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Clinico-statistical and morphological aspects of severe traumatic brain injuries

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Abstract

Traumatic brain injuries (TBIs) represent a problem of public health all over the world if we consider its incidence, mortality and the big social costs. The increase of road and train traffic, the development of industry, the growth of alcohol consumption, the emergence and increase of terrorist attacks have led to more frequent and severe TBIs. There were registered 3260 deaths at the Institute of Forensic Medicine in Craiova, Romania, between 2010 and 2014; they were the result of severe traumas, 622 (19.07%) being caused by TBIs. The most affected by TBIs were men (the men/women ratio was of 3/1) and the elderly, mainly in the rural area. The main risk factor was alcohol intake; about 44% of the deceased people were under alcohol influence. The forensic examination highlighted the severity of cerebral meningeal lesions, the most frequent being cerebral and vascular lesions. The histopathological and immunohistochemical examinations emphasized various microscopic changes in accordance with the severity of the trauma and the time passed from impact until death.

Keywords: traumatic brain injury, traumatic impact, brain edema, morbidity, disability.

Introduction

Traumatic brain injuries (TBIs) represent a problem of public health all over the world, with a very high morbidity and mortality. According to the specialized research, there are about 10 million cases of TBIs worldwide every year [1, 2]. It is hard to estimate the incidence and prevalence of TBIs worldwidely and regionally because the statistics rely only on the cases that need to be hospitalized. For example, the data provided by the *Centre for Disease Control and Prevention*, in USA, show that the estimated average incidence of TBIs between 2002 and 2006 was of 576.8 to 100 000 inhabitants; however, these data do not include the patients who were treated in the ambulatory care institutions [3]. Some specialists [4] consider that the incidence of TBIs worldwide is at least 200/100 000 inhabitants, whereas other studies emphasize that the annual incidence is around 600/100 000 inhabitants [5]. Controversial information may also be found in the epidemiological studies in Europe. For example, a study in a certain region of Spain estimated an annual average of TBIs incidence of 91/100 000, whereas a study in Sweden estimated an incidence of 546/100 000 [3].

TBIs can be the result of the physical trauma of the head, which can occur during work (work accident) or sport activities, road accidents, military conflicts, terrorist events, etc. [4].

TBI is the main cause of violent death and invalidity. Thus, there are about 5.3 million people in the USA alone living with a permanent disability because of severe traumatic brain injuries [6]. In 2010, TBI was the main cause of death in 30% of all death cases in the USA and in 40% of all death cases of people less than 45 years old [7, 8]. From a social point of view, TBI represents a continuous problem for the victims, their families and the society they live in, since a mild TBI can lead to invalidity, which implies huge social and medical costs; the total costs generated by moderate or severe TBI (including the direct and indirect medical costs) were estimated at $ 60 billion in 2000 in USA [4, 9] and to $ 8.6 billion in 2008 in Australia [4].

Brain injuries have huge consequences not only on a person's life but on all the members of his/her family. It is not easy to recover and, moreover, he/she cannot do this alone. The person with disability needs help from all the people around him/her and the effort should be continuous, supportive and offered especially by therapists or teachers who are well informed and trained to do this.

Brain injuries generally affect the people's ability to perform complex skills such as reading, speaking or writing. Mild forms may lead to dyslexia or other disorders, while the most severe ones can determine the total loss of these abilities. Such people may never recover, but those with less severe forms have big chances to improve in time and overcome difficulties in expressing themselves

or performing reading or spelling activities. Generally speaking, children with minor brain injuries are likely to learn faster and successfully pass over their learning disabilities if proper teaching methods and strategies are applied. However, the way they develop is unpredictable since children with brain injuries may do really well in one field and poor in other areas. They are all different; therefore, their progress is hard to be anticipated.

Our research aims at assessing the clinico-statistical and morphological aspects of severe TBI, which caused the death of the patients, based on the autopsy reports from the Institute of Forensic Medicine, Craiova, Romania.

Materials and Methods

Our study was retrospective; we analyzed the forensic autopsy reports performed on bodies between 2010–2014 by the Institute of Forensic Medicine in Craiova. Thus, we mainly analyzed the cases where the traumatic brain injury was declared as the cause of death by the forensics report. The statistical processing of data was done using MS EXCEL. We focused on demographical indices as well as on legal ones, on the mechanism that led to the traumatic brain injury, the acute intoxication with alcohol and the influence of alcohol on the production of traumatic brain injury, the time period between the production of the lesion and the victim's death, the morphology and association of various lesions related to the traumatic brain injury. The main macroscopic morphological aspects were emphasized on photos selected from the collection of the Institute of Forensic Medicine in Craiova, which were taken during our research period.

In order to complete the study of the lesions, we analyzed samples of cerebral tissue from the pathological and immunohistochemical point of view. They were taken when the necropsy was done; they were fixed in formalin and included in paraffin, according to the standard pathological protocol. For the classical pathological study, we used the Hematoxylin–Eosin (HE) and Goldner–Szekely (GS) trichrome stainings.

The immunohistochemical study was done on the same pathological material, included in paraffin. The biological material was cut with the help of the spinning microtome HM350, equipped with a system of transferring the sections on water bath (STS, microM). The histological sections were taken on poly-L-lysine covered blades and dried in a thermostat at 37^0C for 24 hours. Then, the sections followed the classical protocol: deparaffinization and rehydration. In order to reveal the antigen, the blades were boiled in a sodium citrate solution, pH 6, for 21 minutes (seven cycles of three minutes each) in a microwave oven. When the blades cooled down after the boiling process, they were washed with tap water and distilled water for 15 minutes. The blocking of the endogenous peroxidase was achieved by incubating the histological sections in 3% oxygenated water, for 30 minutes at room temperature, followed by their washing in distilled water for 10 minutes and a washing in 1% phosphate-buffered saline (PBS) solution, for 5 minutes. The next step was the blocking of non-specific sites using 2% skimmed milk for 30 minutes. The sections were then incubated with primary antibodies for 18 hours (overnight) in a fridge at 4^0C. The second day, we applied the secondary biotinylated antibody for 30 minutes at room temperature, then the washing in 1% phosphate buffered solution (three baths, five minutes each), and in the end the HRP (Horseradish Peroxidase) Streptavidin for 30 minutes, at room temperature; finally, the blades were washed in 1% PBS 3×5 minutes. The signal was detected using 3.3'-Diaminobenzidine (DAB) (Dako) and the reaction was stopped in 1% PBS. We counterstained the sections with Mayer's Hematoxylin; we dehydrated them in alcohol, cleared in xylene and mounted on slides with DPX (Fluka).

