ISSN 1220-8841 (Print)
ISSN 2344-4959 (Online)

ROMANIAN
NEUROSURGERY

Vol. XXXVI | No. 4 December 2022

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DOI: 10.33962/roneuro-2022-072

Romanian Neurosurgery (2022) XXXVI (4): pp. 393-398
DOI: 10.33962/roneuro-2022-072
www.journals.lapub.co.uk/index.php/roneurosurgery

The assessment of risk factors for brainstem injuries and supratentorial brain injuries in patients with traumatic brain injury

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ABSTRACT

Traumatic brain injury (TBI) is an important cause of death with a significant worldwide percentage. In the United States, there are approximately 2.8 million TBIs yearly with 250,000 hospitalized patients and 50,000 TBI-related deaths. Every year, there are one million hospitalizations in the European Union, resulting in more than 50,000 deaths, most of which occur due to road traffic accidents. Needless to say, these estimations varied based on the different sources of data. The patient's outcome is determined by the context of the trauma, the type of lesion, as well as other factors.

The aim of the study was to assess variables associated with brainstem injury and supra-tentorial brain injury in patients with TBI. This cohort included 70 consecutive TBI-related deaths from the Institute of Legal Medicine Cluj-Napoca. There was a significant difference in brainstem contusion (haemorrhage contusion) in patients younger than 60. According to the computed tomography (CT) data, brain contusion and laceration were observed in association with brainstem contusion in a significant percentage of TBI-related deaths (p=0.016). Neither the meningo-cerebral blood collections nor the intraparenchymal hematomas had a significant occurrence with brainstem contusion. The diffuse axonal injuries were detected on a CT scan in a significant number of cases with brainstem contusion (p=0.011). The mass effect with brain herniation in the posterior fossa was associated with the occurrence of brainstem contusion, possibly as an extensive process (p=0.041).

Keywords
brainstem injury,
supratentorial brain injury,
severe traumatic brain injury,
imagistic data,
histopathological data

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ISSN online 2344-4959
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First published
December 2022 by
London Academic Publishing
www.lapub.co.uk

Analyzing the histopathological data, we observed the significant presence of intracranial haemorrhage in association with a hemorrhagic contusion in the brainstem (p=0.004), but not with meningeal haemorrhage. The poor neurological assessment evaluated by GCS was not an independent variable in relation with this brainstem lesion. That was probably caused by the complexity of the TBI. We did not include this variable in a multivariate analysis considering the poor outcome for all patients

Introduction

Traumatic brain injury (TBI) has an important impact regarding the overall mortality rate and the permanent disability. The brain injuries result from various mechanisms, the most common of which are related to falls (35%) and motor vehicle collisions (17%) (1). Also, the head wounds complete the high incidence of death. TBI is clinically divided into mild, moderate and severe; and the lesions are described histologically as primary and secondary brain tissue injuries. In the majority of cases the primary lesions involve the occurrence of secondary mechanisms such as brain edema, elevated intracranial pressure and brain herniation. These secondary lesions are the consequence of impaired cerebral blood flow regulation and brain metabolism alterations with upregulation of inflammatory mediators, oxidative stress, and vasospasm (2).

The prognostic of TBI depends on multiple factors, some of which are: the anatomical localization of the primary lesion, the type of injury, the secondary mechanisms, the proportion of damaged brain tissue, and also the accurate management for TBI. An acute hemorrhage or a contusion is clearly detected with an appropriate technique (computer tomography) or during the autopsy as morphopathology aspects. These aspects should explain the prognostic of TBI. Diffuse axonal injury (DAI) is often observed in extensive brain damage with intracranial hemorrhage, after rapid and sustained deceleration or acceleration of the brain (3). DAI occurred in up to 50% of traumatic brain injuries (TBIs), detected by magnetic resonance imaging (MRI), in the United States (4). The brainstem injury is an important cause of death, related to the anatomical and functional mechanisms of the cardio-respiratory control in the lower brainstem and spinal cord (5). Some types of posterior fossa lesions are difficult to detect on the MRI and are not completely understood. Also, the correlation between the brainstem injury and the outcome is still unclear. Of course, the researchers assumed a relationship between the brainstem lesions and other brain lesions, from the supratentorial fossa. These could be explained by secondary lesions that occurred as a consequence of the primary lesions. Brain edema is one of the most important secondary lesions that occurs almost in every TBI, including the brainstem injury or the supratentorial brain injury. Beside of the common mechanism of brain edema, cytotoxic or vasogenic, there is currently discussed about a new term "CSF(cerebrospinal fluid) - shift edema" that defined a new mechanism of brain edema occurred in traumatic subarachnoid hemorrhage, as a consequence of rapid shift of CSF from the cisterns. (6) There are many instances where the initial cortical contusion develops at the white/gray border with expansion into overlying grey matter (7). Contusion progression was found with a frequency of 63%-70% (8)(9). TBI is frecquently associated with coma status, caused by alteration of ascending arousal system, that could be observed in DAI with widespread damage white matter or mainly in bilateral brainstem injury.(10) Despite the preclinical and clinical management during hospitalization which is mainly focused on preventing the secondary lesion, the outcome of patients with brainstem injury is still discouraging.

