Delayed Cerebellar Injury is Affected by Multiple Organ Dysfunction Syndrome Caused by Heat Stroke, a Retrospective Cohort Study

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Research

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Abstract

Objective Nervous dysfunction is the main manifestation of heat stroke (HS). Here we investigated the clinical signs for HS-induced nerve injuries.

Methods Retrospective data were collected on 119 patients who got HS from 2016 to 2020. Patients were divided into 4 groups, including the cerebellar injury group, the other nerve injuries group, non-cerebellar injury group and non-nerve injury group. The age, body temperature (Tc), degree of consciousness disorder, liver and kidney function, blood coagulation function, blood routine and cardiac indicators within 24 h after HS were summarized. Moreover, we performed regression analyses to identify risk factors for nervous dysfunction. The Activity of Daily Living (ADL) score was assessed 3 months after HS to evaluate the prognosis of HS.

Results Compared with other groups, the cerebellar injury group had shorter Tc recovering time, lower GSC scales, longer coma time and more hypotension, gastrointestinal bleeding, multiple organ dysfunction syndrome (MODS) and metabolic acidosis significantly. The cerebellar injury group had higher myocardial enzymogram and indexes of liver and kidney dysfunction, immune and coagulation dysfunction significantly. Risk factors associated with HS-induced cerebellar injury are Tc, recovery time of Tc, NSE, GCS scale, lymphocyte count, HLA-DR/CD14, coagulation dysfunction, cardiac injury, metabolic acidosis and MODS. The ADL scale of the cerebellar injury group and the other nerve injury group were significantly lower than other groups.

Conclusions Patients with severe coma and MODS are more prone to cerebellar injury after HS and the HS-induced nerve injury leaded to a worse prognosis.

Introduction

Heat stroke (HS) is diagnosed with hyperthermia (core temperature ≥ 40°C), nervous system dysfunction and multiple organ dysfunction syndrome (MODS). Central nervous system (CNS) damage is the main feature of severe HS. Neurological sequelae are difficult to avoid even if the treatment is timely [1]. There are various manifestations of nervous system damage after HS, including cerebellar injury, subarachnoid hemorrhage, peripheral nerve injury, brainstem injury, Guillain-Barré syndrome and so on. However, there is few analyses of clinical signs and risk factors for these nerve injuries induced by HS. Some nerve injury, such as cerebellar injury, has no clinical manifestations in the early period of HS, leading to delayed treatment and neurological sequelae. When to start the treatment of nerve injury due to HS is a problem.

Therefore, this study aimed to analyze the clinical features and relevant factors of the nerve injuries after HS to help prevent and diagnose nervous disorders.

Methods

Study design

In this retrospective single-center study, we reviewed the electronic medical records for 119 patients who had HS from March 1st, 2016, to October 1st, 2020. Patients who diagnosed with HS according to the Consensus on diagnosis and treatment of HS in China were included [2]. Patients were divided into 4 groups according to the type of injuries, including the cerebellar injury group, the other nerve injuries group, non-cerebellar injury group and non-nerve injury group. The average age, body temperature (immediately after admission), degree of consciousness disorder (DOC), liver and kidney function, blood coagulation function, blood routine and cardiac indicators within 24 h after HS were summarized.

Variables

Factors demonstrated to impact nerve injury or thought by the investigators to potentially impact nerve injury were defined as independent variables. These were patient demographics (age and sex), core temperature (Tc), recovery time of Tc, background diseases, hospitalization time, Glasgow coma scale (GCS), Neuron-specific enolase (NSE), hypotension, convulsion, gastrointestinal bleeding, MODS, the blood routine index (WBC, neutrophil count, lymphocyte count, blood platelet count and HCT), blood clotting index, including DD-dimer, prothrombin time (PT), activated partial thromboplasting time (APTT), liver and renal function (ALT, AST, creatinine and AST/ALT), CK, cardiac function index, including Lactate dehydrogenase (LDH), myohemoglobin and hypersensitive troponin T (hs-tnt), sequential organ failure assessment (SOFA) and Acute Physiology and Chronic Health Evaluation-Ⅱ (APACHE-Ⅱ). Compared with the non-cerebellar injury group and the other nerve injuries group, the related factors (RF) of HS-induced cerebellar injury were analyzed by regression analysis.

Prognosis

To compare the prognosis of patients with or without cerebellar injury after HS, the Activity of Daily Living (ADL) score was assessed 3 months after HS using Barthel index. Death records were excluded. Because all death cases died within 1 month after the onset of HS, the Barthel index of death cases cannot be measured 3 months later.

Statistics

Descriptive statistics were calculated for the variables of interest. Categorical data are presented as counts and percentages and continuous data are presented as median in an interquartile range. Missing dates were deleted. After the homogeneity of variance test, multiple comparisons among different groups were compared using one-way analysis of variance (ANOVA) followed by the Student–Newman–Keuls (SNK) test, and differences between two groups were compared by the two independent-samples Student's *t*-test. Risk factors which might be associated with HS-induced cerebellar injury were assessed via univariate and, if significant, multivariate logistic regression analysis (LRA). Results from the LRA are

given as odds ratios (ORs) with 95% confidence interval. All statistical analyses were performed using IBM SPSS v19.0. A p value < 0.05 was considered statistically significant.

