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Adult Respiratory Distress Syndrome

A Histopathologic Study

S. D. Ferrara and G. Pertile

Istituto di Medicina Legale e delle Assicurazioni, Università di Padova, Via Falloppio 50, Padova, Italy

Summary. The results of an anatomohistopathologic study carried out on subjects who died from various causes in resuscitation centers are reported with specific reference to the evolutive phases of the adult respiratory distress syndrome (ARDS).

While a precise anatomohistopathologic diagnosis of non-clinically diagnosed ARDS in its initial phase is considered possible, the importance of recognizing this pathology in cadavers and living patients is emphasized because of the medico-legal implications involved.

Key words: Adult respiratory distress syndrome (ARDS) – Shock lung – Hyaline membrane

Zusammenfassung. Ergebnisse pathologisch-anatomischer und histologischer Untersuchungen in verschiedentlich verursachten Todesfällen in Reanimationszentren, unter besonderer Berücksichtigung der evolutiven Phasen des ARD-Syndroms.

Verff. halten die exakte pathologisch-anatomische und histologische Diagnose eines anfänglichen ARDS auch in den klinisch nicht diagnostizierten Fällen für möglich und heben die gerichtsmedizinische Bedeutung der Feststellung einer solchen Pathologie in Todesfällen und bei Überlebenden hervor.

Schlüsselwörter: ARD-Syndrom – Schocklunge – Atemnotsyndrom – Hyaline Membranen

Pneumopathy due to hyaline membranes in infants (infant respiratory distress syndrome, IRDS) is a well known clinical entity which was first described by Hockerm [1]. On the other hand, the concept of a pulmonary shock syndrome in adults is a recent acquisition which is poorly known outside the field of resuscitation. A deeper knowledge of this disease entity is a necessity particularly felt by

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anatomo- and medico-legal pathologists who may be asked to evaluate these cases at autopsy.

During the course of a study on the pathology of resuscitation [2] in several subjects dead with a picture of severe respiratory insufficiency we observed that one of the most characteristic and constant morphological findings was the presence of thick PAS-positive hyaline membranes lining the pulmonary alveoles. These membranes have already been reported by various collagues [3—21] in very severe and fatal cases of the pulmonary syndrome commonly known as shock lung, or better still according to Ashbaugh et al. [22], adult respiratory distress syndrome (ARDS).

In many clinically diagnosed cases of ARDS which we observed hyaline membranes were not present. However, we repeatedly observed apparently aspecific alterations, which in the absence of the clinical diagnosis or a specific anatomopathologic preparation would not have allowed this syndrome to be identified. On the other hand, each time these findings were observed in an adult, there was a corresponding clinical diagnosis of ARDS. Therefore, it followed that an accurate histopathological investigation would disclose certain signs that not only would confirm or deny the precision of the clinical diagnosis, but would also provide useful information for a suitable evaluation of the clinical symptoms so that ARDS could be diagnosed in its initial stage. In the study reported here, we examined 48 subjects that had died in resuscitation centers. The patients had been selected on the basis of pathological findings suggesting ARDS, which was confirmed following a retrospective study of the clinical, biochemical and instrumental data obtained during life. Ten cases which survived until the terminal phase of ARDS are reported in detail since they demonstrate the etiologic variety and the evolutive pathological stages of the syndrome.

Materials and Methods

The material for our study came from 48 autopsies carried out at the Institutes of Legal Medicine and Pathologic Anatomy of Padua from December 1, 1975 until May 31, 1977. The decedents had been admitted for various causes to the Resuscitation Center, where death occurred within a period from 1—2 days to 3 weeks. A complete autopsy had been carried out in each case and specimens of each organ, even if it appeared unaltered, had been taken. In each case, 3 specimens from each pulmonary lobe were taken from the parahilar, peripheric, and intermediate sites, for a total of 15. The material was fixed in 10% formalin, embedded in paraffin. Stains employed were hematoxylin-eosin, PAS, Van Gieson and Weigert.

