Human & Veterinary Medicine
International Journal of the Bioflux Society HVM

OPEN ACCESS
Research Article

Particular aspects of dementia syndromes in the context of traumatic brain injury

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Abstract. Aim: to obtain additional data about the particularities of dementia syndromes in the context of traumatic brain injuries. Material and methods: We included 49 patients with a mean age of 70.20±15.1 years old, among which 37 (75.5%) men and 12 (24.5%) women, diagnosed with various types of dementia (Alzheimer's disease (AD), vascular dementia (VD), mixed dementia (MD) or other types of dementia syndromes (DS)) that presented a history of cranio-cerebral trauma. In this study, we included the patients who met the inclusion criteria: evidence of cranio-cerebral trauma in the patient's history; brain changes on CT and / or MRI examinations (native/ contrast substance); the appearance of cognitive changes at more than 6 months after the occurrence of the traumatic event. The following data were recorded: sex, age, context and mechanism of traumatic brain injury. From the posttraumatic imaging examination (CT or MRI), we have retained the following parameters: the type of posttraumatic brain injury and the type of pre-existing degenerative lesions. From the anamnestic data, we recorded: the presence of post lesional amnesia, loss of posttraumatic consciousness, Glasgow score, MMSE. Results: Comparison between the different types of dementia revealed that AD patients were older, experienced more accidents, and were more likely to had skull fractures. Patients with subdural hematoma were more prone to develop MD. The age of AD patients was significantly higher than that of patients with other dementias (75.71±16.15 years vs. 64.92±12.25 years, p=0.01). Among the patients with skull fractures, 13 (54.2%) had AD, and 6 (24%) other types of DS (p=0.04). Mild trauma was recorded in 16 (32.7%) patients, medium trauma in 28 (57.1%) patients and severe trauma in 5 (10.2%) patients. Conclusion: The severity of trauma could be associated with higher frequency of dementia syndromes. The patients that suffered skull fractures were more likely to develop AD. Age was also a factor associated with AD.

Key Words: traumatic brain injury, dementia, legal medicine.

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Introduction

Since the beginning of the last century, it has been known that repetitive brain trauma associated with certain sports or activities may cause a progressive neurodegenerative disease later in life (Savica 2014).

Traumatic brain injury is thought to be a major risk factor for dementia (Smith et al 2013). Despite intensive research into etiologic factors, little is known about the factors that cause the neurodegeneration (Kenborg et al 2015). The pathologic entity associated with repetitive head trauma is currently referred to as chronic traumatic encephalopathy (CTE) (Gavett et al 2011). This entity cannot, however, be diagnosed with confidence antemortem, and clinically may have features that resemble Alzheimer's disease (AD), frontotemporal dementia (FD), Parkinson disease (PD), Parkinson disease with dementia and amyotrophic lateral sclerosis (Gavett et al 2011).

Due to this trouble of diagnosis, the outcome of traumatic brain injuries might pose very serious problems for the survivors both from the medico-legal and juridical points of view. The difficulty in establishing a causal link between a traumatic brain injury event in the patient's history and the development of a certain type of dementia syndrome might lead to an unfair outcome in the juridical process, especially when we take into consideration the high social and medical costs. This is because the victims might try to malinger the neurodegenerative symptoms.

From the medico-legal point of view there are two types of mechanisms of inflicting traumatic brain injuries: accidental and aggressions. In the accidental class we include car accidents, work accidents, sports injuries and military activities. In the aggression category, we think only to the hetero inflicted injuries and not to the self-inflicted ones, due to the lack of juridical importance of the later.

In view of these previous findings, we conducted a study in order to obtain additional data about the particularities of dementia syndromes in the context of traumatic brain injuries.

Material and method

The study is a retrospective, observational, analytical, longitudinal, and cohort type.

