Isolated Adrenocorticotropic Hormone Deficiency: An Autopsy Case of Adrenal Crisis: A Case Report

[Articles]

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Abstract
We present a case of fatal adrenal crisis due to isolated adrenocorticotropic hormone (ACTH) deficiency. Autopsy revealed each adrenal gland weighed 0.9 g and the adrenal cortices were very thin and atrophic. Additionally, cortisol could not be observed in the adrenal cortex by immunohistochemical staining. Furthermore, urine cortisol and 17-OHCS concentration had decreased to a very low level, 20 mg/L and 0.8 mg/L respectively. The anterior pituitary gland was atrophic, and showed fibrosis and lymphocytic histiocytes with clusters of lymphocytes. Thus, lymphocytic hypophysitis was suspected. Immunohistochemically, growth hormone (GH)-stained pituitary gland cells were observed, but there were no cells stained with anti-ACTH antibody. From the history and pathological findings, no other deficiencies of pituitary hormones were evident. Therefore, isolated ACTH deficiency was suspected. Furthermore, as the thyroid gland showed lymphocytic thyroiditis, it was considered that isolated ACTH deficiency was associated with an autoimmune cause. Generally, as patients of chronic adrenocortical insufficiency are exposed to stress and, therefore, have an increased requirement for glucocorticoids, the blood pressure falls, leading to hypovolemic shock called "an adrenal crisis." Without treatment, patients die in crisis within several hours. In our case, the deceased had drunk alcohol without sleep for 2 days. We believe that the stress of drinking and sleeplessness induced adrenal crisis and caused his death.

Adrenocortical insufficiency includes all conditions in which the secretion of adrenal steroid hormones, glucocorticoids (cortisol), mineralocorticoids (aldosterone), and adrenal androgen falls below the requirement of the body (1-4). As a patient of chronic adrenocortical insufficiency is exposed to stress and, therefore, has an increased requirement for glucocorticoids, the blood pressure falls and hypovolemic shock develops. This state of shock is called an adrenal crisis, in which a patient dies within several hours (1-4).

An autopsy case of adrenal crisis, with undiagnosed adrenocortical insufficiency is reported. Both the cause of the crisis and of adrenocortical insufficiency are briefly discussed.

CASE REPORT
A 37-year-old man was found dead on his stomach with evidence of vomiting on October 5th. Since the evening of October 3rd until about 12:30 AM on October 4th, he had been drinking with his family in his hotel. Then he went out and continued to drink in another pub until about 3 o'clock in the morning. At 6 o'clock an employee saw him bring rice wine to his room. After that nobody saw him until his body was discovered the early morning of October 5th, after a guest sleeping in the next room reported hearing a big noise from his room.

Past History
For 2 years, the decedent had complained of vertigo, general fatigue, easy fatigability, and appetite loss. He had not been hospitalized.

**Autopsy Findings**

Height was 166.0 cm, and weight was 52.0 kg. Nutrition was slightly bad, and skin color was relatively pale (Fig. 1). Many injuries, such as discolorations and desquamations, could be observed on the face, elbows, and knees. The pituitary gland weighed 0.4 g (normal weight: 0.5-0.7 g) and macroscopically had no tumor or bleeding lesions. The adrenal glands were highly atrophic (Fig. 2), and each adrenal gland weighed 0.9 g (normal weight: left, 5.9 ± 1.9 g; right, 5.5 ± 1.61 g in 36- to 40-year-old man) (6). The adrenal cortices were very thin. The thyroid gland weighed 11.0 g (normal weight: 17.4 ± 5.04 in 36 to 40-year-old man) (6), and no abnormalities were observed macroscopically. Thickness and length of his pubic hair had a normal appearance (5.2 cm in length). There were no abnormalities in his penis and scrotum. In all other organs, including brain, heart, and lungs, there were no pathological findings to have caused his death. Alcohol was not found in his blood or urine.

**Histological Findings**

The anterior pituitary gland was atrophic; fibrous and lymphocytic infiltration, including clusters of lymphocytes, were observed (Fig. 3). Immunohistochemically, the pituitary gland was stained with antihuman adrenocorticotropic hormone (ACTH) (Chemicon, U.S.A.) and antihuman growth hormone (GH) (Dako, Denmark) antibodies by the labeled streptavidin biotin (LSAB) method (LSAB kit; Dako, Denmark). GH could be observed in cells (Fig. 4), but no ACTH-stained cells were found.

The adrenal cortices were highly atrophic with fibrosis (Fig. 5). In the adrenal cortices, cortisol was not observed immunohistochemically (anticortisol antibody; Chemicon, U.S.A.).

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The thyroid gland showed slightly varying sized colloidal cysts with focal fibrosis and lymphocytosis. In the testis, spermatozoa was observed. In other organs there were no pathological changes histologically.

**Endocrinological Findings**

The concentrations of cortisol and its metabolite, 17-OHCS, in cystic urine were at a very low level, 20 mg/L (normal range; 300–400 mg/L) and 0.8 mg/L (2–0.9 mg/L), respectively (as a control, urine was obtained from a deferent decedent who was almost the same age and died at almost the same time without any abnormalities in pituitary and adrenal glands, cortisol was 365 mg/L and 17-OHCS was 9.7 mg/L). On the other hand, androgen metabolite 17-KS in his urine was at a normal level; 4.6 mg/L (3.0–8.0 mg/L).

