X-ray findings and morphologic changes in lungs after thermal injury

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Purpose

Thermal injury accounts for 4.1% of all trauma types. In the recent years, there has been reported an increase in the number of those affected by the fires [1, 2, 3]. In fire, a human body is exposed to flame and heat, and also to smoke containing toxic products of incomplete combustion of organic substances. Hot air and flames inflict damage to the skin and upper airways; and the smoke and toxic combustion products penetrate deeper into the respiratory tract, reaching the alveoli, and causing a severe injury to the tracheobronchial tree (TBT) and the lung parenchyma [4, 5].

Generally, fire victims admitted to a Burn Unit may have either isolated smoke inhalation injury, or skin burn only, or may suffer a combined inhalation injury and cutaneous burns that represent the most severe course of burn injury [6, 7]. Airway injury is present in up to one-third of patients with major burns. The risk of concurrent pulmonary damage is high. Pulmonary complications arising in thermal injury patients may vary by their nature, severity, time of their occurrence [8, 9]. An early accurate diagnosis, prevention and treatment of life-threatening complications are very important to decrease morbidity and mortality of burn patients.

The purpose of the study was to identify and characterize X-ray signs of abnormalities occurring in the lungs after thermal injury and to define the types of possible complications and the time of their occurrence in patients with various types of thermal injury resulted from fire accidents.

Methods and materials

The study included 240 burn patients who were admitted after fire accidents to the Burn Center of the Sklifosovsky Research Institute from January 2010 to December 2012. The patients sustained either isolated inhalation injury, or skin burn only, or a combined inhalation injury and cutaneous burns. Each patient was subjected to the following standard diagnostic work-up.

1. History taking

Demographic data, patient's history including chronic or congenital diseases were recorded. Patients under 18 years old were excluded from the study, as were the patients whose severe chronic diseases had a poor prognosis.
2. General examination and laboratory studies

Initially at admission, the vital signs (blood pressure, pulse rate) were measured in all patients to know the degree of hypovolemia. Breathing rate and pulse oximetry parameters were taken to assess the degree of respiratory failure and hypoxemia. Glasgo Coma Scale was used to assess the level of consciousness and raise the suspicion of intoxication with combustion products. After exclusion of a vital-organ-threatening dysfunction, the skin burn assessment was performed.

Laboratory studies included: hematology, biochemistry, electrolytes, base-acid balance, blood gases, and urinalysis.

3. Cutaneous burn assessment

Cutaneous burns were assessed in percent of total body surface area (TBSA) affected by the burn, by evaluating the burn depth, after identifying the burn sites. After primary wound treatment, the burn wounds were covered with sterile dressings soaked with antiseptics (solutions or ointments).

4. Evaluation of inhalation injury

We suspect a smoke inhalation injury in the patients who were trapped in a confined space with large quantities of heavy smoke or fire. A skin burn on the face and neck does not reliably indicate the inhalation injury, but the soot present on the face, in the nose or the mouth of a fire victim must raise the suspicion of the inhalation injury. Clinical manifestations of inhalation injury may vary. The injury may be limited to the upper airways and manifested by nasopharyngeal irritation, hoarseness, stridor, dry cough, or may extend deeper causing tracheobronchial and alveolar destruction with the symptoms of dyspnoea, chest discomfort, bronchial breath sounds, wheezing, rales, cyanosis, and carbonaceous sputum [1].

In all patients with clinically suspected inhalation injury, the following tests were performed:

a. Blood gas analysis

Arterial hypoxemia and reduced oxyhemoglobin saturation (SaO₂) were the indicators of inhalation injury.

b. Respiratory function tests

Respiratory function tests, used as a bedside procedure, allowed an early detection and grading of the inhalation injury and helped to identify the obstruction in terminal bronchioles.

c. Fiberoptic bronchoscopy (FOB)
All patients with a suspected inhalation injury underwent bronchoscopic evaluation within 24 hours of admission for the presence of inhalation injury. Bronchoscopy was a useful tool to determine the severity of inhalation injury. The initial diagnostic FOB included the examination of tracheo-bronchial tree, assessing the length of carbonaceous deposits within trachea and bronchial mucosa. Based on the FOB findings, the inhalation injury was graded according to bronchoscopic criteria [4, 10]. Serial tracheobronchial washings for clinical care purposes were performed using an antiseptic solution (miramistin, chlorhexidine gluconate).

