EMBRACE

20 THE FUTURE OF ENDOCRINOLOGY 20

A Case of Waterhouse-Friderichsen Syndrome in a Patient with Streptococcus Pyogenes Bacteremia

D. I. BACAL, B. E. CATALDO, P. M. LUCERI, G. VARALLO

Rowan University School of Osteopathic Medicine, and Jefferson University Hospital System, NJ

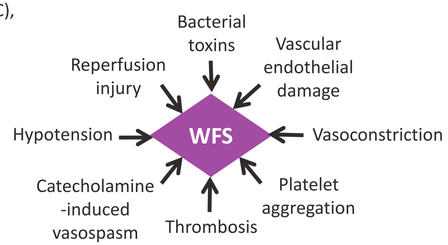
INTRODUCTION

Waterhouse-Friderichsen Syndrome (WFS) is a rare condition of adrenal insufficiency (AI) due to adrenal hemorrhage after a severe infection. The incidence of WFS has been estimated at 0.14-1.8% based on post-mortem studies.[1] It has been associated with a 55-60% mortality rate.[2] Meningococcal disease comprises up to 80% of WFS, but additional causative agents continue to be identified.[3]

This is the case of a 52-year-old female with toxic shock syndrome from Group A Streptococcal (GAS) bacteremia who developed bilateral adrenal hemorrhage & subsequent AI. Septic shock occurred during an initial hospitalization & resolved. Four weeks after discharge she presented with evidence of an adrenal crisis. CT scans demonstrated bilateral adrenal enlargement concerning for adrenal hemorrhage. Primary AI was confirmed via ACTH stimulation testing. A literature search found fewer than ten cases of WFS described due to streptococcal bacteremia.

BACKGROUND OF WATERHOUSE-FRIDERICHSEN SYNDROME

- Bilateral adrenal hemorrhage has multiple causes: coagulopathies, sepsis from infection, hypotension (i.e. MI), severe volume loss, or surgical intervention [4]
- Signs include pallor, weakness, fatigue, anorexia, nausea, vomiting, and lethargy [5,6] & labs often depict hyponatremia & hyperkalemia
- Increased skin pigmentation develops due to an increase in proopiomelanocortin (POMC), the precursor to adrenocorticotropic hormone (ACTH) [7]
- If untreated, patients suffer eventual cardiovascular collapse and death [8]
- The pathogenesis of WFS is multifactorial
- Some causative bacterial organisms include pneumococcus, streptococcus, staphylococcus, haemophilus, & pseudomonas [9]
- In a cross-sectional study of primary & secondary AI, fewer than 30% of women & 50% of men were diagnosed in the first 6 months after symptom onset; 20% of patients had symptoms for over five years before formal diagnosis [11]
- A study of several cases has shown that some patients may recover, & may not need mineralocorticoid & glucocorticoid treatment long-term[7]



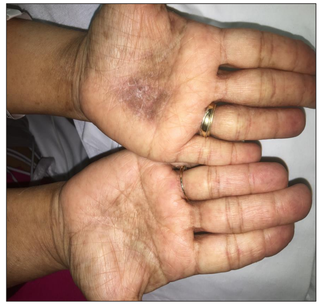


Figure 1: Hyperpigmentation of the patient's palmar creases.

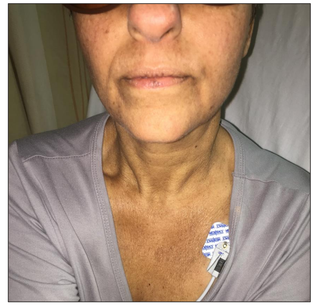


Figure 2: Hyperpigmentation on the patient's lips, face, and chest

CASE DESCRIPTION

A 52-year-old woman presented with left sided axillary swelling & discomfort of her her left upper flank. This was accompanied by fevers, weakness, & malaise. She was septic on admission, with hyponatremia (**125 mmol/L**, NL: 133-145 mmol/L), acute kidney injury (GFR 42) with no prior kidney dysfunction, & elevated creatinine kinase (**728 U/L**, NL: 59-135 U/L).

A CT scan of the chest with & without contrast revealed inflammation of the left chest wall musculature with edema & changes of myositis. She was started on IV antibiotics & copious IV fluids. A CT of the abdomen was unremarkable.

On day 3, blood cultures confirmed *S. pyogenes* bacteremia. She was moved to the ICU due to progression to toxic shock syndrome. By day 4, the patient was started on two pressor medications despite aggressive hydration. On day 5 stress-dosed IV steroids (hydrocortisone 50 mg IV Q6 hours) were initiated. A daily dose of IV immunoglobulin therapy was given on days 4 & 5. Her condition slowly improved thereafter. She was transferred out of the ICU on day 13 & discharged home in stable condition after a 19-day hospital stay.

