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Case Report

Emphysematous Pyelonephritis and Cystitis: Unusual Adverse Events during Concurrent Chemoradiotherapy for Lung Cancer

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Keywords

Lung cancer · Chemoradiotherapy · Adverse event · Emphysematous pyelonephritis · Emphysematous cystitis

Abstract

Various adverse events can occur during antineoplastic therapy. A 67-year-old diabetic woman developed an emphysematous urinary tract infection (UTI) associated with chemoradiotherapy for lung cancer. She had received weekly carboplatin plus paclitaxel with thoracic radiotherapy and developed a fever on day 19. Computed tomography showed a large quantity of gas within the urinary tract. She was therefore diagnosed with emphysematous UTI. Poor diabetes control due to the weekly administration of dexamethasone, an existing urinary tract obstruction, and bone marrow suppression were involved in her serious infection. The potential development of emphysematous UTI during chemoradiotherapy should be considered in at-risk patients.

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Introduction

Serious infection is one of the most critical adverse events of antineoplastic therapy. Emphysematous urinary tract infection (UTI) is rare and life-threatening and is often associated with poorly controlled diabetes mellitus (DM). We herein report a case of emphysematous UTI that was affected by worsening diabetes control occurring in association with the weekly administration of dexamethasone for antiemesis during chemoradiotherapy.

Case Report

A 67-year-old diabetic woman, whose hemoglobin A_{1c} level was 7.7%, was being treated with a dipeptidyl peptidase-4 inhibitor. She was found to have anemia (hemoglobin 8.6 g/dL), and subsequent upper gastrointestinal endoscopy revealed gastric cancer with poorly differentiated adenocarcinoma. Computed tomography showed multiple mediastinal lymphadenopathies, right renal aplasia, and left megaureter. Although we could not identify the primary lesion in the lungs and other organs by ^{18}F-fluorodeoxyglucose positron emission tomography, transbronchial needle biopsies of mediastinal lymph nodes revealed metastases of squamous cell carcinoma. Finally, we diagnosed the patient with locally advanced non-small-cell lung cancer (cT0N2M0, cStage IIIA). Urological evaluation revealed congenital right renal aplasia and ruled out ureteral stenosis (such as a stone or neoplasm).

The patient was admitted for concurrent chemoradiotherapy before surgery for gastric cancer because her lung cancer seemed to be more serious than her gastric cancer. The predefined treatments were as follows: total radiation doses 60 Gy in 2-Gy fractions, and chemotherapy with weekly paclitaxel (40 mg/m^2) plus carboplatin (area under the curve: 2). Dexamethasone was administered for antiemesis at 10 mg/day (intravenously) on day 1 and 8 mg/day (orally) on days 2 and 3; this protocol was repeated every week. Her preprandial blood glucose level was elevated beyond 200 mg/dL on days 1–3, despite the administration of sliding-scale insulin therapy.

The patient had a white blood cell (WBC) count of 3,500 cells/mm^3 with 77% neutrophils on day 14. We administered chemotherapeutic agents as planned on day 15. She developed a fever on day 19, but did not complain of any other symptoms. Laboratory tests showed a WBC count of 6,700 cells/mm^3 with 96% neutrophils, an elevated C-reactive protein level (17.9 mg/dL), 3+ urine leukocytes, and 1+ urine nitrite. Contrast-enhanced computed tomography showed enlargement of her left kidney compared with the state before chemoradiotherapy as well as a large quantity of gas within the kidney pelvis, ureter, and bladder (Fig. 1). She was diagnosed with emphysematous pyelonephritis and cystitis. *Klebsiella pneumoniae* was subsequently isolated from urine, but not from blood. Transurethral insertion of a urethral stent and intravenous administration of antibiotics (meropenem followed by oral levofloxacin) resulted in symptom relief and disease remission. Two weeks after the onset of disease, the remaining chemoradiotherapy was restarted and completed with the insertion of a urethral stent.

Discussion

We describe a case of emphysematous UTI that occurred in association with concurrent chemoradiotherapy for lung cancer. A variety of adverse events can occur during the course

of chemoradiotherapy; serious infection represents one of the most critical adverse events. Emphysematous UTI is a rare form of bacterial infection that often causes sepsis and sometimes results in death. Emphysematous pyelonephritis is associated with a mortality rate of approximately 10–25% [1–4]. The pathogenesis of emphysematous UTI is believed to be as follows: the infecting pathogen induces the fermentation of high concentrations of glucose and produces carbon dioxide [5]. DM is a major risk factor for this life-threatening disease [6]. A systematic review showed that DM was the most common underlying disease in patients with emphysematous pyelonephritis (96%), and that urinary tract obstruction was seen in 29% patients [1]. Our patient had 2 risk factors: DM and left megaureter of unknown cause. We suspect that chemoradiotherapy caused the development of emphysematous UTI in the present case. More than 60% of patients receiving concurrent chemoradiotherapy develop grade ≥3 neutropenia, and 0–23% develop infection (based on the Common Terminology Criteria for Adverse Events version 3.0 or later) [7–9]. In the present case, the patient's WBC count was within normal limits despite the serious infection, which indicated the existence of bone marrow suppression by chemoradiotherapy. Bone marrow suppression is thought to be a factor that influences the development of emphysematous UTI.

