ORIGINAL ARTICLE

The importance of hemosiderin deposition in the infant brain: an autopsy study

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Abstract

Background/aim: Iron is an essential element involved in many metabolic processes. Presence and accumulation of iron in various body systems can result in different outcomes. Its accumulation in the central nervous system (CNS) cannot be detected routinely by application of hematoxylin-eosin staining. Detection of the presence of hemosiderin in the brain and cerebellum by application of Perls' dye is of importance in cases of infant deaths.

Material and Methods: In this study, brain and cerebellar specimens obtained from 52 eligible infants (aged 0-1 years) autopsied in our institute between the years 2010 and 2013, independent of the cause of death, were analyzed in order to detect possible presence of hemosiderin. Perls' dye was used to detect histopathological staining intensity and distribution of hemosiderin in the brain and cerebellum.

Results: Cases did not differ significantly as for the patients' age and gender (p =0.473), type of the culprit trauma (p =0.414), death/crime scene (p =0.587), and diagnosis groups (p =0.550). In this autopsy study blue colored hemosiderin granulations, stained with Perls' dye were detected in the brain (n: 39, 75%), and cerebellum (n: 35, 67.3%). A weakly negative, but significant correlation was detected between the postmortem interval and intensity values of cerebellar hemosiderin (Spearman's correlation coefficient: -0.381, p =0.024). A statistically significant difference was found between the distribution scores of cerebral hemosiderin in cases with and without trauma history (p =0.03). Median cerebral hemosiderin distribution scores were 2.5 and 2, respectively.

Conclusions: The detection of a correlation between the presence of cerebral and cerebellar hemosiderin, and postmortem interval in the age group of 0-1 years, should be interpreted as an important finding in the analysis of cerebral iron. The presence of hemosiderin in the CNS may be a significant finding in the elucidation of infant deaths and this procedure should be carried out on a routine basis.Hippokratia 2015; 19 (2):164-171.

Keywords: Brain, hemosiderin, infant, autopsy

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Introduction

Although processes related to iron metabolism and its accumulation in the body have been the subject of different investigations, we have limited knowledge about these processes, especially in children[1-5]. The number of available publications about the accumulation of iron in the central nervous system is still limited[3,4,6]. It has been indicated that cerebral iron load increases with oxidative stress and *vice versa.* Also, it has been stated that iron load is important in the etiopathogenesis of neurovegetative pathologies[6]. Sudden fetal death and neonatal death can occur respectively in fetuses and neonates with increased cerebral tissue hemosiderin levels who were previously exposed to oxidative stress[3]. Iron is an essential microelement for cerebral metabolism; iron also plays critically important roles in many metabolic processes including

numerous enzymatic activities. Besides, it acts as a co-factor for cytochromes required in the energy production and is involved in neurotransmitter synthesis and many distinct physiological processes[1,4,7,8]. Excessive amounts of iron are encountered in cerebral, and cerebellar tissues in Parkinson's disease, hemosiderosis, various neurodegenerative hereditary diseases, and Friedreich ataxia[3,9,10]. Accumulation of iron in various cerebral structures is generally detected with the aging process, including specialized cerebral regions like basal ganglia[1,6,9,11,12].

Owing to the critical role of iron in metabolism, the inability to be detected on histopathological examination of hematoxylin-eosin (H&E) stained slides, and the potential significance of cerebral/cerebellar hemosiderin detection in the clarification of infant deaths we design this study. We aimed to detect histochemically the accumulation of hemosiderin, in cerebral and cerebellar tissues from autopsied infants (0-1 year of age), using Perls' stain and also to discuss the results in comparison with those of other studies.

Material and methods

In this study were included 52 infants (0-1 year of age) who were among the 5,334 cases been autopsied from 2010 until 2013 in Bursa morgue department of the council of forensic medicine of Turkey, for whom we had complete data regarding clinical status, death/crime scene, and postmortem interval. Cerebral and cerebellar tissue specimens of these cases amenable to staining with Perls' dye were analyzed within 24 hours after their death. Without taking into consideration the causes of death, all cerebral and cerebellar tissue specimens obtained were immersed for at least five days in 10% formaldehyde solution, so as to analyze the blocks. After completion of the follow-up procedures, paraffin blocks were cut into 5-micron sections and stained with H&E before their microscopic examination.