Four weeks after discharge she presented again with fatigue, dizziness upon standing, nausea, & vomiting. There was new hyperpigmentation of her palms (**Fig. 1**), face, chest, & lips (**Fig. 2**). Her sodium level was **121 mEq/L**. On day 2 of this admission, an early morning cortisol was **4.9 µg/dL**. A CT of the abdomen & pelvis with oral contrast showed asymmetric enlargement of her adrenals bilaterally with concern for adrenal hemorrhage. A 250 µg ACTH stimulation test was done & her cortisol rose from **5.5 µg/dL** to only **6.2 µg/dL** one hour later. A baseline plasma ACTH was **785 pg/mL** (10-60 pg/mL).

She was diagnosed with primary adrenal insufficiency & started on IV corticosteroids. The patient's symptoms improved dramatically within hours. Her official diagnosis was adrenal crisis as a result of bilateral adrenal hemorrhage in the setting of Group A Streptococcal bacteremia.

CONCLUSIONS

WFS is a rare, often fatal, clinical condition that can develop after a severe infection & leads to adrenal hemorrhage. Many factors contribute to the pathogenicity of WFS, including coagulopathy, ischemia & bacterial toxins. WFS resulting from severe GAS infection has been sparsely described in the literature. Here we presented a case report of this rare condition. Patients presenting with persistent fatigue, hypotension, hyponatremia, or new onset skin hyperpigmentation after a severe infection should be strongly considered for an AI workup. After diagnosis & treatment, it is important to continue routine long-term follow-up & assessment of the adrenal axis.

REFERENCES

1 Rao, R. H. (1995). Bilateral massive adrenal hemorrhage. *Medical Clinics of North America*, *79*(1), 107–129. doi: 10.1016/s0025-7125(16)30087-6

2 Tormos, L. M., Schandl, C. A. (2013). The Significance of Adrenal Hemorrhage: Undiagnosed Waterhouse-Friderichsen Syndrome, A Case Series. *Journal of Forensic Sciences*, 58(4), 1071-4. doi: 10.1111/1556-4029.12099

3 National Institutes of Health. (2016). Waterhouse-Friderichsen Syndrome. https://rarediseases.info.nih.gov/diseases/9449/waterhouse-friderichsen-syndrome

4 Simon, D. R., & Palese, M. A. (2009). Clinical update on the management of adrenal hemorrhage. *Current Urology Reports*, *10*(1), 78–83. doi: 10.1007/s11934-009-0014-y

5 Ogino, J.,Toda, J., Onitsuka, S., & Hashimoto, N. (2013). Idiopathic bilateral adrenal haemorrhage related to acute adrenal insufficiency. *BMJ Case Reports*, 2013, bcr2013009626. doi.org/10.1136/bcr-2013-009626

6 Picolos, M.K., Nooka, A., Davis, A.B., Ravel, B., Orlander, P.R. (2007). Bilateral adrenal hemorrhage: an overlooked cause of hypotension, *Journal of Emergency Medicine*, 32(2): 167–169.

7 Jahangir-Hekmat, M. Taylor, H. C., Levin, H., Wilbur, M., & Llerena, L. A. (2004). Adrenal Insufficiency Attributable To Adrenal Hemorrhage: Long-Term Follow-Up With Reference To Glucocorticoid And Mineralocorticoid Function And Replacement. *Endocrine Practice*, *10*(1), 55–61. doi: 10.4158/ep.10.1.55

8 Ingelfinger, J., Rushworth, R.L., Torpy, D.J., Falhammar, H. (2019). Adrenal Crisis. *New England Journal of Medicine*, 381(9), 852-61. doi: 10.1056/NEJMra1807486

9 Nosé, V. (2018). Infectious Disorders, Adrenal Glands. In *Diagnostic Pathology: Endocrine, 2nd ed* (pp. 415–418). Elsevier.

10 Bowen, A. D., Keslar, P. J., Newman, B., & Hashida, Y. (1990). Adrenal hemorrhage after liver transplantation. *Radiology*, *176*(1), 85–88. doi: 10.1148/radiology.176.1.2191375

11 Bleicken, B., Ventz, M., Quinkler, M., & Hahner, S. (2010). Delayed Diagnosis of Adrenal Insufficiency Is Common: A Cross-Sectional Study in 216 Patients. *The American Journal of the Medical Sciences*, *339*(6), 525–531. doi: 10.1097/maj.0b013e3181db6b7a