In this study we assessed the variables associated with brainstem injury and supratentorial brain injury in patients with TBI, and to assess imagery data related to the TBI.

METHODS

The study was retrospective, longitudinal, observational, analytical, cohort type. In this study we included 70 TBI-related deaths from the Institute of Legal Medicine Cluj-Napoca, from January 2017 to December 2021. The data were noted from the reports of eligible patients for this study. This study was approved by the Clinical Ethics Committee of the ˝Iuliu Haţieganu˝ University of Medicine and Pharmacy in Cluj-Napoca.

The eligible cases for this study were: the autopsied cases with TBI who were admitted in a department of neurosurgery before death. Patients with TBI who died immediately after trauma were excluded from the study, because we considered that they had a fatal brain injury.

In the first part of the analysis, we noted the demographical information and the following clinical

data: the neurological status related to Glasgow Coma Scale (GCS) on initial evaluation, the classification of TBI (mild, moderate and severe), the comorbidities, the type of surgical intervention used, the complications developed during hospitalization, the number of days of hospitalization until death occurred. We recorded the imagistic data detected on the initial CT: the primary cerebral lesions - subdural hematoma and its maximal thickness (in millimeters, mm), intraparenchymal hematoma and its maximal thickness (mm), subarachnoid hemorrhage, contusion and laceration, diffuse axonal injuries, cranial fracture; and the secondary brain lesions – brain edema, brain herniation and the midline shift. In the next part we noted the microscopic aspects of the brain lesions from the histopathological reports. We distinguished the cases with brainstem injuries from cases without them and we established two groups on this criterion. We defined the brainstem contusion as the lesion with a hemorrhagic character in the brainstem tissue, as viewed microscopically. We considered that the brainstem contusion would be a primary lesion or a consequence of an expansive process from the other brain lesions. Also, we noted the presence of meningeal hemorrhage or intracranial hemorrhage from the histopathological reports.

Statistical analysis was carried out using the MedCalc Statistical Software version 19.4.1 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2020). Quantitative data was tested for normality of distribution using the Shapiro Wilk test and was characterized by median and 25, 75 percentiles. Qualitative data were expressed as frequency and percentage. Comparisons between groups were performed using the Mann-Whitney or chi-square tests, whenever appropriate. A p value <0.05 was considered statistically significant.

Results

The demographical and clinical data are described in detail, in table I. In this study there were 36 patients with histopathological brainstem contusion. Patients with brainstem contusions were significantly younger than patients without them, but there was no difference noted between males and females. Also, we analyzed the impact of the brainstem lesion on the clinical status of patients. We did not observe a correlation between the consciousness state and the patients with brainstem contusion, neither with the severity of the TBI. Patients with comorbidities such as chronic consumption of alcohol, arterial hypertension and atrial fibrillation presented a significant occurrence of brainstem contusion. The surgery status was not related with the localization of the lesions.

