

## Case Report

# Therapy-Related Acute Myeloid Leukemia 2 Months after Chemoradiotherapy for Esophageal Cancer: A Case Report

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## Keywords

Acute adverse event · Chemoradiotherapy · Esophageal cancer · Therapy-related acute myeloid leukemia

## Abstract

Therapy-related acute myeloid leukemia (AML) is a rare but potentially fatal adverse event caused by chemotherapy or radiotherapy. Herein we report a patient diagnosed with therapy-related AML 2 months after chemoradiotherapy for esophageal cancer. A 61-year-old man with dysphagia was diagnosed with locally advanced esophageal cancer with para-aortic lymph node metastasis. Laboratory blood test did not reveal any abnormality except mild macrocytic anemia. To alleviate dysphagia due to malignant esophageal stenosis, the patient underwent concurrent chemoradiotherapy of 60 Gy in 30 fractions with cisplatin and 5-fluorouracil at a local area in thoracic esophagus. Dysphagia alleviated during chemoradiotherapy; however, pancytopenia did not recover after the completion of chemoradiotherapy, and general fatigue with fever developed 13 weeks after the last day of chemoradiotherapy. To rule out hematological malignancy, bone marrow biopsy was performed. The bone marrow smear and flow cytometry analysis indicated the development of AML. Chromosomal test revealed a complex karyotype, suggesting that AML was associated with myelodysplastic syndrome. The patient died 1 month after the diagnosis of therapy-related AML. Thus, the findings indicate that therapy-related AML may develop during the acute phase of chemoradiotherapy and bone marrow biopsy is necessary when prolonged pancytopenia exists after chemoradiotherapy.

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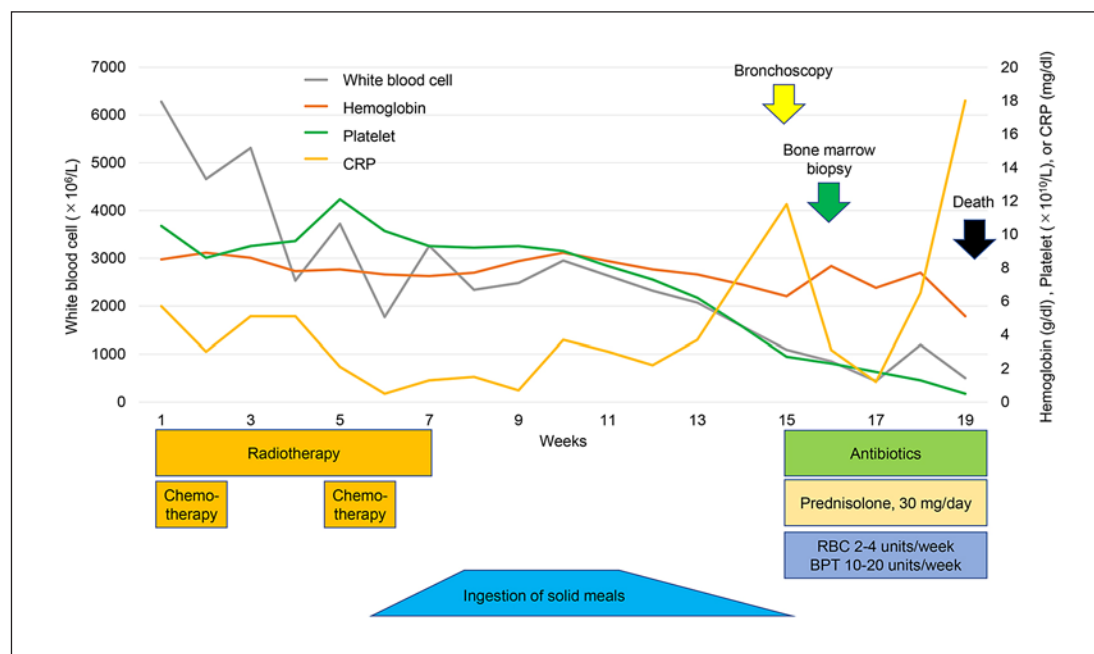
## Introduction

Secondary acute myeloid leukemia (AML) is a rare but potentially fatal adverse event after chemotherapy or radiotherapy for malignancy. Secondary AML has two types of origin as follows: AML developing after chemotherapy or radiotherapy (therapy-related AML) and AML resulting from a disease progression of myelodysplastic or myeloproliferative neoplasm [1]. Therapy-related AML accounts for 8% of all AML. The interval between the onset of therapy-related AML and chemotherapy or radiotherapy was reported to be 5–7 years [2, 3]. Therapy-related AML prognosis is poor, with a 5-year overall survival of 4% in patients who had undergone an allogeneic transplantation [1, 2, 4].

Chemoradiotherapy plays an important role in the treatment of esophageal cancer. Chemoradiotherapy is conducted with curative, preoperative, salvage, and palliative intents [5, 6]. The acute and late adverse events for chemoradiotherapy have been previously reported [3, 6]; however, the reports on therapy-related AML after chemoradiotherapy for esophageal cancer are limited with only one report describing four patients with therapy-related AML after chemoradiotherapy for esophageal cancer. Overt AML from myelodysplastic syndrome was reported in two of four patients, and its onset after chemoradiotherapy was 19–41 months [7]. Herein, we report a patient with therapy-related AML 2 months after chemoradiotherapy for esophageal cancer.

