DRUG-ASSOCIATED STOMATITIS IN METASTATIC COLORECTAL CANCER PATIENTS UNDERGOING AN EPITHELIAL GROWTH FACTOR RECEPTOR INHIBITOR (PANITUMUMAB): A CASE SERIES

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INTRODUCTION

Panitumumab (PmAb) is an epithelial growth factor receptor inhibitor (EGFRI) recombinant monoclonal antibody which has been used for advanced metastatic colorectal cancer (mCRC). EGFR, which is expressed in normal and several types of cancer cells, has a pivotal role in promoting cellular proliferation by activation of multiple downstream signaling pathways, including the RAS/RAF/MAPK/PI3K/AKT/mTOR pathway. Therefore, blocking this cell surface protein have demonstrated improved outcomes compared to the previous standard therapies but exclusively in a subset of non-mutated RAS Wild-Type (WT) colorectal adenocarcinomas. Although mucositis/stomatitis has been reported in patients undergoing PmAb for colorectal cancer, no consensus on reporting this phenomenon is available in the literature and the clinical characterization seems to be unclear at this point. The aim of this study was to report a case series with emphasis on clinical characterization of this oral adverse event associated with PmAb.

METHODS

A retrospective review of patients' charts which underwent the EGFRI PmAb referred to dental evaluation was conducted. Demographic, medical background and clinical information were recorded for each case. The data analyzed included information about gender, age, tumor location, cancer stage (AJCC, 7th edition) and site of metastasis. Oral affected sites, clinical presentation, time of evolution, local and systemic treatments employed for the oral lesions, as well as follow-up data were assessed from the dental records.

RESULTS

Over a 4-year period, 6 patients that underwent PmAb and was referred to oral evaluation were identified in medical records. The clinical-demographic data is presented in table 1. The oral symptoms appeared in a mean time of 8 days (7-10 days) following irinotecan (IRI) and PamAb combined doses. All patients complained of feed discomfort, 5 patients with moderate pain and 2 patients with mild and severe pain, respectively. All of them presented round/ovoid-shaped shallow ulcerations associated with a surrounding erythematous halo, that showed an aphthous-like appearance. Additionally, 2 patients presented circinate and reddish atrophic tongue lesions that resembled benign migratory stomatitis. The most common affected oral sites were the lips and the tongue (Figure 1). Stomatitis grade 2 and 1 (WHO scale) were recorded for the lesions in 5 patients and in 1 patient respectively. In all, except one case, the oral lesions were accompanied by an acneiform cutaneous rash. The patients were either treated with photobiomodulation or topical corticosteroids with clinical resolution.

Table 1. Patients characterization and antineoplastic treatment information.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Gender/Age	F/56	M/37	F/63	F/50	M/66	F/53
Location	Colon and rectum	Ascending colon	Sigmoid colon	Sigmoid colon	Rectum	Rectum
Stage	IV	IV	IV	IV	IV	IV
Metastasis	Hepatic	Hepatic, Non-regional lymph nodes and Peritoneum	Hepatic	Hepatic	Hepatic	Hepatic
Cancer Treatment	mFLOX + RT + Surgery + IRI monodrug + IRI and PmAb	mFLOX + Roswell Park regimen 5-FU + mFLOX + IRI monodrug + IRI and PmAb	AA surgery + mFLOX + IRI and PmAb	AA surgery + mFLOX + Roswell Park Regimen 5-FU + mFLOX + IRI and PmAb	mFLOX + RT + IRI monodrug + IRI and PmAb	Surgery + mFLOX + IRI monodrug + IRI and PmAb
PmAb dose	400 mg q14w	600mg q14w	300 mg q14w	300 mg q14w	500 mg q14w	400 mg q14w

Figure 1. (A-D) Acneiform cutaneous rash and drug-associated stomatitis in patients that underwent PmAb.

CONCLUSIONS

In summary, we concluded that oral lesions related to PmAb share common features which resemble aphthous and benign migratory stomatitis. Thus, we recommend the use of drug-associated stomatitis for this side effect, similarly to mTOR inhibitor-associated stomatitis. In addition, it is worth to mention that preventive measures, the early recognition and the correct management of this oral adverse event may be helpful to improve patients' treatment, not only avoiding discontinuation of a life-saving therapy as well as maintaining their quality of life at an adequate level during the cancer treatment course.

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