We included 49 patients with a mean age of 70.20±15.1 years old, among which 37 (75.5%) men and 12 (24.5%) women, diagnosed with various types of dementia (Alzheimer's disease, vascular dementia (VD), mixed dementia (MD) or other types of dementia syndromes (DS) that presented a history of cranio-cerebral trauma. The patients were selected from those hospitalized in the Neurology Departments of Emergency County

Table 1. Characteristics of study's patients

Variable		Value
Age (years)		70.2±15.1
Gender	**Men**	37 (75.5%)
	Women	12 (24.5%)
Mechanism of trauma	**Aggression**	14 (28.6%)
	Accidental	35 (71.4%)
Loss of consciousness		31 (63.3%)
Post-traumatic amnesia		31 (63.3%)
GCS (pts)		11.2±2.5
Traumatic cranio-cerebral injuries	**Skull fractures**	19 (38.8%)
	Extradural hematoma	8 (16.3%)
	Subarachnoid hemorrhage	17 (34.7%)
	Subdural hematoma	8 (16.3%)
Type of dementia	**Alzheimer's disease**	24 (49%)
	Mixed dementia	5 (10.2%)
	Vascular dementia	12 (24.5%)
	Other types of dementia syndromes	8 (16.3%)
Presence of ischemic brain lesions		20 (40.8%)
Cerebral atrophy		32 (65.3%)
MMSE		19.8±6.4

Hospitals Cluj and Zalău in the period 2005 - 2015. The study protocol was approved by the Ethics Committee of University of Medicine and Pharmacy "Iuliu Haţieganu" Cluj-Napoca. Patients were enrolled in the study after signing the informed consent form.

In this study, we included the patients who met the inclusion criteria: evidence of cranio-cerebral trauma in the patient's history; brain changes on Computed Tomography (CT) and / or Magnetic Resonance Imaging examinations (MRI) (native/ contrast substance); the appearance of cognitive changes at more than 6 months after the occurrence of the traumatic event. The diagnosis of dementia has been established in accordance with the Diagnostic and Treatment Guidelines for Dementia developed by the Romanian Neurology Society, the Romanian Alzheimer Society, a guide approved by the Romanian Psychiatric Association and the Romanian Legal Medicine Society (Bucharest Amaltea 2007).

We have not included patients diagnosed with dementia syndrome prior to the traumatic event or the patients with a history of cranio-cerebral trauma prior to the traumatic event for which the forensic expertise was requested.

The following data were recorded: sex, age, context and mechanism of traumatic brain injury. From the posttraumatic imaging examination (CT or MRI), we have retained the following parameters: the type of posttraumatic brain injury and the type of pre-existing degenerative lesions. From the anamnestic data we recorded: the presence of post lesional amnesia, loss of posttraumatic consciousness, Glasgow score (GSCS), Mini-Mental State Examination (MMSE).

The statistical analysis was performed with the MedCalc Statistical Software version 17.6 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2017). The data were analyzed for normality of distribution with the Kolmogorov Smirnov test. The quantitative variables were expressed by mean and standard deviation, and the qualitative ones by absolute and relative frequency. The comparison between groups in terms of a quantitative variable was performed with the T-test for independent variables or ANOVA, depending on the situation. Comparison between groups in terms of a qualitative variable was performed with the chi-square test. A $p < 0.05$ value was considered statistically significant.

Results

Patients' demographic, clinical and imagistic characteristics are summarized in Table 1.

Comparison between the different types of dementia revealed that AD patients were older, experienced more accidents, and were more likely to had skull fractures. Patients with subdural hematoma were more prone to develop MD (Table 2).

