CLINICAL AND AUTOPSY DIAGNOSES OF VISCERAL AFFECTIONS OF PATIENTS WHO DIED BECAUSE OF COMPLICATED BURNS WITH MULTI-ORGAN FAILURE

Taran A., Baciu N., Rafulea V., German A.

Nicolae Testemitanu State Medical University and Hospital of Orthopaedics and Trauma, Chisinau, Republic of Moldova

SUMMARY. The anatomicopathological investigations carried out in a total number of 186 cadavers during the last decade were reviewed. In these retrospective studies of necropsy protocols related to different affections of visceral organ systems that evolved asymptomatically, 30.1% involved the neurological system, 36.0% the uropoiesis system, 34.4% the gastrointestinal system, 52.0% the hepatobiliary system, and 39.7% the cardiovascular system, with a prevalence in the pulmonary system of 64.2%. A comparative analysis of the incidence of affections detected in various visceral organs (on the basis of necropsy data in the 186 burn patients) and the incidence of their clinical manifestations showed that in 35% of patients with extensive and deep burns all of these conditions developed asymptomatically and were diagnosed only through autopsy.

Introduction

When patients die, autopsy is considered to be the optimal standard to confirm clinical diagnosis. Not only does autopsy enable the clinician to verify the accuracy of the primary clinical diagnosis but post-mortem pathological findings are also relevant to medical education. In this study we attempted to tackle exhaustively all severe burns in order to outline the wide range of visceral alterations caused by thermal traumatism, which, after comparison with clinical and pathomorphological data, would enable us to define a set of criteria for the prognosis, diagnosis, and appropriate treatment of the disturbances observed.

In particular, we intended to specify the relationship between burn severity, the manifestation of secondary organic modifications, and the safety of the perfusion therapy prescribed, thus emphasizing the qualitative specifics of dangers occurring, with a view to improving the modalities of their identification and operative treatment.

Methods

With these objectives in mind, we considered 186 reports specifying the findings of autopsies of victims with complex burns performed at the National Centre of Thermal Injuries of the Republic of Moldova in the period 1989-2003, with the intention of comparing the pathomorphological and organic-systemic deteriorations with their clinical manifestations on the basis of a retrospective analysis of the relevant records.

Autopsy was performed within 24 h of death in each patient. The procedure included a macroscopic and a microscopic assessment of all internal organs and of the brain, when indicated. The following information was extracted from each patient’s record: burn size percentage, age, sex, the score algorithm of the organic pathology for patients with thermal injuries, pre-mortem clinical diagnosis, and autopsy findings.

Results

On the basis of our observations, we can state that our retrospective analysis of necropsy records denoted a variable incidence of destructive processes in the visceral organs: 30.1% in the neurological system, 36.0% in the uropoiesis system, 34.4% in the gastrointestinal system, 52.0% in the hepatobiliary system, and 39.7% in the cardiovascular system, with a prevalence in the pulmonary system of 64.2% (Fig. 1).

A comparative analysis of the incidence of affections detected in various visceral organs (according to the necropsy data in the 186 burn patients) and the incidence of their clinical manifestations proved that in 35% of patients with extensive and deep burns all of these conditions developed asymptomatically and were diagnosed only through autopsy.

Fig. 1 - Incidence of visceral injuries in patients who died of severe burns in relation to area affected.
extensive and deep burns all of these developed asymptotically and were diagnosed only through autopsy.

**Pulmonary modifications caused by deep and extensive burns and their clinical manifestation**

The investigations of the lungs of persons who died at different stages of development of deep and extensive burn disease identified a pulmonary pathology in 108 cases (58%) of the 186 deceased persons examined. The majority of the deceased persons showed respiratory injuries of a certain degree (Fig. 2).

Data on the incidence of pulmonary embolism in thermally injured persons are rather contradictory. In the opinion of some local and foreign researchers, pulmonary artery embolism is deemed to be a cause of death in 3.7% of cases; in the opinion of others, embolism caused the death of 6% of burn patients with lethal development. Thromboembolism of the pulmonary artery caused three deaths in the cases considered.

Diffuse pulmonary oedema, found in 14 patients (17.5%), remains one of the most frequent occurrences in the first post-burn period.

According to our pathomorphological study, pneumonia had an even higher incidence - 125 persons (67.2%), particularly elderly persons, died during thermal shock. Eighty-two per cent of patients died of pneumonia in the second phase of thermal burn development (4-45 days post-burn), and 21% of patients died of pneumonia at a later phase.

