Supplementary Table S1 Basic characteristics of severe traumatic brain injury (sTBI) patients

Case no.	Age/ gender	Survival time	Cause of head injury	Brain lesion	Skull fractures	Histopathological score (max. Score-16)	Histopathological %	β-APP Score	β-APP %
1	38/M	3	RTA	SAH	A	11	68.75	8	80
2	35/M	1	RTA	SDH	P	6	37.5	7	70
3	44/M	21	Fall	MLS, SDH	A	11	68.75	9	90
4	65/M	1	RTA	FTP -SDH, SAH	P	10	62.5	8	80
5	21/M	1	RTA	EDH	P	7	43.75	6	60
6	35/M	6	RTA	FTP- SDH, SAH	P	7	43.75	8	80
7	35/F	20	Fall		P	9	56.25	10	100
8	63/F	5	RTA	FTP- SDH	P	8	50	10	100
9	49/M	1	RTA	SAH	A	12	75	9	90
10	33/M	47	RTA	SAH, SDH	A	12	75	9	90
11	45/M	2	RTA	FTP SDH	P	9	56.25	8	80
12	40/M	2	FALL	SDH, SAH	P	8	50	8	80
13	28/F	3	FALL		A	11	68.75	9	90
14	25/M	1	RTA	SAH, IVH	P	8	50	8	80
15	53/M	2	RTA	FTP- SDH, MLS	A	11	68.75	8	80
16	26/M	2	RTA		A	11	68.75	9	90
17	42/M	11	RTA	SAH	A	11	68.75	9	90
18	53/M	9	RTA		A	13	81.25	8	80
19	32/M	2	RTA	FTP, SAH, SDH, EDH	P	12	75	10	100
20	32/F	10	RTA		A	11	68.75	10	100
21	28/M	1	Fall		A	8	50	10	100
22	23/M	2	fall	FTP, SDH	A	9	56.25	8	80
23	25/M	2	RTA	SDH, SAH	A	9	56.25	10	100
24	33/M	1	RTA	BTA	A	9	56.25	9	90
25	59/M	6	RTA	FTP, SDH, MLS	A	13	81.25	10	100
26	65/M	1	Fall	FTP, SDH	A	10	62.5	10	100
27	35/M	4	RTA	IVH, SAH	P	10	62.5	10	100
28	55/F	4	RTA	FTP, SDH, SAH IVH, MLS	P	10	62.5	9	90
29	38/F	1	FALL		A	9	56.25	10	100
30	39/M	5	RTA	SAH, IVH	P	12	75	10	100
31	40/M	2	RTA		A	10	62.5	9	90
32	50/M	1	Fall		A	7	43.75	8	80
33	40/M	8	RTA	IVH, SDH	P	11	68.75	10	100
34	50/M	4	RTA	IVH	A	13	81.25	10	100
35	25/M	3	RTA	STP, SDH, MLS, IVH	P	11	68.75	8	80

Abbreviations: %, percentage, A, Absent; F, female; IVH, Intraventricular hemorrhage; M, Male; MLS, Midline Shift; FTP, Fronto-tempo-parietal; P, present; RTA, Road Traffic Accident; SAH, Subarachnoid Hemorrhage; SDH, Subdural Hemorrhage; EDH, Epidural Hemorrhage; β APP, Beta amyloid precursor protein.

Supplementary Table S2 Basic characteristics of control patients

Case no.	Age/gender	Survival time	Cause of death	Histopathological score	Histopathological %	β-APP Score	β-APP %
1	36/F	0	Hanging	5	31.25	4	40
2	22/M	0	Gunshot(chest injury)	3	18.75	3	30
3	30/M	0	Fall	5	31.25	3	30
4	35/M	0	Hanging	5	31.25	1	10
5	35/M	0	Hanging	4	25	3	30
6	35/M	0	RTA	6	37.5	3	30
7	52/M	0	RTA	3	18.75	2	20
8	42/M	0	Fall	5	31.25	1	10
9	16/M	0	Drowning	3	18.75	1	10
10	27/M	0	Hanging	4	25	2	20

Abbreviations: %, Percentage; β APP, Beta amyloid precursor protein.
Survival time 0- Patient who either died at the site of accident or immediately after being admitted to the hospital.

