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IMAGES IN FORENSICS

Sudden death due to acute adrenal crisis

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Case report

A 50-year-old man was found dead in the bed of his hotel room. Heavy fecal staining was present on the bed sheets and on the floor adjacent to the bed, as well as on the bathroom floor. According to the man's medical history he had suffered from Addison's disease from the age of 16 years. His history included prescribed medication of 100 mg hydrocortisone per day, but no therapeutic drugs were found at the scene. The man had also been suffering from recurrent respiratory tract infections and mycosis of the nails. A medicolegal autopsy was ordered by a prosecutor to clarify the cause and manner of death, and to rule out third party involvement.

External examination of the body revealed an obese adult male (body length 171 cm, body weight 129 kg, body mass index 44 kg/m^2) with no external injuries. There was marked brownish hyperpigmentation of the skin of the penis and scrotum as well as sporadic depigmentation in the inguinal region (Figs. 1, 2). The surface of the tongue showed a whitish plaque indicating a fungal infection. Autopsy findings included brain edema (weight 1,560 g) and fatty liver. Although slightly enlarged, the heart (weight 480 g) had no valve abnormalities or coronary artery disease. The thyroid gland was unremarkable. The mucosa of the stomach and the small and large intestines showed no evidence of acute inflammation or any underlying chronic bowel disease. Additionally, all of the components of the gastrointestinal tract were completely empty.

Besides the brownish skin pigmentation, the most remarkable aspect of the autopsy was the difficulty to macroscopically identify any adrenal gland tissue. For this reason, all the fatty tissue surrounding the superior pole of each kidney was retained for histological examination. A thorough histological examination of this fatty tissue verified the diagnosis of Addison's disease. The sparse appearance of adrenal gland tissue indicated a notable decrease in the width of the original adrenal cortex, atrophy of the adrenal cortical cells, and a collapsed vascular reticulin framework. Parts of the adrenal cortex had been replaced by dense accumulations of lymphocytic and plasma cell infiltrates (Fig. 3), thus confirming the histological diagnosis of autoimmune adrenalitis. Fibrosis was not observed within the adrenal glands.

Toxicology results were negative for both alcohol and drugs and a urine screen for hyperglycemia was negative. However, the vitreous humor was not examined.

Taking into account the circumstances of the death, the previous medical history of the deceased, and the autopsy findings, cause of death was attributed to acute adrenal crisis (Addisonian crisis).

Discussion

First described by Thomas Addison in 1855, chronic adrenal insufficiency is an uncommon disease with prevalence estimates of 100–140 cases per million [1]. Addison's disease is defined as any pathology leading to the destruction or atrophy of the adrenal cortex. This results in

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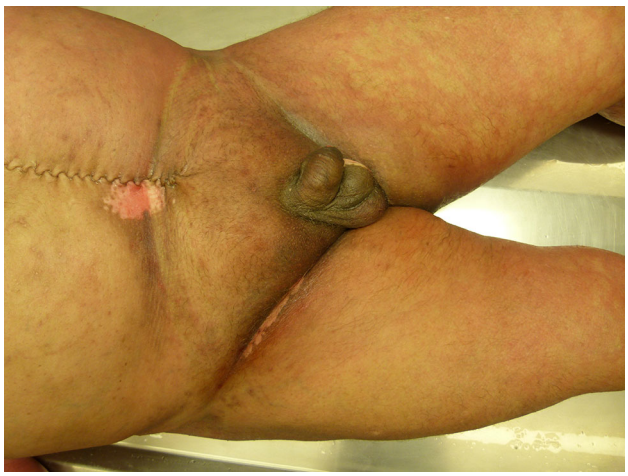

Fig. 1 Brownish hyperpigmentation of the skin of the penis and scrotum, and sporadic depigmentation in the inguinal region

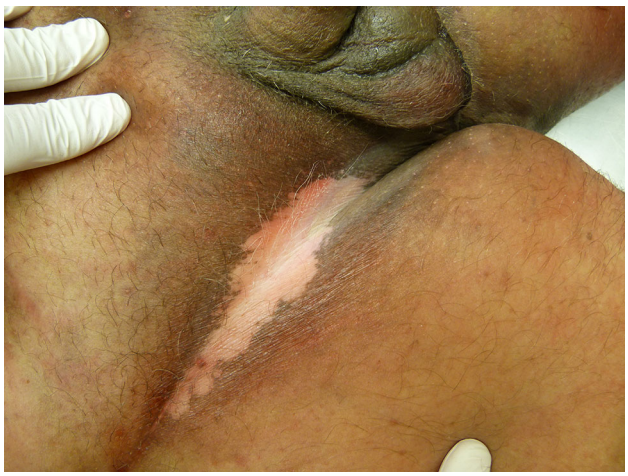

Fig. 2 Close-up view of the brownish hyperpigmentation and whitish depigmentation of the skin in the right inguinal region

a failure to synthesize and secrete glucocorticoids (primarily cortisol), mineralocorticoids (primarily aldosterone), and androgens [2, 3]. A variety of pathological processes may cause Addison's disease. In developed countries the disease is usually related to autoimmune disorders; however, in developing nations, it is still widely associated with tuberculosis [1, 4]. The disease may also be caused by certain hereditary disorders, adrenal hemorrhage of various origin, infections, or medications. It is seen across all age groups and affects equal proportions of males and females [5, 6].