To detect hemosiderin deposition, histochemical staining with Prussian blue was used. In this technique, Perls' dye was applied to produce ferric ferrocyanate and also fixate nonheme ferric ions (Fe^{3+}) which necessitated the combined use of 2% hydrochloric acid (100 ml) and 2% potassium ferrocyanide solutions. Independently from the cause of their death, we utilised the method previously used to detect hemosiderin deposits in the lungs, liver, and spleen in pediatric cases[2,5], in order to determine the hemosiderin distribution scores of the brain and cerebellum. However, intensity scores were evaluated according to the intensity of staining. Specimens of the brain and cerebellum were examined for hemosiderin distribution and intensity scores under magnification (x 10) using an Olympus BX53 microscope (Olympus Europa Holding GMBH, Hamburg, Germany). Regarding the distribution of hemosiderin we determined the iron score for each section (0: no staining, 1: occasional staining with most fields negative, 2: focally abundant staining with most fields without staining, 3: focally abundant staining with most fields showing positive staining, 4: prominent staining throughout the section score). The staining intensity was recorded using a semiquantitative scoring system (0: no staining, 1: weak, small punctate staining, 2: accumulations with greater staining intensity, 3: strong, dark observed staining, 4: very strong, the darkest observed staining). Postmortem interval periods were determined for all cases. The results obtained were subsequently analyzed regarding autopsy findings, sociodemographic characteristics (age, gender), and parameters such as causes of death, postmortem interval, signs of trauma, and toxicological findings. In statistical analyses, diagnoses were grouped as 'absence' or 'presence' (of hemosiderin etc) and evaluted accordingly.

Statistical analysis

Statistical analysis was performed using IBM SPSS (Armonk, NY, USA) version 19.0 for Windows. Continuous variables were expressed as mean and standard deviation (SD) or median and range, while categorical variables as frequencies and percentages. For continuous variables, after controlling for the assumption of normality, non-parametric tests as Mann-Whitney U and Kruskal-Wallis, were used in comparisons. For comparisons of the distribution of categorical variables the Pearson's chi-square and Fisher's Exact test were employed. For correlations between measurements the Kendall's tau b and Spearman's correlation coefficients were calculated. $p < 0.05$ was considered statistically significant.

Results

In total 52 cases were examined. At autopsy, no gross congenital anomaly was detected on external examination. Toxicological examinations could not detect the presence of any illicit substance in the blood, urine samples, and visceral organ specimens that were analyzed during systemic analyses.

Descriptive data of all cases are presented in Table 1. Age of death in these cases ranged between one and 350 days (mean: 79.56, SD: 84.98, median: 60 days). No significant difference was detected between age and gender ($p = 0.473$), history of trauma ($p = 0.414$), death/crime scene ($p = 0.587$), and diagnoses groups ($p = 0.550$).

Blue-coloured hemosiderin granulations that disclosed nonheme iron (Fe^{3+}), after staining with Prussian blue, were detected in the brain and cerebellum in 75% (n: 39) and 67.3% (n: 35) of cases, respectively. Median hemosiderin distribution score in the brain specimens (Figures 1 a,c,d) of male and female infants was two points (mean ± SD: 1.59 ± 1.25 and 1.80 ± 1.26, respectively). Median intensity score (Figures 2 a,c,d) was one point in male and female cases (1.26 ± 1.16 and 1.24 ± 0.93, respectively).

Median hemosiderin distribution scores in the cerebellum (Figures 1 b,e) were two (1.63 ± 1.45) in male, and one (1.40 ± 1.23) in female cases, respectively. However, median hemosiderin intensity value in the cerebellum (Figures 2 b,e) was one in both female and male infants (1.33 ± 1.27 and 1.12 ± 0.97, respectively). Hemosiderin

Table 1: Characteristics of the cases that were evaluated according parameters as gender, signs of trauma, death/crime scene, causes of death and cerebral/cerebellar distribution/intensity scores of the hemosiderin depositions.