The ten cases selected according to the criteria given above consisted of:

— 4 subjects with CNS pathogenesis. Of these, 2 cases of skull trauma, 1 case of cerebral coma from internal hypertensive hydrocephaly in a subject with Arnold-Chiari malformation, and 1 case of massive cerebral hemorrhage in an elderly patient with arteriosclerosis;

— 2 subjects with pulmonary embolism. One patient had diffuse pulmonary and cerebral microembolism (Fig. 1) following multiple traumatic bone fractures, and the other had only pulmonary embolism following a thrombosis of the iliac following application of a coxofemural articulating prosthesis;

— 2 subjects who had recently undergone a mesenteric-cava anastomosis for portal hypertension caused by hepatic cirrhosis;

— 1 case of cardiogenic shock due to complications from a dissecting aneurysm of the aorta (without rupture), and

— 1 case of sepsis with bacterial meningoencephalitis.

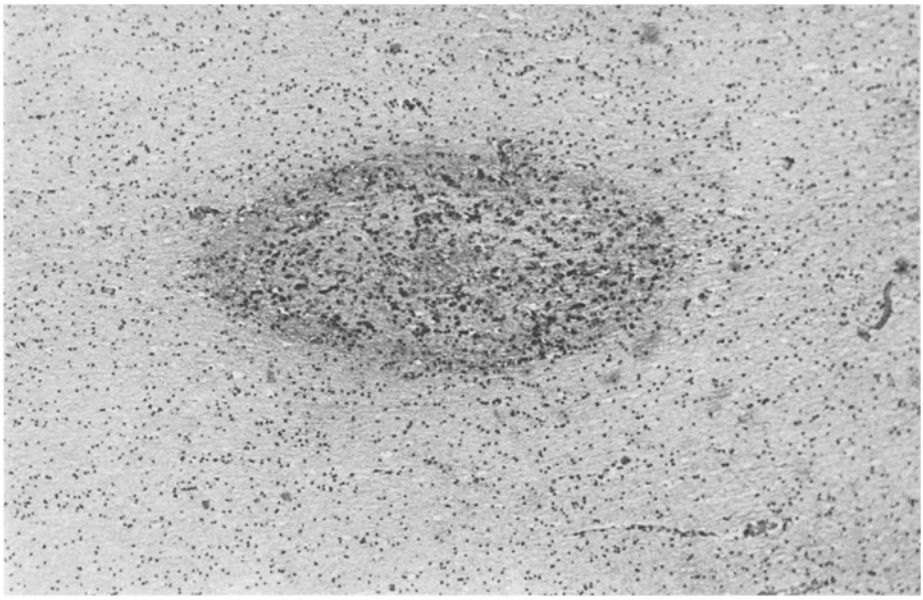

Fig. 1. Foci of microinfarcts in brain white matter

Results and Discussion

The microscopic alterations, like the macroscopic ones, were similar in each of the 10 selected cases with only purely quantitative variations which were related mostly to the different evolutionary stage of the clinical condition causing the patient's death. Only the most pertinent pathological features will be reported. The first alterations visible in the relatively uninjured peripheral zones consisted of interstitial and intra-alveolar edema with congestion of the septal capillaries, and swollen and hypercellular septa. Below the edematous areas, emphysematous zones were observed, and often the endoalveolar fluid was rich in erythrocytes which had passed through the alveolar-capillary membrane be diapedesis.

The hyaline membranes were thick, glassy, and homogeneous and were recognizable with routine hematoxylin-eosin stain, but were better identifiable with the PAS reaction. These were located mostly at the level of the respiratory bronchioles of the alveolar duct, and in the most severe cases they lined the entire alveolar wall. In all the cases observed, along with the picture described, there were also superimposed histological signs of infection with the presence of inflammatory cells at the peribronchial, and/or bronchial, and/or interstitial level.

From our findings and the descriptions in the literature [6, 13, 18, 19], the entire histopathological process may be reconstructed and distinguished into the following various phases. The first alteration observable at the microscope is the interstitial edema (Fig. 2) which is most likely concurrently due to lesions in the endothelium, colloid-osmotic and plasmatic coagulability disorders, hemodynamic, cardiogenic, and neurogenic factors [17, 20, 21, 23, 24].

