Distinguishing Epithelial Growth Factor Receptor Tyrosine Kinase Inhibitor induced Oral Mucositis/Stomatitis from Pseudomembranous Candidiasis: Case Series

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Introduction

Oral mucositis and stomatitis occurs quite frequently with some targeted therapies, namely epithelial growth factor receptor tyrosine kinase inhibitor (EGFR-TKI). The purpose of this report is to show the importance of careful consideration in the administration of antifungal medications through two case studies of EGFR-TKI-induced oral mucositis/stomatitis.

Case presentation

Case1:

A 64-year-old Japanese female was diagnosed with metastatic breast cancer (scirrhous carcinoma, T4N3M1(OSS, BRA)). At first, zoledronic acid and neoadjuvant FEC were administered, followed by a mastectomy. Second-line treatment with PER/HER/DTX was started, and six months later, brain metastasis was observed. After whole brain irradiation was completed, trastuzumab and lapatinib were administered as tertiary therapy. Within 3 weeks after start of treatment, the patient presented oral pain, diarrhea, and a fever of 38.3°C. The patient was hospitalized because of febrile neutropenia and dysphagia. Due to multiple white patches in the oral cavity, the attending physician doubted the merger of pseudomembranous candidiasis. Antibiotics and antifungal agents were prescribed, but the oral white lesions did not improve even after one week. Consultation was held with the oral care team to improve the patient's condition. Dry mouth and poor oral hygiene were observed, which were considered to be deteriorating factors. The team recommended EGFR-TKI induced stomatitis/oral mucositis and performed mouth cleaning and moisturizing. The symptoms greatly improved in a week and was almost cured in 2 weeks.

Conclusion

EGFR-TKI-induced oral mucositis/stomatitis must be distinguished from pseudomembranous candidiasis because drug interaction may prolong oral complications.

Conflict of interest

With regards to the theme of this e-poster presentation, there are no companies in COI relationship that should be disclosed.

Case2:

An 88-year-old Japanese female was diagnosed with metastatic non-small-cell lung cancer (adenocarcinoma, T3N2M1a(PM)). Mutational analysis of the tumor biopsy revealed the presence of an activation mutation (exon 19 deletion). First-line treatment with gefitinib was started and good partial response of the patient's pulmonary tumors, but the primary tumor progressed after 2 years. Docetaxel was administrated as second-line treatment. Stabilization of the disease was obtained, but progression was confirmed after 1 year. Third-line treatment with re-gefitinib was performed, but again progression was confirmed after 1 year. A second biopsy was performed and T790M was revealed, then Fourth-line treatment with osimertinib was performed. In the 6th week after the start of osimertinib, the patient complained of oral pain and lip swelling. There were multiple white lesions on the tongue, lower lip, cheeks, and soft plate. The patient had poor oral hygiene and couldn't use a toothbrush because of oral pain. The patient was instructed on how to use mouthwash with an anesthetic solution. An antifungal agent was prescribed, but the white lesions did not improve.

Discussion

The pathology of molecular targeted therapeutic agent related to stomatitis is still not yet well understood. Since mTOR inhibitor associated stomatitis (mIAS) shows the characteristics of aphthous stomatitis, topical corticosteroid seems to be effective and may also be used to prevent stomatitis. On the other hand, the pathology of EGFR-TKI-related stomatitis remains unknown. In some cases, it is reported that application of topical corticosteroids is effective as with skin rash. But stomatitis showing white patches, it is important to differentiate it from pseudomembranous Candida. The azole-based antifungal agents are metabolized by cytochrome P450 (CYP3A4) in the liver and may present drug interactions. It is known that some EGFR-TKI (gefitinib, erlotinib, lapatinib, osimertinib, etc.) are metabolized by CYP3A4, and metabolic inhibited by drug interaction may prolong oral mucosal disorder. If stomatitis develops while using EGFR-TKI, attention should be paid to the administration of antifungal medications. In these cases, EGFR-TKI treatment caused white patches in the oral cavity, so it was difficult to distinguish between stomatitis and pseudomembranous candida.