Adrenal insufficiency caused by bilateral adrenal macrometastases: a rare case with metastatic colon cancer

Metastatik kolon kanserli bir olguda adrenal yetmezlik

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A 42-year-old male with symptoms of weight loss, fatigue, hyponatremia, hypoglycemia, hypotension and fever was referred to our hospital. A computed tomographic scan of the abdomen and pelvis showed multiple solid masses in the liver, thickened wall of sigmoid colon and bilateral solid adrenal masses, 7x5x3 cm on the right side and 6x4.5x3.5 cm on the left side. A colonoscopic examination showed tumoral mass originating from the sigmoid colon. A biopsy was performed and adenocarcinoma was diagnosed. The patient was suspected of having primary adrenal insufficiency due to bilateral adrenal macrometastases. The diagnosis of adrenal insufficiency was confirmed by levels of ACTH serum, cortisol and ACTH stimulation test. Adrenal metastases are well-recognized, but compared with the prevalence of adrenal metastases, adrenocortical insufficiency in patients with cancer seems to be rare. We report the case of a patient with both bilateral surrenal macrometastases, which is rare in colorectal cancer, and subsequent adrenal insufficiency.

Key words: Adrenal insufficiency; colon cancer; macrometastases.

Kilo kaybı, halsizliği, hipotansiyonu, hiponatremi ve hipoglisemi şikayetleri olan 42 yaşında erkek hasta hastanemize sevkedildi. Karın ve pelvis bilgisayarlı tomografisinde karaciğerde çok sayıda solit kitle, sigmoid kolon duvarında kalınlaşma ve sağda 7x5x3 cm, solda 6x4,5x3,5 cm boyutlarında olmak üzere iki taraflı sürrenal kitleler gözlendi. Kolonoskopik muayenede sigmoid kolondan kaynaklanan tümöral kitle görüldü. Biyopsi yapıldı ve adenokarsinom tanısı kondu. Hastada iki taraflı adrenal makrometastazlara bağlı primer sürrenal yetmezliği düşünüldü. Sürrenal yetmezlik tanısı serum ACTH ve kortizol değerleri ve ACTH uyarı testi ile doğrulandı. Kanser hastalarında sürrenal yetmezlik iyi tanımlanmıştır, fakat sürrenal metastaz sıklığı ile karşılaştırıldığında sürrenal yetmezliği nadir görülmektedir. Bu yazıda, kolon kanserinde nadir görülen iki taraflı sürrenal makrometastazı olan ve buna bağlı sürrenal yetmezliği gelişen bir olgu sunuldu.

Anahtar sözcükler: Kolon kanseri; sürrenal metastaz; sürrenal yetmezliği.

Metastases of the adrenal gland are a frequent finding in patients with advanced solid tumors. In autopsy series, the prevalence of adrenal metastases was 36-44% in bronchiogenic carcinoma, 20-58% in breast cancer, 50-60% in malignant melanoma, 11-21% in gastric cancer, and 4.8-14% in colorectal cancer.[1] The common occurrence of this adrenal lesion is related to its rich sinusoidal blood supply.[2] In most of these patients, the metastases remained clinically silent and did not require specific therapy. Compared with the prevalence of adrenal metastases, clinically apparent adrenocortical insufficiency in these patients seems to be rare, since about 90% of the adrenal gland must be destroyed before an adrenal insufficiency is detectable. Although the adrenal insufficiency rate has been reported as high as 20-80% in some prospective and retrospective studies, most

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Table 1

Hematologic laboratory values and blood chemical values

Variable	First value	At the time of diagnosis (30th day)	After steroid therapy (40th day)
Hematocrit (%)	31	23.3	32.2
White cell count (per mm^3)	7300	4000	4210
Neutrophils (%)	49	48	74
Lymphocytes (%)	40	42	19
Platelet count (per mm^3)	367000	225000	270000
Prothrombin time (sec)	15.4	20.3	14.2
Total albumin (g/dl)	2.7	1.7	2.2
Sodium (mEq/L)	125	120	134
Potassium (mEq/L)	4.6	3.5	3.9
Chloride (mEq/L)	100	92	104
Lactate dehydrogenase (U/L)	190	133	472
Glucose (mg/dl)	116	64	89

of these studies lack clear laboratory proofs. Most data on patients with adrenal insufficiency due to adrenal metastases have been reported as case reports. Fewer than 100 cases have been reported in the literature, and only a few of them concern patients with colorectal cancer.[3,4]

We report the case of a patient with both bilateral surrenal macrometastases, which is rare in colorectal cancer, and a subsequent adrenal insufficiency.