In our study, we used the following markers: anti-GFAP (clone 6F2/ M0761, Dako, 1:200 dilution), anti-CD34 (clone EP373Y/ ab81289 Abcam, 1:100 dilution) and anti-CD68 (clone KP1, Dako, 1:200 dilution).

Results

Between 2010 and 2014, within the Institute of Forensic Medicine in Craiova there were performed 3260 autopsies in order to discover the medical cause of death for injured people or assumed to be injured. The study of the autopsy reports revealed that of the total number of 3260 deceased people, 622 (19.07%) presented brain injuries, the rest 2638 having other causes (Figure 1).

Investigating the distribution of deaths according to sex, of the total number of dead people with brain injuries, 478 (76.85%) were men and only 144 (23.15%) were women, the ratio men/women being of 3/1 (Figure 2).

As for the living environment, we noticed that 392 (63%) cases of brain injury were recorded in rural area, whereas in the urban area only 230 (37%) cases, the ratio urban/rural being of 1/1.7 (Figure 3).

Following the distribution of TBI on age groups, we concluded that they can occur anytime from infant period to old people. Our graph (Figure 4) shows a significant proportional growth of the cases of death caused by TBI once people get older. In the first decade of life (between 0–10 years old), only 22 (3.54%) cases of death caused by TBI were registered, whereas in the seventh decade of age (61–70 years old), 124 (19.93%) cases of TBI were registered as the cause of death. An important number of cases were also registered between 41 and 50 years old (97 cases – 15.39%) and between 51 and 60 (111 cases – 17.85%). The decrease of the number of cases to people aged over 71 may be the result of the low number of people who attain this age, the risk factors for this decade of life being identical with those that characterize the previous age decades.

Analyzing the legal context and the circumstances, which led to TBI, we concluded that the highest number of cases (284 cases, 45.66%) was the result of various accidents (falls, animal aggressions, falls from vehicles, height falls, etc.). We did not take into consideration the aggressions or car and train accidents. The second cause of death because of TBI was the road accident with a total number of 236 (37.94%) cases. The hit-projection mechanism was the most frequent cause of TBI in car accidents (168 cases, 71.19%). There were also other complex mechanisms observed in road accidents based on the association of three simple mechanisms, 164 cases being considered as multiple mechanisms. Twenty-seven cases of death caused by TBI (4.34%) were the result of train accidents. Overall, car and train accidents generated

263 cases of death, representing 42.28%. Besides accidents, 71 cases were the result of murders, mainly the hitting mechanism with hard objects, and a small number was the result of hitting with splitting objects (axe, hoe, scythe, etc.). There were also four suicidal cases (two cases of shooting and two cases of falls from height). The active hitting as a simple mechanism – 72 cases – was observed both in aggressions and in car accidents. Road accidents include other mechanisms, such as compression even splitting (also in train accidents). There were 10 cases of multiple brain injuries with no specified cause. Likewise, 88 cases of TBI occurred as a result of the fall from the same level (fall on ice, from a car, on the stairs); other cases of falling which led to severe TBI occurred after stroke; in this cases, the lack of investigation data raised suspicions regarding the way the traumatic lesions were produced (Figures 5 and 6).

Alcohol is one of the most important risk factors involved in the etiopathogeny of TBI. In order to evaluate the degree of alcohol intoxication to TBI subjects, we took biological samples from 252 people from the total number of 622; in the rest of the cases, we did not take any blood since the long period of survival led to the metabolization of the ethylic alcohol. Evaluating the percent of alcohol and its sex distribution, we concluded that, of a total number of 252 cases, 141 did not have ethylic alcohol in their blood (101 men, 40 women). Of 111 people with TBI and the presence of blood alcohol, 48 cases had the blood alcohol concentration between 0–0.8 g‰ (34 men, 14 women); 34 cases had the blood alcohol concentration between 0.8–2 g‰ (28 men, six women), 25 people (21 men and four women) had an blood alcohol concentration between 2–3 g‰, and to four cases, the values of blood alcohol concentration were bigger than 3 g‰ (Figure 7).

Another parameter that we investigated was the time passed from the production of the lesion until death. Of 622 cases of TBI, 279 survived for more than three days; 90 cases of survival were between one and three days, 147 cases survived between 0 and 24 hours and 85 cases instantly led to death. In the case of 21 subjects, we could not exactly predict the survival period because of the lack of research data, death having occurred outside the hospital (Figure 8).

The macroscopic aspects of the cerebral meningeal lesions observed during the necropsy examination revealed different types of cerebral lesions associated with meningeal lesions in 485 cases: contusions and cerebral dilacerations, diffused cerebral meningeal hemorrhages, intracerebral hematoma, intraventricular hemorrhage, etc.; we noticed massive brain dilacerations to 29 cases (Figures 9–13). Meningeal lesions were either unique or associated with other cerebral lesions. Thus, in 137 cases, the meningeal hemorrhage was identified as a unique lesion and had the form of an extradural hematoma to 28 cases, subdural hematoma in 37 cases and leptomeningeal hemorrhage in 72 cases (Figures 14–17).