Blood gas analysis, functional respiratory tests and FOB results were used to choose an appropriate respiratory support tactics in the patients with inhalation injury.

Based on the initial evaluation data, the 240 study patients were distributed into 3 groups: 115 patients having isolated inhalation injury (Group 1); 43 patients with cutaneous burns only (Group 2); and 82 patients with combined inhalation injury and cutaneous burn (Group 3).

5. Chest X-ray

Chest X-ray (in supine position) was routinely performed in all burn patients at admission to evaluate the intrathoracic organs and to reveal possible complications. Further, in patients with cutaneous burns only (Group 2), chest X-rays were performed when indicated by the burn injury course peculiarities (clinical signs of pneumonia, sepsis etc.). In patients with inhalation injury (Group 1, and Group 3), the chest radiographs were taken daily in the initial 4-5 days, and further on, as indicated, depending on obtained X-ray/clinical findings, and considering the risk of potential pulmonary edema or pneumonia development.

Lung X-ray findings demonstrating the signs of pulmonary abnormalities were studied and compared to clinical findings and fiberoptic bronchoscopy and other diagnostic test results.

Lung morphology

Morphologic changes in the lungs of non-survivors were studied using autopsy material (taken at the root of the lung, at lung periphery, from pneumonia foci, from trachea). Histological examinations of specimen was performed using standard staining techniques (histology HE stain, Van Gieson's stain, MSB for fibrin stain, Loeffler’s methylene blue stain).

Lung morphology findings of non-survivors were compared with the related X-ray findings for their consistency.
**Results**

Group 1 comprised 61 male and 54 female patients with isolated inhalation injury of various severity. Their mean age was 53.20 ± 1.93 years (ranged from 18-90 years). Some of them might also have superficial cutaneous burns of the face, neck, or scalp up to 10% of total body surface area TBSA.

In Group 2, there were 32 male and 11 female patients, their mean age was 57.12±2.47 years. Their cutaneous burn size ranged from 1% to 85% of total body surface area (TBSA), with a mean of 23.12±2.57% TBSA.

In Group 3, there were 46 male and 36 female patients, their mean age made 49.76±1.96 years. The majority of them had extensive cutaneous burns, their size ranging from 11% to 95% TBSA, with a mean of 47.06±12.62% TBSA.

Total mortality in the patients of all three groups was 31.25%.

Having studied X-ray findings of burn patients, we found that pulmonary abnormalities in response to burn injury were similar by types in the patients of the three groups but differed between the groups by the time of their occurrence and their severity.

**Group 1**

In Group 1, the initial X-ray findings varied between patients depending on the severity of their inhalation injury graded by bronchoscopic criteria [4, 10].

In most of isolated Grade 1 inhalation injuries, no abnormalities in lungs were seen (66.7%) at X-ray; the signs of moderate venous congestion were revealed in 33.3 %. (Fig. 1 a, b).

In isolated Grade 2 inhalation injury, we identified an X-ray sign indicating a deep toxic damage to the terminal bronchioles induced by incomplete combustion of organic products, and toxic inhalants. That sign appeared at chest X-ray as peripherally located (mainly in the right lung) small round clear bubbles closely arranged to each other in a shape resembling a mulberry. (Fig. 2 a, b).
That X-ray sign of "mulberry" appeared as result of an impaired expiration and air retention in some alveolar groups, mainly on the right, due to lumen narrowing in the terminal bronchioles caused by their mucosa swelling. Usually, 4-5 such "mulberries" located in peripheral parts of the right lung (due the anatomy of the right bronchus) were identified at X-ray in the initial 3-4 days after thermal injury.

