Sudden Death and Enlarged Adrenal Glands in an Otherwise Healthy Adult Woman

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Questions

1. What are this individual's most striking anatomic autopsy findings?
2. How do you explain these findings?
3. What is the most likely diagnosis consistent with this patient's autopsy histopathologic findings?
4. What is the most common cause of Addison's disease?
5. What laboratory testing can help confirm the diagnosis in this case or in a living patient?
6. What utility does a single, untimed, serum cortisol measurement have in evaluating Addison's disease in a living patient?
7. Why were no tuberculosis (TB) organisms found in stained tissue sections from the decedent?
8. Based on the decedent's most likely diagnosis, what increased risk is there to the decedent's family and close contacts and to autopsy personnel?
9. Why did the decedent's skin darken in the period immediately preceding her death?

Possible Answers

1. Enlarged adrenal glands consisting almost entirely of granulomatous inflammation and scarring and adhesion involving the right lung, the right side of the diaphragm, and the capsule of the liver, in close proximity to a liver granuloma.

2. The presence of caseating necrosis is characteristic of mycobacterial infection and supports an infectious etiology for this

Principal Laboratory Results

Table 1

Additional History

After discussing the autopsy findings with the decedent’s daughter, she mentioned that her mother’s skin had been getting darker in the months preceding her death.

Image 1. Patient's enlarged right adrenal gland, demonstrating a thick, nodular cortex, a firm yellow-tan cut surface, and focal calcification.
individual’s histopathologic findings. Fungal infections can cause similar findings. On the other hand, sarcoidosis is associated with non-caseating granulomas.

3. Most likely diagnosis: Addison’s disease (primary adrenal insufficiency) due to TB infection of the adrenal glands.

4. Up until 20 to 25 years ago, TB was the most common cause of Addison’s disease. Due to the effectiveness of the treatment for TB in developed western countries, autoimmune disease is now the most common cause of Addison’s disease. In less developed countries, however, TB continues to be responsible for most cases of Addison’s disease.

5. Laboratory testing at autopsy is limited by postmortem changes in body fluids, including serum. Vitreous fluid is relatively protected from such changes; however, artifactual increases in potassium can be seen after death. Testing of vitreous fluid for electrolyte (sodium, potassium, chloride) concentrations gives the best approximation of values for these analytes in antemortem serum. In decedents with adrenal insufficiency, their vitreous sodium concentration should be decreased while their potassium concentration should be increased. Both of these changes were observed in vitreous fluid from the decedent presented in this case study (Table 1). In a living patient, provocative testing can be performed to assess adrenal reserve. An abnormal response to cosyntropin [an adrenocorticotropic (ACTH) analogue] stimulation suggests primary adrenal insufficiency.

6. In a living patient with a normal sleep pattern (no shift work) and normal adrenal glands, serum cortisol concentration reaches a peak in the early morning hours (approximately 8:00 AM), declines throughout the day, and reaches a nadir at approximately 8:00 PM before rising again and repeating this cycle. Therefore, a single, untimed cortisol measurement may not be useful in assessing Addison’s disease, unless it is markedly low, as was the case for the decedent (Table 1). On the other hand, the cosyntropin stimulation test can be performed at any time by measuring baseline cortisol concentration and comparing it to 30-minute and 60-minute post stimulation cortisol values. In an individual with adequate adrenal reserve, plasma cortisol concentration should rise by >9 µg/dL over baseline within 30 to 60 minutes after the administration of cosyntropin. Although a cosyntropin stimulation test was not performed on our patient prior to her death, based on the autopsy findings relevant to her adrenal glands, her adrenal reserve would have been clearly insufficient for her to mount an adequate cortisol response to the unknown stress which led to her death.

7. Presumably, the decedent’s TB infection had been treated successfully several years ago with a 4-drug therapy. Because no evidence of active TB was found at autopsy, it is likely that any TB organisms present previously had been cleared. However, effective treatment of TB infection does not restore normal adrenal function in individuals whose adrenal gland(s) have been infected and damaged by the TB organism.
8. Because the decedent’s TB was successfully treated, family members, other close contacts, and autopsy personnel are not at increased risk of contracting TB. In deceased individuals with active TB infection, the required adherence of autopsy personnel to universal precautions procedures, including the wearing of an N95 mask, will reduce the likelihood of TB infection in these individuals.7

9. Decreased glucocorticoid production in primary hypoadrenalism leads to increased production of ACTH by the pituitary. Adrenocorticotropichas significant melanogenic activity which accounts for the hyperpigmentation and skin atrophy that is seen in patients with Addison’s disease or with Nelson syndrome (ACTH-secreting tumors).8,9

Keywords: adrenal glands, cosynthentropin stimulation test, ACTH, cortisol, hypoadrenalism, Addison’s disease