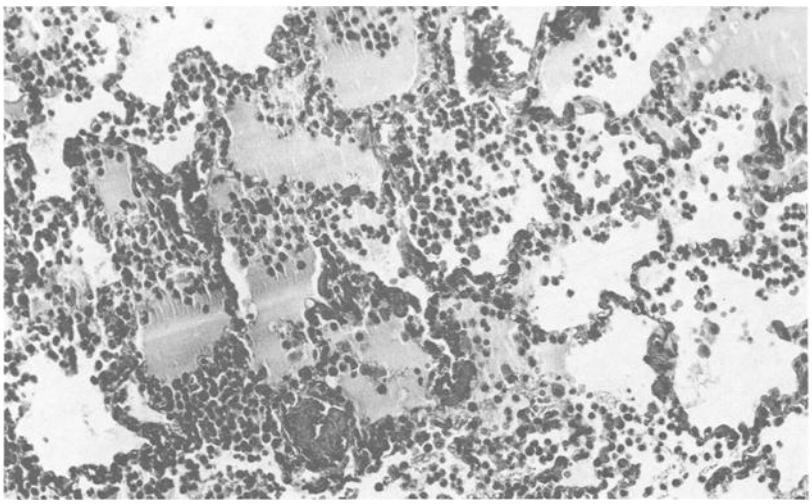

FIG. 3—*Acute inflammation, edema, and hemorrhage in interstitium and alveoli (hematoxilin and eosin, ×125).*

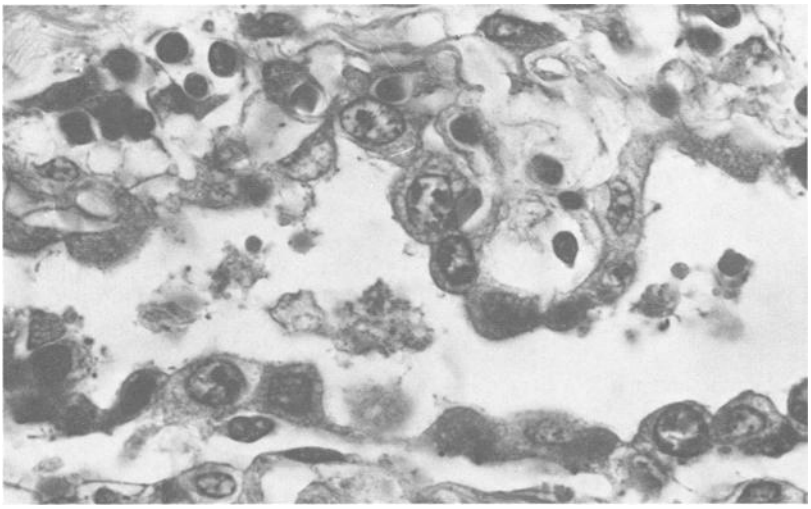

FIG. 4—*Pneumocitary hyperplasia with the typical cuboidal shape and hyperchromatic nuclei (hematoxilin and eosin, ×950).*

At the vascular level we found capillary microthrombus in three cases and arteriolar thrombus in four cases.

Hyaline membranes were encountered in five cases.

The fibrosis affected the arteriolar wall at the subendothelial level.

Six of these cases were of traumatic etiology and two of toxic etiology. In all but one, in which death was related to heroin addition, there had been admission to an intensive care unit.

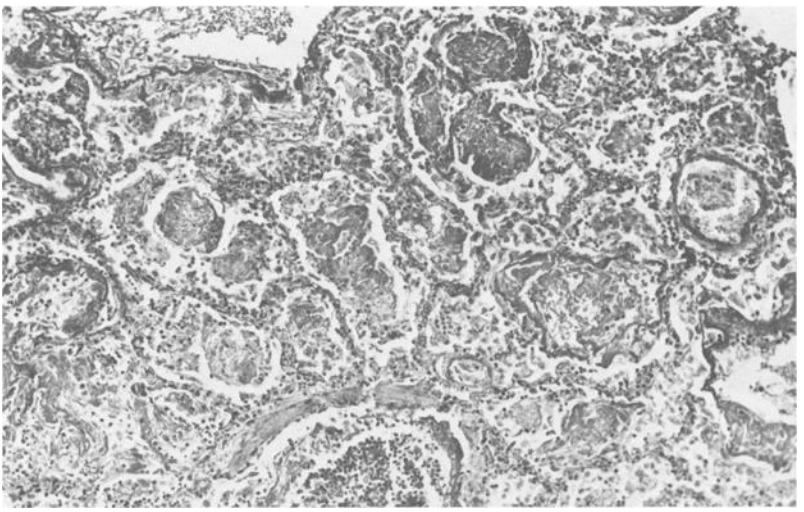

FIG. 5—*Collagen proliferation in wall and alveolar lumen jointed to persistence of inflammatory phenomena (hematoxilin and eosin, ×90).*

3. Edemohemorrhagic lesions (EHL): we have grouped under this heading 25 cases in which we could distinguish several degrees of severity of the lesion.