In the cases of lung edema, the X-ray sign of "mulberries" could not be visualized as they were concealed by the pulmonary edema X-ray appearance. The "mulberry" X-ray sign was revealed in 39% and 50 % of patients with isolated Grade 2 and Grade 3 inhalation injury, respectively (Group 1), and in 51.2 % of patients in Group 3.

Histological examination of lungs revealed a hyperinflation of individual alveoli, the spasm or luminal narrowing in some terminal bronchioles, the bronchial epithelium desquamation (Fig. 3). These abnormalities were consistent with a "mulberry" sign on X-ray.

X-ray signs of hypertension in the pulmonary circulation were more commonly found in the form of venous congestion in the patients with isolated Grade 2 inhalation injury (28.7 %).

Pulmonary edema was more common in isolated Grade 2 inhalation injury; its X-ray signs were seen as early as at day 1-2 in 27.8 % of cases. Lung edema appeared at X-ray as prominent patchy air space opacities at the root of the lung with a distortion of the lung root pattern (Fig. 4 a, b) that were consistent with lung histology findings (Fig. 5 a, b).

Pneumonia without pulmonary edema signs was identified in 21.2% of cases, more commonly in isolated Grade 3 inhalation injury, and more often at day 3-4.

Pneumonia appeared at X-ray either as a non-homogenous ill-defined shadowing of varied density or as confluent focal shadows of varied density (Fig. 6).

In 10-15 % of cases, pneumonia developed in the presence of pulmonary edema that posed certain difficulties for pneumonia identification at X-ray film (Fig. 7 a, b).

**Group 2**

In 45.1% of patients with cutaneous burns only (Group 2), no X-ray signs of pulmonary abnormalities were present (Fig. 8). Complications, if any, occurred in 46.5 % of patients and were seen at a later stage post-burn, usually at week 2 or 3.
In Group 2, lung edema occurred in 22.2% of patients at day 8-10, and pneumonia developed in 46.5% patients at day 7-31 (Fig. 9).

No "mulberry" sign was seen at chest X-ray in the patients of this Group; the absence of corresponding abnormalities in the chest was confirmed histologically in non-survivors (Fig. 10).

**Group 3**

The most severe course of burn injury was observed in 82 patients with combined inhalation injury and cutaneous burn (Group 3). Chest X-ray revealed a paradoxical response of the human body to thermal injury in 48.7 % of patients of this group: no X-ray signs of pronounced pulmonary abnormalities such as edema and/or pneumonia were seen on the initial 4-6 post-burn days (Fig 11a, 12a). But from the first post-burn day, we saw multiple "mulberry signs" at X-ray indicating a deep toxic insult to the tracheobronchial tree in the form of obstruction of terminal bronchioles (Fig. 13). This sign was most commonly seen in Grade 3 inhalation injury in combination with the skin burn of over 40 % (up to 95 %) TBSA.

Pulmonary edema was seen only in 24.3 % of patients in Group 3, being identified at day 5-7 in the patients with Grade 2 or Grade 3 inhalation injury and skin burns up to 40%-55% TBSA (Fig. 12 b). Venous congestion was found in 48.7 % of patients of Group 3 at day 1-3, more commonly in Grade 2 inhalation injury with the skin burn of 40-80 % TBSA.

Pneumonia was revealed in 34 of 82 patients (41.5 %) at day 5-10 post-burn: mainly in Grade 3 inhalation injury with the skin burn of 11-40 % TBSA, and in Grade 2 inhalation injury with the skin burn of 30-60 % TBSA. Pneumonia (more commonly bilateral) appearing at X-ray as infiltrated confluent shadows was found in 38.2 % of patents in the presence of pulmonary edema (Fig. 11 b, 12 c). We emphasized difficulties of diagnosing pneumonia and its abscess formation in the presence of lung edema and hydrothorax.