Out of the 108 patients who died because of their pulmonary injuries, 45 (41.7%) underwent a bilateral pneumatic inflammatory process, including nine patients with all lung lobes affected by this inflammatory process. Only the lower lobes were affected in 32 other patients and only the upper lobes in 23 patients. The pneumonia was unilateral in eight patients. The extended pneumatic process proved to be the most frequent cause of fatal development among burn patients.

The retrospective analysis of clinical records of the 108 patients with pulmonary affections diagnosed through necropsy established that pulmonary affections occurred clinically in only 62 patients (57%).

The clinical manifestations of pulmonary injuries caused by thermal shock are shown in Fig. 3.

The analysis of statistical data describing clinical manifestations of pulmonary alterations diagnosed through the pathomorphological examination of deceased burn patients revealed that they increased in comparison with the initial stages of burn disease development.

**Pathomorphological data featuring injury to the cardiovascular system versus the victims’ clinical conditions**

In our opinion, it would be more reasonable to distinguish two categories of burn-related cardiovascular complications: 1. accidents resulting directly from the burn disease; and 2. complications occurring in patients with cardiac antecedents, when a thermal trauma only aggravated pre-existing cardiac dysfunctions.

**Myocardial affections of patients who died of thermal shock**

Cardi ovascular affections were diagnosed in 74 patients (39.7%) who died at different stages of burn disease development. We carried out morphological examinations on 53 hearts of burn patients who died during thermal shock and we identified cardiovascular affections in 21 deceased patients, i.e., about 39.6% of the total number of hearts of persons who died during thermal shock. The majority of the hearts presented deep, extensive burns in over 20% of the tegumentary surface, while 15 hearts (28.3%) also had burns in the respiratory tract. The great majority of hearts did not present cardiomegaly; 17 deceased patients had subepicardial punctate and petechial haemorrhages. The cardiac muscle appeared violet in section, while the histological examination identified vast microcirculatory disorders. The blood vessels, especially the veins, appeared dilated, overloaded, and in capillary stasis. Blood clots were distinguished in the lumen of minuscule arteries and in veins, and haemorrhages in the subepithelial stratum.

The clinical morphological disturbances detected in the burn shock stage manifested themselves in retrosternal pains, which were recorded, among other symptoms, in 14 patients from the respective target group, including six patients who suffered from hypertonic disease and cardiac atherosclerosis. Four other patients felt these pains for the first time in their life, i.e. based on other signs typical of severe burn shock. The sensations observed were constrictive and localized retrosternally, but tended to irradiate only in one of these patients. In other deceased patients, these sensations were constrictive or manifested themselves through a stitch. It should be noted that two patients felt retrosternal pain even after minor efforts. Dyspnoea was recorded in the majority of patients with severe
burns in the first days post-trauma, and when their state degenerated into haemodynamic insufficiency it was recorded as being among the prevalent symptoms.

Our observations confirmed the data from other field-related research, showing that diffuse myocardial deteriorations occur during shock, which remain conspicuous during the entire post-burn development interval. We thus deduced that thermal burns were associated with deteriorations in the cardiovascular system.

Myocardial alterations in patients who died in the second and third phases of the burn disease

Severe cardiovascular affections were diagnosed in 33 (17.7%) of the 82 patients who died in phase 2 of the burn disease (4-15 days). Fig. 4 gives an overview of the cardiac phenomena observed.

As shown in Fig. 4, myocardial injuries were detected in a rather large number of patients who died of thermal burns. Sometimes they were less manifest (moderate dystrophies) in the patients’ lifetime and were not absolutely involved in the development of the disease and its termination. In other cases, these were major injuries (myocarditis, infection, diffuse dystrophies), emerging in the foreground, often being the immediate cause of lethal development. However, no considerable alterations of the cardiac muscle were detected by necropsy in any of these cases.

On the basis of the retrospective analysis of the clinical records, it was established that symptoms characterizing cardiac insufficiency during the second and third stages of post-burn disease respectively occurred clinically only in six out of 33 patients (8%) and in 15 out of 20 patients (21.1%) who died at these developmental stages (Fig. 5).

