

The Complexity of Pulmonary Complications in Acute Kidney Injury

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ABSTRACT. Background: Pulmonary complications often occur in patients with acute kidney injury, and represent an important cause of death. Objective: To analyze the complexity of lung disorders in patients with RIFLE class III acute kidney injury undergoing hemodialysis and the physiopathological mechanisms that cause the various pulmonary complications. Methods: Our study included 74 clinical cases of acute kidney injury of various etiologies (severe sepsis, trauma, post-surgery, toxic, etc.). The respiratory function of these patients was monitored from the clinical and radiological points of view. Deceased patients underwent autopsy. Results: Pulmonary complications occurred in 47.24% of cases. Most pulmonary complications (over 50%) occurred in sepsis-induced acute kidney injury. Regarding the clinical aspects of pulmonary complications, the most frequent were ARDS, atelectasis and bronchopneumopathies, determined by the etiological factors that had caused the acute kidney injury in the first place, and by the acute kidney injury-induced physiological effects. Conclusions: 1. The frequency of pulmonary complications in acute kidney injury is very high and has a negative impact on the evolution and prognosis. 2. The etiology of the pulmonary complications is complex, as these are caused by the agents that induced the acute kidney injury in the first place, most frequently by septic shock. 3. Along with clinical and radiological evidence of pulmonary damage, severe pulmonary histological lesions were found in deceased patients, with a high contribution to the increased mortality rate.

KEYWORDS: Acute kidney injury, pulmonary complications, hemodialysis, sepsis, acute respiratory distress syndrome.

Introduction

The lung is an organ where the complications of acute kidney injury frequently occur. A significant number of deaths in acute kidney injury patients are caused by lung damage. The concept of simultaneous lung and kidney distress is old, but several issues still need discussion.

The purpose of this study is to analyze the complexity of lung disorders in patients with RIFLE class III acute kidney injury (AKI) [1] undergoing hemodialysis, and to discuss the physiopathological mechanisms that cause the various pulmonary complications. Regarding these aspects, we set the following objectives:

- To determine the frequency of pulmonary disorders in acute kidney injury patients
- To evaluate the etiological factors that triggered the AKI and their pulmonary impact
- To evaluate the biological disorders regarding the uremic syndrome and the acute kidney injury's triggering factors, as well as their pulmonary impact
- To analyze the histological support of some pulmonary complications
- To analyze the impact of pulmonary complications on the acute kidney injury

Material and method

The study included 74 cases of different etiology acute kidney injury treated by hemodialysis, admitted to Craiova Clinical Emergency Hospital in the Intensive Care Unit, the Nephrology Department, and other surgery departments.

The acute kidney injury's etiology is displayed in Table 1.

Table 1. The acute kidney injury's etiology

AKI etiology	No	%
Severe sepsis	43	58.19%
Surgery	9	12.16%
Trauma	6	8.08%
Chronic nephropathies	4	5.4%
Intoxication	8	10.81%
Leptospirosis	2	2.7%
Burns	2	2.7%
Total	74	100%

The patients were monitored regarding the pulmonary damage, as well as the uremic syndrome (nitrogen retention, ionogram, acid-base balance, and complete blood count). Autopsies were performed for the deceased patients and histological material was obtained from the lungs as well as other organs. Table 2 shows the clinical aspects of pulmonary complications.

Table 2. Clinical aspects of pulmonary complications

ARDS / Atelectasis / Bronchopneumopathies	20	27.02%
Pleurisy	3	4.05%
Pulmonary edema	2	2.7%
Pulmonary embolism	1	1.35%
Airway bleeding	7	9.45%
Respiratory muscle loss	2	2.7%
Total pulmonary complications	35	47.29%
Total AKI cases	74	100%

Results

As Table 2 shows, it can be seen that 47.29% of all cases of acute kidney injury presented different pulmonary complications, indicating lung damage that occurs in almost half of the AKI patients.

Regarding the pulmonary disorders depending on the AKI etiology, the highest percentage can be found in sepsis-induced AKI, where the largest variety of clinical forms can also be seen. In sepsis-induced AKI pulmonary complications exceed 50% of all the cases (52.48%). The clinical aspects are very diverse. Most are related to the septic factor: acute respiratory distress syndrome, bronchopneumonia, atelectasis, and bronchoalveolar damage, representing 25.67%. Other pulmonary complications were: pleurisy (4.05%), sepsis-induced pulmonary edema (2.32%), pulmonary embolism (1.57%), and pulmonary and airway hemorrhage (9.30%). Histology analysis has shown that these pulmonary complications are caused by shock-specific factors (IDC, ARDS), as well as local pulmonary factors (atelectasis, bronchopneumopathy, coagulation disorders, etc. [2-4]

Histological material (Figs. 1 and 2) brings extra diagnostic elements, adding information to the image investigations. These have constantly shown interstitial pulmonary edema, capillary congestion, intra-alveolar hemorrhage and edema, and atelectasis areas. These histological features were also present in the early deceased cases, in which the etiologic factor, along with the disruption of the coagulation balance [4,5] and the uremic factor, were decisive.

Half of the cases that underwent necropsy presented pulmonary damage that, along with other factors and complications, contributed to the patient's death.

