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Rapid progression of gastric cancer with liver metastasis after discontinuation of lenalidomide in a patient with concurrent multiple myeloma: A case report

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ABSTRACT

INTRODUCTION: The synchronous incidence of multiple myeloma (MM) and other primary malignant solid tumor is rare. No detailed studies have been published regarding the perioperative management of patients with concurrent MM and malignant solid tumor. We report a patient with concurrent MM and gastric cancer who experienced rapid progression of liver metastasis after lenalidomide was discontinued. **PRESENTATION OF CASE:** An 82-year-old woman with MM was diagnosed with clinical T3N2M0 gastric cancer, and MM had been maintained in remission with lenalidomide. Preoperatively, pancytopenia was found, and lenalidomide was discontinued and lenograstim was administered. Blood transfusions were also administered preoperatively due to anemia caused by tumor bleeding. Surgery was performed after her pancytopenia improved. Intraoperatively, several nodules were found on the liver, which were diagnosed as adenocarcinoma metastases. On postoperative day 13, a low density mass in the liver that was not observed before surgery was shown. The patient received best supportive care because she did not desire adjuvant chemotherapy for gastric cancer or resumption of treatment for MM. She died of progressive gastric cancer on postoperative day 80.

DISCUSSION: Discontinuation of lenalidomide in our case may have promoted tumor angiogenesis and lowered antitumor immunity, causing rapid tumor growth and liver metastasis. Continuation of the MM agent may be preferable in patients who do not have marked myelosuppression.

CONCLUSION: Surgeons should be familiar with the risks associated with discontinuation of MM drugs when operating on patients with MM and concurrent malignant solid tumor.

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1. Introduction

The synchronous incidence of multiple myeloma (MM) and other primary malignant solid tumors is rare [1]. The most common synchronous malignant solid tumor is gastric cancer but colorectal and lung cancers have also been reported [2,3]. Some reports have noted that MM may be associated with an increased risk of secondary malignancy [2,3]. However, continuation of MM treatment in the perioperative period in these patients has not been well studied.

We report a MM patient with rapidly progressed liver metastasis of gastric cancer after discontinuation of lenalidomide. Our case highlights the need to devise a perioperative management strategy

for MM patients presenting with concurrent malignant solid tumor. This work has been reported in line with the SCARE criteria [4].

2. Presentation of case

An 82-year-old woman with MM presented with bloody stools and anemia. She had been diagnosed with symptomatic MM five years ago, and administered melphalan, prednisolone, and bortezomib. Afterward, her condition had been maintained in remission with lenalidomide and dexamethasone. Upper gastrointestinal endoscopy and series showed a type 2 tumor in the posterior wall of the gastric antrum (Fig. 1). Enhanced computed tomography (CT) showed thickening of the posterior wall of the gastric antrum and enlargement of three local lymph nodes suspicious for metastases; no distant metastases were found (Fig. 2). An endoscopic biopsy indicated papillary adenocarcinoma. The patient was clinically diagnosed with T3N2M0, stage III adenocarcinoma of the stomach [TNM classification, 8th version]. The patient provided

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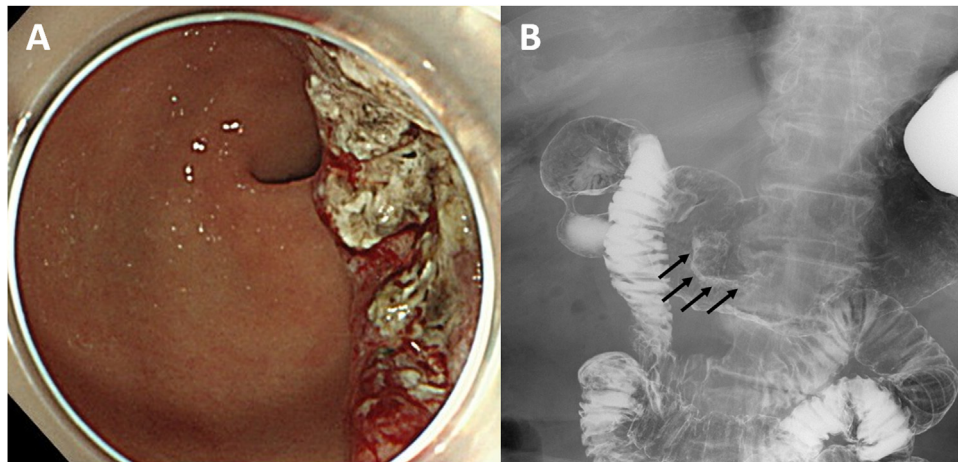


Fig. 1. Upper gastrointestinal endoscopic findings (A) and upper gastrointestinal series findings (B). A: a type 2 tumor in the posterior wall of the gastric antrum; B: an upper gastrointestinal series shows an irregularly shaped tumor in the gastric antrum (arrows).