Results

Patient demographics and clinical characteristics

A total of 119 HS patients admitted from March 2016 to December 2020 were counted. The mean age of these patients was 23.53 ± 0.72 years, and 116 (97.48 %) were men. 116 (97.48%) patients developed HS under high temperature, high humidity, and high heat radiation conditions, 1 (0.84%) patient developed symptoms in a poorly ventilated room and 2 (1.68%) patients developed HS when training without high temperature. Prevalent comorbidities identified among the cohort were hypertension (2 patients, 1.68%) and ankylosing spondylitis (1 patients, 0.84%).

Of the 119 total patients, 34 (28.57 %) cases had neurological dysfunction, 13 (10.92 %) cases had cerebellar dysfunction, 6 (5.04%) cases of multiple intracranial lesions, 5 (4.2%) cases of epilepsy, 4 (3.36%) cases of severe peripheral nerve injury, especially the 2 (1.68%) cases of Guillain-Barré syndrome, 2 (1.68%) cases of subarachnoid hemorrhage, 2 (1.68%) cases of diffuse cerebral edema, 1 (0.84%) case of brain abscess and 1 (0.84%) case of brain stem injury. Magnetic resonance images (MRI) of different nerve injuries caused by HS were shown in Fig. 1. Cerebellar injury accounted for the highest rate of all nerve injuries induced by HS. Among all patients with nervous injuries, the rate of patients with severe coma is 52.94%. The number of cases in the cerebellar injury group was 13, 21 cases in the other nerve injuries group, 85 cases in no-nerve injury group and 106 cases in non-cerebella injury group. The period from HS to the appearance of cerebellar injury was 18.6 ± 1.59 days, longer than other nervous injury induced by HS significantly (Table 1). The screening process of the clinical data is shown in Fig. 2.

Table 1
Clinical manifestations of the 34 patients with nervous system injury induced by HS

Clinical dates	**nervous injury**		**HS**		
	n	% of nerve injury	n	% of HS	
Sex (male)	33	97.06	116	97.48	
Basic illness	3	8.82	5	4.2	
Degree of DOC	n	% of nerve injury	n	% of HS	
Light coma	8	23.53	20	16.8	
Moderate coma	6	17.65	6	5.04	
Severe coma	18	52.94	20	16.8	
nervous system symptoms	n	% of nerve injury	n	% of HS	Time from HS to nerve injury (days)
cerebellar dysfunction	13	38.24	13	10.92	18.6 ± 1.59
multiple intracranial lesions	6	17.65	6	5.04	12.5 ± 2.7
epilepsy	5	14.71	5	4.2	2 ± 0.45
peripheral nerve injury	4	11.76	4	3.36	10.5 ± 3.2
diffuse cerebral edema	4	11.76	4	3.36	3 ± 0
Ischemic-hypoxic encephalopathy	3	8.82	3	2.52	1.7 ± 0.67
Guillain-Barré syndrome	2	5.88	2	1.68	14 ± 1
weakened muscle strength	2	5.88	2	1.68	7.5 ± 4.5
subarachnoid hemorrhage	2	5.88	2	1.68	10.5 ± 5.5
stroke	1	2.94	1	0.84	5
brain abscess	1	2.94	1	0.84	14
brainstem injury	1	2.94	1	0.84	10

The time from onset to admission of the patients is between 30 min and 5 hours, with an average time of 6.01 ± 1.01 hour. Patients with cerebellar injury were older than the patients with other nerve injuries or no nerve injury. Compared with other groups, the cerebellar injury group had slower temperature recovering, lower GSC scales, longer coma time and more hypotension, gastrointestinal bleeding, MODS, cardiac damage, coagulation disorder and metabolic acidosis. (Table 2)