Supplementary Table S3 CT findings post severe TBI

S. no.	Variables	TBI	Non-TBI	p-Value
		$n = 35$, n (%)	$n = 10$, n (%)	
1	**Contusion**			
	Absent (0)	18 (51.4)	10 (100)	0.005*
	Present (1)	17 (48.6)	0 (0.0)	
2	**Extradural hemorrhage (EDH)**			
	Absent (0)	32 (91.4)	10 (100)	0.999
	Present (1)	3 (8.6)	0 (0.0)	
3	**Subdural hemorrhage (SDH)**			
	Absent (0)	19 (54.3)	10 (100)	0.008*
	Present (1)	16 (45.8)	0 (0.0)	
4	**Subarachnoid hemorrhage (SAH)**			
	Absent (0)	23 (65.7)	10 (100)	0.03*
	Present (1)	12 (34.3)	0 (0.0)	
5	**Intraventricular hemorrhage (IVH)**			
	Absent (0)	29 (82.9)	10 (100)	0.16
	Present (1)	6 (17.1)	0 (0.0)	
6	**Basal cisterns open**			
	Absent (0)	23 (65.7)	10 (100)	0.031*
	Present (1)	12 (34.3)	0 (0.0)	
7	**Mass effect**			
	Absent (0)	31 (88.6)	10 (100)	0.5
	Present (1)	4 (11.4)	0 (0.0)	
8	**White cerebellar sign positive**			
	Absent (0)	31 (88.6)	10 (100)	0.5
	Present (1)	4 (11.4)	0 (0.0)	
9	**Midline shift (MLS) classified according to Wilcoxon's classification**			
	Absent (0)	23 (65.7)	10 (100)	0.16
	Present (<5)	8(22.9)	0 (0.0)	
	Present (>5)	4 (11.4)	0 (0.0)	

Abbreviations: CT, computed tomography; non-TBI, other than head injury TBI, traumatic brain injury.
*Significant p-values.

Supplementary Table S4 Correlation of histopathological score and β-APP score with length of stay

Length of stay	Histopathological score		β-APP score	
	In no. (max. 16)	%	In no. (max. 10)	%
1 day	8.6 ± 1.7	53.75 ± 1.1	8.5 ± 1.3	85 ± 13.5
3 day	10.18 ± 1.3	63.63 ± 7.8	8.63 ± 0.8	86.36 ± 8.9
5 day	10.6 ± 2	66.25 ± 12.2	9.8 ± 0.4	98 ± 4.5
7 day	10 ± 4.2	62.5 ± 26.5	9 ± 1.4	90 ± 14.1
2 weeks	11.5 ± 1	71.87 ± 6.3	9.25 ± 0.9	92.5 ± 9.5
2 weeks-1 month	10 ± 1.4	62.5 ± 8.8	9.5 ± 0.7	95 ± 7.07
> 1 month	12	75	9	90

Abbreviations: %, percentage; Max, maximum; β APP, beta-amyloid precursor protein.
Data shown in mean ± standard deviation.

Supplementary Table S5 Histopathological characteristics in corpus callosum and thalamus after DAI-associated TBI

S.no.	Histopathological character	Corpus callosum			Thalamus		
1	Degenerative changes score	Case (n = 35)	Control (n = 10)	p-Value	Case (n = 33)	Control (n = 10)	p-Value
	Absent (0)	26 (74.3)	10 (100)	0.56	8 (24.2)	8 (80)	0.01*
	Mild (1)	6 (17.1)	0 (0.0)		11 (33.3)	2 (20)	
	Moderate (2)	1 (2.9)	0 (0.0)		8 (24.2)	0 (0.0)	
	Severe (3)	2 (5.7)	0 (0.0)		6 (18.1)	0 (0.0)	
2	Infarction						
	Absent (0)	17 (48.6)	10 (100)	0.003*	24 (72.7)	10 (100)	0.063
	Present (1)	18 (51.4)	0 (0.0)		9 (27.3)	0 (0.0)	
3	Transection changes						
	Absent (0)	34 (97.1)	10 (100)	0.999	31 (94.0)	10 (100)	0.999
	Present (1)	1(2.9)	0 (0.0)		2 (6)	0 (0.0)	
4	Cellularity						
	Absent (0)	17 (48.6)	9(90)	0.02*	23 (70)	10(100)	0.04*
	Present (1)	18 (51.4)	1 (10)		10 (30.3)	0 (0.0)	
5	Axonal swellings						
	Absent (0)	5 (14.3)	6 (6.67)	0.01*	13 (39.4)	9 (90)	0.04*
	Mild (1)	11 (31.4)	2 (22.22)		13 (39.4)	1 (10)	
	Moderate (2)	12 (34.3)	1 (11.11)		6 (18.2)	0 (0.0)	
	Severe (3)	7 (20.0)	0 (0.0)		1 (3.0)	0 (0.0)	
6	Neovascularization						
	Absent (0)	29 (82.9)	10(100)	0.31	26 (78.8)	10(100)	0.11
	Present (1)	6 (17.1)	0		7 (21.2)	0	
7	Lipid-laden macrophages						
	Absent (0)	29 (82.9)	10(100)	0.31	29 (87.9)	10(100)	0.55
	Present (1)	6 (17.1)	0		4 (12.1)	0	
8	Gemistocytic astrocytes						
	Absent (0)	35 (100)	10(100)		33 (100)	10(100)	
	Present (1)	0	0		0	0	