The age of AD patients was significantly higher than that of patients with other dementias (75.71±16.15 years vs. 64.92±12.25 years, p=0.01). Among men, 18 (75%) developed AD and 19 (76%) other dementia syndromes. Among women 6 (25%) developed AD, and 6 (24%) other dementia syndromes. The difference was not statistically significant (p=1). The GCS score did not differ statistically significantly between the patients with AD (10.79±2.53) and the patients with other dementias (11.6±2.53) (p=0.2). The MMSE score did not differ statistically significantly between the group of patients with AD (19.08±2.53) and that of patients with other dementias (11.6±2.53) (p=0.2). Among the patients with skull fractures, 13 (54.2%) had AD, and 6 (24%) other types of dementia syndromes (p=0.04). Among the patients with an extradural hematoma, 3 (12.5%) developed AD, and 3 (12.5%) other types of dementia syndromes (p=0.7). Among the patients with subarachnoid hemorrhage, 6 (25%) developed AD, and 11 (44%) other types of dementia syndromes (p=0.2). Among the patients with subdural hematoma, 2 (8.3%) developed AD, and 6 (24%) other types of dementia syndromes (p=0.2). Among the patients with posttraumatic amnesia, 15 (62.5%) developed AD, and 16 (64%) other types of dementia syndromes (p=0.1). Among the patients with posttraumatic consciousness loss, 14 (58.3%) developed AD, and 17 (68%) other types of dementia syndromes (p=0.6).

The age of the patients with accidental trauma was higher than that of the patients with aggression injuries (72.26±15.11 vs. 65±14.54 years old) (p=0.1). The trauma mechanism did not differ in males compared to women (p=0.7). The trauma mechanism (aggression vs. accident) did not cause the occurrence of significantly more frequent fractures (p=0.1). The GCS scores did not differ depending on the trauma mechanism (p=0.5). The MMSE scores did not differ depending on the trauma mechanism (p=0.8). The trauma mechanism (aggression/accident) was not associated with the occurrence of extradural hematoma (p=0.6), subarachnoid hemorrhage (p=0.1), subdural hematoma (p=1), or of subdural hematoma (p=1). The presence of cerebral ischemic lacuna lesions did not result in more accidental trauma (p=0.2). The preexistence of a cerebral atrophy more frequently caused accidental trauma, but without reaching the

Table 2. Comparison between the different type of dementia

Variable			AD	MD	VD	Other DS	P
Age			75.71±16.15	73±11.79	65.92±12.07	58.38±10.43	0.02
Gender	**Men**		18 (75%)	3 (60%)	9 (75%)	7 (87.5%)	
	Women		6 (25%)	2 (40%)	3 (25%)	1 (12.5%)	
GCS			10.79±2.53	12±0.7	12.08±2.02	10.63±3.7	0.4
MMSE			19.08±6.04	19.2±7.8	19.25±7.64	23.25±4.4	0.4
Mechanism of trauma		**Aggression**	4 (16.7%)	1 (20%)	6 (50%)	3 (37.5%)	0.1
		Accidental	20 (83.3%)	4 (80%)	6 (50%)	5 (62.5%)	
Skull fractures			13 (54.2%)	1 (20%)	3 (25%)	2 (25%)	0.1
Extradural hematoma			3 (12.5%)	1 (20%)	3 (25%)	1 (12.5%)	0.7
Subarachnoid hemorrhage			6 (25%)	2 (40%)	6 (50%)	3 (37.5%)	0.5
Subdural hematoma			2 (8.3%)	2 (40%)	1 (8.3%)	3 (37.5%)	0.09
Posttraumatic amnesia			15 (62.5%)	3 (60%)	7 (58.3%)	6 (75%)	0.8
Posttraumatic consciousness loss			14 (58.3%)	3 (60%)	9 (75%)	5 (62.5%)	0.8

Table 3. The association between the severity of trauma and several parameters

Variable			Mild trauma	Medium trauma	Severe trauma	p
Age			69.7±16.5	70±14.5	72.8±17.3	0.9
Gender	**Men**		14 (87.5%)	19 (67.9%)	4 (80%)	0.3
	Women		2 (12.5%)	9 (32.1%)	1 (20%)	
Types of dementia		**AD**	7 (43.8%)	14 (50%)	3 (60%)	0.4
		MD	1 (6.2%)	4 (14.3%)	-	
		VD	6 (37.5%)	6 (21.4%)	-	
		Other DS	2 (12.5%)	4 (14.3%)	2 (40%)	
MMSE			21.8±6.1	19±6.2	18±7.8	0.3
Mechanism of trauma		**Aggression**	4 (25%)	10 (35.7%)	-	0.2
		Accidental	12 (75%)	18 (64.3%)	5 (100%)	
Skull fractures			5 (31.2%)	12 (42.9%)	2 (40%)	0.7
Extradural hematoma			2 (12.5%)	6 (21.4%)	-	
Subarachnoid hemorrhage			5 (31.2%)	11 (39.2%)	1 (20%)	
Subdural hematoma			3 (18.8%)	4 (14.3%)	1 (20%)	
Posttraumatic amnesia			7 (43.8%)	21 (75%)	3 (60%)	
Posttraumatic consciousness loss			8 (50%)	20 (71.4%)	3 (60%)	