## Case Report

A 61-year-old male experiencing severe dysphagia for 3 months was referred to our clinic. Computed tomography and esophagogastroduodenoscopy revealed esophageal squamous cell carcinoma with metastatic mediastinal and abdominal para-aortic lymph nodes, clinical stage IVB, cT4bN2M1, according to the Union for International Cancer Control eighth edition. Laboratory test did not reveal any abnormality except mild macrocytic anemia. To alleviate dysphagia due to malignant esophageal stenosis, the patient underwent 60 Gy of local radiotherapy in 30 fractions with concurrent chemotherapy with cisplatin 70 mg/m<sup>2</sup> (days 1, 29) and 5-fluorouracil 700 mg/m<sup>2</sup> (days 1–4, 29–32). Dysphagia alleviated during chemoradiotherapy; however, pancytopenia did not and it continued 6 weeks after the start of chemoradiotherapy (Fig. 1). No abnormal cells were found in the peripheral blood. Moderate fatigue and low-grade fever without respiratory symptoms developed 13 weeks after the start of chemoradiotherapy. To determine the cause of fever, computed tomography was performed 15 weeks after the start of chemoradiotherapy, which revealed diffuse ground-glass opacity in the bilateral lungs. Based on this finding combined with bronchoalveolar lavage fluid and *Pneumocystis jirovecii*, a diagnosis of *Pneumocystis* pneumonia was made. To rule out hematological malignancy, bone marrow biopsy was performed. The bone marrow smear, chromosomal test, and flow cytometry analysis indicated the development of AML. Chromosomal test revealed a complex karyotype as follows: 47,XY,add(5)(q13),add(6)(p21),add(18)(q21),-21,+mar×2[13]/48,idem,+8[1]/46,idem,der(1)add(1)(p34)add(1)(q21),-add(6)[5]. Thus, a diagnosis of therapy-related AML was made by the multidisciplinary team that included hematological oncologists. The complex karyotype suggested the possibility of myelodysplastic syndrome-overt AML. Considering poor pulmonary function and the coexistence of incurable advanced esophageal cancer and unfavorable AML karyotype, the best supportive care was recommended for the patient. After consenting, the patient received the best supportive care and died 1 month after the diagnosis of therapy-related myelodysplastic syndrome-overt AML.



**Fig. 1.** Time course after chemoradiotherapy. CRP, C-reactive protein (mg/dL); RBC, red blood cell transfusion; BPT, blood platelet transfusion.

## Discussion

We report the case of therapy-related AML that developed 2 months after chemoradiotherapy for esophageal cancer. There are two important clinical findings of this case study. First, therapy-related AML may occur during the acute phase of chemoradiotherapy, which mimics prolonged pancytopenia after chemoradiotherapy. Second, the existence of myelodysplastic syndrome may accelerate the onset of therapy-related AML.

Therapy-related AML may develop during the acute phase of chemoradiotherapy for esophageal cancer. Pancytopenia including leukocytopenia and general fatigue are the initial signs of AML [8]. Similarly, leukocytopenia and general fatigue are also common acute adverse events in chemoradiotherapy for esophageal cancer [9, 10]. Persistent pancytopenia with general fatigue due to AML is potentially misunderstood as a prolonged acute hematological adverse event after chemoradiotherapy. Previously, the development of therapy-related AML during the acute phase of chemoradiotherapy has not been reported. Therapy-related AML may develop as an acute adverse event of chemoradiotherapy for esophageal cancer. In case of prolonged pancytopenia with general fatigue after chemoradiotherapy, bone marrow biopsy is necessary to rule out hematological malignancy even during the acute phase of chemoradiotherapy.

The early onset of therapy-related AML might be associated with myelodysplastic syndrome. In the present case study, chromosomal test showed a complex karyotype involving three or more chromosomes or chromosomal arms/segments. A complex karyotype is not common in de novo AML, but it is in myelodysplastic syndrome-overt AML [11]. The chromosomal abnormality +8 is frequently observed in myelodysplastic syndrome [12]. Mild macrocytic anemia without leukopenia and thrombocytopenia are common laboratory findings in asymptomatic myelodysplastic syndrome [13]. These findings possibly support the existence of myelodysplastic syndrome in our patient. DNA damages due to chemoradiotherapy result

in chromosomal instability [14]; this might possibly have accelerated the unusual onset of therapy-related AML in our patient.

In conclusion, therapy-related AML may develop during the acute phase of chemoradiotherapy, which may accelerate the onset of myelodysplastic-overt AML. Bone marrow biopsy is necessary even during the acute phase when prolonged pancytopenia with general fatigue exists after chemoradiotherapy.

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### Statement of Ethics

This study was conducted in accordance with the Declaration of Helsinki and Ethical Guidelines for Medical and Health Research Involving Human Subjects in Japan. General written consent for the use of clinical data for research purposes was obtained from the patient before starting radiotherapy.

### Disclosure Statement

The authors have no conflicts of interest.

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### Author Contributions

Shinya Hiraoka and Katsuyuki Sakanaka participated in the study design, performed treatment, acquired data, and drafted the manuscript. Takahiro Iwai, Kota Fujii, and Hiroyuki Inoo performed treatment and radiotherapy planning. Hiroyuki Inoo and Takashi Mizowaki provided writing assistance of the manuscript. All authors read and approved the final manuscript.

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