Table 2
Clinical features and complications to heat stroke-induced brain injury

	cerebellar injury	the other nerve injuries	non-cerebellar injury	non-nerve injury
time from onset to visit (h)	2.12 ± 0.44	4.74 ± 2.46*	6.52 ± 1.1**	6.88 ± 1.22
Age (year)	29.77 ± 3.89	23.38 ± 2.08**	22.76 ± 0.55**	22.61 ± 0.38**
Tc (℃)	40.52 ± 0.47	39.35 ± 0.43	38.85 ± 0.18**	38.71 ± 0.19**
Time of Tc recovering(h)	8.38 ± 1.90	4.71 ± 0.60	2.92 ± 0.27**	2.49 ± 0.32**
GSC scales	6.3 ± 1	9.95 ± 1.11*	13.7 ± 0.48**	14.6 ± 0.54**
coma time (day)	9.96 ± 3.26	14.21 ± 3.86	3.05 ± 1.75**	0.15 ± 1.88**
Systolic pressure(mmHg)	88.08 ± 3.81	103.85 ± 6.32	113.17 ± 2.71**	115.56 ± 3.0**
Diastolic pressure(mmHg)	51.85 ± 3.9	57.8 ± 3.89	65.43 ± 1.79**	67.39 ± 2.00**
	cerebellar injury	the other nerve injuries	non-cerebellar injury	non-nerve injury
Hypotension	10 (76.92%)	12(57.14%)	18(16.98%)**	6(7.06%)**
gastrointestinal bleeding	9 (69.23%)	9 (42.86%)	16 (15.09%)**	7 (8.24%)**
MODS	13 (100)	17 (80.95)	66 (62.26)**	49 (57.65)**
cardiac damage	13 (100)	14 (66.67)	38 (35.85)**	24 (28.24)**
coagulation disorder	12 (92.31)	15 (71.43)	39 (36.8)**	24 (28.24)**
metabolic acidosis	8 (61.54)	10 (47.62)	18 (16.98)**	8 (9.41)**
convulsion	7 (53.85)	9 (42.86)	39(36.79)	30(35.29)
rhabdomyolysis	12(92.3)	15(71.43)	63(59.43)	48(56.47)
Data are shown as mean ± S.E.M., * $P < 0.05$, ** $P < 0.01$ vs the cerebellar injury group.				
Laboratory examination				
Compared with other groups, the cerebellar injury group had higher indexes of creatine kinase (CK), Alanine transaminase (ALT), Aspertate Aminotransferase (AST), lactic dehydrogenase (LDH), serum bilirubin levels, SOFA scales, increased Prothrombin time (PT), lower levels of lymphocyte count, plaquettes count, hematocrit (HCT) and the ratio of HLA-DR/CD14 significantly. (Table 3)				

Table 3
Myocardial enzymogram and indexes of liver and kidney function, immune function, coagulation function and MODS in each group

	cerebellar injury	the other nerve injuries	non-cerebella injury	non-nerve injury
CK	6553 ± 4012	3813 ± 1327	1835 ± 591.6	1383 ± 644.2
myohemoglobin	1390 ± 303	900.9 ± 246.3	729.1 ± 110.3	667.5 ± 121.9
hs-tnt	752.1 ± 166.1	916.6 ± 376.2	324.3 ± 167.8	106 ± 187.4
ALT	838.3 ± 417	137.9 ± 51.1**	209.5 ± 22.4**	227.2 ± 25.2**
AST	1158 ± 571.1	534.4 ± 372.3	231.4 ± 165.9**	156.6 ± 185.3**
bilirubin	50.4 ± 11.2	35.6 ± 8.6	24.7 ± 3.8	22.1 ± 4.3
creatinine	144.9 ± 20.1	126.3 ± 16.4	114 ± 7.4	111 ± 8.1
LDH	1197 ± 337	963 ± 269	471 ± 123	351 ± 135
DD-dimer	15.12 ± 1.9	11.18 ± 2.4	8.7 ± 1.1	7.8 ± 1.2
PT	25.9 ± 2.3	19.8 ± 1.6	16.2 ± 0.7	15.3 ± 0.8
APTT	0.92 ± 0.08	0.71 ± 0.1	0.38 ± 0.05	0.29 ± 0.05
AB	20.7 ± 1.33	23.2 ± 0.59	21.9 ± 0.26	21.1 ± 0.28
SB	21.8 ± 1.09	23.1 ± 0.49	22.1 ± 0.22	21.5 ± 0.23
potassium concentration	3.52 ± 0.16	3.68 ± 0.07	3.86 ± 0.03	3.90 ± 0.04
sodium concentration	141.7 ± 0.77	141.8 ± 0.90	141.57 ± 0.4	141.5 ± 0.37
WBC	8.44 ± 0.7	11.4 ± 1.4**	9.6 ± 0.65*	9.17 ± 0.7*
neutrophil count	7.36 ± 0.68	8.87 ± 1.27	7.16 ± 0.57	6.76 ± 0.65
lymphocyte count	0.6 ± 0.1	1.7 ± 0.2	1.7 ± 0.1	1.7 ± 0.1
blood platelet count	70 ± 17	149 ± 24*	178 ± 11*	185 ± 8.8*
HCT	0.37 ± 0.016	0.38 ± 0.014	0.41 ± 0.006	0.42 ± 0.007
NSE	18 ± 1.66	108 ± 38.3	66.9 ± 19.5	12.6 ± 21.7
HLA-DR/CD14	64.1 ± 7.3	74.5 ± 3.3	82.1 ± 1.6	85.9 ± 1.8
CD14	34.5 ± 7.3	24.2 ± 3.2	16.1 ± 1.6	12 ± 1.8
SOFA	7.7 ± 0.8	5.2 ± 1.0	2.0 ± 0.4	1.3 ± 0.5

Data are shown as mean ± S.E.M., * $P < 0.05$, ** $P < 0.01$ vs the cerebellar injury group.

	cerebellar injury	the other nerve injuries	non-cerebella injury	non-nerve injury
APACHE Ⅱ	16.15 ± 1.69	15.85 ± 1.81	15.85 ± 0.77	14.69 ± 0.89
Data are shown as mean ± S.E.M., * *P*< 0.05, ** *P*< 0.01 vs the cerebellar injury group.				

