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Primed neutrophil infiltrations into multiple organs in child physical abuse cases: A preliminary study

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ABSTRACT

Physical abuse of the elderly induces a massive primed neutrophil infiltration into the lung and liver through chemotaxis by interleukin (IL)-8, similar to cases of traumatic or hemorrhagic shock. Here, we used immunohistochemical analyses to investigate this infiltration in cases of physically abused children. In addition, we examined the expression of neutrophil elastase (NE) as the inflammatory mediator and α1-antitrypsin (AAT) as the elastase inhibitor. The number of neutrophils in the abuse cases was increased significantly in the heart, lung, liver, and kidney, compared with that of control cases. IL-8-positive cells and NE-positive cells in all organs of abuse cases were significantly greater than those in control cases. Large quantities of oxidized AAT, which fails to inactivate NE and results in tissue damage, was detected in the liver of abuse cases. Neutrophil infiltration showed positive correlation with the degree of systemic accumulation of non-fatal injuries caused by repetitive abusive behavior. Although further investigation using more autopsy samples is necessary, results of our preliminary study indicate that massive neutrophil infiltration induced by IL-8 in multiple organs is a new complementary diagnostic indicator of physical abuse in children. Moreover, the demonstration of NE-positive cells and oxidized AAT provides firm evidence of tissue damage.

1. Introduction

Studies have suggested that 'primed' polymorphonuclear neutrophils may contribute to multiple organ injury in cases of extensive trauma and following traumatic or hemorrhagic shock. These cells produce inflammatory mediators, such as neutrophil elastase (NE), leukotrienes, cyclooxygenase (COX)-2, reactive oxygen species (ROS), and proinflammatory cytokines [1–11]. Multiple injuries of different ages are usually observed over the whole body in cases of physical abuse [12,13]. Recently, we reported that the physical abuse of the elderly induces massive primed neutrophil infiltration into the lung and liver. This infiltration is accompanied by activation of a multistep cascade mediated by the endothelial cell adhesion molecule P-selectin and the chemotactic factor interleukin (IL)-8. Our previous studies indicate that immunohistochemical demonstrations may be useful as new complementary diagnostic markers for elder physical abuse [14]. In the present study, we conducted similar analyses in cases of child physical abuse. Moreover, we examined the expression of NE, an inflammatory mediator of neutrophils, and α1-antitrypsin (AAT), a protease inhibitor (intrinsic protective molecule against elastase) [15–17], to confirm that massive neutrophil infiltration can cause tissue damage in multiple organs. Finally, we discuss whether these immunohistochemical analyses may represent supportive diagnostic methods of the physical abuse of children.

2. Materials and methods

2.1. Autopsy samples

Eleven autopsy cases of child physical abuse (age range, 2 months to 8 years; mean age, 2.25 years; 5 males and 6 females) were collected from affiliated institutions over a 34-years period (1982–2015). The abuse cases were defined based on autopsy findings and police reports. The degree of physical abuse in each case was determined by estimating the whole area of injured skin on the entire body surface based on the Lund-Browder chart [18], and by calculating the Injury Severity Score (ISS; designated as ISS of the whole injury) [19]. For the ISS, the abbreviated injury scale (AIS) score of the 3 most severely injured body regions of a

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Table 1
Details of child physical abuse cases.

Case no.	Age and Gender	Direct cause of death	Nutritional condition	BMI	Weight of thymus	Pathology of thymus	Survival time	Postmortem period	Injured skin area	ISS of whole injury	ISS of fatal injury	Total score of non-fatal injuries	Estimated age of skin wounds (Duration of abuse)
A1	4 M	SDH	Good	15.2	11.1	Hypotrophy	24 d	36 h	11%	38	16	22	4d – several months
A2	2 M	SDH, SAH	Good	21.6	9.7	Hypotrophy	3d 10 h	32 h	11%	30	25	8	3d – several months
A3	2 F	Liver injury, lacerations of mesenterium	Good	15.3	8.4	Hypotrophy	4 h	24 h	10%	18	16	2	<3d – 1 m
A4	1 F	SDH, SAH, CC	Slightly poor	13.1	7.1	Hypotrophy	6 d	15 h	2%	27	25	4	4d – 2w
A5	4 m F	Smothering	Poor	11.8	11.6	Hypotrophy	Short	17 h	2%	-	-	-	<3d – 1 m
A6	6 m M	SDH	Good	18.9	50	Normal	2.5 h	20 h	4%	26	25	1	<3d – 2w
A7	1 F	Shock due to duodenal perforation	Slightly poor	14.0	13.1	Normal	Short	19 h	12%	18	9	9	<3d – several months
A8	4 F	SDH, SAH	Poor	8.7	1.8	Atrophy	10 h	15 h	13%	27	25	4	<3d – several months
A9	2 m M	Smothering	Slightly poor	14.6	20	Normal	Short	96 h	2%	-	-	-	<3d – 1w
A10	8 M	Ligature strangulation	Slightly poor	14.6	40	Normal	Short	20 h	3%	-	-	-	<3d – 1w
A11	1 F	Severe burn	Slightly poor	14.0	7.8	Hypotrophy	56 h	12 h	2%	27	25	3	<3d – 1 m

M, male; F, female.
SDH, subdural hematoma; SAH, subarachnoidal hemorrhage; CC, cerebral contusion.
BMI, Body Mass Index.

Table 2
Details of child control cases.

Case no.	Category	Age and Gender	Cause of death	Nutritional condition	BMI	Weight of thymus	Pathology of thymus	Survival time	Postmortem Period	Mechanism of trauma
C1	I-S (n = 4)	3 M	Exsanguination due to incised wound of the neck	Good	17.4	30	Normal	Short	39.5 h	Insulted by his mother with mental disorder (single episode)
C2		3 m M	Exsanguination due to stab wound of the abdomen	Good	15.6	35	Normal	Short	17 h	Insulted by his mother with mental disorder (single episode)
C3		9 M	Exsanguination due to stab wound of the chest	Good	16.5	60	Normal	Short	27 h	Insulted by unrelated person
C4		9 M	Exsanguination due to incised wound of the neck	Obese	27.7	50	Normal	Short	28 h	Insulted by his mother with mental disorder (single episode)
C5	I-B (n = 4)	1 F	SDH	Good	17.6	22.2	Normal	4 h	8 h	Insulted by acquaintance of her mother (single episode)
C6		1.6 F	SDH, SAH, CC	Good	15.9	19.5	Normal	68 h	18 h	Insulted by acquaintance of her mother (single episode)
C7		8 F	SDH	Good	15.1	65	Normal	Short	18 h	Accidental fall
C8		1 M	SDH	Good	15.6	23	Normal	Short	24 h	Insulted by unrelated person
C9	Poly (n = 4)	6 M	Respiratory failure due to multiple rib fractures	Good	17.4	42	Normal	Short	16 h	Traffic accident
C10		2 M	Brain disruption, liver disruption	Good	15.8	27.6	Normal	Short	29 h	Traffic accident
C11		8 F	Multiple fracture	Good	15.1	30	Normal	Short	12 h	Traffic accident
C12		3 M	Multiple fracture	Good	16.0	24.2	Normal	1 h	15 h	Traffic accident

M, male; F, female.
SDH, subdural hematoma; SAH, subarachnoidal hemorrhage; CC, cerebral contusion; I-S, sharp instrument injury; I-B, single fatal blunt injury; Poly, polytrauma.
BMI, Body Mass Index.