(*Continued*)

Supplementary Table S5 (*Continued*)

S.no.	Histopathological character	Corpus callosum			Thalamus		
9	Congestion/edema						
	Absent (0)	8 (22.9)	7(70)	0.009*	6 (18.2)	5 (50)	0.09
	Present (1)	27 (77.1)	3 (30)		27 (81.9)	5 (50)	
10	Hemorrhage						
	Absent (0)	16 (45.7)	8(80)	0.07	24 (72.7)	9 (90)	0.40
	Present (1)	19 (54.3)	2(20)		9 (27.3)	1 (10)	
11	Vasculitis						
	Absent (0)	32 (91.43)	10(100)	0.999	32 (97)	10(100)	0.999
	Present (1)	3 (8.6)	0		1 (3)	0	
12	Hyalinized blood vessels						
	Absent (0)	29 (82.9)	10(100)	0.31	32 (97)	10(100)	0.999
	Present (1)	6 (17.1)	0		1 (3)	0	

Abbreviations: non-TBI, other than head injury, TBI, traumatic brain injury.
*significant *p*-values.

Supplementary Table S6 Histopathological characteristics in brain stem (midbrain, pons, and medulla oblongata) after DAI-associated TBI

S.no.	Histopathological character	Midbrain			Pons			Medulla oblongata		
		Case (*n* = 30)	Control (*n* = 10)	*p*-Value	Case (*n* = 34)	Control (*n* = 10)	*p*-Value	Case (31)	Control (*n* = 10)	*p*-value
1	Degenerative changes score									
	Absent (0)	5 (16.7)	7 (70)	0.006*	4 (11.8)	6 (60)	0.01*	9 (29.0)	6 (60)	0.05*
	Mild (1)	10 (33.3)	3 (30)		19 (55.9)	4 (40)		18 (58.1)	3 (30)	
	Moderate (2)	4 (13.3)	0 (0.0)		2 (5.9)	0 (0.0)		0 (0.0)	1 (10)	
	Severe (3)	11 (36.7)	0 (0.0)		9 (26.5)	0 (0.0)		4 (12.9)	0 (0.0)	
2	Infarction									
	Absent (0)	24 (80)	10 (100)	0.012*	30 (88.2)	10 (100)	0.55	30 (97.1)	9(90)	0.43
	Present (1)	6 (20)	0 (0.0)		4 (11.8)	0 (0.0)		1 (3.2)	1 (10)	
3	Transection changes									
	Absent (0)	17 (56.7)	5 (50)	0.73	27 (79.4)	5 (50)	0.10	24 (79.4)	10 (100)	0.09
	Present (1)	13 (43.3)	5 (50)		7 (20.6)	5 (50)		7 (20.6)	0 (0.0)	
4	Cellularity									
	Absent (0)	26 (86.7)	8(80)	0.62	32 (94.1)	10(100)	0.99	27 (87.1)	10100)	0.55
	Present (1)	4 (13.3)	2 (20)		2 (5.9)	0 (0.0)		4 (13.0)	0 (0.0)	
5	Axonal swellings									
	Absent(0)	15 (50.0)	5 (50.0)	0.999	14 (41.2)	8 (80.0)	0.20	7 (22.6)	6 (60.0)	0.20
	Mild (1)	10 (33.3)	4 (40.0)		14 (41.3)	2 (20.0)		13 (42.0)	2 (20.0)	
	Moderate (2)	4 (13.3)	1 (10.0)		5 (14.8)	0 (10.0)		9 (29.0)	2 (20.0)	
	Severe (3)	1 (3.3)	0 (0.0)		1 (2.3)	0 (0.0)		2 (6.5)	0 (0.0)	
6	Neovascularization									
	Absent (0)	26 (86.7)	10 (100)	0.55	32 (94.1)	10 (100)	0.99	29 (93.5)	10 (100)	0.999
	Present (1)	4 (13.3)	0		2 (5.9)	0		2 (6.5)	0	