Univariate analysis

In univariate regression analyses, factors that demonstrated borderline statistical significance (defined as $p < 0.05$) in their association with cerebellar injury included: Tc > 40°C ($p = 0.13$), recovery time of Tc > 3 h ($p = 0.14$), NSE > 16.3 ($p = 0.004$), GCS scale < 9 ($p < 0.01$), lymphocyte count > 3.2×10^9/L ($p = 0.001$), HLA-DR/CD14 < 75% ($p = 0.039$), gastrointestinal bleeding ($p = 0.008$), DD-dimer > 0.5 ($p = 0.037$), coagulation dysfunction ($p = 0.004$), cardiac injury ($p = 0.004$), CK > 1000 ($p = 0.001$), hs-tnt > 100 ($p = 0.002$), LDH > 500 ($p = 0.001$), metabolic acidosis ($p = 0.003$), MODS ($p < 0.01$) and SOFA scale ($p = 0.042$) (Table 4). Among them, GCS < 9, APTT > 44s, lymphocyte count < 1.1×10^9/L, PLT < 120×10^9/L and ALT > 80 U/L were associated with cerebellar injury compared with the other nerve injury group (Table 5). In addition, there were 5 missing dates in HLA-DR/CD14, 12 missing dates in NSE and 9 missing dates in hs-tnt.

Table 4
Multiple regression analysis of relevant factors(RF)of HS-induced cerebellar injury compared with non-cerebellar injury

relevant factors(RF)	B	SE	Wald	*P*	Exp(B)	95%*CI*	*OR*
Tc (℃) > 40℃	1.86	0.75	6.19	0.13	6.42	1.49–27.80	9.75
recovery time of Tc > 3h	2.1	0.86	6.01	0.14	8.17	1.52–43.8	10.7
NSE > 16.3	2.48	0.87	8.12	0.004	11.89	2.165–65.28	15.26
GCS < 9	3.35	0.78	18.7	0.01	28.54	6.25-130.35	32
lymphocyte count < 1.1×10^9/L	2.71	0.83	10.62	0.001	15.06	2.95–76.97	9.75
HLA-DR/CD14 < 75%	2.09	1.01	4.28	0.039	8.06	1.12–58.31	12.12
gastrointestinal bleeding	-2.21	0.833	7.05	0.008	0.11	0.021–0.561	12.66
DD-dimer > 0.5	2.79	1.33	4.37	0.037	16.23	1.19-221.39	33.43
coagulation dysfunction	-1.101	0.372	8.772	0.003	0.333	0.161–0.689	20.62
cardiac injury	1.879	0.645	8.483	0.004	6.550	1.849–23.200	20.62
CK > 1000	2.23	0.69	10.31	0.001	9.29	2.38–36.2	12.54
hs-tnt > 100	4.09	1.33	9.52	0.002	60	4.45-808.643	62.82
LDH > 500	2.21	0.65	11.6	0.001	9.11	2.56–32.46	9.1
metabolic acidosis	-1.031	0.346	8.895	0.003	0.357	0.181–0.702	7.82
MODS	-11.85	618.89	55.435	0.01	20.750	9.339–46.101	8.2
SOFA > 5	2.54	1.25	4.13	0.042	12.63	1.095–145.6	33.37
AST/ALT > 1	2.14	0.85	6.39	0.11	8.48	1.62–44.45	3.61

Table 5
Multiple regression analysis of relevant factors(RF)of HS-induced cerebellar injury compared with the other nerve injury

relevant factors(RF)	B	SE	Wald	*P*	Exp(B)	95%*CI*	*OR*
GCS < 9	1.68	0.82	4.17	0.041	5.38	1.07–27.05	8.75
APTT > 44s	-2.4	1.2	4	0.045	0.09	0.01–0.09	0.786
lymphocyte count < 1.1×10^9/L	2.18	0.9	5.95	0.015	8.86	1.53–51.18	6.25
PLT < 120×10^9/L	1.8	0.88	4.14	0.042	6.05	1.07–34.23	7.15
ALT > 80U/L	1.9	0.81	5.56	0.018	6.67	1.38–32.28	7.62

Prognosis

The Barthel index of the cerebellar injury group was 67.7 ± 7.43, significantly lower than no nerve injury group (99.8 ± 3.64) and no cerebella injury group (95.6 ± 3.58), but the difference fell short of statistical significance compared with the other nerve injuries group (73.8 ± 9.08) (Fig. 3). There were no deaths in patients with cerebellar injury. All death cases happened in the group of the other nerve injuries. The average time from the onset of HS to death in the death cases was 14.2 ± 5.28 days and with diffuse cerebral edema and subarachnoid hemorrhage.

