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Adrenal apoplexy caused by fulminant sepsis in 20-year-old healthy male?: case report

Case report

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Abstract: Introduction. Bilateral massive adrenal hemorrhage (BMAH) is a rare catastrophic condition that manifests with acute adrenal insufficiency. Death can occur within a few hours or after many days. BMAH in association with fulminant septicemia and sepsis occurring in children and young adults is also known as the Waterhouse-Friderichsen syndrome. Fulminant sepsis associated with purpura is lethal in 40-70% of patients. Case report. The abrupt onset of fever with sore throat occurred in a 20-year old man. Next day in the early morning, he complained of severe symptoms: generalized weakness, shortness of breath and myalgia. Few hours later petechial rash occur. Within 30 hours from first symptoms he died in hospital. On autopsy, there were macroscopic bilateral areas of adrenal hemorrhage. Autopsy also revealed hemorrhage in almost all organs and tissues. Microbiological blood culture and toxicological finding was negative. Discussion. In our case, very high levels of procalcitonin and D-dimer, with all other clinically and autopsy findings, was directing medical examiners that a main cause of death was fulminant bacterial sepsis. Blood culture did not reveal any bacteria, so the cause of BMAH stays uncovered. The bacteria that most often cause fulminant sepsis connected with BMAH and death within 12-24 hours from first symptoms is N. meningitidis. It is very likely that N. meningitidis caused BMAH in our case, but it will stay in domain of speculation.

Keywords: *Adrenal apoplexy • Fulminant sepsis • Autopsy*

1. Introduction

Bilateral massive adrenal hemorrhage (BMAH) is a rare catastrophic condition that manifests with acute adrenal insufficiency due to irreversible destruction of the adrenal cortices [1,2].

Risk factors connected to BMAH are: sepsis or severe infection, advanced age, congestive heart failure, postoperative state (especially cardiovascular or orthopedic surgery, suggested to be due to the common practice of using anticoagulants), significant hypotension, spontaneous or iatrogenic coagulopathies, certain prothrombotic disorders, trauma, adrenocorticotropin (ACTH) administration, vasculitis, adrenal venography and pheochromocytoma [1-6].

In the precrisis interval of BMAH, patients present with a combination of pain in the chest, back, or abdomen; fever; nausea or vomiting; neuropsychiatric manifestations (such as, confusion, weakness or obtundation); and, less frequently, hypotension. Frequent laboratory features include a significant drop in the hemoglobin and electrolyte changes of adrenal insufficiency that often take several days to develop [6-8]. Death can occur within a few hours or after many days [1].

It is uniformly fatal if glucocorticoid treatment is not initiated shortly after onset of the crisis but can be very difficult to diagnose prospectively because of its nonspecific symptoms [1,9].

BMAH, in association with fulminant septicemia and sepsis, occurring in children and young adults, caused by Neisseria meningitidis or other gram-negative, endotoxin-producing bacteria (like Pseudomonas aeruginosa, Haemophilus influenzae type b), or gram-positive

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bacteria (like Streptococcus sp.-Pneumococcus), is also known as the Waterhouse-Friderichsen syndrome (WFS) [10-16]. This condition is characterized with all above mentioned symptoms and primarily by the abrupt onset of fever, petechiae, arthralgia, weakness and myalgias.

Fulminant sepsis associated with purpura is defined as septicemia, shock, disseminated intravascular coagulation and circulatory failure leading to multiple organ dysfunction [17,18]. 40-70% of patients with fulminant sepsis associated purpura die. [19]

Measurement of serum PCT concentration can be applied in doubtful cases to facilitate the differentiation between WFS and other putative conditions leading to bilateral adrenal hemorrhage, especially when the medical history of the deceased is unclear for the present and a toxicologic analysis was not performed [20-25]. While the serum PCT concentration is below 0.5 ng/ml in healthy individuals, PCT levels rise above 10 ng/ml in sepsis [21-23].

2. Case report

In the following we present the forensic investigations and technical examinations in chronological order.

History: The abrupt onset of fever with sore throat occurred in a 20-year old man in late evening hours on 08 February 2012. Next day in the early morning, he complained of severe symptoms: generalized weakness, shortness of breath, myalgia and diarrhea. A few hours later a petechial rash occurred.

The patient arrived in hospital at 1:30pm. On physical exam he was conscious, pale, with agonal breathing, petechial rash was all over the body, hypotensive (TA 60/45 mmHg). During examination he became unconscious with irregular breathing and IPPV was indicated. He was sent to the Intensive Care Unit. Initial laboratory workup was significant with a Procalcitonin: >200ng/ml, PLT: 26 x10^9/L, D-dimer >10000 ng/ml, immeasurable time of bleeding and coagulation, urea: 6,6 mmol/L and creatinine: 258 mmol/L.

After massive bloody diarrhea at 2:15pm, cardiac arrest occurred, but cardiopulmonary resuscitation was successful. At 4:45pm another cardiac arrest occurred and death was pronounced at 5:15 pm.

Ten days later, the microbiological findings were finalized: blood culture was negative.

Autopsy: On autopsy, there were macroscopic bilateral areas of adrenal hemorrhage consistent with Waterhouse-Friderichsen syndrome. Autopsy also revealed hemorrhage in almost all organs and tissues: conjunctiva, skin, brain and leptomeningies, lungs,

Figure 1. A) Petechial rash; B) Hemorrhage in heart; C) Hemorrhage in stomach; D) Hemorrhage in intestines.

