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## Adrenal failure due to bilateral adrenal metastasis of rectal cancer: A case report

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## ABSTRACT

**INTRODUCTION:** It is rare for a patient to present with adrenal insufficiency secondary to bilateral adrenal metastases from a malignant colorectal tumor.**CASE PRESENTATION:** An 82-year-old Japanese man presented to our hospital with high fever and malaise. He was receiving oral chemotherapy for the treatment of rectal cancer with multiple metastases. Computed tomography showed new bilateral adrenal gland metastases. A rapid adrenocorticotropic hormone (ACTH) test showed adrenal insufficiency. Treatment with hydrocortisone provided immediate symptom improvement.**DISCUSSION:** Adrenal insufficiency secondary to bilateral adrenal metastases from rectal cancer is rare. A rapid ACTH test is useful to diagnose adrenal insufficiency.**CONCLUSION:** The incidence of adrenal insufficiency may be underestimated in patients with multiple metastasis. Appropriate therapy with adrenal corticosteroid hormone supplementation may lead to a significant improvement in the patient's symptoms and quality of life.© 2016 The Author(s). Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

Addison's disease, the result of adrenal insufficiency, has various etiologies [1]. It develops when >90% of adrenal tissue is destroyed [2]. It is rare for a patient to present with Addison's disease secondary to bilateral adrenal gland metastases from a malignant colorectal tumor; only five cases have been published in the English literature [3–7]. Herein, we describe a sixth case of adrenal insufficiency in a patient with bilateral adrenal gland metastasis from rectal cancer, based on Surgical Case Report (SCARE) Guidelines [8].

## 2. Case presentation

In May 2016, an 82-year-old man presented with a 2-week history of a high fever and malaise. His medical history was significant for rectal cancer (pT3, pN1a, pM0, pStage IIIB), diagnosed in 2015, for which he underwent a laparoscopic ultra-low anterior resection. He developed metastases in the liver, lung, right adrenal gland,

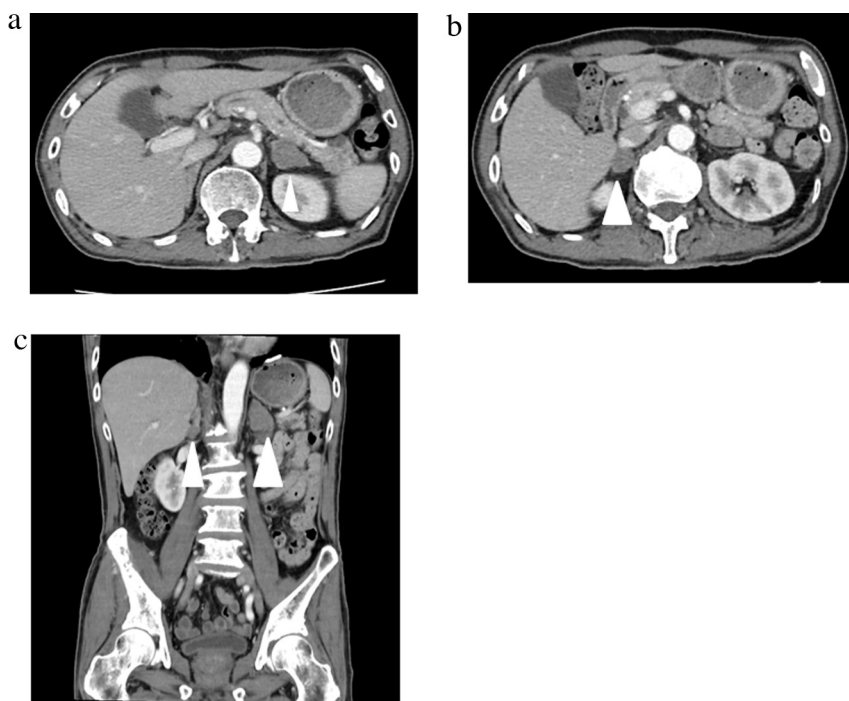
right fourth rib, and right ilium in February 2016. Subsequently, oral chemotherapy (capecitabine 2400 mg/day) was begun. He had been receiving oral chemotherapy until admission on May 25, 2016, at which point it was interrupted.

Physical examination revealed a tired-looking man with a body weight of 52 kg. His blood pressure was 141/91 mmHg; pulse rate, 101 beats/min; and body temperature, 37.2 °C. No abnormalities were noted on physical examination. The results of his laboratory investigations are shown in Table 1. Blood and urine culture tests revealed no bacteria. Computed tomography (CT) of the abdomen revealed that the normal tissue of both adrenal glands had been replaced by tumor tissue (Fig. 1a–c). Unfortunately, the patient refused further invasive examination, including the biopsy.