Discussion

We performed a retrospective cohort study of 119 adult patients who suffered from HS. The patients with higher Tc, longer temperature recovering time, lower GSC scales, longer coma time, higher NSE, lower lymphocyte count, coagulation dysfunction, cardiac injury, metabolic acidosis and MODS are more prone to suffered from cerebellar injury after HS. The degree of coma, shock and multiple organ damage within 24 h after HS are RFs for cerebellar injury. Moreover, patients with HS-induced nerve injuries had worse prognosis than non-cerebellar injury and non-nerve injury presented. These results indicated that patients with MODS and severe DOC in the early period of HS are more likely to give rise to cerebellar injury.

There are various types of nervous injuries related to HS. In this study, all patients with diffuse cerebral edema died. This warned us to pay great attention to cerebral edema after HS and start brain protection therapy, necessary dehydration and decreasing intracranial pressure as soon as possible. Cerebellar dysfunction occurred frequently 18.6 days after HS and the sequelae lasted for about 1–2 years. It is also the main factor affecting the life ability of HS patients in the later period. This suggested us to pay attention to early recognition of the signs of cerebellar dysfunction and start the treatment and rehabilitation early.

At the early stage of HS, evaluation of nervous system function is very important for predicting nervous injury. Among all the factors, GCS < 9 had the most significant correlation. The coma time of patients with cerebellar injury were also longer than those without cerebellar injury. These results suggested that the degree and time of coma in the early stages of HS patients predicted the occurrence of later cerebellar injury. The degree of coma is also an indicator of cerebral hypoxia[3]. Moreover, NSE > 16.3 was also a RF for HS-induced cerebellar injury in this study. NSE has been suggested as a prognostic biomarker for neuronal injuries suffering from traumatic brain injury, neurodegenerative disease, or cardiac arrest and found increased in HS models[4–6]. NSE expression was significantly higher in cerebellar cortex than whole-brain expression as investigated in the whole brain and whole genome-wide atlas of the Allen Institute for Brain Sciences (Seattle, WA)[4]. These results are consistent with our analysis, suggesting that NSE in serum may be a biomarker of HS-induced cerebellar injury.

Previous literature suggested that cerebellar dysfunction after HS was related to acute vertebrobasilar territory infarcts, leading to acute posteromedial midbrain and cerebellar infarcts [7]. Patients often behaved as scanning speech and limb ataxia after being conscious. Early cranial imaging examinations often fail to see structural abnormalities. Cerebellar atrophy can be observed six months after HS. The patients who developed infarction/posterior reversible encephalopathy syndrome (PRES)-like lesions in the early stage and survived often developed cerebellar sequelae. Among the PRES-like lesions, most exhibited the dominant parietal-occipital pattern (DPOP)[8]. Brain lesions caused by HS are mostly bilaterally symmetrical[9]. Under normal circumstances, these small lesions will not cause serious neurological deficits and serious sequelae. But in this study, the corresponding injury symptoms are severe and the prognosis is poor. It suggested that high fever and its secondary inflammatory reaction, apoptosis, etc. might cause serious damage to neurons or nerve fibers and extensive tissue necrosis[10]. The HS-induced injuries of liver and kidney function and coagulation function is severe, but the prognosis is better and the affects on life ability is small. Because neurons cannot regenerate and the repair and connection of nerve fibers progresses slowly and incompletely[11], it may provoke separations of the nerve stumps and the axonal proliferation of the conduits is restricted, the treatment and rehabilitation to nerve injury is very difficult, leading to a worse prognosis and a lower quality of life for patients with HS-induced nerve injury.

Cardiac injury is the correlative factor of cerebellar injury, manifested by increased myocardial enzyme profile. The mechanism of the association between HS-induced heart injury and brain injury remains unclear so far. The incidence of cardiac dysfunction in patients with severe HS is 43.4%~65.2% [12]. HS-induced cardiac injury is considered to be associated with cardiomyocytes and endothelial cells injury caused by direct heat damage, calcium overload and ROS [13, 14]. Endothelial cell injury can lead to microvascular embolism, resulting in myocardial cell ischemia, hypoxia and causing myocardial infarction like symptoms[15]. Impairment of cardiac function, such as reduced cardiac output and high burden of cardiovascular risk factors, could aggravate hypotension, leading to intracranial hypoperfusion, and thus aggravating cerebral ischemia. Neurohormonal, nutritional, and inflammatory mechanisms were also involved in this complex process of cardiac injury-induced brain injury[16, 17]. Neuronal death,

including apoptosis, autophagy, necroptosis and ferroptosis, are delayed for hours or days after ischemia-reperfusion of brain[16]. Perhaps that may explain why nerve injury occurred several days after HS rather than immediately. Why do Purkinje cells die so easily after global brain ischemia? Deficiencies in aldolase C and EAAT4 that allow Purkinje cells to survive after the restoration of blood flow might explain the particularity of cerebellar injury[18].