Supplementary Table S6 (*Continued*)

S.no.	Histopathological character	Midbrain			Pons			Medulla oblongata		
7	Lipid-laden macrophages									
	Absent (0)	23 (76.7)	9 (90)	0.65	26 (76.5)	10 (100)	0.16	22 (71)	10 (100)	0.08
	Present (1)	7 (23.3)	1 (10)		8 (23.5)	0		9 (29)	0	
8	Gemistocytic astrocytes									
	Absent (0)	29 (96.7)	10 (100)	0.999	33 (97.0)	10 (100)	0.999	30 (96.8)	10 (100)	0.999
	Present (1)	1 (3.3)	0		1 (3)	0		1 (3.2)	0	
9	Congestion									
	Absent (0)	10 (33.3)	6 (60)	0.15	14 (41.2)	7 (70)	0.15	15 (48.4)	6 (60)	0.71
	Present (1)	20 (66.7)	4 (40)		20 (58.8)	3 (30)		16 (51.6)	4 (40)	
10	Hemorrhage									
	Absent (0)	15 (50)	7 (70)	0.46	14 (41.1)	7 (70)	0.15	26 (83.7)	9 (90)	0.999
	Present (1)	15 (50)	3 (30)		20 (58.9)	3 (30)		5 (16.3)	1 (10)	
11	Vasculitis									
	Absent (0)	30 (100)	10(100)		33 (97.0)	10(100)	0.99	31 (100)	10(100	
	Present (1)	0	0		1 (3)	0		0	0	
12	Hyalinized blood vessels									
	Absent (0)	29 (96.7)	10 (100)	0.999	33 (97.0)	10 (100)	0.99	29 (93.5)	10 (100	0.999
	Present (1)	1(3.3)	0		1 (3)	0		2(6.5)	0	

Abbreviations: non-TBI, other than head injury, TBI, traumatic brain injury;
*Significant *p*-values.

Supplementary Table S7 βAPP scoring for corpus callosum (amount per field at 200x magnification) in sTBI study patients

