



**A CASE OF HEPATOCELLULAR CANCER WITH ADRENAL GLAND METASTASIS  
PRESENTED WITH SERIOUS HYPERKALEMIA**

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Article Received on 25/10/2018

Article Revised on 15/11/2018

Article Accepted on 06/12/2018

**ABSTRACT**

A 66-year-old male patient was admitted to our emergency department with complaints of weight loss, drowsiness, fatigue, and anorexia. Laboratory examination showed hyperkalemia, acute renal failure, elevation of liver enzymes and cholestasis. Hyperkalemia was resistant to medical treatment and hemodialysis. Radiologic evaluation revealed the findings of chronic liver disease, portal thrombosis and hepatocellular carcinoma (HCC) in the liver, and the masses were found in the left adrenal gland and adrenal insufficiency was observed. His complaints regressed dramatically after methylprednisolone replacement. Clinical and laboratory parameters were improved. Histopathology of the adrenal gland was completely necrosis. The radiological image, clinical and laboratory findings supported the metastasis of HCC to the adrenal gland.

**KEYWORDS:** Hyperkalemia, adrenal Insufficiency, hepatocellular cancer.

**INTRODUCTION**

The global incidence of HCC is estimated to be one million and is one of the most common cancers especially in Southeast Asia.<sup>[1]</sup> The extrahepatic metastases of HCC have been reported in approximately 50% of cases. Oral and perioral region, diaphragm, large veins adjacent to the liver, adrenal glands, abdominal glands, lungs are typical target organs.<sup>[2]</sup> Although adrenal glands are the most common site of metastasis in autopsy studies, adrenal insufficiency is rarely seen.<sup>[3]</sup> In a review by Guttman<sup>[4]</sup>, a statistical analysis of 566 cases revealed that metastatic carcinoma-related adrenal insufficiency were less than 1%.

However, detection of metastasis-induced adrenal insufficiency increases with the development of hormone-sensitive measurements, imaging techniques such as ultrasonography and computed tomography.<sup>[5-7]</sup> Metastasis-induced adrenal insufficiency occurs when more than 90% of the adrenal tissue is damaged.<sup>[8,9]</sup> Lymphoma, melanoma, breast cancer, lung cancer metastases are often go to adrenal glands.<sup>[3]</sup>

We report a case of adrenal insufficiency due to metastasis of HCC with clinical, biochemical and radiological evidence.

**CASE REPORT**

A 66-year-old male patient was admitted to the emergency department with weakness, fatigue, loss of appetite, yellowing of the eyes, darkening of the skin, difficulty in walking and change in mental status. These complaints have appeared for a month. During this time, he lost about 10 kg weight as a result of anorexia. He has no history of alcohol or smoking. He also have no family history. He was not taking any medication for any chronic disorder. Physical examination was as follows; height: 177 cm, weight: 71.5 kg, blood pressure: 100/60 mmHg, pulse 50/ min, fever: 36.5°C, conscious but sleepy. The scleras were icteric. In addition to hypovolemia findings, there was a decrease in reflexes and hyperpigmentation in the skin. But the pigmentation of mucous membranes was normal. His pubic hair was preserved. In the abdominal examination, the traube area was closed and the spleen was palpable. Abdominal percussion was compatible with ascites. Examination of other systems was normal. In laboratory values hyponatremia (Na: 122 mEq/ L), hyperkalemia (K: 7.9 mEq/ L), hypoglycemia (glucose: 56 mg/ dL), deterioration of liver function tests and cholestasis enzymes (AST: 324 u/ L, ALT: 135 u/ L, GGT: 195 u/ L, Total bilirubin: 3.9 mg/ dL, direct bilirubin: 3.1 mg/ dL), elevation in renal function tests (urea: 154 mg/ dL, creatinine: 1.82 mg/ dL), leukocytosis (wbc: 11.73 10<sup>3</sup>/ L).