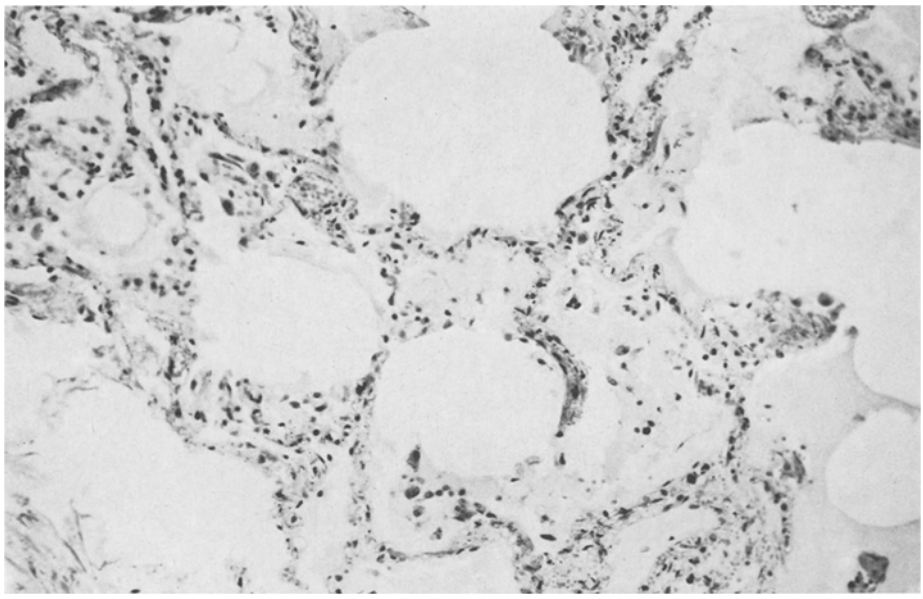

Fig. 2. Interstitial edema with hypercellular swollen septa, and partial endoalveolar edema

