Waterhouse Friderichsen Syndrome Report of Two Cases

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Waterhouse Friderichsen Syndrome

This syndrome is characterized by necrohemorrhage of the adrenal glands in the course of a serious infectious disease, which is characterized by septic shock with multiple organ failure (prevailing neurological, renal and hematological failure even with criteria for disseminated intravascular coagulation), disseminated purpura and data on acute adrenal insufficiency. Initially described by an English physician in 1911, Dr. Rupert Waterhouse and later studied further by a Danish pediatrician, Dr. Carl Friderichsen in 1917 [1-3].

Within the etiology, it is mentioned that more than 90% of the cases are due to infectious agents, the rest to hematological pathologies or to certain added drugs. Of the infectious agents, Neisseria meningitidis is mentioned as responsible for 75-80% of the cases, the rest is distributed in a wide range of bacterial and rarely viral agents. In immunocompromised patients, the cases associated with cytomegalovirus that usually affect predominantly at the neurological level initially, CSF analysis including culture is recommended, as well as detection of meningococcal antigens in various biological fluids and polymerase chain reaction, which helps to identify specific serogroups without requiring the presence of live microorganisms.

The confirmation of the diagnosis is made with imaging studies that demonstrate an adrenal hemorrhagic lesion or often during a necropsy, in cases where only in this last way they are diagnosed, going unnoticed [3,10].

Risk Factor’s

The main risk factors are: Immunosuppression, anatomical or functional asplenia/hyposplenia states (mainly congenital asplenia and that associated with thalassemia and sickle cell anemia), in patients who have not received the appropriate specific prophylaxis against pneumococci, meningococci and haemophilus influenza [1,8,9].

Diagnosis

The initial clinical diagnosis is sudden and persistent high fever, associated with a picture of severe sepsis, the presence of rapidly progressive purpura, as well as evidence of adrenal insufficiency.

The biochemical findings demonstrate consumption coagulopathy fulfilling criteria for DIC (platelet penia, prolonged clotting times, dysfibrinogenemia and elevation of D-dimer), renal, hepatic, metabolic, respiratory lesions of varying magnitude. Likewise, you can find leukocytosis, normal leukocytes, or even leukopenia. It is important to emphasize the importance of taking diverse cultures in order to identify the etiological agent. We can use serum procalcitonin as a marker of bacterial sepsis. To rule out the presence of meningococci that usually affect predominantly at the neurological level initially, we can use serum procalcitonin as a marker of bacterial sepsis and use specific serogroups without requiring the presence of live microorganisms.

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The two main aspects to take into account are the start of broad-spectrum or specific antimicrobial therapy, which covers the most frequent possibilities, mainly meningococcus and gram-positive cocci, using penicillins, cephalosporins, glycopeptides and carbapenems; and on the other hand, start treatment of the shock state, always taking into account adrenal insufficiency, which will also require energetic fluid resuscitation, use of vasopressor amines, use of steroids such as fludrocortisone or hydrocortisone at stress doses, although

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**Table 1:** Two cases are presented in young, apparently healthy patients, who presented with disseminated purpuric symptoms and multiple organ failure that led to death, confirming the presence of Waterhouse Friderichsen syndrome due to adrenal involvement (Figure 1 and Figure 2).

|                      | Case 1                                                                 | Case 2                                                                 |
|----------------------|------------------------------------------------------------------------|------------------------------------------------------------------------|
| **Genre, age**       | Female, 24-years-old                                                   | Male, 42-years-old                                                     |
| **Medical history**  | Apparently healthy                                                     | Apparently healthy                                                     |
| **Symptoms**         | Fever, vomiting, disorientation                                        | Fever, disorientation, anuric                                           |
|                      | Purple spread 12 hours later                                           | Purple spread 6 hours later                                            |
| **Initial evaluation** | Deep shock (80/40 mmHg), metabolic acidosis, multiple organ failure including adrenal and respiratory failure. | Deep shock (88/53 mmHg), metabolic acidosis, multiple organ failure including adrenal and respiratory failure. |
| **Hemoglobin**       | 12.6 g                                                                | 13.2 g                                                                |
| **Leukocytes**       | 9,800                                                                  | 31,900                                                                 |
| **Platelets**        | 43,000                                                                 | 15,000                                                                 |
| **Creatinine**       | 2.3 mg                                                                 | 6.0 mg                                                                 |
| **Creatine phosphokinase** | 5,000 U                                                              | 4,000 U                                                               |
| **Bilirubins**       | 1.0 mg/dl                                                              | 2.2 mg/dl                                                             |
| **Transaminases**    | 65/70 U                                                                | 120/178 U                                                             |
| **Lactic dehydrogenase** | 816 U                                                              | 980 U                                                                 |
| **Na/K**             | 132/3.2 mmol                                                           | 128/4.5 mmol                                                          |
| **Prothrombin time** | does not coagulate                                                    | 32.6 seg                                                              |
| **Partial thromboplastin time** | 78.4 seg                                                             | 42.6 seg                                                              |
| **Fibrinogen**       | does not coagulate                                                    | 480 mg                                                                 |
| **pH, pO₂, pCO₂, HCO₃⁻** | 7.06, 87, 37, 10.1                                                   | 6.8, 78, 40, 8.2                                                      |
| **Isolated pathogen** | *Staphylococcus haemolyticus*                                         | None                                                                  |
| **Adrenal imaging**  | Adrenal necrosis                                                       | Adrenal necrosis                                                      |
| **Evolution and prognosis** | Stay in ICU with organic support, broad spectrum antimicrobials, steroids, despite this poor prognosis | Stay in ICU with organic support, broad spectrum antimicrobials, steroids, despite this poor prognosis |

**Figure 1:** Case 1-Female, 24-years-old, with disseminated purpura and multiple organ failure; purpuric lesions are confluent and scattered macules of different sizes.
dexamethasone can also be used, mainly in cases in which concomitant neuroinfection is documented.

Once these areas are covered, it is recommended to continue the indications of the campaign guidelines surviving sepsis for the management of septic critically ill patients.

Recently, cases of survivors have been reported, although with major sequelae, mainly of a neurological nature, who benefited from early therapies with continuous veno-venous hemodiafiltration and extracorporeal membrane oxygenation (ECMO), however these therapies are only available in centers highly specialized, often limited to a small number of patients [3,11-13].

Waterhouse Friderichsen Syndrome should be suspected in all patients with acute febrile syndrome, who appear critically ill (often encephalopathic, dehydrated or swollen, hyperdynamic, anuric or jaundiced), hypotensive or in shock, and with disseminated purpuric lesions, until proven otherwise.

Two cases are presented in young, apparently healthy patients, who presented with disseminated purpuric symptoms and multiple organ failure that led to death, confirming the presence of Waterhouse Friderichsen syndrome due to adrenal involvement (Table 1, Figure 1 and Figure 2).

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