CASE REPORT

A 42-year-old male with weight loss (>15 kg in last 3 months) and fatigue was admitted to our medical polyclinic. Laboratory tests were performed (Table 1). An abdominal ultrasonographic examination showed multiple masses in liver, bilateral adrenal masses and a thickened wall of sigmoid colon. After one week, the patient was admitted for an advanced evaluation and treatment in the gastroenterology department. The colonoscopic examination showed an annular tumoral mass originating from sigmoid colon, and biopsy was performed. A computed tomographic (CT) scan of the abdomen (Fig. 1), which was obtained after oral administration of contrast material, showed multiple solid masses in liver, a thickened wall of sigmoid colon and bilateral solid adrenal masses, 7x5x3 cm on the right side and 6x4.5x3.5 cm on the left side. The spleen, kidneys, pancreas, gallbladder, omentum, and other sites of gastrointestinal tract were normal. Three weeks later, the patient began to pass four or more loose stools daily, without bleeding, and diarrhea developed, with an abdominal pain and temperature of 37.8°C. Test for *Clostridium difficile* toxin

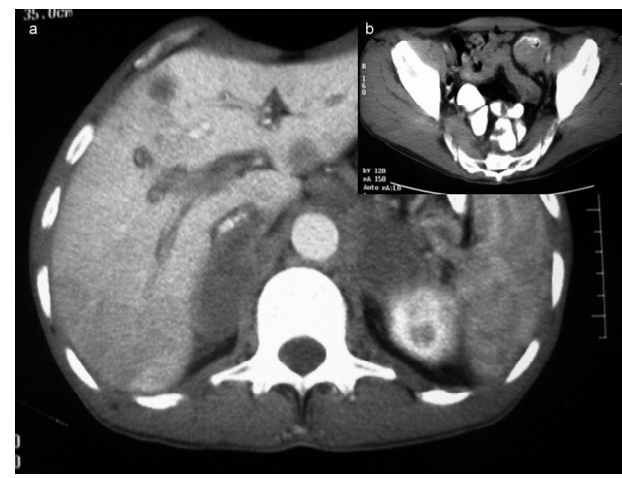

Fig. 1. (a) Axial contrast-enhanced CT image showing bilateral adrenal masses, 7x5x3 cm on the right side and 6x4.5x3.5 cm on the left side, and multiple small liver metastatic lesions. **(b)** CT image shows severe wall thickening of the sigmoid colon with fat stranding.

Table 2

Clinical signs and symptoms

Signs/symptoms	First value	At the time of diagnosis (30th day)	After steroid therapy (40th day)
Blood pressure	100/60	80/54	124/78
Pulse	72	114	68
Fever	36.5	37.8	36.7
Diarrhea	No	Four or more	No
Fatigue	Yes	Yes	Yes
Weight loss	>15 kg	–	Stable

Table 3

Diagnostic tests for adrenal insufficiency

Variable	Value	
Cortisol (µg/dl)	2.5 (5-25)	
ACTH (pg/ml)	428 (0-46)	
Cortisole after standard ACTH stimulation test (more than double the basal level at 30th and 60th minute) (µg/dl)	2.7 (30th minute)	2.7 (60th minute)

in stool specimen was negative. Blood culture was also negative. A physician prescribed ciprofloxacin and metronidazole for the treatment of gastroenteritis. On the 30th day, hypoglycemia, lower hyponatremia, tachycardia and hypotension developed (Table 2). In the meantime, a pathologist diagnosed adenocarcinoma (Fig. 2). The patient was transferred to the medical oncology department.