Fig. 3 - Clinical phenomena signalling early pneumonia caused by thermal traumatism

Fig. 4 - Myocardial affections detected in patients who died in the second and third stages of post-burn development (53 cases with cardiovascular injuries).
Our study confirms that cardiovascular alterations start in the first hours and even minutes after the accident. The subsequent development of these haemodynamic dysfunctions depends totally on the severity of the thermal injury. Most of the haemodynamic dysfunctions observed immediately after the accident reflect feedback of the organism attacked by thermal injury and are part of the burn disease concept.

Pathomorphological analysis of ulcerous and erosive affections of the digestive tract of deceased burn patients

Our retrospective analysis of the results of necropsies of 186 persons who died because of severe burns in the period 1989-2003 revealed that ulcerous and erosive affections were diagnosed in 64 deceased patients (34.4%) and that these affections proved to be the defining cause of death (by severe perforations and haemorrhages) in 4.3% of the burn victims examined, including acute ulcers in 26.7% of the victims (Fig. 6). If other erosive and haemorrhagic processes are added to these, the percentage of such injuries rises to 42.5%.

Over the last three years a clear decrease in the incidence of ulcerous and erosive affections was observed through necropsy. The clinical diagnosis of ulcerous and erosive injuries of the digestive tract of persons with severe burns is rather difficult, since these injuries develop asymptomatically and are detected more often by necropsy. Conditions of shock or septicaemia, especially in deep, extensive burns, make anamnestic, clinical, and instrumental examinations very difficult.

It should be noted that ulcerous and erosive injuries developed asymptomatically and were identified only during the autopsy of 75% of patients with severe burns. The incidence of digestive tract injuries found in patients with severe burns and their clinical manifestation is presented in Fig. 7.

In the cases that we studied and analysed retrospectively, the most characteristic sign of digestive tract affections was the sensation of heaviness in the epigastrium, identified in respectively 48 cases (26.6%) and 57 deceased patients with lethal burns in 1989-2003.

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Fig. 5 - Incidence of clinical manifestations characterizing cardiovascular injuries diagnosed by necropsy.

Fig. 6 - Incidence of ulcerous affections of gastrointestinal tract of persons with lethal burns.

Fig. 7 - Incidence of symptoms relevant to digestive tract lesion in patients who died of burns in 1989-2003.

Fig. 8 - Incidence of ulcerous and erosive affections of digestive tract of persons who died at different post-traumatic stages.
patients (30.4%). “Coffee-grounds” vomiting and melena, as relevant phenomena of ulcerous and erosive injury of the digestive system, manifested themselves in respectively 34 patients (18.1%) and 12 deceased burn patients (6.4%) in our study. In respectively 26 patients (40.6%) and 14 deceased patients (21.8%), digestive tract affections manifested themselves clinically in epigastric pains and pyrosis.

It is also worth mentioning the fact that over the last three years the incidence of acute ulcers underwent a relative increase in the shock and toxemia phases, as also those caused by burn cachexia. On the one hand, this phenomenon could be accounted for by endoscopic investigations, now available for the earlier stages of disease development after the accident, and, on the other, by more appropriate and timely treatment for the prevention of acute digestive ulcerations (Fig. 8).

Gastrointestinal affections diagnosed by necropsy are represented by localization in Fig. 9.

Massive haemorrhages occurring suddenly from the digestive mucous membrane remained as dangerous as before. In all, 19 haemorrhages were estimated in the period 1989-2003 (Fig. 10), including nine cases in which acute gastric ulcers were found and seven with intestinal ulcers (five duodenal ulcers and two ulcers in the caecum and colon). Perforations of gastric and duodenal ulcers were diagnosed on incision in three deceased patients (two gastric ulcer perforations, one duodenum perforation, and one intestine perforation).

Haemorrhage or ulcer perforation of the abdominal compartments very often occurred as the first symptom of digestive tract injury. Clinical pre-monitoring signs of these incidents are presented in Fig. 11: “coffee grounds” were detected in 11 deceased patients, vomiting with blood in five, and melaena in three. Signs of peritoneal irritation were detected in only two patients.

Comparing the results of anatomopathological investigations of the 186 cadavers examined in the last decade, we concluded that ulcerous and erosive affections of the digestive tract constituted phenomena that frequently complicated the development of severe burns, often becoming the cause of lethal developments. Their identification, and especially their timely prognosis, are therefore a must, in order to diminish their severity and effectively eliminate them.