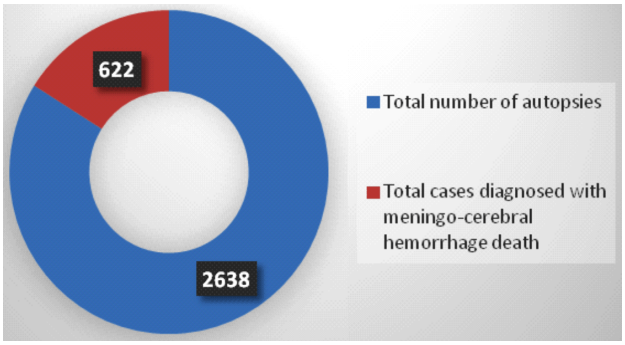

Figure 1 – ***Ratio between cases of TBI-caused death and death by other causes; the autopsy was done in the Institute of Forensic Medicine in Craiova.***

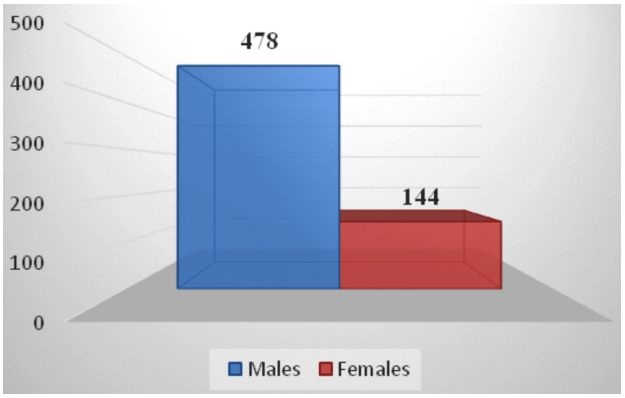

Figure 2 – ***Distribution of TBI cases on sexes.***

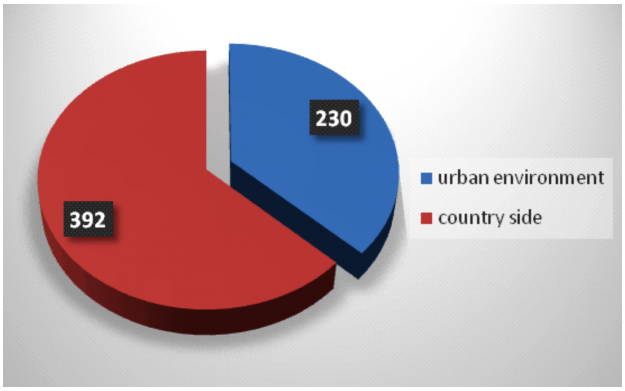

Figure 3 – ***Distribution of severe cerebral injuries according to the living environment.***

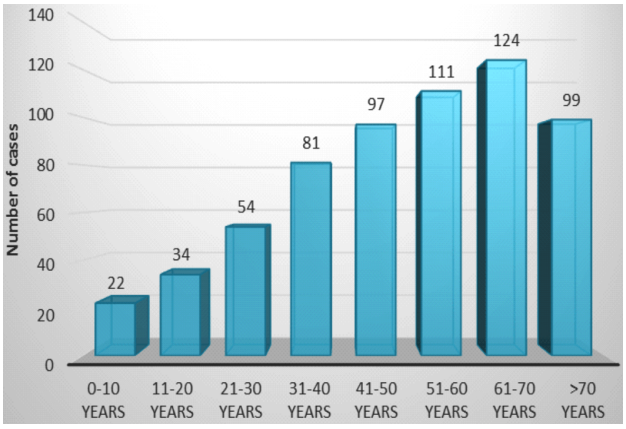

Figure 4 – ***Distribution of TBI cases based on the age of patients.***

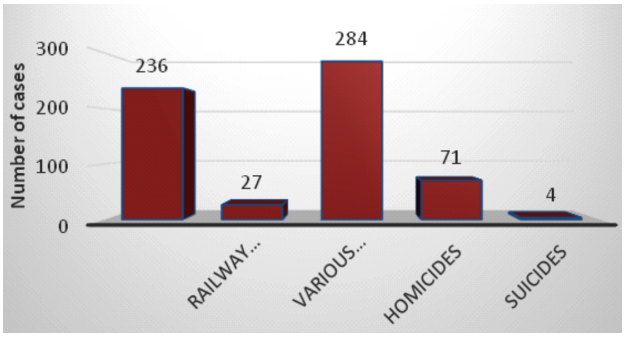

Figure 5 – ***Distribution of TBI cases according to the legal framework.***

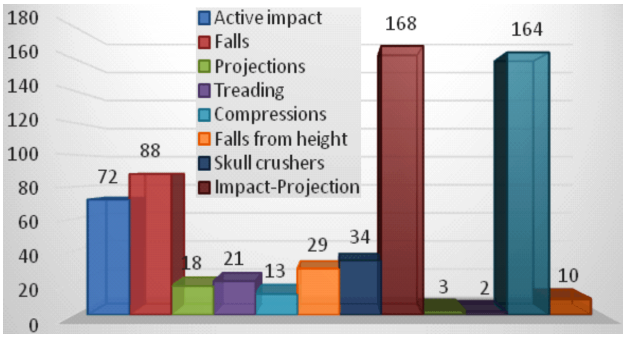

Figure 6 – ***Distribution of cases according to the mechanism of production determined after autopsy.***

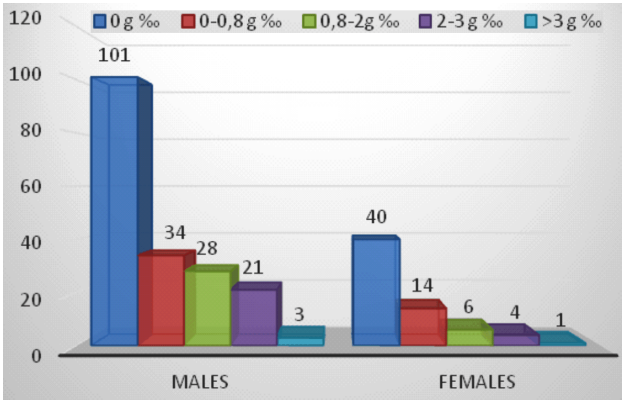

Figure 7 – ***Distribution of TBI cases according to alcohol concentration and sex.***