threshold of statistical significance (p=0.5). The trauma mechanism did not cause the occurrence of posttraumatic amnesia more frequently (p=1).

Mild trauma was recorded in 16 (32.7%) patients, medium trauma in 28 (57.1%) patients and severe trauma in 5 (10.2%) patients. We tried to find associations between the severity of trauma and several parameters (table 3).

Discussions

This study attempted to demonstrate the association between the different etiology of cranio-cerebral trauma, post-traumatic injuries and the appearance of dementia. Also, in our attempts we analyzed the correlation of structural cerebral changes and the mechanism of trauma.

The cranio-cerebral trauma is a particularly important public health problem with an annual incidence of 180-220 per 100,000 inhabitants in the United States. Most (80%) are represented by minor injuries, 10% are moderate and 10% are severe injuries. The socio-economic costs generated by the management of long-term trauma are high, given that nearly 100% of the severe trauma patients and 70% of those with moderate trauma will have a degree of disability that will not allow them to continue their lives as well as they used to do, prior to the trauma (Lu et al 2012).

The mean age of the patients in our study was 70 years. Over the age of 65 years old there is an increase risk of brain trauma, especially over 75 years. Most traumas in the elderly occur accidentally: 51% by falling from the same level and 9% by car accident (pedestrians) (Langlois et al 2004). In our study the

prevalence of accidents was even higher (71%), as sports accidents were also included here. Approximately 75% of patients in our study were males, this being consistent with literature data that showed the higher risk of developing AD in men suffering from brain injury (Coronado et al 2005; Fleminger et al 2003). The mean age of the patients with AD (75 years) was significantly higher than in those with other dementia syndromes. This is in ascent with literature data showing that brain trauma is associated with development of Alzheimer's disease (AD) later in life (Johnson et al 2010), and also with the data provided by Gavett et al (Gavett et al 2000).

The prevalence of medium cerebral trauma was much higher than in the general population (57% vs. 10%), while mild traumas were rarer (32% vs. 75-80%) (Coronado et al 2011). This is due to the fact that the patients from our study were diagnosed with dementia at more than six months after the trauma. The patients with minor trauma are much less likely to develop severe neurological pathologies, most of them only experiencing functional, sensory, linguistic, emotional deficits rather limited in severity and more likely in the short term.

On the other hand, in patients with moderate or severe trauma, there was a higher incidence of Alzheimer's disease, as evidenced by our study data (Fleminger et al 2003). We also demonstrated that the intensity of trauma, proved by the existence of skull fractures, was associated with a higher AD incidence. In one study, Barnes et al found that veterans that were diagnosed with AD, suffered three times more skull fractures, as compared to those without AD (Barnes et al 2014).

The patients with severe trauma have diffuse lesions of the axons associated with overproduction of β-amyloid, which favors the Alzheimer's disease (Franz et al 2003; Povlishock et al 2005). Plassman et all have demonstrated that patients who have experienced moderate or severe trauma have a risk of developing dementia in time, while in those with mild trauma the possibility of developing Alzheimer's disease is insignificant (Plassman et al 2000).

Cognitive impairment is one of the most important sequelae of traumatic brain injury in the long-term. Montero-Odasso et al followed the cognitive changes over time through repeated MMSE evaluations and showed a reduction in their values after trauma. The reduction was higher in patients who sustained major trauma (Montero-Odasso et al 2012). Also in our study, the MMSE values were lower in patients with moderate or severe trauma.