To this effect, it is necessary to extend the implementation of oesophagogastroduodenoscopy techniques and to develop more informative and reliable methods for the diagnosis and treatment of these incidents, which may become decisive for the final curative outcome of patients with deep, extensive burns.

Pathomorphological modifications of kidneys in persons with thermal burns and their clinical manifestations

Pathomorphological modifications of the kidneys in persons with thermal burns were identified in 67 cases (36%). On the basis of the findings reported in Fig. 12, we can conclude that in young patients renal functions usually recovered quickly with adequate treatment, even in cases of extensive burns. Irreversible renal dysfunctions were identified in 11 (5.9%) of the 186 patients examined by necropsy (average age, under 31 yr).

Our retrospective analysis of the clinical records found that clinical and laboratory symptoms of renal affections
were present in 49% of cases.

**Hepatic morphostructural alterations found in deceased burn patients**

Hepatic morphostructural alterations were found in 97 patients (52%) who died of their burns, of whom 34 had deep burns in more than 50% body area. Fourteen persons were in burn shock, 48 died in 4-45 days post-trauma, and 15 died of burn-related cachexia at later phases.

Our retrospective analysis indicated that clinical and laboratory symptoms of hepatic affections occurred in 58 cases (31.1%).

The pathomorphological examination of patients who died soon after their injury showed considerable sanguine repletion of the liver, firm when palpated, with a twisted internal margin that was violet or red-brown in section. The persons who died a few hours after their accident presented large quantities of condensed blood running out of the organ’s texture.

It was our intention to specify the pathological morphology of hepatic degradations using necropsy material from patients who died as a result of burn cachexia, and we established that the most conspicuous modifications occurred at the hepatic parenchyma level, where atrophy and fat necrosis were observed.

**Pathomorphological alterations of the nervous system**

For a more complex understanding of the multiple clinicopathogenetic aspects that characterize visceral injuries from burns degenerating subsequently into multi-organ failure, it is indispensable to thoroughly examine the pathomorphological deteriorations of the nervous system at different phases of post-burn development.

The pathomorphological examinations of 56 patients (30.1%) who died between two hours and two months post-trauma revealed modifications of the central and peripheral nervous system. Clinical signs of inhalation injury of various degrees were diagnosed in 27 (48.2%) of these 56 deaths. Our retrospective analysis of the clinical records showed clinical and laboratory symptoms of affection of the neurological system in 28 patients (15%) (Fig. 13).

Moderate oedema of the soft meningeal structures and cerebral substance was discovered in all the cases studied macroscopically. The histological examination of the cerebral substance identified oedema and compression of the meningeal teguments, moderate dissociation of the fibrous structures, and signs of stasis in average and small vessels.

**Discussion**

A burn is not only one of the most severe skin injuries but also a very complicated disease with a large variety of morphological and functional multi-system lesions. Autopsy findings provide an appropriate morphological analysis when oriented to an adequate investigation and retrospective evaluation of the overall clinical findings during the hospitalization of patients. A properly conducted autopsy has a very practical value, because it permits comparison between clinical and post-mortem diagnosis and yields the true cause of death.¹,²

Systemic inflammatory response syndrome (SIRS) leading to multiple organ failure (MOF) continues to be a major problem after surgery and trauma. MOF is a critical condition developing in patients with overwhelming bodily injury resulting from severe traumas, extensive burns, and sepsis. MOF accounts for up to 80% of all intensive care unit (ICU) deaths and costs millions of dollars due to prolonged ICU-bed occupancy.³,⁴ MOF is one of the major causes of death in patients with severe burns. The pathogenetic mechanism that links these conditions is SIRS. SIRS is defined as a failure of local control of the inflammatory response to injury or infection, allowing the inflammatory process to spill over and damage organs remote from the site of injury.⁵ As the component parts of the integrated inflammatory response to injury and infection are identified, and their potential role in the development of SIRS studied, experimental attempts have been
made to modulate key mediators in an attempt to attenuate this response. Because the release of key inflammatory mediators is extremely rapid, it is now becoming clear that for such an approach to be successful, patients at risk must be identified very early in the course of their injury or insult.

Zhang presents an analysis of the relationship between invasive infection and the multiple organ dysfunction syndrome (MODS) in 158 burn cases. Morbidity in MODS is high, reaching 81.6%, and there is a 50% possibility that it will become progressive MOF. Death is associated with MOF rather than with MODS. Mortality in MOF is very high - over 90%. Among various microbes, Pseudomonas pyocyanea causes the highest morbidity in MODS. The diagnosis and treatment of MODS are difficult, and it is therefore essential to control invasive infections.

