

Systemic Manifestations of Traumatic Brain Injury

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Degree
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By

Mohamed Mohamed Abdelatty Shararibo
(M.B., B.Ch.)

Faculty of medicine – Mansoura University

Under Supervision of :

Prof. Dr. Hesham Mohammed El-Azzazi

*Professor of Anesthesiology, Intensive Care and pain
management*

Faculty of Medicine - Ain Shams University

Dr. Ahmad Kamal Mohammed Ali

*Lecturer of Anesthesiology and Intensive Care
Faculty of Medicine - Ain Shams University*

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LIST OF ABBREVIATIONS

| | |
|-------|--|
| A10 | Clot amplitude at 10 minutes after the beginning of clot formation |
| ACTH | Adrenocorticotrophic hormone |
| ADH | Antidiuretic hormone |
| ALI | Acute lung injury |
| ARDS | Acute respiratory distress syndrome |
| ASPEN | American Society for Parenteral and Enteral Nutrition |
| ANS | Autonomic nervous system |
| APTT | Activated partial thromboplastin time |
| BBB | Blood brain barrier |
| BD | Brain damage |
| BG | Blood glucose |
| BTF | Brain trauma foundation |
| CARS | Compensatory anti-inflammatory response syndrome |
| CBF | Cerebral blood flow |
| CK | Creatinine kinase |
| COPD | Chronic obstructive pulmonary disease |
| CO | Cardiac output |
| CPIS | Clinical pulmonary infection score |
| CPP | Cerebral perfusion pressure |
| CSF | Cerebrospinal fluid |
| CSW | Cerebral salt wasting |
| CT | Clotting time |
| CVP | Central venous pressure |
| DAMPs | Damage associated molecular patterns |
| DI | Diabetes insipidus |
| EXTEM | Extrinsically activated thromboelastography test |
| EVD | Extra ventricular device |

| | |
|-------------------|--|
| FSH | Follicular stimulating hormone |
| FibTEM | Fibrin based thromboelastometric test |
| GCS | Glasgow-coma scale |
| GH | Growth hormone |
| GFAP | Glial fibrillary acidic protein |
| GOS | Glasgow-outcome scale |
| HBOT | Hyperbaric oxygen therapy |
| HO | Heterotopic ossification |
| HR | Heart rate |
| HRT | Hormonal replacement therapy |
| HTS | Hypertonic Saline |
| HPA | Hypothalamus pituitary-adrenal |
| IL | Interleukin |
| ICP | Increased intracranial pressure |
| <i>INR</i> | International normalized ratio |
| LMWH | Low molecular weight heparin |
| LV | Left ventricle |
| MCF | Maximum clot firmness |
| MDR | Multi-drug resistant |
| MIH | Mild induced hypothermia |
| NPE | Neurogenic pulmonary edema |
| NSE | Neuron specific enolase |
| NSM | Neurogenic stunned myocardium |
| ODS | Osmotic demyelination syndrome |
| PAID | Paroxysmal autonomic instability and dystonia |
| PTH | Phenytoin |
| PTHP | Post-traumatic hypopituitarism |
| PT | Prothrombin time |
| PRIS | Propofol infusion syndrome |
| ROS | Reactive oxygen species |
| SAH | Subarachnoid hemorrhage |
| ScvO ₂ | Central venous saturation |
| SIADH | Syndrome of Inappropriate Antidiuretic Hormone |

| | |
|------|---|
| SIRS | Systemic inflammatory response syndrome |
| SCCM | Society of critical care medicine |
| TBI | Traumatic brain injury |
| TEE | Trans-esophageal echo |
| TF | Tissue factor |
| TTE | Trans-Thoracic echo |
| TSH | Thyroid stimulating hormone |
| VAE | Ventilator associated events |
| VAP | Ventilator associated pneumonia |
| VILI | Ventilator induced lung injury |
| VPA | Valporate |

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Abstract:

Traumatic brain injury (TBI) affects functioning of various organ systems in the absence of concomitant non-neurologic organ injury or systemic infection. The systemic manifestations of TBI can be mild or severe and can present in the acute phase or during the recovery phase. Non-neurologic organ dysfunction can manifest following mild TBI or severe TBI. The pathophysiology of systemic manifestations following TBI is multifactorial and involves an effect on the autonomic nervous system, involvement of the hypothalamic-pituitary axis, release of inflammatory mediators, and treatment modalities used for TBI. Endocrine dysfunction, electrolyte imbalance, and respiratory manifestations are common following TBI. The influence of TBI on systemic immune response, coagulation cascade, cardiovascular system, gastrointestinal system, and other systems is becoming more evident through animal studies and clinical trials. Systemic manifestations can independently act as risk factors for mortality and morbidity following TBI.

Key words: Endocrine dysfunction; autonomic dysfunction; coagulopathy; immune response; neurogenic pulmonary edema

Introduction



Introduction

The pathophysiology of traumatic brain injury (TBI) involves the initial primary brain injury that occurs at the time of accident and the secondary brain injury that follows which results in increased intracranial pressure (ICP) and decreased cerebral perfusion. Secondary brain injury is due to the several biochemical cascades that occur in brain after TBI. Systemic insults such as hypoxia, hypotension, fever, and anemia can potentiate the process of secondary brain injury. The current evidence-based management of TBI mainly includes intensive monitoring of physiological parameters like ICP and cerebral perfusion pressure (CPP), anticipation of secondary insults, their early recognition and adequate management (medical and/or surgical). However, there is an increasing awareness that apart from the cerebral manifestations there are several systemic manifestations of TBI which can act as independent prognostic factors (*Zygun et al., 2005*).

The systemic manifestations occur in the absence of any coexisting specific organ injury or systemic infection. The nature and severity of the systemic manifestations of TBI mainly depend on the severity of the brain injury. Mild TBI causes systemic manifestations such as fatigue and

dizziness whereas severe TBI can adversely affect the functioning of multiple organ systems. Following severe TBI, endocrine dysfunction and electrolyte imbalances are common while renal and hepatic manifestations are unusual. These systemic manifestations can occur either in the acute phase following severe TBI or/and during the chronic phase of rehabilitation. The manifestations in any particular organ system can vary from mild organ dysfunction to organ failure. Zygun et al. reported organ dysfunction in 89% of patients, and organ failure in 35% of patients in their observational study of 209 patients with severe TBI (*Zygun et al., 2005*).

The systemic manifestations can result in both increased mortality (with one organ system involvement mortality is 40%, with two organ systems 47%, while with no organ system dysfunction it is 26%) and adverse outcomes following severe TBI (*Lim and Smith, 2007*).

Endocrine dysfunction is common and the symptoms of these hormonal abnormalities overlap with the chronic symptoms that persist after TBI, especially fatigue, weakness, memory and attention problems. Current recommendations for screening of TBI patients include acute assessment for cortisol and thyroid deficiency and

treatment is indicated for documented deficiency of these hormones. At 3–6 months, the additional following screening is recommended: morning cortisol level, insulin-like growth factor, thyroid stimulating hormone, free thyroxine, luteinizing hormone, follicle stimulating hormone, estradiol (females), and testosterone (males) (*Ghigo et al., 2005*).

Zygun et al., (2005) reported pulmonary complications in 80% of patients with severe TBI. In patients with severe brain injury (GCS <8), acute lung injury (ALI) is seen in 20% of patients.

Following TBI there is a surge in catecholamines in the blood. This sympathetic hyperactivity results in tachycardia and systemic hypertension which increases the work load of heart. As catecholamines can also cause constriction of coronary vessels, ischemia of the myocardium especially in the subendocardial regions may result. This myocardial ischemia is responsible for the several ECG changes that are seen after TBI. Prolonged QTc on ECG is more common after traumatic SAH and can result in cardiac arrhythmias (*Collier et al., 2004*).

Although coagulation abnormalities after TBI is common and contribute to devastating complications of delayed intracranial hemorrhage, the pathophysiology of coagulation abnormalities after TBI is not well understood and may involve tissue factor release from injured tissue, fibrinolysis, thrombocytopenia, and activated protein C and other cytokines (*Laroche et al., 2012*).