	Case	n	%
Gender	Male	27	51.9
	Female	25	48.1
Trauma	None	36	69.2
	Resuscitation	13	25.0
	Head trauma	1	1.9
	Chest trauma	1	1.9
	Neck trauma	1	1.9
Death/crime scene	Home	39	75.0
	Hospital	12	23.1
	Workplace	1	1.9
Cause of death	Sudden unexpected death (SUD)	11	21.2
	Bacterial pneumonia	16	30.8
	Viral pneumonia	3	5.8
	Fetal Distress Prematurity	4	7.7
	Food aspiration	5	9.6
	Congenital Diaphragmatic Hernia, Pulmonary Hypoplasia	3	5.8
	Epilepsy	2	3.8
	Congenital Cardiac Anomaly	1	1.9
	Myocarditis	2	3.8
	Subdural Cranial Bleeding due to Head Trauma	1	1.9
	Metabolic Disease	1	1.9
	Subarachnoidal Cerebral Bleeding due to Shaken baby syndrome	1	1.9
	Mechanic asphyxia due to strangulation with a rope	1	1.9
	Congenital Renal Anomaly	1	1.9
Brain-distribution scores	1	8	15.4
	2	16	30.8
	3	12	23.1
	4	3	5.8
Brain-intensity scores	1	20	38.5
	2	15	28.8
	3	1	1.9
	4	3	5.8
Cerebellum-distribution scores	1	10	19.2
	2	9	17.3
	3	13	25.0
	4	3	5.8
Cerebellum –intensity scores	1	15	28.8
	2	13	25.0
	3	5	9.6
	4	2	3.8

deposition in the brain was detected in 70% (n: 19) of male and 80% (n: 20) of female cases. However, positive staining for hemosiderin in the cerebellum was observed in 63% (n: 17) of male and 72% (n: 18) of female cases, respectively. In all cases, hemosiderin depositions were detected in the interstitial area of the brain parenchyma, and in neurons and interstitial area of the cortex.

Among cases (n: 11) with sudden unexpected death (SUD), positive staining for Prussian blue dye was detected in the brain (n: 6), cerebellum (n: 6), and in both (n: 4). Also positive staining was detected in cases with fetal distress prematurity (75%), food aspiration (80%), congenital diaphragmatic hernia-pulmonary hypoplasia (100%), epilepsy (50%), myocarditis (50%), traumatic subdural bleeding (50%), metabolic disease (100%), shaken baby syndrome (100%), strangulation with a ligature (100%), congenital cardiac abnormality (100%), and congenital kidney abnormality (100%). Hemosiderin deposition was not detected in the brain and cerebellar specimens in only 3 cases with pneumonia, while hemosiderin accumulation was observed in the brain (n: 13 and n: 2) and cerebellum (n: 12 and n: 1) in cases with bacterial and viral pneumonia, respectively.

No significant difference was found between postmortem intervals (PMI) and patients' gender (p =0.054), type of the trauma (p =0.683), death/crime scene (p =0.907), and diagnosis (p =0.464). Similarly, distribution scores of hemosiderin calculated for the brain did not differ significantly with respect to patients' gender (p =0.577), death/crime scene (p =0.300), and diagnosis (p =0.253); and intensity scores of hemosiderin calculated for the brain did not differ significantly with respect to patients' gender (p =0.847), death/crime scene (p =0.722), and diagnosis (p =0.138).

However, hemosiderin distribution scores in the brain were different in the presence of trauma and this was statistically significant (p =0.030). In the traumatic group, median hemosiderin distribution score estimated for the brain was 2.5 compared to the non-traumatic group where it was 2 (mean ± SD: 2.25 ± 1.24 *vs.* 1.44 ± 1.18).

No statistically significant difference was detected between hemosiderin distribution scores in the cerebellum and gender of the patients (p =0.630), traumatic incident (p =0.443), and diagnosis (p =0.595). Also, for hemosiderin intensity scores in the cerebellum and gender of the patients (p =0.641), traumatic incident (p =0.427), and diagnosis (p =0.744). In 33 of the 35 cases (94.3%), diffuse hemosiderin distribution was detected both in the brain and cerebellum. In 11 of the 17 cases (64.7%), scattered areas of hemosiderin distribution both in the cerebellum and brain were detected. However, in 6 (35.3%) cases diffuse hemosiderin distribution was detected in the brain (p =0.0004).