In addition, coagulation dysfunction is also associated with cerebellar injury induced by HS. Disseminate intravascular coagulation (DIC) is an independent cause of death in HS [19]. HS-induced coagulation dysfunction is triggered by changes of coagulation factors ,thrombocytopenia, inflammatory activation and endothelial injury[19, 20]. We all know that tissue-type plasminogen activator (t-PA) or urokinase-type plasminogen activator (u-PA) promotes fibrin breakdown. T-PA had been shown to not only have key roles in modulating astrocytes, neurons and microglia, but also to have profound effects in a number of CNS conditions, including ischemic stroke, severe traumatic brain injury and also in neurodegenerative disorders[21]. However, the mechanism of cerebellar injury caused by HS-induced coagulation dysfunction is still unclear.

Moreover, immunological indexes were also associated with occurrence of cerebellar injury. The ratio of HLA-DR/CD14 and lymphocytopenia indicated an immune deficiency and hyperinflammatory state. This result indicated that inflammatory response and decreased immune function could also lead to cerebellar injury after HS, which is related to the mechanism of HS-induced inflammatory response to brain tissue. In the last few years, more and more evidence suggested that cerebellar ataxias in some patients develop through immune-mediated mechanisms[22]. Cell-mediated mechanisms responsible for myelin injury have been proposed to be lymphocytes activated by antigens entering the blood brain barrier and lymphocyte-induced myelin damage mediated through the actions of tumor necrosis factor or other certain substances[22]. In our study, we also found two cases of HS-induced Guillain-Barre syndrome, a typical demyelinating disease. These results suggested that myelin injury caused by immune system disturbance may play an important role in the mechanism of cerebellar injury caused by HS.

The deficiency of this study is that the sample size of patients with various types of nerve injury is small, so that the sample size of imaging evaluation indexes is insufficient for statistical analysis. The degree of coma and multiple organ damage within 24 hours after HS are RFs for cerebellar injury of HS, suggesting the role of inflammation, blood coagulation and immunity in the mechanism of cerebellar injury after HS. Patients with nerve injury had worse prognosis, suggesting us to identify the related factors of cerebellar injury in the early stage of HS, and to start the treatment and prevention to brain injury early to improve the prognosis of HS.

Conclusions

Patients with severe coma and MODS are more prone to cerebellar injury after HS and the HS-induced nerve injury leaded to a worse prognosis than those without nerve injury. These results suggested us that it is important to diagnose and treat the HS-induced nerve injuries early, especially cerebellar injuries.

Declarations

Ethics approval and consent to participate

We confirm adherence to ethical guidelines and ethical approvals (IRB).

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

Xiao-xiao Ni: Data curation-Writing- Original draft preparation, Cong-lin Wang: Data curation, Jie Wang: Investigation, Ye-qun Guo: Methodology, Yan Chen: Conceptualization, Bo Zheng: Data curation, Rong-hao Yu: Supervision, Zhi-feng Liu: Funding acquisition, Writing- Reviewing and Editing.