Table 1. Demographic and clinical data

Variable		Non histopathological brainstem contusion (n=34)	Histopathological brainstem contusion (n=36)	p
Age		65 (56; 82)	59.5(32.5; 73.5)	0.014
Sex, n (%)	M	21 (61.8%)	27 (75%)	0.3
	F	13 (38.2%)	9 (25%)	
GCS		4 (3.75; 7.25)	3.5 (3; 7)	0.4
TBI, n (%)	mild	5 (14.7%)	4 (11.1%)	0.7
	moderate	7 (20.6 %)	6 (16.7%)	
	severe	22 (64.7%)	26 (72.2%)	
Comorbidities, n (%)	None	7 (20.6%)	22 (61.1%)	0.01
	Arterial hypertension	7 (20.6%)	6 (16.7%)	
	Chronic alcohol composition	4 (11.8%)	5 (13.9%)	
	Atrial fibrillation	16 (47.1%)	3 (8.3%)	
Surgery, n (%)	No	9 (26.5%)	12 (33.3%)	0.7
	Applied	25 (73.5%)	24 (66.7%)	
Complications, n (%)	None	25 (73.5%)	26 (72.2%)	0.1
	Hemorrhagic shock	0 (0.0%)	2 (5.6 %)	
	Septic shock	3 (8.8%)	0 (0.0%)	
	Bronchopneumonia	6 (17.6%)	8 (22.2%)	
Days of hospitalization		8.5 (4.5; 15.25)	6 (3; 10)	0.8

Table 2. Imagistic data

Variable		Non histopathological brainstem contusion	Histopathological brainstem contusion	p
Subdural hematoma, n (%)	Absent	5 (14.7%)	8 (22.2%)	0.6
	Present	29 (85.3%)	28 (77.8%)	
Thickness of subdural hematoma, mm		9.5 (6.75; 19.50)	15.50 (11; 24.5)	0.3
Intraparenchymal hematoma, n (%)	Absent	25 (73.5%)	20 (55.6%)	0.1
	Present	9 (26.5%)	16 (44.4%)	
Thickness of intraparenchymal hematoma, mm		32.5 (11; 71.5)	31 (6.25; 41)	0.9
Subarachnoid hemorrhage, n (%)	Absent	25 (73.5%)	24 (66.7%)	0.7
	Present	9 (26.5%)	12 (33.3%)	
Brain contusion and laceration, n (%)	Absent	23 (67.6%)	13 (36.1%)	0.01
	Present	11 (32.4%)	23 (63.9%)	
Midline shift, mm		10.5 (5.5; 14.5)	7 (4; 9.5)	0.4
Diffuse axonal injury, n (%)	Absent	30 (88.2%)	21 (58.3%)	0.01
	Present	4 (11.8%)	15 (41.7%)	
Brain edema, n (%)	Absent	7 (20.6%)	6 (16.7%)	0.9
	Present	27 (79.4%)	30 (83.3%)	
Brain herniation, n (%)	Absent	26 (76.5%)	18 (50.0%)	0.04
	Present	8 (23.5%)	18 (50.0%)	
Cranial Fracture, n (%)	Skull dome	19 (59.9%)	16 (44.4%)	0.5
	Skull base	9 (26.5%)	8 (22.2%)	
	Skull dome and base	4 (11.8%)	7 (19.4%)	

Table 3. Histopathological data

Variable		Non histopathological brainstem contusion	Histopathological brainstem contusion	p
Meningeal hemorrhage, n (%)	Absent	3 (8.8%)	5 (13.9%)	0.7
	Present	31 (91.2%)	31 (86.1%)	
Intracranial hemorrhage, n (%)	Absent	19 (55.9%)	7 (19.4%)	0.004
	Present	15 (44.1%)	29 (80.6%)	

CT detected all the other brain lesions, beside the brainstem injury. The supratentorial brain lesions were assessed according to the presence or absence of brainstem contusion. The cerebral blood collections did not seem to have a direct relation with the brainstem injury. The meningocerebral collection such as the subdural hematoma (SDH) was an independent factor of TBI. Neither the thickness of the subdural hematoma or the midline shift did not describe a causal relation with the posterior fossa lesion. Beside this, a direct relation was found between the supratentorial brain laceration and the brainstem contusion. Diffuse axonal injuries were detected in a significant number of patients with brainstem contusion (p= 0.011). Another diffuse brain injury, namely brain herniation as a consequence of brain edema, was a significant information which showed a correlation with brainstem contusion. All the supratentorial lesions and their comparisons are mentioned in Table II.