A significant correlation was not detected between postmortem interval and distribution, and intensity scores of hemosiderin in the brain and cerebellum (Table 2). However a weakly negative, but statistically significant correlation was detected between patients' age and hemosiderin distribution scores in the brain (Spearman's rho: -0.306) (Table 2). Also, a moderately positive and significant correlation was observed between hemosiderin distribution scores in the brain, and distribution, and intensity scores in the cerebellum. (Kendall's Tau b correlation coefficients: 0.532 and 0.580, respectively) (Table 2). In addition, between hemosiderin intensity and distribution scores in the brain and cerebellum, a highly positive and significant correlation was observed (Kendall's tau b correlation coefficients: 0.805 and 0.909, respectively) (Table 2).

In our study, in the early neonatal period (first few days of life), Prussian blue stain-positivity was detected in the brain (13/17, 76.5%; p =0.0735) and cerebellum (12/17; 70.5%; p=0,722), whereas no statistically significant difference was found between the brain and the cerebellum as for positive staining with Prussian blue.

Table 2: Correlations between clinical parameters postmortem interval, age, and cerebral/cerebellar distribution/intensity scores of the hemosiderin depositions of the cases.

Correlation Coefficients and p-values	PMI Hours	Brain Distribution	Brain Intensity	Cerebellum Distribution	Cerebellum Intensity
Brain Distribution	-0.018*				
	0.901				
Brain Intensity	0.042*	**0.805**			
	0.770	**<0.001**			
Cerebellum Distribution	-0.122*	**0.532**	**0.533**		
	0.390	**<0.001**	**<0.001**		
Cerebellum Intensity	-0.145*	**0.580**	**0.589**	**0.909**	
	0.305	**<0.001**	**<0.001**	**<0.001**	
Age Days	0.017*	**-0.306**	-0.150	-0.168	-0.238
	0.912	**0.046**	0.336	0.282	0.125

PMI:Postmortem interval, *Spearman's rho; the others Kendall's Tau b correlation coefficients

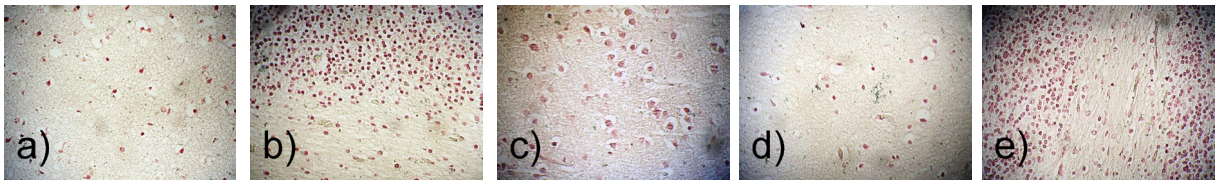

Figure 1: Iron distribution scores (Perls' dye, x200). a) Brain score 0: no staining. b) Cerebellum score 1: occasional staining with most fields negative. c) Brain score 2: focally abundant staining. d) Brain score 3: focally abundant staining with most fields showing positive staining. e) Cerebellum score 4: prominent staining throughout the section.

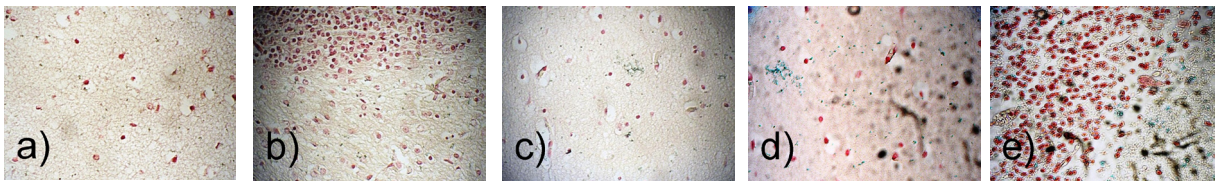

Figure 2: Iron staining intensity scores (Perls' dye, x200). a) Brain score 0: no staining. b) Cerebellum score 1: weak, small punctate staining. c) Brain score 2: accumulations with greater staining intensity. d) Brain score 3: strong, dark observed staining. e) score 4: very strong, observed staining.