The symptoms of chronic primary adrenal insufficiency are varied and nonspecific, including weakness, fatigue, dysphagia, hypotension, nausea, and weight loss [1–7]. One of the most characteristic signs of Addison's disease is hyperpigmentation of the skin. Isolated darkened areas are commonly observed in (but not restricted to) flexural areas,

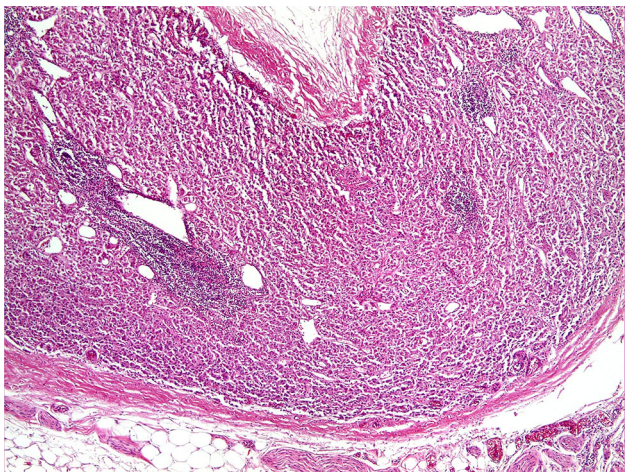

Fig. 3 Histology of Addison's disease. There is atrophy of the adrenal cortical cells and a collapsed vascular reticulin framework, with partial replacement of the adrenal cortex by dense accumulations of lymphocytic and plasma cell infiltrates. Note the absence of fibrosis

sites of friction, recent scars, and genital skin [3, 7]. In addition, patients may also exhibit vitiligo, alopecia areata, and mucocutaneous candidiasis [3].

In this autopsy case, the brownish hyperpigmentation of the skin of the penis, scrotum, and inguinal regions, together with the indications of vitiligo and the fungal infection of the tongue are all consistent with the documented clinical symptoms of Addison's disease.

The most severe and potentially life-threatening complication of Addison's disease is acute adrenal crisis (Addisonian crisis). Possible indications of this sudden decompensation of chronic adrenal insufficiency include nausea, vomiting, diarrhea, orthostatic hypotension, agitation, confusion, circulatory collapse, abdominal pain, and fever [3, 6]. The most common symptoms related to adrenal crisis have been identified as vomiting and diarrhea, which seem to be associated with more than half of the documented cases of adrenal crisis. Other conditions such as flu-like illness and associated major infections, surgical procedures carried out with insufficient steroid cover, respiratory and urinary tract infections, septicemia, myocardial infarction, migraines, allergic reactions, and severe diabetic hypoglycemia could all play a role in the onset of adrenal crisis. In the case reported here, the previous medical history (recurrent respiratory tract infections) as well as the findings at the scene (liquid fecal staining on some surfaces of the hotel room) and at autopsy (the completely emptied gastrointestinal tract) are clearly indicative of acute adrenal crisis. There was no evidence of the coexistence of diabetes mellitus or any other autoimmune disease such as Hashimoto's disease, as previously described in rare cases of particular autoimmune syndromes. In this particular case diarrhea may be interpreted

as both a contributing factor to and a symptom of the sudden onset of adrenal crisis.

The most remarkable outcome of this autopsy was the difficulty to clearly identify any adrenal gland tissue. This autopsy observation has been described previously in cases of Addison's disease, in addition to the atrophy and low weight of the adrenal glands when they can be macroscopically identified [2, 8]. The histological findings here can be attributed to autoimmune Addison's disease [2, 3, 8].

In summary, it is important to conduct a comprehensive evaluation of all the macroscopic and histological observations in an autopsy case such as this [2, 8, 9]. The combination of characteristic postmortem findings and known preexisting conditions assisted in the determination of acute adrenal crisis as the cause of this sudden death.

Unsurprisingly, adrenal crisis is often diagnosed only after exclusion of all other possible causes of death. The forensic pathologist must be aware of its specific pathology, otherwise this uncommon cause of sudden death could easily remain undiscovered during a postmortem examination.

References

1. Erichsen MM, Løvås K, Fougner KJ, Svartberg J, Hauge ER, Bollerslev J, Berg JP, Mella B, Husebye ES. Normal overall mortality rate in Addison's disease, but young patients are at risk of premature death. Eur J Endocrinol. 2009;160:233–7.
2. Al Sabri AM, Smith N, Busuttil A. Sudden death due to autoimmune Addison's disease in a 12-year-old girl. Int J Legal Med. 1997;110:278–80.
3. Nieman LK, Chanco Turner ML. Addison's disease. Clin Dermatol. 2006;24:276–80.
4. Hiatt JR, Hiatt N. The conquest of Addison's disease. Am J Surg. 1997;174:280–3.
5. Krishnamoorthy A, Mentz RJ, Hyland KA, McMillan EB, Patel CB, Milano CA, Hernandez AF. A crisis of the heart: an acute reversible cardiomyopathy bridged to recovery in a patient with Addison's disease. ASAIO J. 2013;59:668–70.
6. Bornstein SR. Predisposing factors for adrenal insufficiency. N Engl J Med. 2009;360:2328–39.
7. Zargar AH, Laway BA, Masoodi SR, Bashir MI, Wani AI, Salahuddin M. A critical evaluation of signs and symptoms in the diagnosis of Addison's disease. J Assoc Physicians India. 2001; 49:523–6.
8. Burke MP, Opeskin K. Adrenocortical insufficiency. Am J Forensic Med Pathol. 1999;20:60–5.
9. Langlois NE. Sudden adult death. Forensic Sci Med Pathol. 2009;5:210–32.