Analyzing the histopathological data, we observed a significant presence of intracranial hemorrhage in patients with brainstem contusion (p=0.004), but this association was not reported for meningeal hemorrhage. The comparisons of these histopathological aspects are described in table III.

Discussion

In some cases of brain trauma, the exact mechanism which lead to death is difficult to explain. The physiopathological mechanism that follows TBI is not completely known and is still an investigated subject. The fatal head impact was characterized by a depression activity on electrophysiology in both cortex and brainstem and of course, death occurred immediately. (11) In mild and severe TBI, the lesion could be limited at a part of the brain. In terms of its location, it does not always include the vital centers from the brainstem that generate and maintain the cardiac and respiratory rhythm. It is well known that

the mechanisms of central control are complex, by receiving signals from other sites while also having a nervous, reflex and humoral regulation. It is still challenging to know the mechanism of death in TBI when the primary lesion does not include the vital centers from the brainstem or spinal cord. In this study we were interested to find out the variables associated with the brain lesions from different locations of the brain. We were looking at the supratentorial and the brainstem lesions, focusing on their imagistic and microscopic aspects.

In regard to the relation with the supratentorial injuries, Mannion et all studied the aspects of the brain lesions, detected mostly on MRI. (12) In their study, the brainstem injuries were observed in association with severe diffuse axonal injury or in the context of a significant mass lesion and all of those patients had a poor outcome.(12) Only two patients from their study had a good outcome and that was in association with minor supratentorial abnormalities. (12) Evaluating the outcome, John R Williams showed in their study that the patients with associated brainstem and cerebrum injury had an unfavorable outcome compared with Duret hemorrhage alone or brainstem contusion.(13) In contrast, the Duret hemorrhage was associated with transtentorial herniation as a consequence of severely elevated intracranial pressure (14) In our study we showed a significant association of brainstem injury with supratentorial lesions, including diffuse axonal injuries and brain herniation.

Despite worse outcome, Moen et all evaluated through MRI the traumatic axonal injuries and they demonstrated the reduction of non-hemorrhagic lesions from hemispheres and corpus callosum and the complete absence of brainstem lesions, 3 months after TBI. (15) The hemorrhagic axonal injuries were only attenuated at the 3 months examination. (15) Even though, they observed an important evolution of traumatic axonal injury, the number of lesions and their volume on MRI predicted a worse clinical prognosis. (15) In the same study, quoted at 4 points, the authors found that isolated traumatic axonal injury or other brainstem lesions with a volume less than 1 ml measured on the CT-scan, predicted a favorable outcome. (4) In contrast, the brainstem lesions (contusion or Duret hemorrhage) with a volume larger than 1 ml were against the favorable long-term outcome. (4) Isolated TAI in brainstem are caused mostly after rotational acceleration mechanism and they tend to have the prospect of recovery. (16) (17) (18) Besides, the hemorrhagic brainstem contusion and Durret hemorrhage are the result of more complex intracranial mechanisms and they could lead to a more severe brainstem injury. (16)

The poor neurological assessment evaluated by GCS was not an independent variable in relation with brainstem lesions in our study. That was probably caused by the complexity of TBI. We did not include this variable in a multivariate analysis considering the poor outcome for all patients. Two extensive studies, the International Mission on Prognosis and Analysis of Clinical trials in Traumatic brain injury database (IMPACT models) and the Corticosteroid Randomisation After Significant Head Injury trial data (CRASH models) were performed to predict the mortality and unfavourable outcome and in both the GCS variable predicted it. (19)(20)

Conclusion

The brainstem contusion was reported to the clinical, imagistic and other histopathological aspects of TBI. Related to the primary supratentorial lesions, the extensive brain laceration was significantly associated with the brainstem injury. Diffuse axonal injuries were detected on CT for a significant number of cases with brainstem contusion (p =0.01). The mass effect with brain herniation in the posterior fossa was associated with the occurrence of brainstem contusion, possibly as an extensive process. The histopathological data showed a significant presence of intracranial hemorrhage with hemorrhage contusion in brainstem, but not with meningeal hemorrhage. The poor neurological assessment evaluated by GCS was not an independent variable in relation with brainstem lesions. That was probably caused by the complexity of TBI.

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