Discussion

Though processes related to iron metabolism in the body have been investigated in many studies, our knowledge about fetal, postnatal periods, and infancy is still based on a limited number of studies[1-5]. Specifically only few publications exist regarding detection of hemosiderin deposition in the central nervous system (CNS) and determination of iron scores using various methods[3,4,6].

Many studies have indicated that increased cerebral iron load augments predisposition to endogenous oxidative stress and enhances during stress. Its important pathogenetic role in the development of neurodegenerative processes has been revealed[6,11].

In cases of sudden fetal death and neonatal mortality in infants exposed to oxidative stress, it has been indicated that hemosiderin concentrations can increase in the brain[3]. Also, many reports noted that hemosiderin deposition in cases with hemosiderosis can be associated with accumulations of abnormal protein types, such as synuclein and tau protein[13].

Iron is an indispensable element for many biological functions and plays an important role in various processes. It is involved in many enzymatic processes and functions as a cofactor in cytochromes required for energy production. It also participates in many physiological events namely oxygen transport, production of mitochondrial energy, DNA synthesis, and DNA repair[2,3,7,8].

Two-thirds of the iron stores of the body are contained in erythrocytes as "heme iron". Iron is also an essential element for cerebral metabolism and plays a role in the synthesis and metabolism of neurotransmitters, and diverse physiological processes. Non-heme iron binds to transferrin and is distributed via systemic circulation into all tissues except for CNS. It passes from the systemic circulation into the CNS through the blood-brain barrier[2].

It has been also indicated that both deficiency and excessive amounts of iron are considered potential risk factors during the development of the CNS. Besides, iron is stored in ferritin, which maintains its higher concentration in the basal ganglia throughout one's lifetime[14]. As reports assert, iron accumulates mostly in the globus pallidus, substantia rubra, substantia nigra, and dentate nucleus in the cerebellum[9,14].

Excessive iron depositions in the brain and cerebellum are encountered in various neurodegenerative diseases, such as Parkinson's disease, hereditary cerebellar ataxia, and aceruloplasminemia[1,4].

Accumulation of iron in various cerebral structures is seen in association with aging process. Bartzokis et al, emphasized on increased iron accumulation in the brains of patients with Alzheimer's disease; however in our study, no significant correlation was detected between age and hemosiderin distribution scores[12].

Based on radiological imaging modalities, various researchers revealed statistically significant correlations between hemosiderin deposition in the brain and age groups, and asserted that radiological evaluations are valuable, especially in the monitoring of neurodegenerative processes and changes in iron deposition with age[15]. In our study, no significant difference was detected between patients' gender and hemosiderin distribution/intensity scores.

In the literature, hemosiderin depositions have been reported in male cases with neurodegenerative diseases; in Alzheimer's disease iron deposits have been associated with amnesia[12]. In genetic studies, researchers found that in syndromes associated with human hemochromatosis protein (HFE) gene mutations, commonly associated with the iron overload (ie. hereditary hemochromatosis), the detection of expression of genes might be effective in the prediction of the presence of iron depositions in the brain. Their diagnostic role in neurodegenerative processes including Parkinsonism, Alzheimer's disease, and

ischemic infarct has been disclosed[16,17]. Some authors have insisted on the evaluation of synuclein and tau proteins in cases with hemosiderosis[13,18]. In our study, in 17 cases in the early neonatal period (first few days of life), positive staining for Prussian blue was detected in their brain (n: 13) and cerebellum (n: 12). A significant difference could not be found between cerebral and cerebellar staining scores of other infants.