The least severe lesions appeared in cases of carbon monoxide intoxication, presenting a severe and diffused congestion with interstitial hemorrhage, producing a picture of tightly packed red cells in the wall without extravasation into the alveolar lumen.

In nine cases capillary congestion was accompanied by alveolar hemorrhage. All of them had a traumatic etiology and the majority had a very quick evolution.

In the remaining fifteen cases we found congestion, hemorrhage, and intra-alveolar edema. In eight of them it was attributed to a direct lesion of the parenchyma produced by stab wounds, bullet wounds, traffic accidents, or falls. Two cases had a diffused and slight character and were terminal. The remaining five cases corresponded to mechanical asphyxia.

4. Chronic lesions not related to the cause of death: we found nine cases in which there was only a chronic unspecific pathology, namely: chronic bronchitis; bronchiectasia; and subpleural, perivascular, or peribronchial fibrotic phenomena.

Discussion

The interstitial widening, which is the dominant pathology at the wall level, is the manifestation of a whole series of phenomena that produce alterations in the morphology of the alveolocapillary membrane provoking in the "thin zones" of its structure a separation of the capillar and epithelial basal membrane [*15*]. Among this phenomena, fibrosis stands out taking the form of an accumulation of collagen and reticulin in a lineal or aggregated form, being found in localized areas of scar tissue, and in a diffused frame, in several cases of diffuse alveolar damage. Hypercellularity of a diffuse predominance and constituted by both acute and chronic inflammatory cells illustrates the response of the defense mechanism of the alveolocapillary membrane when faced with aggression.

In the capillaries, diffused congestion is, as in certain other series [*16–18*], the most frequent observed phenomena. In the alveolar epithelium, the hyperplasia manifests a direct sign of aggression of the alveolocapillary membrane, appearing in all the cases of diffuse alveolar damage and also in certain instances of inflamed alveolar lesions and edemohemorrhagic lesions.

With reference to the alveolar lumen we should mention first the presence of macrophages which form part of the natural population of the alveoli [*19*], and which accompany the rest of the inflammatory cells in both the chronic and acute conditions. Edema and hemorrhage appear in an isolated form or joined with other inflammatory signs like leukocytes.

The presence of collagen, fibroblasts, hyaline membranes, and aspiration are rarer, the first three being indications of severe affectation of the parenchyma, suggesting an evolution towards a chronic state.

As a criteria for classification of the various responses of the lung to violent and harmful agents we have used: (1) the presence of inflammatory material which allows the differentiation between IAL and EHL groups, and (2) the existence of diffused involvement of the wall, separating two different types of IAL.

The Inflammatory alveolar lesions without participation of the wall take the form of localized structural alterations that affect the alveolar level of the alveolocapillary membrane, and when they affect the wall, do so in a limited way. Usually they are either contusions [*20*], when the lungs react to a direct aggression, or lobular pneumonias or bronchopneumonias, these being frequent complications in cases of direct or indirect aggressions—traumatic or not [*21*]—and especially in situations when there is a debility of the defense mechanisms. They are characterized by the presence of inflammatory exudation with a predominance of polimorphonuclear neutrophils in the interior of the alveoli. The wall presents, in an irregular form, focal signs of acute lesion which accompany the alveolar lesion.

The inflammatory alveolar lesions with diffused participation of the wall constitute generalized affectations of the parenchyma, comparable with the different phases of DAD [*13*]. The sequence defined and described in our series is consistent with the pathogenetic hypothesis defended by several authors [*2,22–24*] who advocate an initial lesion of the capillary structure of the wall with interstitial edema and widening [*14*]. The phenomena which increases capillary permeability produces a direct lesion of the alveolar epithelium with destruction of pneumocytes Type I and substitution by hyperplastic pneumocites Type II. In this situation, the defensive cells of the alveoli, macrophages, and neutrophils are stimulated, and some of their free enzymes may complete the process deepening the tissue lesion and preparing the way for the development of fibrosis [*25–30*].

In spite of their differences, it would not be correct to establish a rigid division between both, with and without diffuse interstitial affectation, lesions. In fact, in several instances, the lesions are convergent. So, the contusions may produce a diffuse alveolar damage either by their large size or by inducing, despite being small, the generalized defensive reactions described above [*31*]. Pneumonia may be complicated with diffuse alveolar damage [*32–34*] by this same motive, and multilobar bronchopneumonia presents so many morphological similarities to it that certain authors consider bronchopneumonia as one of the phases of diffuse alveolar damage [*2*].

The edemohemorrhagic lesions are characterized by presenting a series of phenomena ranging from severe capillary congestion to hematic and plasma extravasation into the interstitial and alveolar space, without any inflammatory response at any stage. This is the most numerous group and it can constitute the preliminary phase of any other type of lesion. Its relationship with direct aggression is evident, but even in indirect aggressions the congestive exudative phenomena can appear, giving rise to lesioned edema. Anyway, congestion, hemorrhage, and edema are suitable breeding groups for the development of any of the above mentioned complications.

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