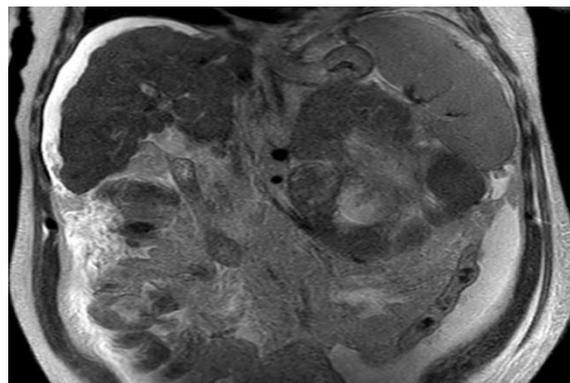
Calcium gluconate was given immediately to antagonize the cardiac effects of hyperkalemia. Antihyperkalemic medical treatment (fluid replacement, glucose & insulin, sodium bicarbonate, salbutamol, furosemide, cation exchanger resin, lactulose) was given. His renal functions returned to normal after fluid replacement. Acute renal failure was attributed to lack of oral intake. When ECG findings of hyperkalemia and mental status disorder persisted, hemodialysis was performed twice. However potassium level did not improve.

The causes of hyperkalemia were examined. In the endocrinological examination, urinary 17-hydroxycorticosteroid (1.07 mg/ day), 17-ketosteroid (0.41 mg/ day), and aldosterone was too low. Serum anterior pituitary hormones were within normal limits. Plasma renin activity was high, serum aldosterone and dehydroepiandrosterone sulfate levels were low (> 3.0 ng/ ml/ hr, <21.0 pg/ ml, <6 pg/ dl, respectively). Serum corticosteroid-binding globulin level was also low. Severe low serum cortisol (cortisol: 0.6 mcg/ dL) and ACTH elevation (ACTH: 123 pg/ ml) were found. He had adrenal insufficiency and hyperreninemic hypoaldosteronism. The abnormalities in serum ACTH and cortisol levels supported this. Therefore, high-dose cosyntropin stimulation test was not required.

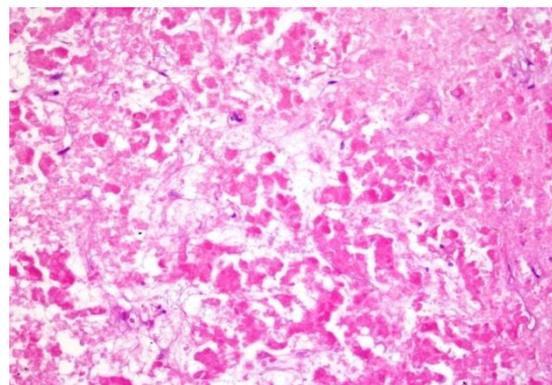
Liver disease was examined; hepatitis B surface antigen and hepatitis C antibody were negative. The antimitocondrial antibody for primary biliary cirrhosis detection was negative. The hepatocellular cancer marker AFP was high at the border. In magnetic resonance imaging of the abdomen; findings were supporting HCC, chronic liver disease, right portal vein thrombosis, ascites and splenomegaly. Metastatic involvement was observed in the left surrenal gland (Fig. 1). Adrenal gland biopsy was performed from the and histopathological material consisted of necrosis. Necrotic tissue could not be evaluated with immunohistochemical staining (fig. 2). Biopsy could not be performed for the second time because of the patient's poor general condition.

Oral 48 mg/ day methyl prednisolone was started and the dose was titrated over days. After treatment with methylprednisolone, his appetite and fatigue improved dramatically. In the control laboratory; Na: 136 mEq/ L, K: 4.5 mEq/ L, urea: 54 mg/ dL, creatinine: 0.9mg/ dL, glucose: 75mg/ dL. Electrolyte, hemogram and glucose values were normal.

There was a mental state change in the patient's admission. Brain magnetic resonance imaging was performed to exclude pituitary diseases and cranial metastasis. The pituitary gland and other parts of the brain were normal. Oncology consultation did not consider chemotherapy because of his age and poor performance and, proposed a conservative approach. Liver failure was attributed to primary tumor and chronic liver failure.