Histological studies of the lungs revealed pulmonary abnormalities in the form of impaired microcirculation with sludge and thrombi formation in the vessels of all sizes. These abnormalities were the most prominent in Grade 3 inhalation injury with an extensive cutaneous burn (Fig 14 a, b, c, d).

In combined inhalation injury with cutaneous burn, the burn injury course was seriously affected by the severity of tracheobronchial tree toxic lesion that caused a respiratory failure and deteriorated the outcome.
Fig. 1: a. Antero-posterior (AP) chest (supine) radiograph. Grade 1 isolated inhalation injury on the 1st post-burn day. No pulmonary abnormalities are seen. b. Histological examination of lung specimen. Grade 1 isolated inhalation injury on the 1st day of burn injury. Vascular congestion in alveolar septa and respiratory bronchioles are seen.
Fig. 2: a. AP chest (supine) radiograph. Grade 2 isolated inhalation injury on the 1st post-burn day. A distortion of the lung pattern is seen in the distal right lung with the presence of X-ray signs resembling mulberries by shape. b. The same radiograph magnified, demonstrating the "mulberries".
**Fig. 3:** Histopathology of the lung specimen. Grade 2 inhalation injury on the 3rd post-burn day. An inflation of some alveoli is seen in the presence of moderate pulmonary edema consistent with an X-ray sign of “mulberries”.
Fig. 4: a. AP chest (supine) radiograph. Grade 2 inhalation injury on the 2nd post-burn day. Pulmonary edema signs are seen, more prominent at the root of the lung. b. Grade 3 inhalation injuries on the 1st day of burn injury. X-ray signs of pulmonary edema are seen all over the lung fields.
Fig. 5: a. Histopathology of the lung specimen. Grade 2 inhalation injury on the 3rd post-burn day. Fluid collections in alveoli suggest a pulmonary edema. b. Grade 3 inhalation injury on the 3rd post-burn day. Prominent signs of pulmonary edema and microfocal pneumonia are present.
**Fig. 6:** AP chest (supine) radiograph. Grade 2 inhalation injury on the 3rd post-burn day. A prominent non-homogenous opacity in the left medial lung is seen in the form of patchy air space shadowing and extended root of the lung manifesting the signs of pneumonia.
Fig. 7: a. AP chest (supine) radiograph. Grade 3 inhalation injury on the 10th post-burn day. More prominent opacities suggesting pneumonia are seen against the signs of pulmonary edema. b. Histopathology of lung tissue specimen. Grade 2 inhalation injury on the 4th post-burn day. The signs of macrofocal pneumonia are identified in the presence of vascular congestion in alveolar septa and moderate pulmonary edema. c. Grade 3 inhalation injury on the 5th post-burn day. Signs of macrofocal pneumonia are seen in the presence of pulmonary edema.
Fig. 8: AP chest (supine) radiograph. Skin burns of the 1-2-3 degrees in the area of 45% TBSA (with 3 degree burn of over 20% TBSA). The 1st day of burn injury. No pulmonary abnormalities are seen.
Fig. 9: AP chest (supine) radiograph. Skin burns of 45% TBSA. The 7th post-burn day. Pulmonary edema signs and more prominent patchy air space shadowing are seen suggesting pneumonia.
**Fig. 10:** Histopathology of lung specimen. Skin burns of 42% of TBSA. The 14th post-burn day. The slide demonstrates the signs of confluent pneumonia with necrosis sites and fibrin.
Fig. 11: Serial AP chest (supine) radiographs. Grade 3 Inhalation injury, skin burns in the area of 40% TBSA: a. The 1st day of burn injury. No signs of pulmonary abnormalities are seen. b. The 7th post-burn day. The X-ray signs of bilateral hydrothorax, and pulmonary edema are seen.
Fig. 12: Serial AP chest (supine) radiographs. The combination of Grade 2 inhalation injury and skin burn of 95% TBSA. a. The 2nd post-burn day. No signs of pulmonary abnormalities are seen. b. The 7th post-burn day. Pulmonary edema signs are identified. c. The 10th post-burn day. Against the signs of pulmonary edema, more prominent infiltrated shadows are revealed indicating pneumonia. Opacification in inferolateral parts of the left pulmonary field raises the suspicion of the pleural effusion.
**Fig. 13:** AP chest (supine) radiograph. Grade 3-4 inhalation injury with skin burns of 14% TBSA. The 1st day of burn injury. Multiple "mulberries" in the right lung periphery are seen in the absence of any other abnormalities.
Fig. 14: Histopathology of lung specimen. Grade 2 inhalation injury with the skin burn of 65% TBSA. a. At 5 hours post-burn. A vascular congestion in alveolar septa is revealed. Erythrocyte sludges are present within the vessels. Inflation of some alveoli is seen corresponding to a "mulberry sign" identified at X-ray. b. Grade 2 inhalation injury with the skin burn of 95% TBSA. At 36 hours of burn injury, histology demonstrates the signs of the capillary congestion, emphysema, blood clots, and sludges in the blood vessels. c. Grade 2 inhalation injury with the skin burn of 57% TBSA. At 48 hours of burn injury, the histological examination demonstrates the signs of alveolar inflation consistent with X-ray "mulberry signs", emphysema, blood clots in vessels. d. Grade 3 inhalation injury with the skin burns of 75% TBSA. At 60 hours post-burn, the signs of capillary congestion, emphysema, clot formation are seen.
Conclusion