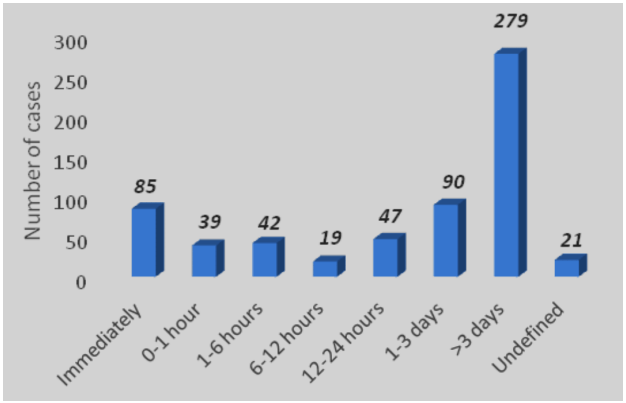

Figure 8 – ***Distribution of TBI cases according to the time passed from injury to death.***

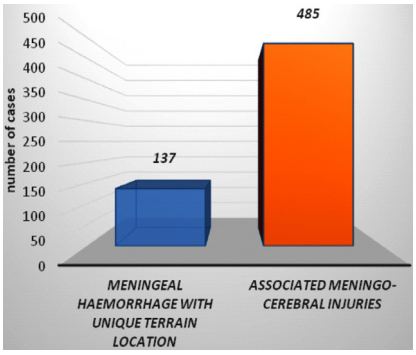

Figure 9 – ***Distribution of cases according to the presence of meningeal lesions as a unique location and the association with brain lesions.***

Figure 10 – ***Association of lepto-meningeal hemorrhage with cortical and sub-cortical contusions. Pitres sections (road accident, man, age 71).***

Figure 11 – ***Severe TBI of sub-arachnoid hemorrhage associated with sub-cortical millimetric contusions – Pitres sections (an accident – pieces of ice, which fell from the roof of a block), man, aged 80.***

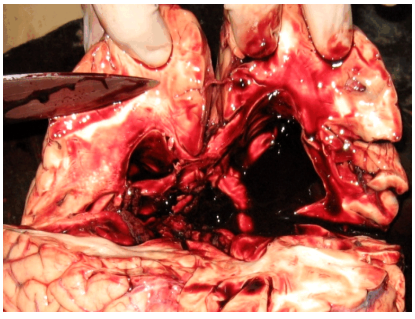

Figure 12 – ***Intraventricular hemorrhage caused by falling (man, aged 76).***

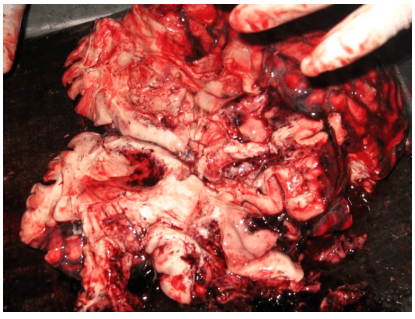

Figure 13 – ***Massive cerebral laceration on the left fronto-temporo-parietal region, man, aged 64, lesion of counter-hitting with occipital impact, road accident. Pitres sections.***

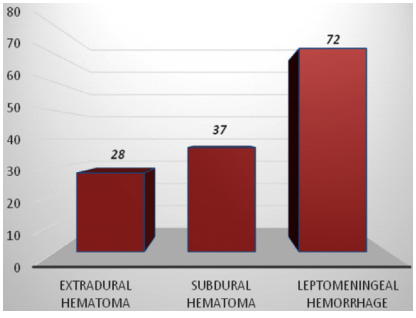

Figure 14 – ***Distribution of types of meningeal hemorrhage at the studied group with TBI.***

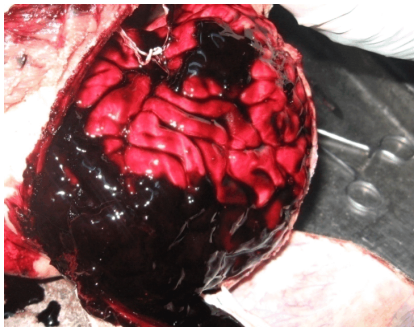

Figure 15 – *Acute subdural hematoma (the period of survival – two days) on the left fronto-temporo-parieto-occipital side of the brain (man, aged 50, hurrying (fall from height).*

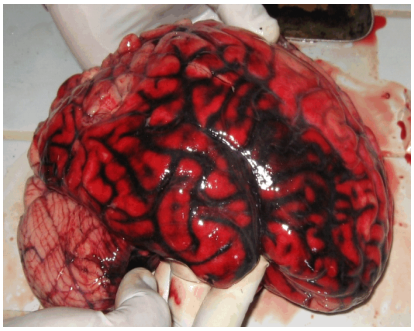

Figure 16 – *Leptomeningeal hemorrhage at the level of the right side of the brain (aggression, man, aged 48).*

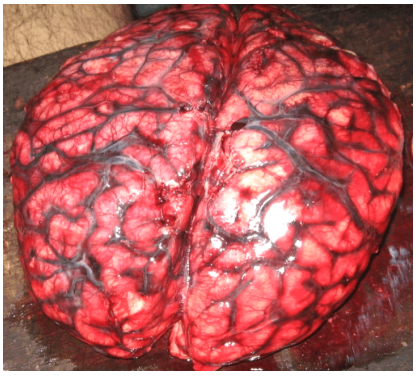

Figure 17 – *Diffused leptomeningeal hemorrhage "in the canvas" (road accident, man, aged 21).*

The microscopic examination of the cerebral tissue samples taken during necropsy emphasized a great number of lesions that varied in accordance with the severity of the lesion impact and the time period between the trauma and death. The most frequent lesions were the meningeal and/or intraparenchymal hemorrhages (Figures 18–21). The recent leptomeningeal hemorrhages were characterized by the diffused lepromeningeal infiltration with different quantities of blood, where red cells appeared to be intact; the old hemorrhages presented hemolysed red blood cells and a great number of macrophages. We discovered vessels of angiogenesis at the level of the leptomeninges, as well as incipient processes of collagen fibrillogenesis. Intraparenchymally, we also found hematomas of various sizes, either recent or old, diffused petechial hemorrhages or perivascular ones in the Virchow–Robin spaces.

The immunohistochemical examination was meant to point out the changes of the cerebral microvascularization, the reaction of glial and macrophage cells at the level of the traumatized brain tissue.

