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Mallory-Weise syndrome in a patient treated with EGFR-TKI

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Occurrence of Mallory-Weise syndrome after chemotherapy for lung cancer has been rarely reported.[1–3] We observed a case of Mallory-Weise syndrome following oral erlotinib, one of the epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKI).

A 68-year-old woman presented with lung adenocarcinoma. The patient had metastases to lungs, bones, and cervical lymph nodes. Chemotherapy with cisplatin plus pemetrexed, docetaxel, and gemcitabine plus bevacizumab was done for the disease. Seventeen months later the initiation of first-line chemotherapy, a recurrence in pulmonary nodules was observed in chest CT scan. Although the patient had wild type of EGFR gene, she strongly hoped to receive EGFR-TKI therapy. Therefore, erlotinib (150 mg, once a day) was given as a fourth line chemotherapy. The patient tolerated this well having only slight nausea and vomiting (National Cancer Institute Common Terminology Criteria for Adverse Event version 4: grade 1). One month afterward, decrease in size on metastatic pulmonary lesions was found in chest CT scan. However, the patient still had nausea and vomiting and was admitted to our hospital due to hematemesis. Bright red blood clots were obtained by nasogastric tube aspiration. Endoscopy, shortly after admission, showed a 4 cm tear in the mucosa of the gastro-esophageal junction (Figure 1). There was an adherent clot over the lesion, which was not actively bleeding. No other lesions or sites of bleeding were identified. The endoscopic diagnosis was a Mallory-Weiss tear of the mucosa of the gastro-esophageal junction. Over the next few days, the patient's midepigastric pain abated and there were no further signs of active gastrointestinal bleeding. Fortunately for our patient, the Mallory-Weiss tear was self-limiting, which was confirmed by endoscopy 2 weeks later, and was managed without blood transfusions.

The most common adverse events (AEs) associated with EGFR-TKIs include skin rush, diarrhea, hepatotoxicity, and pulmonary toxicity. Among them, pulmonary toxicity is the most sensitive one, although its incidence is less than 5%.[4] The profiles are somewhat different in the three TKIs. Incidence of elevation of liver enzyme and that of diarrhea is somewhat higher than the other TKIs, respectively. In a postmarketing surveillance study of erlotinib in 10 708 Japanese patients, overall AE incidence was 81.8% (mostly grade 1/2); skin disorders (68.5%) including rash (63.0%).[4] ILD-like events were reported in 158 patients (4.5% of interim population) with a mortality rate of 1.6% (55 patients).[4]

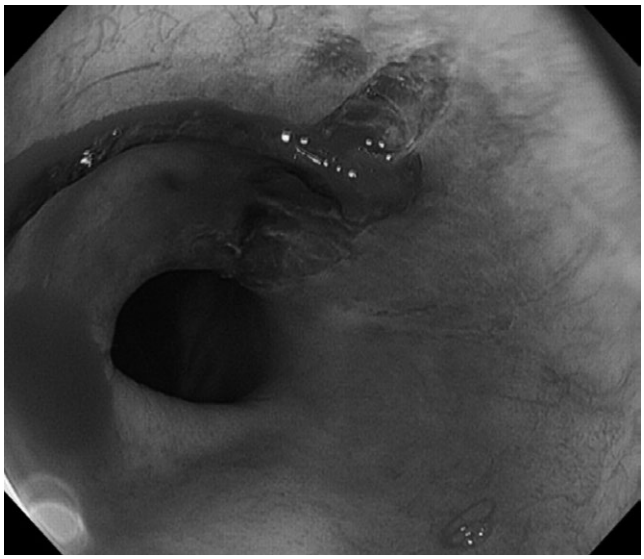

FIGURE 1 Endoscopy showed a 4 cm tear in the mucosa of the gastro-esophageal junction

In 1977, Enock reported on a patient with a Mallory-Weiss lesion following chemotherapy with 5-fluorouracil and methyl-CCNU.[1] As then, there have been three patients with Mallory-Weiss syndrome flowing cancer chemotherapy.[2,3] All of them were treated with

cytotoxic chemotherapeutic agents. They developed Mallory-Weiss syndrome within a day after cytotoxic chemotherapy, and two of them had the syndrome soon after cisplatin-induced nausea and vomiting.[2,3] There have been two case reports of gastrointestinal bleeding.[5,6] Bai et al.[5] reported positive fecal test in an elderly patient treated with gefitinib and erlotinib, but bleeding site was not evaluated with endoscope. Honda et al.[6]described a patient treated with gefitinib, who developed gastroesophageal variceal hemorrhage induced by metastatic liver tumor of lung cancer. The patient had not only gefitinib but also steroid therapy.[6] To our best knowledge, however, there have been no Mallory-Weiss syndrome following EGFR-TKI therapy. The incidence of erlotinib-induced nausea is around 10%[7,8], but this complication may be ignored because of lack of severity. Our patient developed Mallory-Weise syndrome 1 month after the initiation of erlotinib therapy. The reason why the patient had Mallory-Weiss tear was beyond our knowledge. Persistent nausea and vomiting might have relation with the development of the syndrome. Togashi et al.[9] evaluated differences in adverse events between 250 mg daily gefitinib and 150 mg daily erlotinib in Japanese patients with nonsmall cell lung cancer. According to their report, more adverse events including gastrointestinal bleeding were observed in the erlotinib group and in a dose dependent manner.[9]

Our experience suggested that we should alert this possible complication even in the cases treated with EGFR-TKIs.

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All authors participated sufficiently in the work to take responsibility for appropriate portions of the content.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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