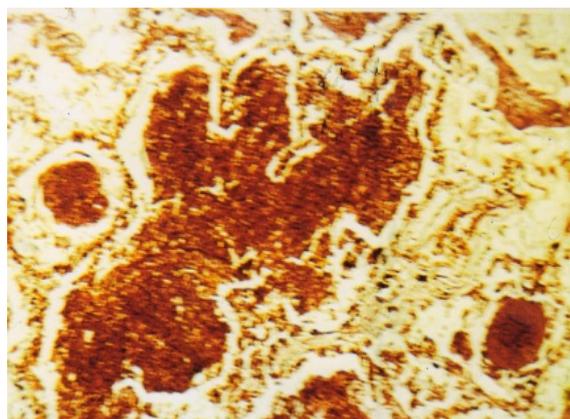


Fig. 1. Pulmonary interstitial and alveolar hemorrhage, HE staining 4x

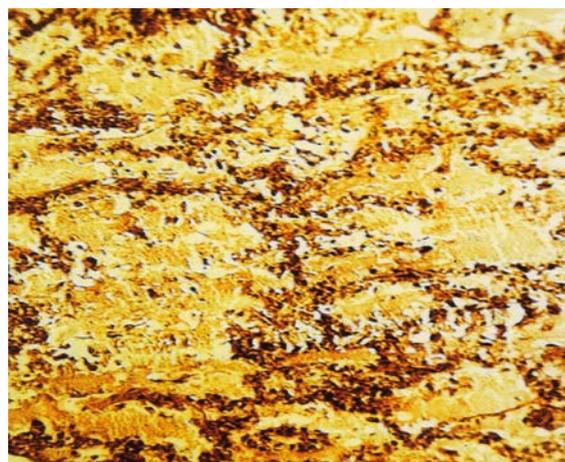


Fig. 2. Pulmonary interstitial hemorrhage and alveolar damage, HE staining 10x

Discussion

In order to interpret the pulmonary manifestations that occur during acute kidney injury, it is necessary to assess the lung damage from AKI's early stage, considering multiple factors: the etiologic factor that triggered the AKI [3,6]; the patient's comorbidities; and the biological, physiopathological, and clinical disorders caused by the AKI (the uremic factor). [5-7]

The acute kidney injury's etiology is most often represented by various types of shock. It is well-known that respiratory failure, as well as kidney failure, is a complication that occurs in shock.

Most pulmonary manifestations were found in patients with sepsis-induced acute kidney injury (severe sepsis and septic shock) [3,6], at times when the lungs were primarily affected. In these cases, multiple factors affected the lungs: IDC, pulmonary blood flow redistribution, pulmonary surfactant alteration, chemical mediators (cytokines, elastase, etc.) [8,9,10], bacteria and endotoxins, and kinins that trigger

bronchospasm. Another element with a pulmonary impact that contributed to the so-called fluid lung syndrome was hyperhydration [11]. Hyperhydration is sometimes caused by an excess of fluid replacement therapy in shock in situations in which the kidneys are unable to eliminate the fluid excess [12].

Regarding the comorbidities, these were very diverse, considering the acute kidney injury patient's history (chronic bronchopulmonary disease, emphysema, cifosis, thoracic trauma, tuberculosis, etc.).

The biological alterations that occur during acute kidney injury are not without pulmonary consequences. The high blood urea level can increase membrane permeability, contributing to the pathogenesis of the so-called "uremic lung".

Dyspnea can also occur in acidosis, anemia, and electrolyte imbalance, in the absence of pulmonary lesions.

Bleeding pulmonary disorders can occur in different types of shock, especially septic shock, but also in the context of certain nephropathies that cause hematuria [13] or in Goodpasture syndrome, a typical situation of glomerular nephropathy associated with hemoptysis [14]. There are also toxic factors (e.g., carbon tetrachloride) with kidney impact. Certain therapeutic procedures used to treat acute kidney injury (hemodialysis, blood transfusions) contributed to increased lung damage. Emergency hemodialysis has pulmonary effects [15,16]-hypoxia, hypoventilation, and pulmonary hypertension are described. Granulocytes and monocytes are activated, releasing inflammation mediators with pulmonary impact.

Preserved blood, if needed for transfusion, affects the lung by causing capillary obstruction determined by platelets, leucocyte cellular debris, and microemboli. It also causes an increase of serotonin level and pulmonary immunological effects.

A significant number of acute kidney injury patients required surgery to treat the main cause of the kidney damage. Surgical procedures were required to treat peritonitis, pancreatitis, colecistitis, etc. These procedures caused pulmonary damage through anesthetic factors (intubation, mechanical ventilation [17], pulmonary impact of anesthetics, airways damage). Surgical procedures in the upper abdomen, as well as post-surgery distension, can also cause pulmonary complications.

The clinical aspects of pulmonary complications included respiratory muscle reduction (2.70%) in patients with severe sepsis. The patients underwent surgical procedures, presented long periods of anuria, and lacked proper nutrition, sometimes because the enteral or parenteral input was not properly assimilated by the altered cells. These cases evolved with a decrease of the pulmonary functional capacity, followed by other pulmonary complications.

The acute kidney injury's pulmonary complications did not remain without consequences on the evolution and prognosis. Therefore, out of 15 deceased patients, 6 involved pulmonary damage as the main cause of death, along with other organ failure.

In patients with sepsis-induced acute kidney injury, especially with pulmonary complications, the oliguric or anuric periods were prolonged. Sometimes, a sudden and explosive restart of the diuresis process was noticed after management of the pulmonary complication.

Conclusions

1. The pulmonary complication rate in acute kidney injury is very high (47.24%).

2. Most of the pulmonary complications occurred in patients with sepsis-induced acute kidney injury (septic shock and severe sepsis). These were caused by multiple factors:

- Physiopathological modifications that occur in septic shock and severe sepsis that can have an impact on both the kidney and the lung;
- Various therapies used to treat acute kidney injury in shock conditions (hemodialysis and preserved blood transfusions);
- Surgical procedures that may affect the lungs by anesthetic factors.

3. The most severe pulmonary complication was the acute respiratory distress syndrome that required ventilatory support.

4. In many cases, the pulmonary complications influenced the evolution and the recovery of the kidney function.

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