The cerebral microvascularization changes vary according to the type of cerebral lesion, the age of the patient and the time passed from aggression to death. The recent or old leptomeningeal hemorrhages led to a significant decrease of the micro vascularization in the lining brain tissue and, most probably to the growth of intracranial pressure (Figures 22 and 23). Some blood vessels had the wall broken because of the cerebral injury, probably because of the presence of shearing forces at this level (Figure 24). A 21-year-old man with a seven-day injury had an increased number of vessels of angiogenesis in the intraparenchymal hemorrhage (Figures 25 and 26).

The reaction of the macrophage system cells (microglias, blood macrophages) was low at recent brain injuries but very intense in older injuries (more than a week) (Figures 27 and 28). The presence of a large number of macrophages in the areas with meningeal hemorrhage (Figure 29) led us to believe that the largest number of the macrophages found in the cerebral parenchyma came from the blood monocytes and only a small number came from the activation of the local microglias.

The evaluation of the glial cells reaction emphasized that the intensity of the reaction of these cells depended on the age of the trauma and on the time passed between lesion and death. In recent injuries, under 48 hours, the reaction of the glial cells was highly reduced (Figure 30), whereas in the case of old lesions (especially in young people), the reaction was very intense (Figure 31).

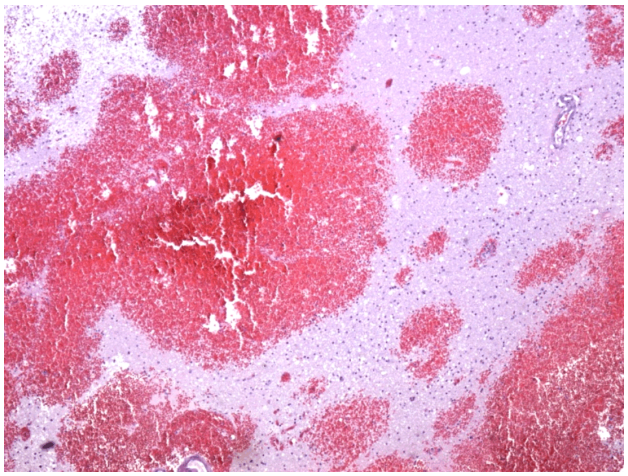

Figure 18 – *Recent intraparenchymal hemorrhage with intact red blood cells to a 2-day-old dead person. HE staining, ×100.*

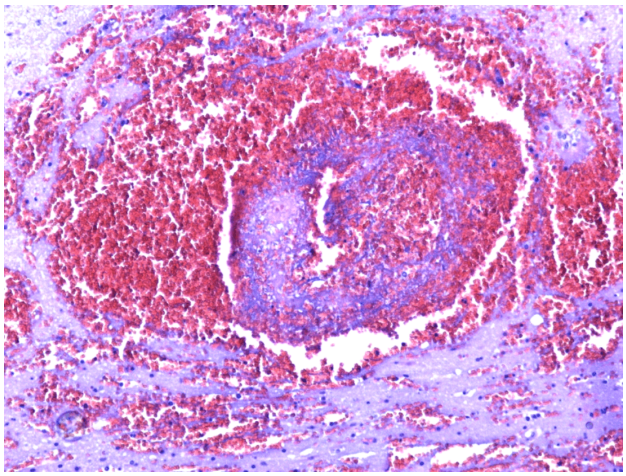

Figure 19 – *Microscopic image of an intraparenchymal hematoma, six days after the injury. HE staining, ×100.*

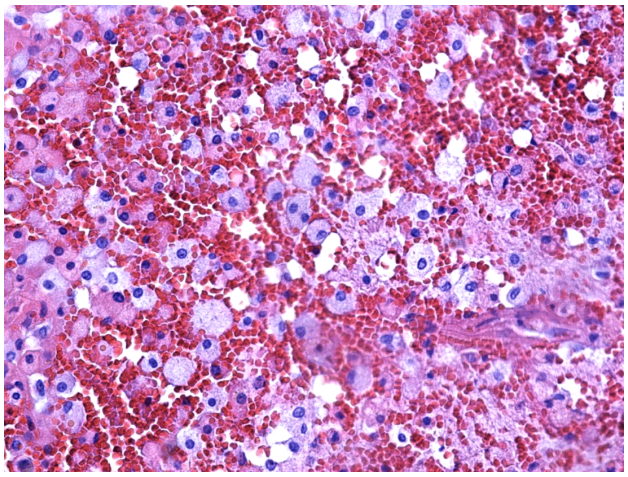

Figure 20 – ***Old intraparenchymal hematoma, 14 days after the injury, with multiple macrophages in the focus. HE staining, ×200.***

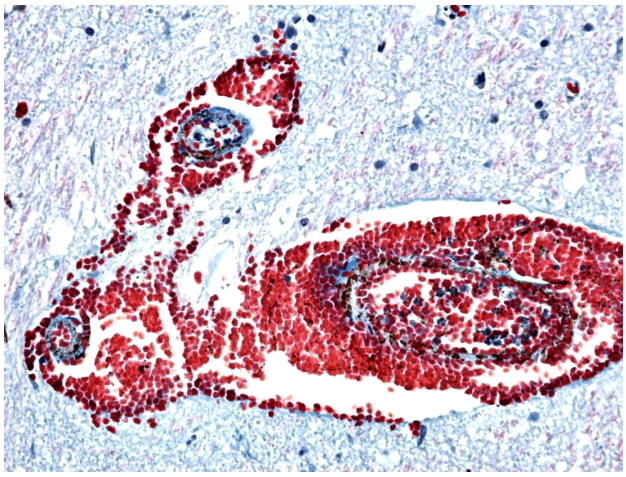

Figure 21 – ***Leptomeningeal hemorrhage associated with the diffusion of the intra-cerebral hemorrhage at the level of Virchow–Robin spaces. GS trichrome staining, ×200.***