**Figure 1: Hepatocellular cancer and adrenal metastatic mass.**



**Figure 2: Adrenal histopathological material entirely consists of necrosis.**

## DISCUSSION

Increased life expectancy of cancer patients and increased use of imaging technics allows identification of adrenal metastases. Adrenal gland involvement by metastatic cancers is common. It is probably due to abundant blood supply.<sup>[10]</sup> Most autopsy series report adrenal metastasis in 40-60% of breast or disseminated lung cancer patients, 30% in melanoma, 20% in colon or gastric cancer, but clinically visible adrenal insufficiency is rare.<sup>[9]</sup> Most of the adrenal cortex tissue must be destroyed before hypofunction is obvious<sup>[8,9]</sup> and symptoms are mistakenly attributed to underlying cancer.

The sporadic cases of adrenal hypofunction secondary to adrenal metastasis were first described by Addison in 1855.<sup>[11]</sup> Most of these reports are considered as single case information and include bronchogenic<sup>[12]</sup>, pulmonary<sup>[5,13,14]</sup>, breast<sup>[15]</sup>, stomach<sup>[16]</sup> and lymphomas.

Otabe et al. described a patient with HCC causing hyperreninemic hypoaldosteronism. They confirmed the radiological, histological and endocrinological tests.<sup>[7]</sup> Toshinari et al. described another case of adrenal metastasis with clinical and biochemical findings of adrenal insufficiency. In contrast to the case of Oteba et al., they described hyporeninemic hypoaldosteronism caused by glycyrrhizic acid.<sup>[17]</sup> Poojary et al. described a third case of HCC-related gingival mass and adrenal insufficiency.<sup>[18]</sup>

We report a case of adrenal insufficiency due to HCC metastasis with clinical, biochemical and radiological findings. Similar to the case of Oteba *et al.*, hyperreninemic hypoaldosteronism was present. To our knowledge, this is the fourth case in the literature. Our case had a different feature than the other cases with mortal hyperkalemia. He did not respond to conservative treatment and hemodialysis and this makes our case special.

In Japan, Primary Cancer Study and Follow-up between 1986 and 1995 revealed that 13.6% of patients with 3857 HCC had adrenal metastasis in autopsy.<sup>[19]</sup>

In our case, adrenal insufficiency findings were leading before the findings of HCC. Only one patient with bronchogenic carcinoma<sup>[20]</sup> had similar characteristics in the literature. Even if a primary tumor does not appear immediately, such cases may suggest metastatic cancers in the differential diagnosis of Addison's disease. Inflammation, necrosis, fibrosis, sustained regeneration characterize cirrhotic liver and contribute to HCC.<sup>[21]</sup> In our case, HCC developed on the basis of chronic liver disease and portal thrombosis occurred due to liver malignancy. In our case, we could not find a cause of chronic liver disease. Therefore, we decided it to be idiopathic.

Adrenal insufficiency is characterized by gastrointestinal and non-specific findings. Fatigue, loss of appetite, nausea, vomiting, abdominal pain, diarrhea, constipation, weight loss are common symptoms. In patients with hypotension, dehydration and postural hypotension may occur, and in the case of adrenal crisis, syncope and shock may occur. In almost all cases, hyperpigmentation is evident in the extensor areas of the body and mucous membranes. In laboratory examination; hyponatremia, hyperkalemia, mild metabolic acidosis, hypoglycemia, anemia and lymphocytosis may be seen.<sup>[22,23]</sup> When we look at the literature, we have seen a high incidence of hyperkalemia in a few cases in patients with adrenal insufficiency. Our case was also resistant to conservative antihyperkalemic treatment and hemodialysis. This case improved dramatically after methylprednisolone replacement.

In a case series reported by Rajaratnam *et al.*, an adrenal mass with a diameter of more than 5 cm in computed tomography showed irregular necrosis/ haemorrhage areas (no lipomatous component) in the central tumor, and constituted the diffusion characteristic of malignant melanoma.<sup>[24]</sup> In our case, the histopathology of the adrenal gland was completely necrotic tissue. However, the radiological image was in favor of HCC-induced adrenal metastasis. The patient was old and his biopsy was not repeated because the performance score was not favorable.

Nowadays, adrenal insufficiency is a condition that can cause the life-threatening condition that clinicians should

be aware. Because the occurrence of hypoaldosteronism-mediated hyperkalemia is common and occurs particularly in acute conditions such as malignancies, shock and circulatory disorders; malignancy and adrenal insufficiency should be considered in cases of hyperkalemia.

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