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Figures

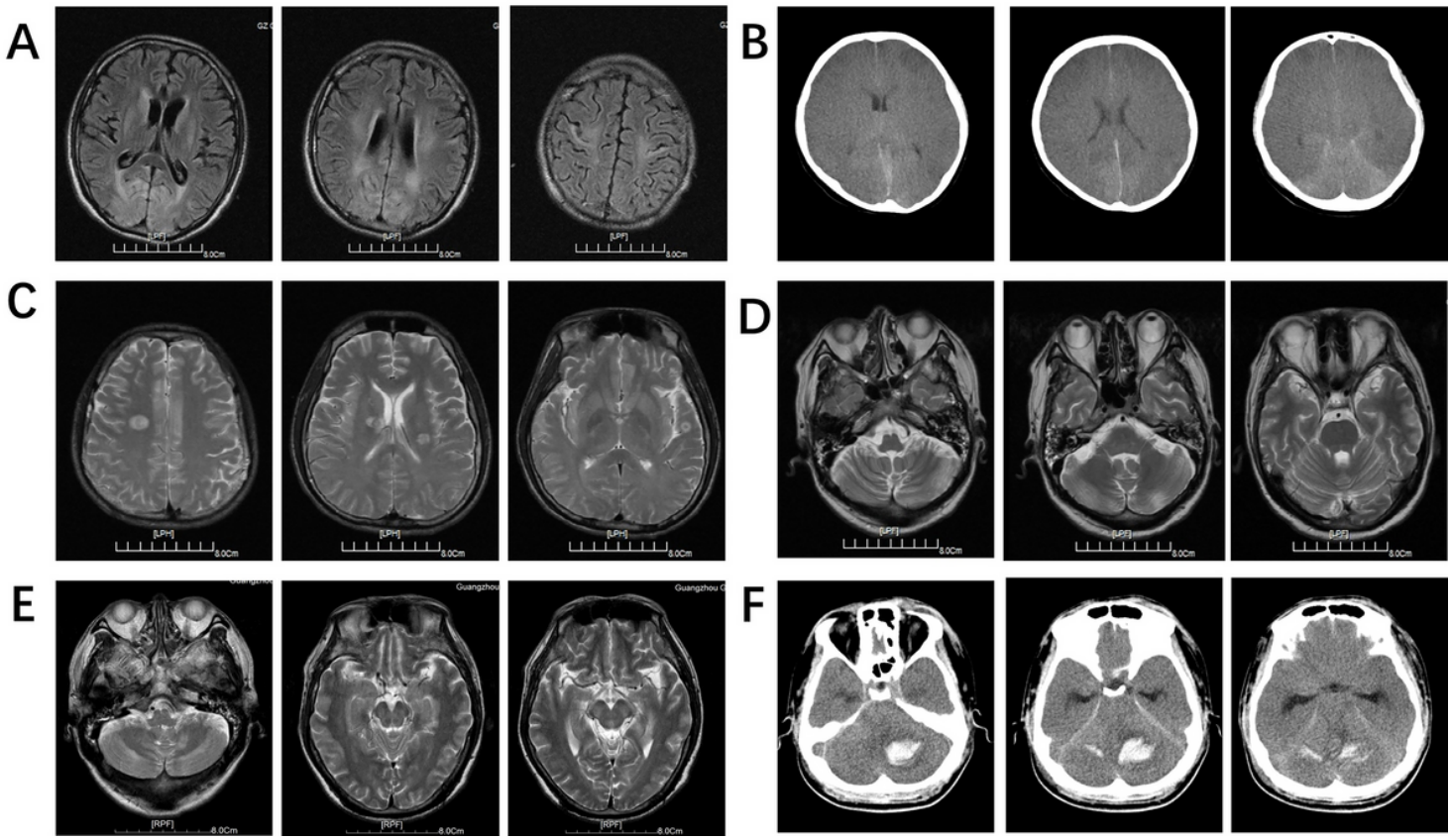

Figure 1

Imaging manifestations of brain injury after heatstroke A: MRI imaging (T1 sequence) of ischemic hypoxic encephalopathy; B: CT imaging of diffuse cerebral edema with subarachnoid hemorrhage; C: MRI

imaging (T2 sequence) of brain abscess; D: MRI imaging (T2 sequence) of cerebellum atrophy; E: MRI imaging (T2 sequence) of brainstem ischemia with multiple intracranial lesions; F: CT imaging of cerebral edema and cerebellar hemorrhage.