Lack of correlations between cerebral and cerebellar staining scores might be related to the degree of maturation of the blood-brain barrier, as revealed by more recent studies[1,3,4,7,8,19]. These findings were evaluated so as to guide future studies and based on newly understood mechanisms, transport of Iron/transferrin complex into the brain by blood circulation, takes place in endothelial cells of capillaries of the blood-brain barrier, through receptor-dependent endocytosis[1,3].

In another study, hemosiderin deposition in the endothelial cells of capillaries detected in cases with sudden intrauterine unexpected death (SIUD) and sudden infant death syndrome (SIDS) was underlined as a reflection of hemosiderin deposition[3]. However, in none of our cases comparable hemosiderin accumulation pattern was observed. As indicated in many other studies, hemosiderin depositions are frequently concentrated on interstitial space and in neurons[3,6,8,9].

The presence of immature blood-brain barrier in the neonatal period has been claimed to be the basic etiological factor of advanced iron deficiency or on the contrary of cerebral hemosiderin accumulation in the brain, in the early neonatal period[2,3]. Deficiency or excess of this important cofactor, has been specially indicated as a potential risk factor and its critical roles during various developmental stages of one's lifetime, have been emphasized in various studies[14].

In similar studies, in consideration of the metabolic processes involved in iron homeostasis, the elucidation of systemic metabolic events and physiological mechanisms occurring at a cellular level, has made us to believe that some favourable results can be obtained for the arrangements of treatment protocols for iron deficiency and iron excess[2,4,14,19]. An important study, performed on cerebral iron scores, revealed that especially cerebrospinal fluid ferritin levels can be meaningful in the monitoring of the developmental processes[20].

A statistically significant difference was detected between our traumatic and non-traumatic cases regarding hemosiderin distribution scores. However, Wu et al in their study on cases with intracerebral bleeding, detected that changes in cerebral iron deposition and related proteins such as ferritin could occur during long-lasting processes. They also determined that based on incompletely enlightened mechanism, accumulation of hemosiderin was closely associated with microglial elements in the brain[21]. Similarly in neurodegenerative diseases, Koeppen et al demonstrated the presence of apparent microglial reaction and degeneration in cases with increased cerebellar iron scores[10].

Within this context, assumptions that cerebral degeneration independent of iron distribution can be associated with the potential of iron to generate oxidative radicals, appear to be in compliance with the outcomes of various studies[3]. In our previous study, hemosiderin deposition in the organs of the reticuloendothelial system (i.e. liver, spleen, and lungs) had been associated with trauma, and increased hemosiderin scores in these organs and increased hemosiderin load were found in cases, aged between 6 months and 6 years[5].

In our recent study, cerebral hemosiderin distribution scores differed significantly between groups with and without traumatic etiology. In these groups, median hemosiderin distribution scores were 2.5 and 2 in the groups, with and without traumatic etiology, respectively. In this study, regardless the cause of death, the presence of blue-coloured hemosiderin, stained with Perls'dye has been histochemically investigated in a wide spectrum of indications including SUD, pneumonia, congenital renal abnormalities, and myocarditis. No significant differences could be detected for the cerebral/cerebellar hemosiderin distribution scores between cases with pneumonia and other conditions. Similarly, no significant difference could be found for the hemosiderin distribution scores between our SIUD and other diagnostic groups. Lavezzi et al reported in their study, that they had detected various concentrations of hemosiderin depositions which were stained blue with Perls'dye and localized on certain areas or scattered within parenchymal tissues of the brainstem and cerebellum in 33 % of their SIUD cases. However, they couldn't determine hemosiderin depositions in the control group[3]. In the same study, they demonstrated hemosiderin depositions in 11 cases with SIUD of mothers that were smokers and hemosiderin depositions had been associated with the formation of free radicals. However, our study was devoid of any data regarding the smoking status of the mothers and detection of hemosiderin depositions in the cerebral specimens of 3/4 of the cases with fetal distress can be interpreted in the light of the findings of the above-mentioned study[3].