In conclusion, the chest X-ray performed in 240 patients with thermal injury in the initial days post-burn demonstrated differences between the three designated groups of patients in the time when pulmonary complications occurred.

1. We identified the X-ray sign of "mulberry" indicating the presence of a deep toxic damage inflicted by inhalation injury to the tracheobronchial tree (TBT), involving terminal bronchioles. This sign of multiple "mulberries" is usually seen at lung periphery (predominantly on the right side). This sign suggests an impaired patency of terminal bronchioles due to their constriction in spasm or mucosal toxic injury that leads to an impaired expiration and air retention in individual alveoli, which was confirmed clinically and histologically.

The "mulberry" X-ray sign may be detected in the initial 3-4 days of inhalation injury. It is generally absent in cutaneous burn alone. It cannot be visualized against the pulmonary edema signs present at X-ray.

In isolated inhalation injury, pulmonary edema and pneumonia are identified early: on the 1\textsuperscript{st}-2\textsuperscript{nd} day, and the 3\textsuperscript{rd}-4\textsuperscript{th} day post-injury, respectively; the most pronounced pulmonary abnormalities being observed in Grade 2 and Grade 3 inhalation injury.

2. In combined inhalation injury and cutaneous burn, no X-ray signs of pronounced abnormalities (pulmonary edema, pneumonia) are seen in the lungs on the initial 5-6 days post-burn. Meanwhile, the X-ray signs of moderate venous congestion may be revealed in 43.6 % of patients; and X-ray "mulberry signs" may be seen in 51.2 % of patients indicating a severe toxic injury of the terminal bronchioles.

Histological examination of lung specimen from non-survivors of Group 3 demonstrated pulmonary abnormalities in the form of impaired microcirculation at all levels with sludge and thrombi formation in the vessels of all sizes that were seen neither in the patients with isolated inhalation injury (Group 1), nor in those with cutaneous burn alone (Group 2).

Lung edema and pneumonia in the patients of Group 3 are revealed at X-ray at later stages: at day 5-9, and day 6-7, respectively. Absent X-ray signs of pulmonary abnormalities (pulmonary edema and/or pneumonia) in patients with combined inhalation injury and cutaneous burn in the initial days post-burn may suggest a severe thermal injury with a deep toxic damage to the tracheobronchial tree and an impaired
microcirculation at all levels. In our study that was confirmed by histological studies of lung specimen from non-survivors.

In combined inhalation injury with cutaneous burn, the burn injury course is seriously affected by the severity of tracheobronchial tree toxic lesion that may cause a respiratory failure and deteriorate the outcome.

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