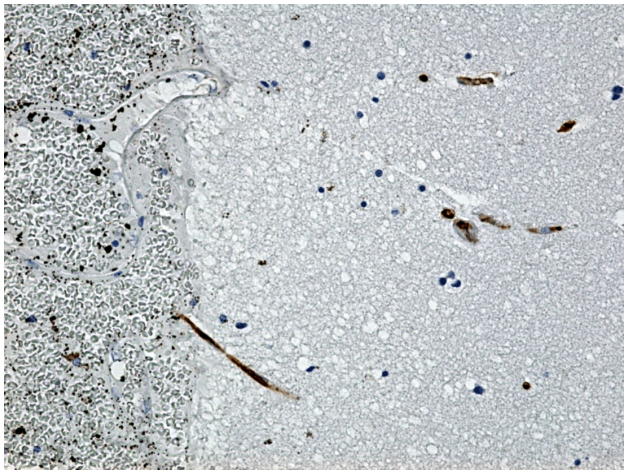

Figure 22 – ***Image of the surface of the encephalon, which shows the presence of a hemorrhage in the leptomeninges (on the left) and the decrease of the capillaries in the cerebral parenchyma (on the right). Immunostaining with anti-CD34 antibody, ×100.***

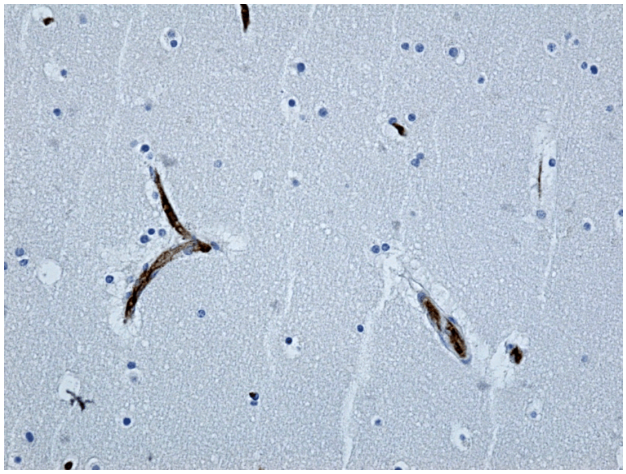

Figure 23 – ***Cerebral parenchyma at a distance from the hemorrhagic focus with a reduced number of blood vessels. Immunostaining with anti-CD34 antibody, ×200.***

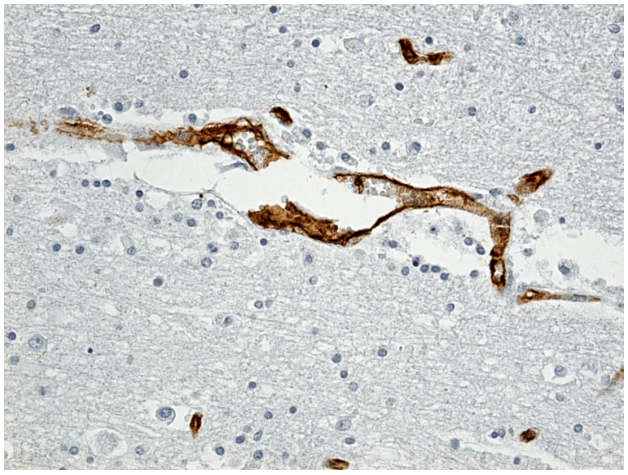

Figure 24 – ***Intra-cerebral blood capillary with broken wall. Immunostaining with anti-CD34 antibody, ×200.***

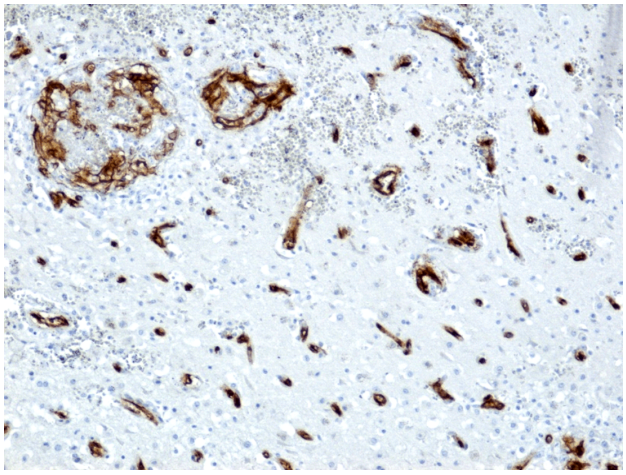

Figure 25 – ***Ten-day-old intraparenchymal hemorrhage with numerous vessels of angiogenesis. Immunostaining with anti-CD34 antibody, ×100.***

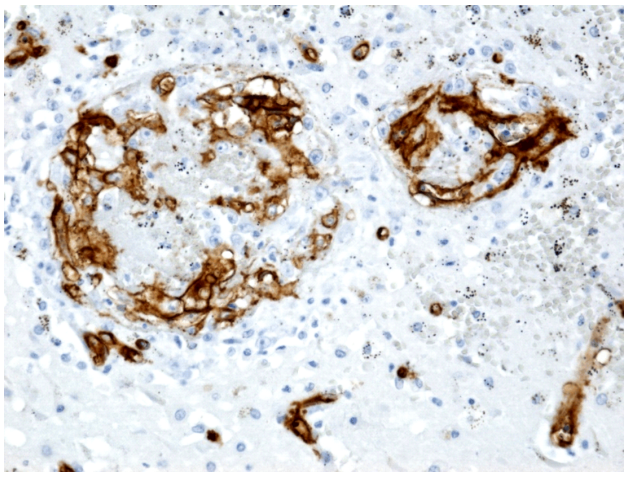

Figure 26 – *Vessels of angiogenesis in a focus of old cerebral hemorrhage. A detail from the previous figure. Immunostaining with anti-CD34 antibody, ×200.*