Rao et al, in their experimental study, revealed that conditions with iron deficiency led to a prominent decrease in the number of iron-positive cells in hippocampal neurons that demonstrated increased sensitivity to hypoxia. They also indicated that findings detected in animal model studies might demonstrate parallelism with neonatal outcomes and asserted that studies, especially with diabetic mothers and cases with placental deficiency, elucidated this issue[11]. However, in our study, hemosiderin depositions were detected in 75% (n: 3) of the cases with fetal distress and prematurity. In a study performed with infants, the researchers reported that iron depositions *per se* had an important place in the development of preterm destructive changes in the oligodendroglial cells of the white matter[22].

The authors reported that the increase in cerebral iron load, especially with age, might rise predisposition to endogenous oxidative stress, and also stated that this

conveys importance in the development of neurodegenerative processes[6]. Other researchers revealed that iron stores could be used as an extremely effective marker for hypoxic cerebral events[23]. In our study, a statistically significant negative correlation was detected between age and cerebral hemosiderin distribution scores.

Darrrow et al conducted a study on the presence of iron pigments in macrophages in preterm babies with subependymal intraventricular bleedings. In this study, it was disclosed that hemosiderin depositions in macrophages and astroglial cells together with histomorphological findings might be helpful as a marker in the determination and staging of intracerebral bleeding times[24]. In addition, in their experimental study on intracerebral bleeding, Wu et al indicated that changes in cerebral iron and related proteins could become evident in the processes lasting up to 4 weeks, whose mechanisms had not been fully elucidated. However, in relation to the correlations between traumatic processes and cerebral iron deposition, the authors couldn't explain the emergence of oxidative stress findings induced by iron ions after bleeding episodes[21].

Similarly, Italian researchers asserted that the presence of insoluble diffuse hemosiderin depositions in the brain of a newborn might essentially indicate oxidative stress in the brain due to accumulation of iron. As an alternative assumption, they also claimed that insoluble iron overload, which could not be eliminated by the organism, could be associated with iron deficiency at a neuronal level and SIDS[3].

In the present study, we think that the statistically significant findings related to cerebral and cerebellar hemosiderin distribution scores should be accepted as an indicator of the distribution of cerebral iron stores, as a consequence of the normal metabolic processes. Moreover, these findings should be further evaluated as consistent criteria for demonstrating the general impact of the metabolic processes of iron[1-4].

In experimental animal studies, the authors have suggested that areas of iron deficiency and supersaturation demonstrate regional differences in the brain and cerebral tissues, which can respond differently to these conditions based on their developmental stage, and emphasized the need for confirmation of these findings in further studies performed on human subjects[25].

At the experimental level, it has also been indicated that decreased stain uptake by glial cells and neurons had been priorly associated with decreased iron intake[26]. In the present study, blue-coloured hemosiderin granulations, stained with Perls' Prussian blue, were detected in the cerebral and cerebellar specimens in 75% (n: 39) and 67.30% (n: 35) of all cases. In the scientific literature, it has been reported that increased iron intake is important in the development of brain; and hemosiderin deposition in brain might be associated with infant deaths, whose pathogenetic mechanisms has not been completely resolved yet[1-4]. Iron depositions observed in the neonatal period have been reportedly involved in the regulation of iron homeostasis during development of the body systems[1-3]. Besides, it has been indicated that immature blood-brain barrier can be the basic etiological factor, responsible for iron deposition in brain and severe iron deficiency[1-4,6-8]. Also, various authors have underlined the importance of iron in processes involved in the systemic metabolism and asserted that brain should be analyzed from a genetic perspective[16-17]. Besides, evaluation of the diverse entities of iron deposition and studies aiming at comprehension of fundamental pathophysiological processes, might contribute to elucidation of this issue.

Conclusion

In our study, weakly negative, but significant correlation between postmortem interval and cerebellar hemosiderin intensity scores in infants (0-1 year of age) was detected. Besides, detection of a statistically significant difference between traumatic and non-traumatic cases as for hemosiderin distribution scores in the brain, have led us to think that iron accumulation revealed at autopsy, should be interpreted as a significant finding in the analysis of brain iron metabolism. We also assume that detecting the presence of hemosiderin in the CNS will contribute to the clarification of various aspects of infant deaths. As a concluding remark we conceive that Perls' Prussian blue should be routinely used in such cases.

Conflict of interest

Authors report no conflict of interest related to this study.

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