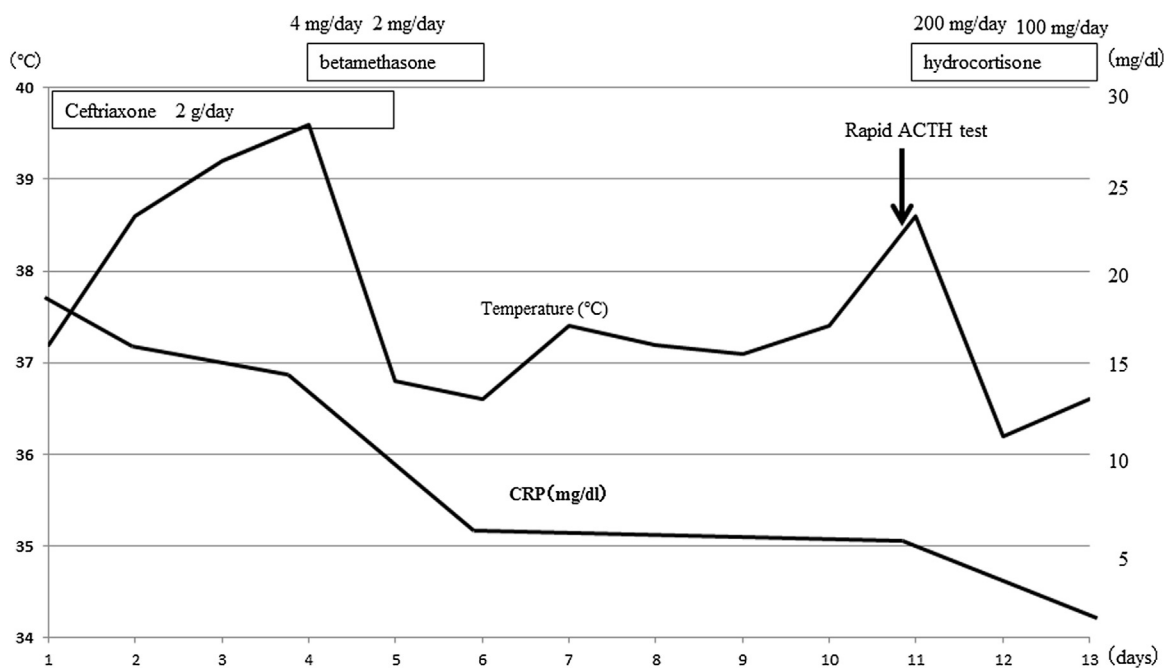
The patient developed a fever (>39 °C) despite administration of intravenous antibiotic therapy (ceftriaxone 2 g/day) and antipyretic analgesics. On the fourth day of hospitalization, betamethasone 4 mg was administered intravenously, and his fever immediately resolved. Ten days after admission, using a sample obtained early in the morning, the adrenocorticotropic hormone (ACTH) level was found to be normal (28 pg/mL) and the cortisol level was low (7.8 µg/dL), but other hormone levels, such as catecholamines, aldosterone, and renin, were normal. A rapid ACTH stimulation test was performed 11 days after admission; the result indicated primary adrenal failure, with a basal cortisol level of 14.8 µg/dL and a maximal increase to only 18.1 µg/dL (Table 2). Hydrocortisone therapy (200 mg/day) was begun, with tapering every second day.

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**Fig. 1.** (a) Computed tomography (CT) scans showing metastases in the left adrenal gland (25 × 23 mm); (b) CT scans showing metastases in the right adrenal gland (19 × 13 mm); (c) Coronal CT scans showing new bilateral adrenal gland metastasis.



**Fig. 2.** Body temperature and CRP levels before and after hydrocortisone therapy.

The patient’s fever and elevated C-reactive protein levels gradually resolved (Fig. 2). He was discharged 25 days after admission and prescribed hydrocortisone 20 mg/day.

On July 19, 2016, he was re-admitted for management of cancer-related pain. At that point, he had no symptoms of adrenal failure, but the cancer had progressed, with evidence of new brain metastases. The patient died on September 3, 2016. His death was unrelated to the adrenal insufficiency.