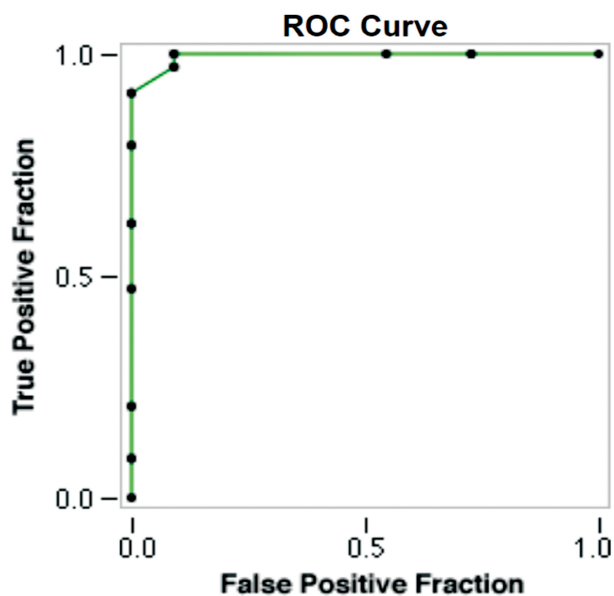| S.no.		Corpus Callosum – *n* (%)			Thalamus - n(%)		
1	Granular Changes	Case (*n* = 35)	Control (*n* = 10)	*p*-Value	Case (*n* = 33)	Control (*n* = 10)	*p*-Value
	Absent (0)	2 (5.7)	2 (20)	0.001*	1 (3.03)	4 (40)	0.007*
	1 to 5 (1)	4 (11.4)	6 (60)		9 (27.27)	2 (20)	
	6 to 20 (2)	13 (37.1)	2 (20)		16 (48.48)	0 (0)	
	>20 (3)	16 (45.7)	0 (0)		7 (21.21)	4 (40)	
2	Axonal swellings						
	Absent (0)	6 (17.1)	9 (90)	<0.001*	11 (33.33)	9 (90)	0.02*
	1 to 5 (1)	9 (25.7)	1 (10)		11 (33.33)	1 (10)	
	6 to 20 (2)	5 (14.3)	0 (0)		6 (18.18)	0 (0)	
	>20 (3)	15 (42.9)	0 (0)		5 (15.15)	0 (0)	
3	Retraction bulb						
	Absent (0)	7 (20)	10 (100)	<0.001*	18 (5 4.55)	10(100)	0.008*
	Present (1)	28(80)	0 (0)		15 (45.45)	0 (0)	
4	Granular bands						
	Absent (0)	6 (17.1)	10 (100)	<0.001*	16 (48.48)	10 (100)	0.003*
	Present (2)	29(82.9)	0 (0)		17 (51.52)	0 (0)	
5	Non Granular band						
	Absent (0)	10 (28.6)	10 (100)	<0.001*	13 (39.39)	10 (100)	0.001*
	Present (1)	25 (71.4)	0 (0)		20 (60.61)	0 (0)	

Abbreviations: non-TBI, other than head injury, TBI, traumatic brain injury.
*Significant *p*-values.

Supplementary Table S8 βAPP Scoring for brain stem (midbrain, pons, and medulla oblongata) in sTBI study patients

S.no.	Amount per field at 200x magnification	Midbrain			Pons			Medulla oblongata		
1	Granular changes	Case (n = 30)	Control (n = 10)	p-Value	Case (n = 34)	Control (n = 10)	p-Value	Case (n = 31)	Control (n = 10)	p-Value
	Absent (0)	3 (10.0)	3(30)	0.40	3 (8.8)	2(20)	0.002*	5 (16.1)	3(30)	0.002*
	1 to 5 (1)	10 (33.3)	4(40)		9 (26.5)	8(80)		6 (19.4)	7(70)	
	6 to 20 (2)	14 (46.7)	3(30)		14 (41.2)	0(0)		12 (38.7)	0 (0)	
	>20 (3)	3 (10.0)	0(0)		8 (23.5)	0(0)		8 (25.8)	0 (0)	
2	Axonal swellings									
	Absent (0)	9 (30.0)	8 (80)	0.05*	6 (17.7)	9(90)	<0.001*	9 (29.0)	9 (90)	0.01*
	1 to 5 (1)	12 (40)	2 (20)		16 (47.1)	1(10)		13 (43)	1 (10)	
	6 to 20 (2)	6 (20)	0 (0)		6 (17.7)	0(0)		6(19.4)	0 (0)	
	>20 (3)	3 (10)	0 (0)		6 (17.7)	0(0)		3(9.7)	0 (0)	
3	Retraction bulb									
	Absent (0)	16 (53.3)	9(90)	0.06*	9 (26.5)	10(100)	<0.001*	14 (45.2)	10(100)	0.002*
	Present (1)	14 (46.7)	1(10)		25 (73.5)	0(0)		17 (54.8)	0(0)	
4	Granular bands									
	Absent (0)	15 (50)	10(100)	0.006*	12 (35.29)	10(100)	0.001*	20 (64.5)	10(100)	0.07*
	Present (2)	15 (50)	0(0)		22 (64.71)	0(0)		11 (35.5)	0(0)	
5	Non granular bands									
	Absent (0)	15 (50)	10(100)	0.006*	16 (47)	10(100)	0.003*	16 (51.6)	10(100)	0.007*
	Present (1)	15 (50)	0(0)		18 (53)	0(0)		15 (48.4)	0(0)	

Abbreviations: non-TBI, other than head injury, TBI, traumatic brain injury.
*Significant p-Values.

ROC Curve

Supplementary **Fig. S1** AUC analysis of the novel classification.