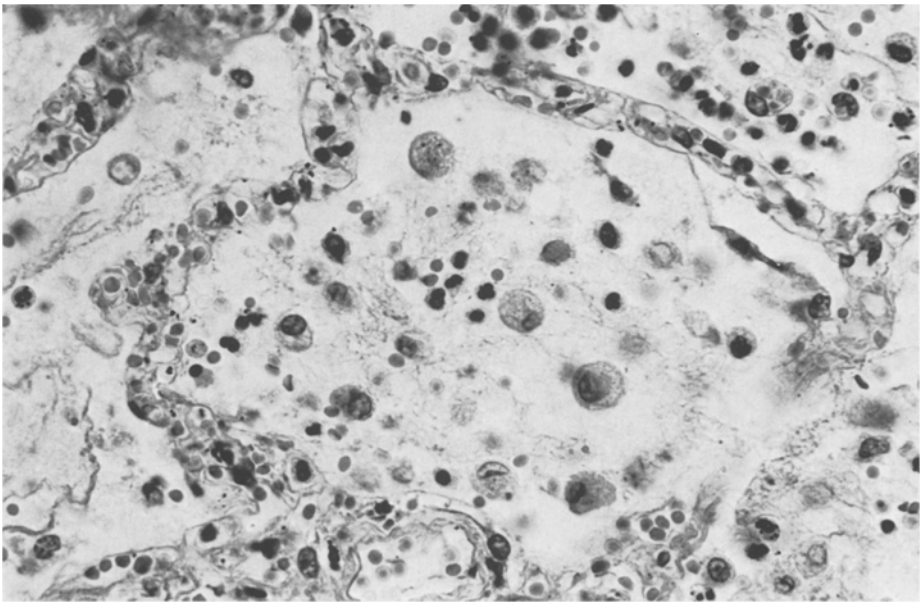

Fig. 3. Endoalveolar cellular elements

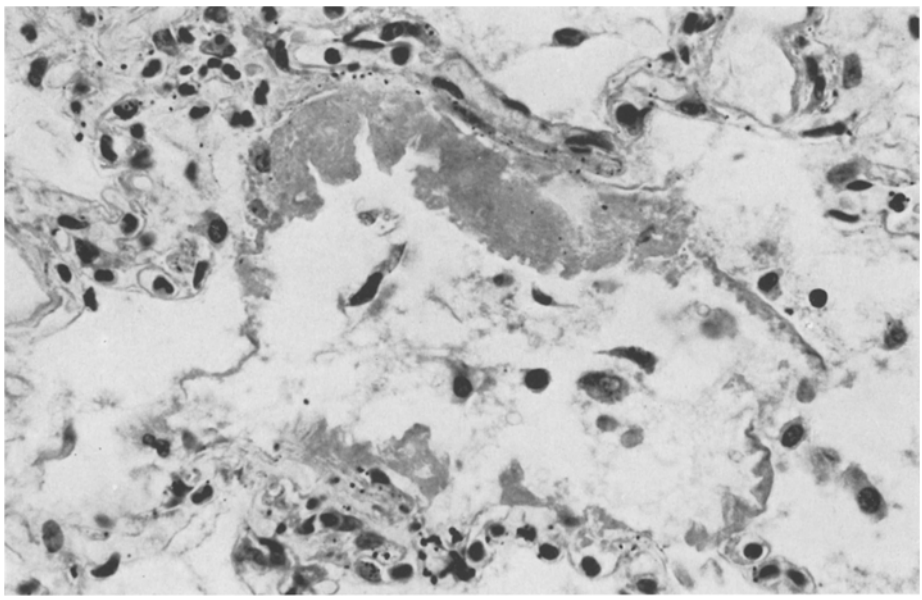

Fig. 4. "Early" hyaline membranes are high, slightly dense, and acidophilous with cleavage planes at the alveolar wall

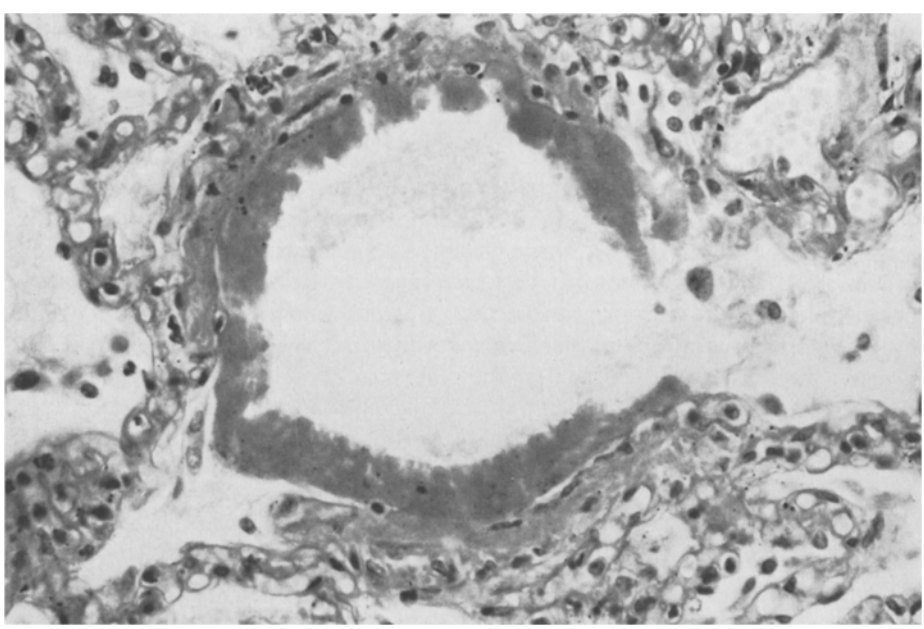

Fig. 5. "Late" hyaline membranes are intensely acidophilic dense; less high and closely adherent to the alveolar wall