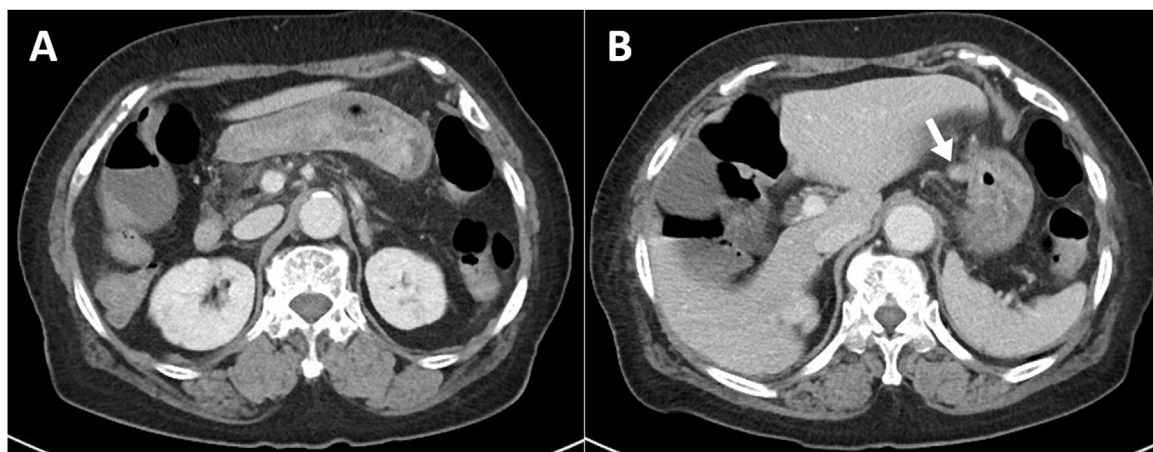


Fig. 2. Preoperative computed tomography findings. A: computed tomography shows thickening of the posterior wall of the gastric antrum. B: image shows enlarged lymph nodes suspicious for metastases (arrow).

written informed consent for surgical treatment after discussed in the cancer board. Preoperatively, blood testing showed pancytopenia: white blood cells (WBC), 2,600/ μ L; neutrophils, 1,340/ μ L; red blood cells (RBC), 1,880,000/ μ L; hemoglobin, 6.6 g/dL; and platelet, 92,000/ μ L. Biochemical examination showed no abnormalities of liver function, and tumor markers were normal. In consultation with a hematologist, lenalidomide was discontinued for three weeks and 100 μ g each of lenograstim were administered twice. Transfusions of 280 mL RBC concentrate were also administered twice preoperatively (Fig. 3). Hematological parameters on the day of surgery were as follows: WBC, 3,800/ μ L; neutrophils, 2,410/ μ L; RBC, 3,210,000/ μ L; hemoglobin, 11.3 g/dL; and platelet, 102,000/ μ L.

The patient underwent open surgery. After laparotomy, ascites and peritoneal dissemination were not observed but several liver nodules were. A surface liver nodule was excised, which was diagnosed as adenocarcinoma metastasis with intraoperative histopathological examination. Distal gastrectomy with Billroth II reconstruction was performed to remove the bleeding tumor. Operative time was 207 min and estimated blood loss was 268 mL; an intraoperative blood transfusion was not administered. Enhanced CT on postoperative day 13 showed a 1 cm sized low density mass in the liver that was not observed before surgery (Fig. 4a, b). The definitive diagnosis was pT4aN3aM1, pStage IV. Postoperative adjuvant chemotherapy for gastric cancer and resumption of MM treatment were not desired, therefore best supportive care

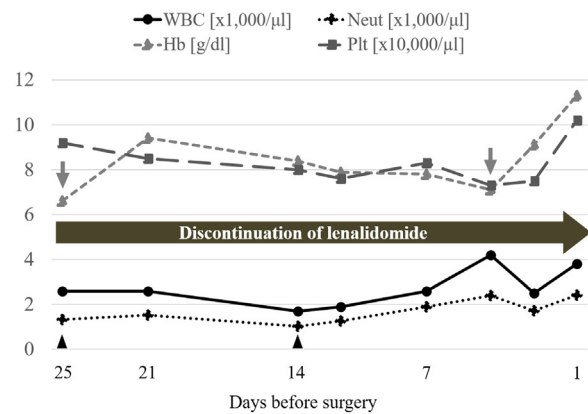


Fig. 3. Transition of hematological parameters from starting date of discontinuation of lenalidomide to operation day. Administration of 100 μ g lenograstim was performed (arrowheads), and transfusion of 280 mL red cell concentrate was administered (arrows).

was provided. The patient was discharged on postoperative day 28, however, she was readmitted to the hospital due to loss of appetite 77 days after surgery. At this time, she was jaundiced and biochemical examination showed a marked increase in aspartate and alanine aminotransferase levels. Her general condition gradually worsened thereafter and she died on postoperative day 80.