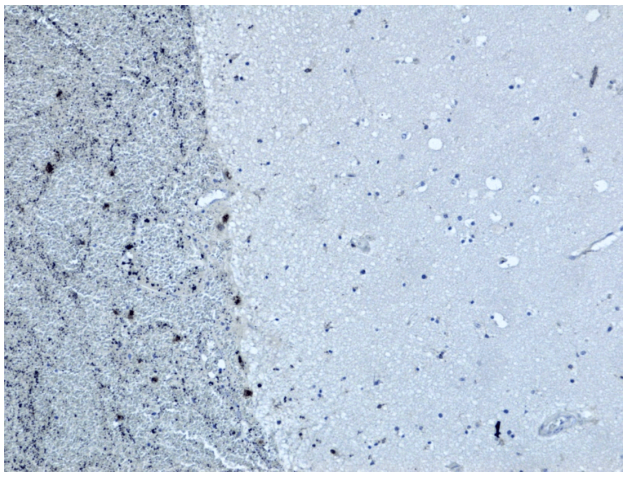

Figure 27 – *Image of recent leptomeningeal hemorrhage (two days) with a reduced reaction of the macrophagic system cells. Immunostaining with anti-CD68 antibody, ×100.*

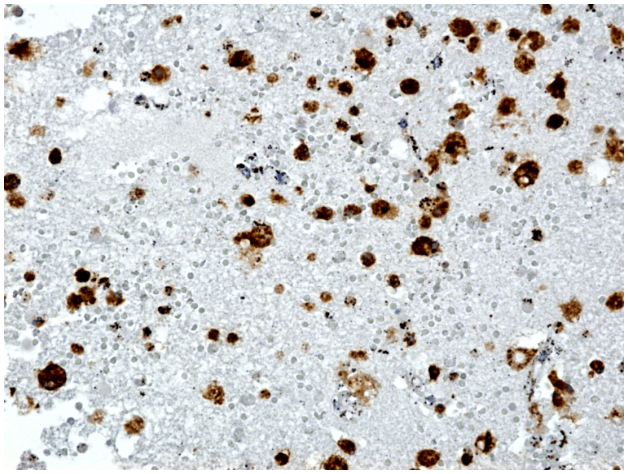

Figure 28 – *Ten-old-day TBI with intraparenchymal micro-hemorrhages and intense reaction of the macrophages. Immunostaining with anti-CD68 antibody, ×200.*

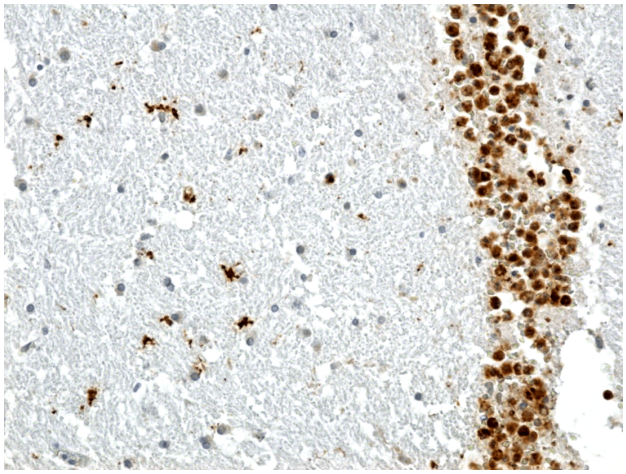

Figure 29 – *Seven-year-old injury associated with meningeal and interscissural hemorrhage, with numerous macrophage cells in the hemorrhagic focus (on the right) and a relatively small number of activated microglial cells in the cerebral parenchyma (on the left). Immunostaining with anti-CD68 antibody, ×200.*

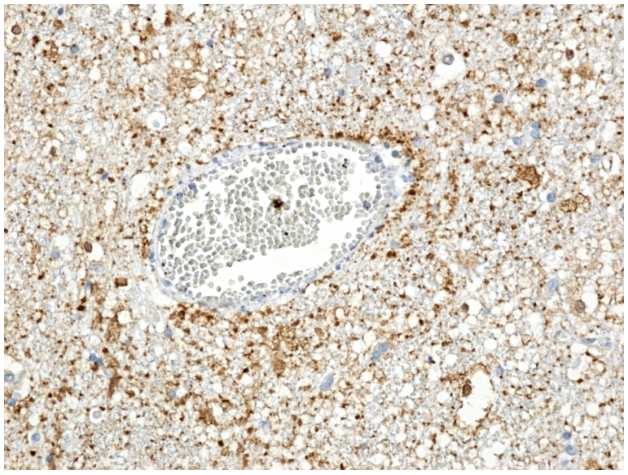

Figure 30 – *Recent TBI (two days) with reduced glial reaction. Immunostaining with anti-GFAP antibody, ×200.*

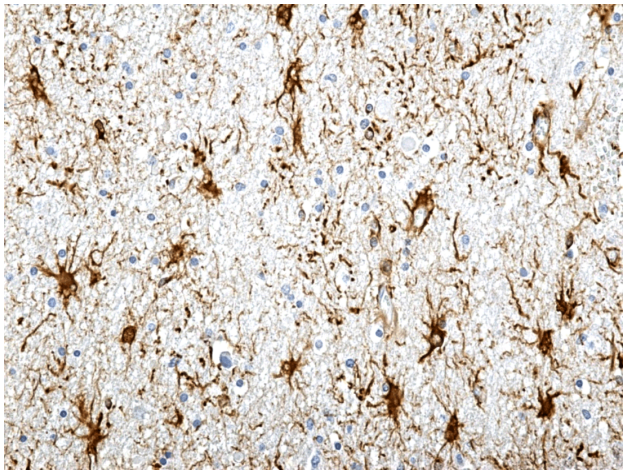

Figure 31 – *Intense glial reaction in a 10-day-old TBI. Immunostaining with anti-GFAP antibody, ×200.*

Discussion

Traumatic brain injuries (TBIs) still represent the main cause of death and invalidity [10, 11], despite the efforts made by countries in the last decades to increase the prevention methods and to improve the means and methods of taking care of the patients and rehabilitation [12]. Mild and moderate TBIs, such as concussions or contusions, do not raise important legal problems such as severe traumas that lead to the death of the patient. Numerous studies indicate that TBIs have evolved as a sort of epidemics in the last years especially in under-developed countries, where the number of severe traumas produced by cars has gradually increased from one year to another [13–15]. It is estimated that over one million patients with TBIs are hospitalized annually in the EU (European Union) and that a big number of them generally deceases. According to the predictions of the *World Health Organization* (WHO), TBI will become the third cause of death and invalidity worldwide by the end of 2020 [16, 17].