This patient was suspected of having a primary adrenal insufficiency. His anorexia, fever, fatigue, and weight loss were consistent with this diagnosis, although they could also be explained by the presence of a malignant tumor or an infectious disease. Additional findings that supported the diagnosis of adrenal insufficiency were anemia, hypotension, hypoglycemia, a low serum sodium level, and bilateral adrenal masses. The levels of ACTH serum and cortisol were examined. ACTH stimulation test was performed (Table 3). On the basis of these laboratory results, the patient was diagnosed with adrenal insufficiency due to bilateral macrometastases and was initially treated with intravenous hydrocortisone 200 mg followed by oral hydrocortisone 20 mg daily and fludrocortisone 0.1 mg daily. The patient rejected the adrenal biopsy. A dramatic improvement in clinical and laboratory findings was observed within days (Tables 1, 2). He was then given 2000 mg/m^2 capecitabine on the 1st-14th days and 135 mg/m^2 oxaliplatin on the 1st day and at 21 day-intervals.

DISCUSSION

Adrenocortical insufficiency is a rare but potentially lethal disease. Autoimmune adrenalitis is the most frequent cause, accounting for 70% of

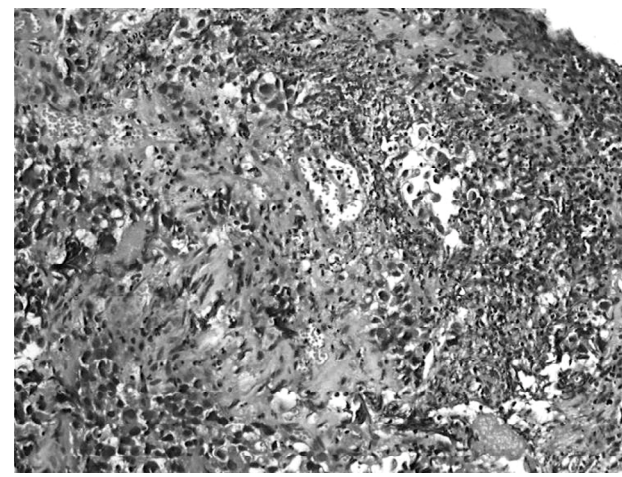

Fig. 2. Tumoral development formed of epithelial cells, with eccentric nucleus, and which are irregular, hyperchromatic, huge, atypic, spreading separately, and completely eliminating the mucosa (H-E x 100).

the cases, followed by adrenal tuberculosis (15%). Adrenal metastases are well-recognized, but compared with the prevalence of adrenal metastases, adrenocortical insufficiency in these patients seems to be rare. Particularly, adrenal insufficiency due to metastasis of colorectal cancer is rarer than in others cancer such as lung cancer and lymphoma according to the literature.[5] The low incidence of adrenocortical insufficiency in adrenal metastases may be attributed to the fact that over 90% of the adrenal glands must be destroyed before there is a functional adrenal cortical loss. The prevalence of adrenal insufficiency in patients with adrenal metastases as reported in the literature ranges from 0 to 80%. These differences seem to be mainly due to the preselection of patients and variable criteria for the diagnosis of adrenal insufficiency.[1] However, there is not a systematic, prospective evaluation of the prevalence of adrenal insufficiency.

Clinically, patients with cancer frequently have signs and symptoms suggestive of adrenal insufficiency. These symptoms are more likely due to the underlying malignancy than caused by a relative glucocorticoid deficit. Clinical assessment of adrenal insufficiency, therefore, is of little value in these patients, and the prevalence of adrenal impairment will be overestimated if the diagnosis of adrenal insufficiency is based only on features like weakness, fatigue, anorexia, weight loss, and vomiting.[1,6] Recently, Lutz et al. showed that adrenal insufficiency was only found in a patient with large (>4 cm) bilateral adrenal metastases.[1]

Consequently, in a patient with cancer, symptoms and signs such as anorexia, fever, fatigue, weight loss, hypotension, anemia, hypoglycemia and low serum sodium level, which are consistent with a malignant tumor or an infectious disease, can also be explained by the presence of adrenal insufficiency. Therefore, as was the case with our patient, adrenal insufficiency should be taken into consideration in patients suffering from bilateral surrenal macrometastases and showing these symptoms and findings.

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