The weekly administration of dexamethasone during chemoradiotherapy can give rise to the development of emphysematous UTI due to worsening diabetes control. Although the patient's creatinine level was normal, she had a single kidney. Thus, we selected a weekly carboplatin-based chemotherapy regimen. Carboplatin is less nephrotoxic than cisplatin and is administered with adjustment for the patient's renal function. A weekly carboplatin plus paclitaxel regimen with thoracic radiotherapy is generally selected for patients with locally advanced non-small-cell lung cancer. The weekly regimen was considered to have equivalent efficacy and to be less toxic than standard cisplatin-based regimens [8]. Dexamethasone is usually administered in chemotherapy for antiemesis. According to a recent guideline, the administration of dexamethasone (8 mg/day) for 3–4 days is recommended for patients receiving carboplatin-containing regimens [10]. However, the regular weekly administration of dexamethasone is expected to worsen diabetes control. Although our patient's hemoglobin A_{1c} had actually increased to 8.8% at the time, the time to the onset of the patient's disease seemed to be short. We therefore suspect that dexamethasone-induced hyperglycemia, in addition to other risk factors, accelerated the development of emphysematous UTI. The administration interval of chemotherapeutic agents is generally longer in patients receiving cisplatin-containing regimens, which results in a lower dosage of dexamethasone being administered in comparison to carboplatin-containing regimens. Nonetheless, we still believe that the weekly regimen was the only acceptable regimen for the present patient, who had a single kidney.

We describe a case of emphysematous UTI associated with concurrent chemoradiotherapy for lung cancer. The weekly administration of dexamethasone during chemoradiotherapy can give rise to the development of emphysematous UTI as a result of worsening diabetes control. In addition, urinary tract obstruction and bone marrow suppression by chemoradiotherapy contributed to the disease development in the present case. Although emphysematous UTI associated with antineoplastic therapy is a rare condition, we should be alert for the development of serious infection and select optimal chemotherapy regimens for patients who have risk factors for infection.

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Statement of Ethics

Informed consent was obtained from the patient's family for publication of this case report.

Disclosure Statement

The authors declare no conflicts of interest in association with the present study.

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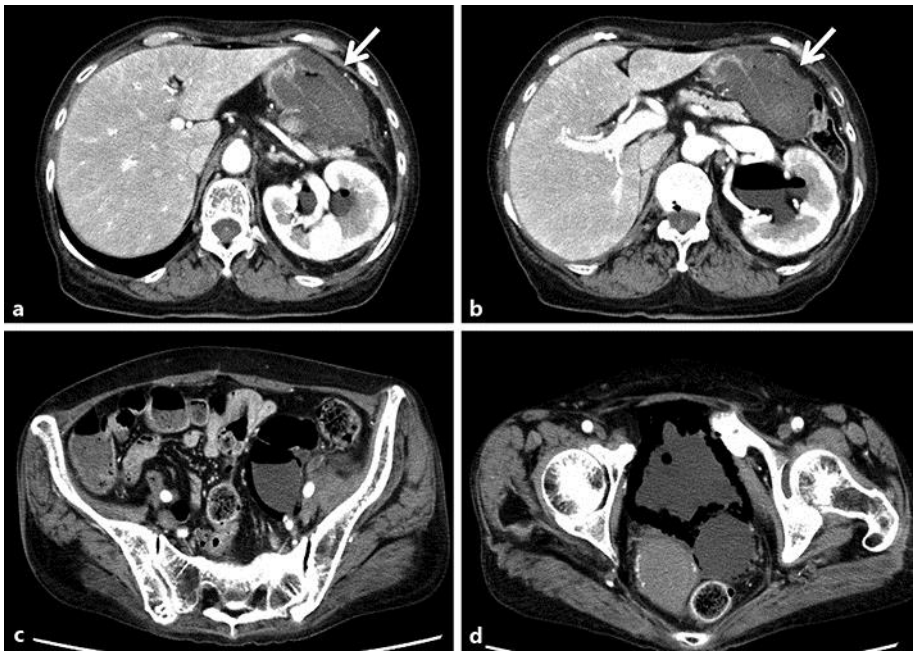

Fig. 1. Contrast-enhanced computed tomography images showing the enlargement of the left kidney, renal pelvis, and ureter (**a–c**) and gas accumulation within the renal pelvis, ureter, and bladder (**a–d**). The patient's right kidney is absent, and a thickened gastric wall can be observed (arrows).