**DISCUSSION**

Adrenal insufficiency is defined by deficient production of adrenal steroid hormones. Adrenal insufficiency may be divided into two general categories: (1) those associated with primary inability of the adrenal cortex to elaborate sufficient quantities of hormone and (2) those associated with a secondary failure due to a primary failure in the elaboration of ACTH. The primary insufficiency is a total lack or deficiency of all three adrenocortical steroid hormones: glucocorticoids, mineralocorticoids, and adrenal androgen. On the other hand, in secondary adrenal insufficiency secretions are deficient of glucocorticoids and adrenal androgen, which are under the control of pituitary ACTH (1–4, 7, 8). In our case, nutrition was slightly bad, and skin color was relatively pale (see Fig. 1). Autopsy revealed no macroscopical changes in organs except the adrenal glands. The adrenal glands were highly atrophic, and each gland weighed 0.9 g (see Figs. 2 and 4). In the adrenal cortexes, cortisol was not observed immunohistochemically. Furthermore, urine cortisol and 17-OHCS concentration were at a very low level, 20 mg/L and 0.8 mg/L, respectively (9, 10). Therefore, adrenocortical insufficiency was suspected. The anterior pituitary gland was atrophic, and fibrosis and lymphocytic infiltration, including clusters of lymphocytes, were found (see Fig. 3). Histologically, lymphocytic hypophysitis was suspected. There were no ACTH-positive cells with immunohistochemical staining. From these findings, his adrenal insufficiency was considered a secondary deficiency due to pituitary lesions.

Pituitary lesions induce deficiencies of anterior pituitary hormones. The condition of the patient depends on the number and extent of hormone deficiencies. In an adult male, from deficiencies in anterior pituitary hormones, hypoglycemia may result in growth hormone (GH) deficiency. Gonadotropin deficiency may induce decreased or absent pubic and axillary hair, and testicular atrophy. Deficiency of thyrotropin (TSH) may cause lethery, constipation, cold intolerance, dry skin, myxema, anemia, and hair loss. Also, declines may develop in intellectual and motor activity and in appetite (7, 8). In our case, GH deficiency was not discovered immunohistochemically (see Fig. 4). On the other hand, there were no findings such as dry skin, myxema, and hair loss. Decreased or absent pubic and axillary hair, and testicular atrophy were not observed, and urine 17-KS content was within normal range (4.6 mg/L). Therefore, deficiency of gonadotropin and TSH were not considered. It was considered that only ACTH was deficient, and isolated ACTH-deficiency was suspected (11, 12).

Isolated ACTH deficiency is a rare cause of adrenocortical insufficiency in which an anterior pituitary lesion shows lymphocytic hypophysitis. There have been occasional associations with chronic lymphocytic thyroiditis, suggesting that it is an autoimmune disorder (13–19). In our case, both lymphocytic hypophysitis and thyroiditis were observed. Therefore, it is considered that our case is associated with an autoimmune cause.

The clinical signs of isolated ACTH deficiency are characterized by deficiencies of two hormones: glucocorticoid and adrenal androgen (1–4, 7, 8). In our case, the deceased complained of vertigo, anorexia, and fatigability for 2 years. Those symptoms agree with the clinical findings of deficiency of glucocorticoid. Therefore, the deceased exhibited secondary insufficiency for 2 years (i.e., chronic adrenocortical insufficiency).

Adrenal crisis is a rapid and overwhelming intensification of chronic adrenal insufficiency. In the presence of severe stress, such as infection, trauma (including surgery), gastrointestinal upsets, or other stress, which requires an immediate increase in glucocorticoid, the blood pressure and pulse fail as hypovolemic vascular shock ensues. This state is usually termed adrenal crisis (1–4). From autopsy and histological findings, infection and gastrointestinal upsets were not suspected. In our case, the deceased had continued to drink without enough sleep for 2 days until his death. It was considered that the stress of drinking and sleeplessness induced adrenal crisis and caused his death.

In the clinical processes of adrenal crisis, patients previously maintained on chronic glucocorticoid therapy may not exhibit severe dehydration or hypotension until postmortem because mineralocorticoid secretion is usually preserved. In contrast, in previously untreated patients, pre-existing symptoms are intensified. Nausea, vomiting, and abdominal pain may become intractable. Fever is frequently severe but may be absent. Lethargy deepens into somnolence (13). Our deceased, untreated patient, was found with vomiting, and it was suspected that he had fallen into such a clinical process before his death.

In this paper, one case of adrenal crisis due to isolated ACTH deficiency was reported. Histologically, as lymphocytic hypophysitis and thyroiditis were observed, the isolated ACTH deficiency may have been associated with an autoimmune cause.

**REFERENCES**


**Keywords:**

Endocrinology; Isolated ACTH deficiency; Lymphocytic hypophysitis; Adrenal crisis; Cortisol

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