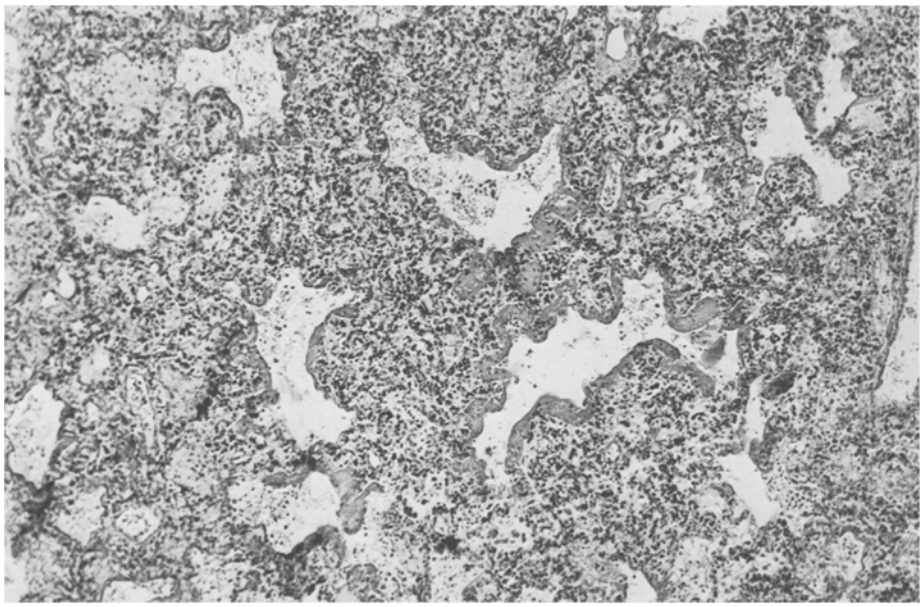

Fig. 6. Marked congestion. Atelectasic areas infiltrated by inflammatory cells alternate with coarse air spaces created by the rupture of the interalveolar septa. Diffuse hyaline membranes

Interstitial edema is followed be endoalveolar edema constituted by a high specific weight proteinaceous fluid which passed inside the alveoles due to alterations in the alveolar-capillary membrane. These alterations are not visible microscopically but have been described ultrastructurally by several investigators [20, 21, 23, 25, 26, 27, 28, 29].

In some cases the severity of the alteration in the alveolar-capillary membrane is demonstrated by its impossibility to retain even cells (Fig. 3). Consequently, large quantities of erythrocytes pour into the alveoles with a picture reminiscent of massive pulmonary hemorrhage in neonates. In less severe and not frankly hemorrhagic cases, reabsorption of the acqueous fraction of the edema liquid follows with re-aeration of the alveoles and progressive concentration of the protein fraction in the residual fluid and its adhesion to the alveolar walls. Further hydrous reabsorption of the edema liquid reduces its characteristic fluidity and brings about the formation of pseudomembranes (Figs. 4, 5) which become progressively denser, more organized, and closely adherent to the alveolar walls.

In the more advanced phases of the disease, fibrosclerotic alteration of the interstices prevails with zones of atelectasia (Fig. 6) alternating with coarse air spaces which formed due to the rupture of the stiffened alveolar septa (Fig. 6).

In the various phases, also inflammatory cells appear, consisting of lymphocytes. They are initially localized at the peribronchial interstice and diffuse centrifugally into the pulmonary interstice. Successively, pronounced lymphocytic and granulocytic infiltration of the bronchial wall occurs with necrosis of the mucosa membrane. In the more advanced phases, very marked inflammatory

phenomena occur and vast zones of granulocytic and lymphocytic infiltration are formed as well as hepatization with multiple foci of abscess formation.

In light of our observations, it may be confirmed that ARDS, a pulmonary syndrome that is stereotyped in its many clinical and radiological manifestations, has numerous etiopathogenetic factors. Its evolution is completely independent of the responsible noxa since the common denominator of this disease consists of a severe alteration in the alveolar-capillary membrane, the mechanism of which has been subject of various hypotheses. This alteration determines the outflow of endocapillary material into the interstice of the alveolar spaces with successive formation of hyaline membranes.

Secondly, the pathological process occurs in a unitarian and constant evolution, in which every histopathological alteration is always produced by the preceding one and coexists with it, so that in an advanced disease phase different histopathological pictures may be always observed in the same pulmonary parenchyma. Because of their punctual repetition, it follows that these pictures acquire a particular characteristic which is useful in confirming not only the clinical diagnosis of an advanced state of ARDS, but also the early stages; moreover, a clinical diagnosis may be formulated from the anatomohistopathological observations.

The interest of the medicolegal examiner emerges clearly from the fact that when possible medical professional responsibilities must be determined, it is necessary to discern what is the direct result of indispensable resuscitation treatment from that which follows incongrous therapeutic manoeuvers (pneumothorax, pneumomediastinum, etc.). Finally, a not less important interest for the medicolegal evaluation of injury derives from the knowledge of the consequences that this pathology assumes in patients surviving resuscitatory treatment. This aspect will be treated in detail elsewhere.

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