A retrospective study was conducted on 5321 burn patients hospitalized in a burn centre in Jinzhou, China, during the period 1980-1998. The overall mortality rate was 0.86%. The high survival rate may be related primarily to the low percentage of elderly patients and patients with severe burns. Inhalation injuries, infections, and MOD are the main causes of death in burn patients and should be key targets to improve clinical care, as also in future studies.

Autopsy data alone provide only a crude measure of trauma system effectiveness, but these data may influence injury severity scoring and hence the probability of survival calculation. Streat and Civil compared clinical and autopsy data to derive the abbreviated injury scale (AIS) and the injury severity score (ISS) in 279 trauma patients. The ISS score derived from post-mortem data were identical to those derived from clinical data in only 31% of patients. Accurate data collection incorporating autopsy is necessary for panel studies using “preventability of death” as the major criterion and for those involving comparison of trauma registries.

Stothert examined the differences between clinical impressions and autopsy findings in a group of patients dying in a university surgical service after blunt injury, penetrating injury, or thermal burns. Major discrepancies in clinical diagnosis versus the anatomical diagnosis at autopsy were found to occur in approximately 30% of patients.

In Wu’s research, 41 patients with extensive burns complicated by severe MOF were studied. This condition was diagnosed in the shock stage in 14 patients (34.1%) and in 27 cases (65.9%) in the infectious stage. Among them, 37 patients presented associated inhalation injuries. Two organs were affected in 29 cases, three organs in six cases, and four organs in four cases. Pulmonary function failures were found in 29 cases, cardiac failures in 21 cases, gastrointestinal function failures in 19 cases, renal function failures in 16 cases, liver function failures in nine cases, and coagulation function failures in four cases. Thirty patients died and 11 survived.

These data support the continued practice of effecting an autopsy in all patients dying from trauma. This information is clinically relevant. In many cases visceral affections develop asymptotically and can therefore be diagnosed only by autopsy.

Over a 4-yr period (1986-1990) we performed 40 autopsies on burn patients. Twenty-three of these survived one to ten days following the accident, eleven died between 11-40 days post-burn, and six patients survived until day 41 post-burn. Almost 70% of the patients (28 cases) presented inhalation injury, and half (20 cases) presented MOF. The organs most frequently affected were the lung (38 cases), followed by the heart (23 cases), the kidney (17 cases), and the liver (15 cases). MOF appeared to be unrelated to the onset and efficacy of fluid replacement. The aim of this study was to demonstrate the importance of close collaboration between clinicians and pathologists and the clinical correlation between burn autopsy, management, and burn injury therapy.

Clinical and pathological diagnosis varies among burn centres and may cause confusion. An international standardization register should be sought to permit comparison of results in order to determine whether the practice of requesting an autopsy for patients who die in medical ICUs continues to be a valid approach to obtain clinically and educationally relevant findings.

Autopsy findings confirmed 81% of clinical diagnoses, and in 16% of cases they revealed a major diagnosis that, if known before death, might have led to a change in therapy and prolonged survival (class I missed major diagnoses). The most frequent class I missed major diagnoses were fungal infections, cardiac tamponades, abdominal haemorrhages, and myocardial infarctions. Another 10% of autopsies revealed a diagnosis that, if known before death, would probably not have led to a change in therapy (class II error).

Conclusions

Autopsy remains an important tool for education and quality control. The anatomopathological investigations were carried out on a total number of 186 cadavers examined during the last decade. In retrospective studies of necropsy protocols related to different affections of visceral organs systems that evolved asymptomatically, 30.1% affected the neurological system, 36.0% the uropoiesis system, 34.4% the gastrointestinal system, 52.0% the hepatobiliary system, and 39.7% the cardiovascular system, with a prevalence of the pulmonary system (64.2%).

Comparative analysis of the incidence of affections detected in various visceral organs (on the basis of necrop-
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Address correspondence to: Anatolie Taran, MD, Ph.D., Teilor 11 ap. 77, Chisinau, MD-2043, Republic of Moldova. Tel: (373) 22 24 34 08; fax: (373) 22 24 - 23 - 44; e-mail: anatol_taran@yahoo.com / ataran@umich.edu