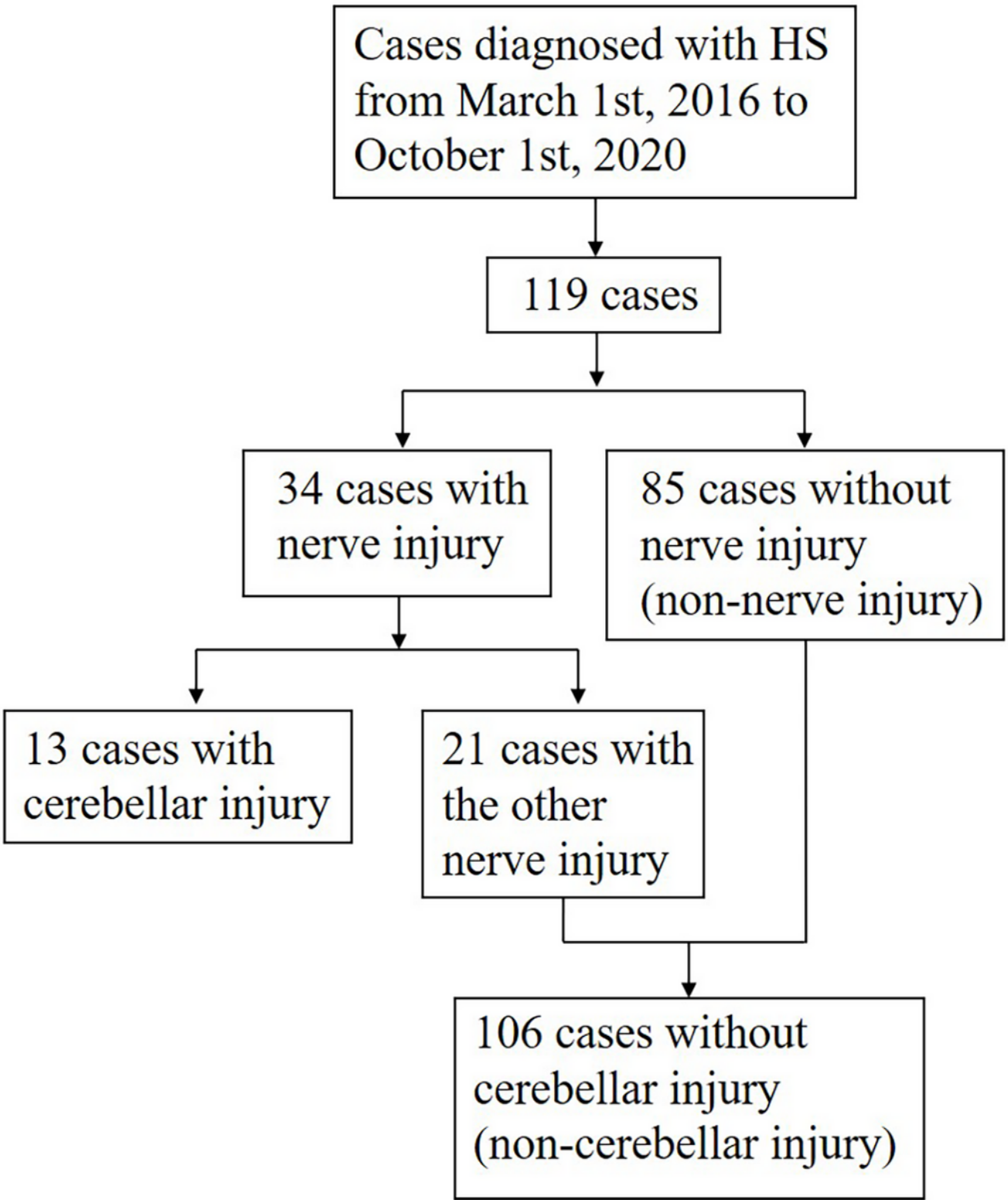

Figure 2

The clinical data screening process of cases in this study

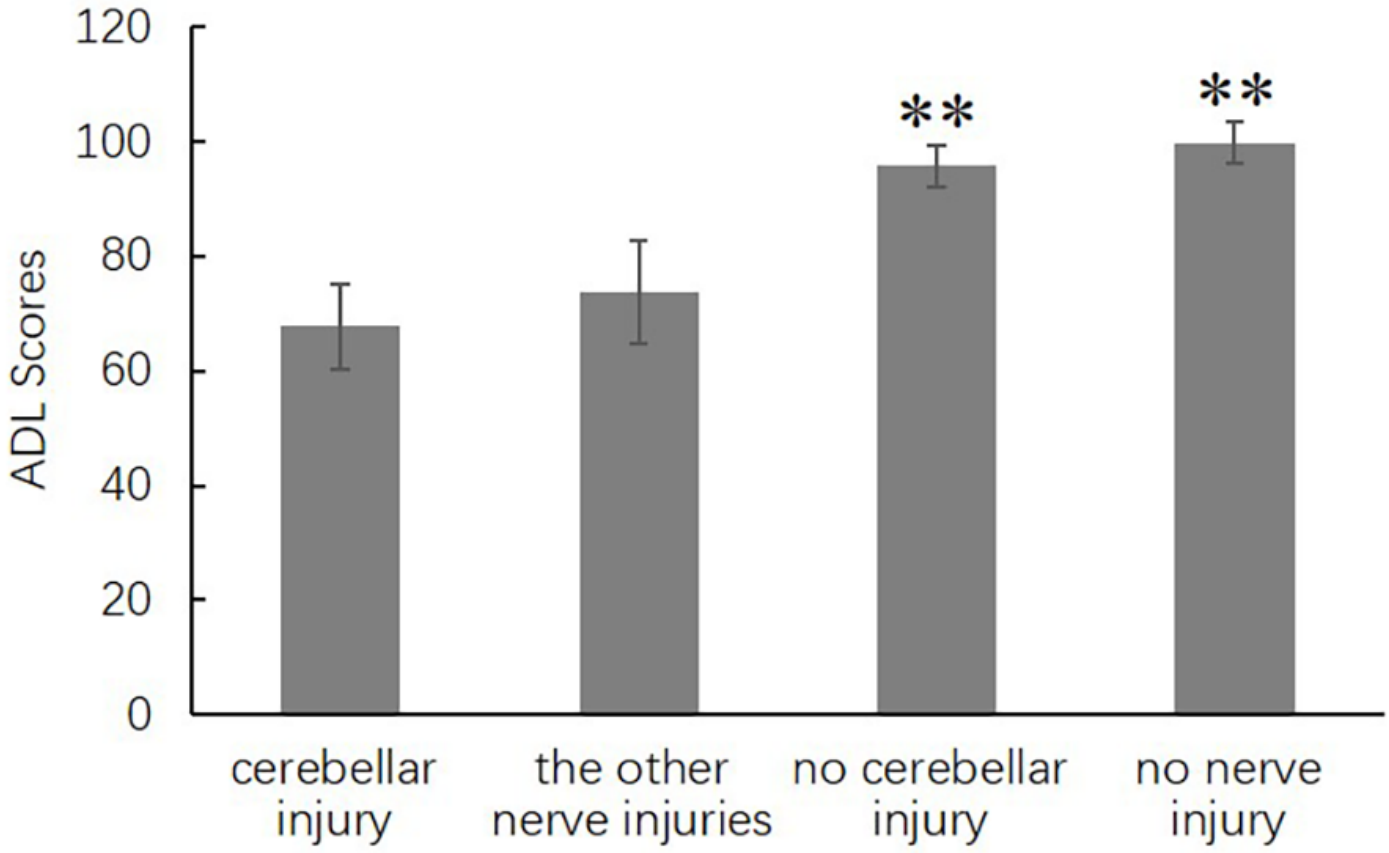

Figure 3

The Barthel index of cerebellar injury and other groups three months after the onset of heatstroke Data are shown as mean ± S.E.M., * P<0.05, ** P<0.01 vs the cerebellar injury group.

Supplementary Files

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