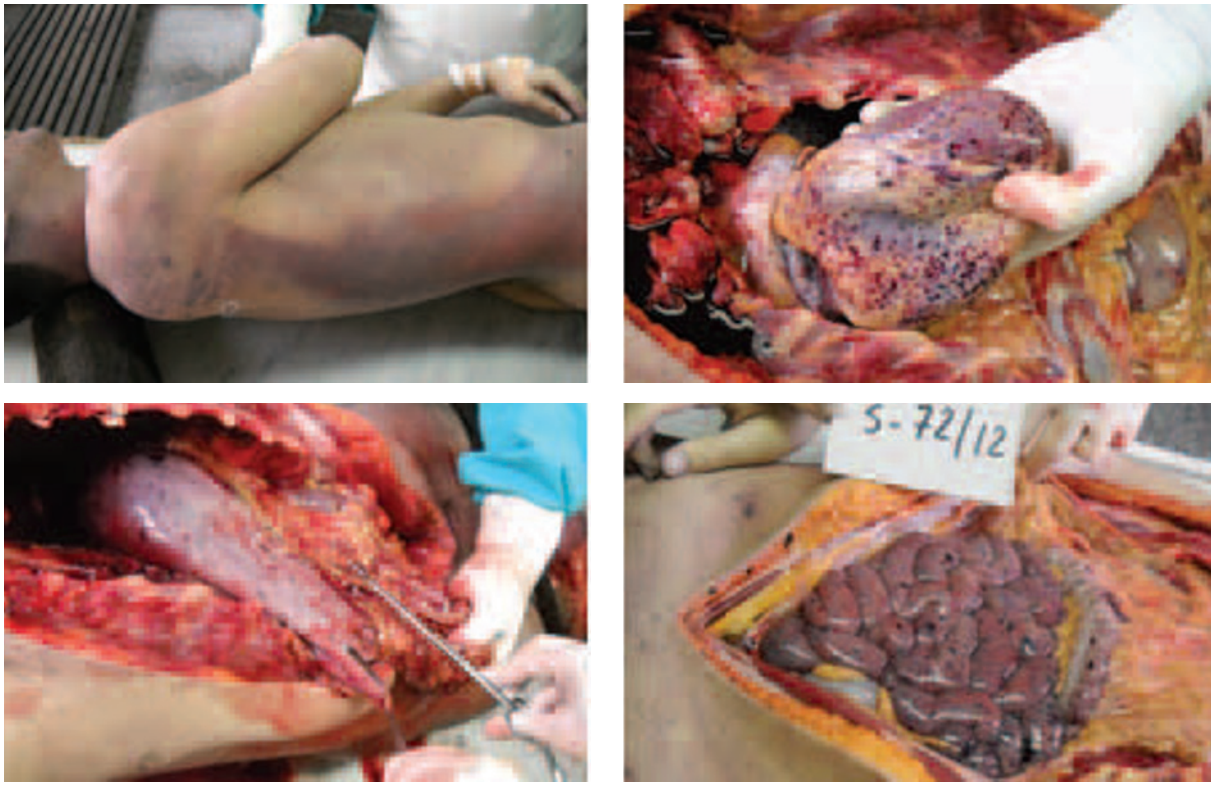
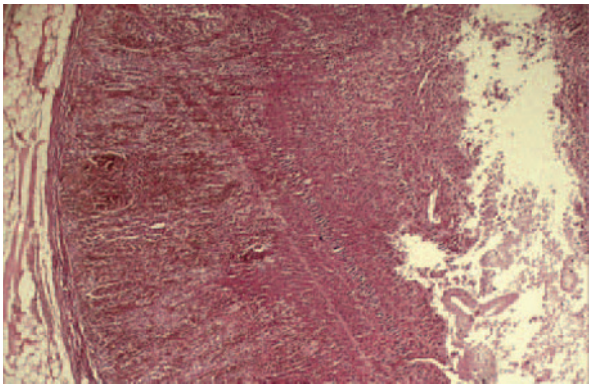


Figure 2. Hemorrhage in adrenal glands (hematoxylin-eosin, original x5).



heart, esophagus, thymus, peritoneum, mesentery, pancreas, stomach and intestines. Forensic examination did not reveal any inflammatory focus or other pathological finding.

During autopsy blood sample from heart was excluded for blood culture. After ten days and appropriate incubation, microbiological finding arrive: blood culture was negative (Figure 1).

Microscopic findings: Patho-histology examination confirmed a massive acute hemorrhage in adrenal glands. Hemorrhage in all others above listed organs with micro thrombosis of small vessels was observed. Exclusion of inflammatory focus or other pathological finding was confirmed by patho-histology examination.

Toxicology findings: Toxicology was negative.

3. Discussion

In our case, it was confirmed that BMAH was (the) direct cause of death [5,6]. Hemorrhage in multiple organs with micro thrombosis of small vessels was also revealed. On the other hand, mechanism of death and main cause of death was not established with certainty.

BMAH is connected with many risk factors, as listed above. In our case, very high levels of procalcitonin and D-dimer, with all other clinically and autopsy findings, was directing medical examiners that a main cause of death was fulminant bacterial sepsis. Blood culture, performed on clinical and autopsy material, did not reveal any bacteria, so the cause of BMAH remained uncertain [26,27]. Double negative blood culture may be explained with fulminant sepsis and with small amount of bacteria in blood that cause sepsis [26,27].

The bacteria that most often cause fulminant sepsis connected with BMAH and death within 12-24 hours from first symptoms is N. meningitidis [4,18,28]. It is very likely that N. meningitidis caused BMAH in our case, but it will stay in the domain of speculation [29,30].

This case is presented to illustrate the difficulty in confirming BMAH as a mechanism causing death. It would be helpful to improve the medico-legal diagnostic criteria for describing probable infectious disease mortality. Future research could elucidate the pathogenesis of fulminant sepsis and the contribution of post-mortem diagnosis.

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