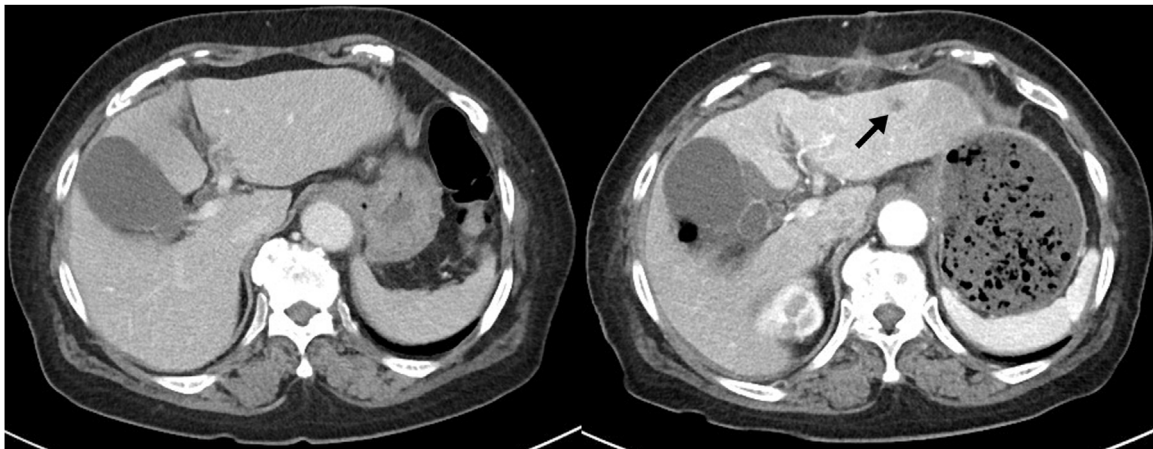


Fig. 4. Preoperative (A) and postoperative (B) computed tomography findings. Distant metastasis was not observed preoperatively. However, on postoperative day 13, a low density mass was found in the liver (arrow).

3. Discussion

Although the synchronous incidence of MM and other primary malignant solid tumors is rare [1], several cases have been reported; however, no detailed reports have been published regarding the perioperative management of these patients, particularly in terms of continuing treatment for MM. In our case, we discontinued oral lenalidomide to improve the patient's general condition in preparation for surgery. Preoperative blood testing showed mild neutropenia and thrombocytopenia, which were considered myelosuppressive effects from lenalidomide. We considered recovery of the patient's blood counts to be of paramount importance before performing the operation; therefore, lenalidomide was discontinued to improve her myelosuppression, and lenograstim were administered. As a result, escalation of her neutrophil and platelet counts was achieved prior to surgery. However, her liver metastasis progressed rapidly.

Lenalidomide is thalidomide derivative, which inhibits tumor angiogenesis and tumor proliferation by inducing apoptosis [5,6]. Lenalidomide is a useful treatment for selected hematologic malignancies such as MM, but its effectiveness against solid tumors is unclear. In animal models, lenalidomide has been reported to normalize tumor vessels in colorectal cancer and enhance anti-tumor immunity in colon cancer [7,8]. Based on these findings, discontinuation of lenalidomide in our case may have promoted tumor angiogenesis and lowered antitumor immunity, causing rapid tumor growth and liver metastasis. Myelosuppression is a well-recognized side effect of lenalidomide and its package insert contains dose adjustments for hematological toxicity, especially for platelets and neutrophils. According to the package insert, dose adjustment is required when platelet or neutrophil count falls below 30,000/ μL or 1,000/ μL , respectively. In our case, the initial platelet and neutrophil counts were both above the standard value that required drug adjustment. Considering this, the discontinuation of lenalidomide may not have been necessary. Had lenalidomide been continued, rapid progression of the liver metastasis may not have occurred.

4. Conclusion

Surgeons should be familiar with the risks associated with discontinuation of MM drugs when operating on patients with MM and concurrent malignant solid tumor. Continuation of the MM agent may be preferable in patients who do not have marked myelosuppression.

Declaration of Competing Interest

All authors have no conflicts of interest to declare.

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This research did not receive any specific grant from funding agencies.

Ethical approval

Ethical approval has been exempted from our institution for this case report.

Consent

Written informed consent was obtained from the patient's family for the publication of this case report and accompanying images.

Author contribution

NU and YE reviewed the patient and discussed the literature review. NU, YE, NT, YK, MZ, and YK collected data of the patient. NU, YE, NT, YK, MZ, and YK treated the patient (perioperative management including operation). NU wrote the manuscript draft. All authors reviewed and edited the manuscript.

Registration of research studies

This paper is a clinical report, no research involved.

Guarantor

Naoto Ujii.

Provenance and peer review

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