Our research investigated only the severe traumatic brain injuries which were autopsied at the Institute of Forensic Medicine in Craiova and which led to death. During five years (2010–2014), the Institute of Forensic Medicine registered 3260 cases of death, 622 (19.07%) deaths caused by a severe traumatic brain injury.

The incidence of severe TBIs is hard to establish since, in most countries, there are different criteria of including and reporting such traumas. For example, in Germany (Hanovra and Münster), Rickels *et al.* (2010) [18] reported a mortality rate of 3 to 100 000 inhabitants, while Koskinen & Alaranta (2008) in Finland and Servadei *et al.* (2002) in Italy, reported a mortality rate of 18.3 to 100 000 inhabitants [19, 20]. Each year, there are about 1.1 million people with TBIs treated in the emergency departments from the USA and about 50 000 people finally die [21, 22].

As far as the sex of the people deceased because of severe TBI is concerned, our research emphasized that most of them were men, women representing a lower percentage, the ratio being of 3/1. Leo & McCrea (2016), on the basis of CDC reports, stated that the ratio of traumatic brain injuries is of 1.6/1, whereas other European studies showed variations of the ratios between men and women with TBI from 1.46/1 to 1.8/1 [6]. We consider that the big number of men deceased because of severe TBI is bigger than women as a result of the increasing number of vehicles, the existence of a poorly developed road infrastructure and the ignorance of preventive driving measures. Road and train accidents, which produced death, represented 42.28% in our research. Our data are similar to other studies, which mention road accidents as the most frequent cause of severe TBIs [23, 24].

Another characteristic of the studied group was the big number of TBIs in the rural area in comparison with the urban one, the ration being of 1.7/1. We would have expected a higher risk of severe TBI in the urban area than the rural one because of the intense traffic and the big number of people.

The analysis of the distribution of cases of severe TBI, which led to death, pointed out the fact that the number of deceased people varies with age, the most numerous cases of deaths being registered in the 61–70 age groups. All the epidemiological studies reveal a non-homogenous distribution of TBIs in report to the age. Relatively recent data provided by CDC show the biggest incidence of TBIs is in the 0–4 age group (small children), in the 15–19 age group (teenagers) and in the 75 and over age group (elderly) [3, 6]. Similar data are also provided by other studies from Asia, which show that the most exposed people to TBI are young men [25, 26], children under [27, 28], and the elderly [29, 30].

We consider that one of the risk factors, which increase the incidence of TBIs in Romania, is alcohol consumption. Our research assessed the alcoholism quantity to 252 people deceased because of TBI and we found that 111 (44%) of them had positive samples for alcohol. If we take into account the fact that some deceased people because of TBIs were aggressed by other drunken people, then we consider that more than 50% of severe TBIs in Romania are produced by alcohol intake. Several studies from the USA show that around 56–72% of the people with TBIs who needed medical care had consumed alcohol and 36–55% had high values of alcohol [31–34]. Unfortunately, alcohol consumption continues to increase especially with young people, which leads to a bigger incidence of TBI cases in the future [35].

The macroscopic aspects of the brain to patients with severe TBI that we examined varied according to the impact force, the direction, the surface contact of the vulnerable agent with the skull, etc.

The microscopic aspects were dominated by the lesions of the nervous tissue and the lesions of the cerebral vascular network. All the examined cases presented vascular lesions, such as: leptomeningeal hemorrhages, intracerebral micro-hemorrhages, hematomas, ventricular hemorrhages.

All the studies admit that the external forces, which produce TBIs, determine vascular lesions with negative effects not only in the acute phase of the trauma but also later on [36, 37]. The vascular lesions occur even in small injuries and their secondary and late effects are important since all types of TBI are characterized by lesions of the blood-brain barrier (BBB). BBB is vital for the proper functioning of the nervous tissue, representing the structure which maintains the cerebral homeostasis, an environment which contains certain concentrations of ions such as sodium, potassium and calcium [38]. The BBB lesion leads to extravasation of blood components in the nervous tissue [39], which produces local inflammatory reactions and the necrosis of the neurons. In addition, it leads to the appearance of cerebral edema, which, in its turn, may generate serious neuronal lesions by reducing the blood flow, the quantity of oxygen at the level of the brain and the increase of the intracranial pressure [40].

Our immunohistochemical study showed that the meningeal hemorrhage determines a significant decrease of the cerebral blood flow, especially in the affected hemisphere, by increasing the intracranial pressure, reducing the number of functional capillaries from the nervous tissue and local hypoxia. All these morphological changes increase the gravity of neuronal and glial lesions induced by the mechanical force, through a multitude of

mechanisms: the emphasis of the neuronal apoptosis [41], the activation of local proteases [42], the growth of intracellular water absorption [43], the growth of permeability of neuronal membrane for ions such as calcium and proteins, which disturb the energetic homeostasis of the neurons [44], the growth of the oxidation stress, etc. [45, 46].

We consider that the mechanisms of post-traumatic neuronal and glial death, of the destruction of neuronal extensions and connections between them are still unknown.

Conclusions

In our research, TBI was the cause of death in 622 people, representing 19.07% of the total number of deaths, which required necropsy. Road and train accidents represented 263 cases, namely 42.28%. Of all the risk factors involved in the studied group, alcohol intake was the most important one; almost 44% of the people were found under alcohol influence. Men and the elderly were mostly affected by this phenomenon. The necropsy emphasized the severity of cranio-cerebral lesions; most cases had vascular lesions and dilacerations of the cerebral tissue. The microscopic analysis revealed the existence of meningeal or intraparenchymal hemorrhages, sometimes situated far from the traumatic impact zone. Moreover, we observed the significant reduction of intracerebral microvascularization because of the increase of the intracranial pressure; this is an intense reaction of macrophages in the cerebral dilaceration areas in an old TBI, reactive gliosis in some areas of ischemic shadow.

Conflict of interests

The authors declare that they have no conflict of interests.

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