Study limitations included the small number of patients, the uneven following period, the heterogeneous diagnosis and the lack of data regarding the cardiovascular diseases.

Conclusion

The severity of trauma could be associated with higher frequency of dementia syndromes. The patients that suffered accidents and skull fractures were more likely to develop AD. Age was also a factor associated with AD.

References

Barnes D, Kaup A, Kirby K, Byers A, Diaz-Arrastia R, Yaffe K. Traumatic brain injury and risk of dementia in older veterans. Neurology 2014;83(4):312-319.

Coronado VG, Thomas KE, Sattin RW. The CDC traumatic brain injury surveillance system: Characteristics of persons aged 65 years and older hospitalized with a TBI. J Head Trauma Rehabil 2005;20:215–228.

Coronado VG, Xu L, Basavaraju SV, McGuire LC, Wald MM, Faul MD, Guzman BR, Hemphill JD. Surveillance for traumatic brain injury-related deaths–United States, 1997–2007. MMWR Surveillance Summaries 2011;60:1–32.

Fleminger S, Oliver DL, Lovestone S, Rabe-Hesketh S, Giora A. Head injury as a risk factor for Alzheimer's disease: the evidence 10 years on; a partial replication. J Neurol Neurosurg Psychiatry 2003;74(7):857–62.

Franz G, Beer R, Kampfl A, Engelhardt K, Schmutzhard E, Ulmer H. Amyloid beta 1-42 and tau in cerebrospinal fluid after severe traumatic brain injury. Neurology 2003;60(9):1457–61.

Gavett BE, Stern RA, Cantu RC, Nowinski CJ, McKee AC. Mild traumatic brain injury: a risk factor for neurodegeneration. Alzheimer's Research & Therapy 2010;2:18.

Gavett BE, Stern RA, McKee AC. Chronic traumatic encephalopathy: a potential late effect of sport-related concussive and subconcussive head trauma. Clin Sports Med 2011;30:179–188.

Johnson VE, Stewart W, Smith DH. Traumatic brain injury and amyloid-β pathology: a link to Alzheimer's disease? Nat Rev Neurosci 2010 May;11(5):361–370.

Kenborg L, Rugbjerg K, Lee PC, Ravnskjær L, Christensen J, Ritz B, Lassen CF. Head injury and risk for Parkinson disease - Results from a Danish case-control study. Neurology 2015;84:17.

Langlois JA, Rutland-Brown W, Thomas KE. Traumatic Brain Injury in the United States: Emergency Department Visits, Hospitalizations, and Deaths. National Center for Injury Prevention and Control; Atlanta. 2004.

Lu J, Gary KW, Neimeier JP, Ward J, Lapane KL. Randomized controlled trials in adult traumatic brain injury. Brain Inj 2012;26 (13-14):1523-48.

Montero-Odasso M, Verghese J, Beauchet O, Hausdorff JM. Gait and Cognition: A Complementary Approach to Understanding Brain Function and the Risk of Falling. Journal of the American Geriatrics Society 2012;60:11.

Plassman BL, Havlik RJ, Steffens DC. Documented head injury in early adulthood and risk of Alzheimer's disease and other dementias. Neurology 2000;55(8):1158-66.

Povlishock JT, Katz DI. Update of neuropathology and neurological recovery after traumatic brain injury. J. Head Trauma Rehabil 2005;20:76–94.

Savica R. Head trauma and neurodegeneration in Veterans. An additional piece of the puzzle. Neurology 2014;83:298–299.

Smith DH, Johnson VE, Stewart W. Chronic neuropathologies of single and repetitive TBI: substrates of dementia? Nat Rev Neurol 2013;9:211–221.

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Citation	Chiroban O, Perju-Dumbravă L. Particular aspects of dementia syndromes in the context of traumatic brain injury. HVM Bioflux 2017;9(3):79-83.
Editor	Ştefan C. Vesa
Received	3 July 2017
Accepted	15 August 2017
Published Online	15 August 2017
Funding	None reported
Conflicts/ Competing Interests	None reported