### 3. Discussion

Adrenal insufficiency secondary to any type of metastatic cancer has been reported in fewer than 100 cases in the literature [9]. It is rare for a patient to present with adrenal insufficiency secondary to bilateral adrenal gland metastasis from a malignant colorectal tumor [3–7]. The survival rate of patients with cancer is increasing, and improvements in imaging techniques have resulted in increased antemortem recognition of adrenal gland metastases. An autopsy series reported adrenal metastases in 14–20% of patients

**Table 1**  
Results of laboratory investigations.

WBC	8900/ $\mu$ l	PCT	negative
(neutrophils 65.5% eosinophils 16%)		$\beta$ -D glucan	negative
RBC	$349 \times 10^4$ / $\mu$ l	CEA	1903 ng/ml
Hb	11.5g/dl	CA19-9	477 mA U/ml
Ht	33.8%	Cortisol	7.8 $\mu$ g/dL
PLT	$47.5 \times 10^4$ / $\mu$ l	ACTH	28 pg/mL
TP	6.5 g/dl	Blood sugar	86 mg/dl
Alb	2.6 g/dl		
T-Bil	0.4 mg/dl		
AST	53U/l		
ALT	36U/l		
ALP	1554U/l		
LDH	884U/l		
Ch-E	154U/l		
BUN	23.4 mg/dl		
Cr	0.93 mg/dl		
Na	141 mEq/l		
K	4.9 mEq/l		
Cl	101 mEq/l		
CRP	17.32 mg/dl		

WBC, white blood cells; Hb, hemoglobin; Ht, hematocrit; PLT, platelets; TP, total protein; Alb, albumin; T-bil, total bilirubin; AST, aspartamine aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; Ch-E, cholinesterase; BUN, blood urea nitrogen; Cr, serum creatinine; Na, serum sodium; K, serum potassium; Cl, serum chloride; CRP, C-reactive protein; PCT, procalcitonin test; CEA, carcinoembryonic antigen; ACTH, adrenocorticotropic hormone.

**Table 2**  
Rapid adrenocorticotrophic hormone test results.

	pre	30 min	60 min
Cortisol( $\mu$ g/dl)	14.8	17.1	18.1
ACTH(ng/dl)	35.4	–	–

ACTH, adrenocorticotrophic hormone.

with stomach or colon cancer [10]. Hence, the incidence of adrenal insufficiency may be underestimated in patients with multiple metastases.

Generally, adrenal insufficiency is diagnosed based on a low early morning serum cortisol level ( $< 3 \mu\text{g/dL}$ ) with a high basal plasma ACTH level [11], and on the results of a cosyntropin stimulation test [12]. Cortisol levels of 3–15  $\mu\text{g/dL}$  may indicate adrenal insufficiency. Adrenal insufficiency is defined as failure of the serum cortisol level to increase to at least 5  $\mu\text{g/dL}$  above its baseline level [13]. The cut-off value for cortisol after rapid ACTH tests in various reports is 18–20  $\mu\text{g/dL}$  [14–16]. The criterion of serum cortisol levels  $< 4.4 \mu\text{g/dL}$  before and 1 h after administration of cosyntropin has also been reported to be clinically important [10].

This patient's main complaints were high fever and lassitude, and it seemed unlikely that these were due to bacterial infection or cancer cachexia. Adrenal insufficiency seemed more likely in view of the low white blood cell count, absence of calcitonin elevation, the lack of effect of non-steroidal anti-inflammatory drugs, and the significant response to a corticosteroid. There were no physical signs of adrenal insufficiency, such as hyperpigmentation, hair loss, low blood pressure, shock, hyponatremia, or hypoglycemia.

#### 4. Conclusion

We described a case of adrenal insufficiency caused by bilateral adrenal gland metastases from rectal cancer. In general, patients with multiple metastases due to advanced cancer should be investigated for organ failure. However, the incidence of adrenal insufficiency can be underestimated. Appropriate adrenal corticosteroid hormone supplementation may lead to a significant improvement in the patient's symptoms and quality of life. More-

over, adrenal crisis may be fatal if not promptly recognized and treated.

#### Conflicts of interest

The authors have no conflicts of interest to declare.

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We have no sponsors involving this paper.

#### Ethical approval

Approval to publish this case report was waived by the institution.

#### Consent

Written informed consent for publication of this case report and accompanying images was obtained from the patient. A copy of the written consent is available for review by the Editor-in-Chief of this journal, on request.

#### Author contribution

YI drafted the manuscript and acquired the data. FK revised the manuscript and has given final approval of the version to be published. All authors read and approved the final manuscript.

#### Guarantor

Yuki Imaoka.

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