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Letter to the Editor

Before Rituximab is Blamed for Ulcerative Esophagitis, all other Possible Causes must be Carefully Ruled Out

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Letter to the Editor

We read with interest the article by Abdulrazzak *et al*. about a 53-year-old patient with stage IV follicular non-Hodgkin lymphoma. She developed ulcerative esophagitis, which was attributed to rituximab (RTX), initially in combination with bendamustine and later as monotherapy [1]. Omeprazole was ineffective, but after discontinuation of RTX and the addition of vonoprazane, the ulcerative esophagitis resolved completely after more than a year of follow-up [1]. The study is interesting but raises some questions.

Firstly, the onset of the lymphoma, the organs affected, the disease course, and the prior treatment are not sufficiently documented [1]. Stage IV means that the lymphoma has spread beyond the lymph nodes to one or more organs outside the lymphatic system [2]. It is important to know which organs were specifically affected in this patient. What symptoms initially occurred? Was the diagnosis made by lymph node biopsy or bone marrow aspiration? What genetic classification was present? Did RTX have a positive effect on the spread of the lymphoma?

The second point concerns comorbidities and concomitant medications, which were not fully documented [1]. What medications did the patient regularly take in addition to bendamustine, rituximab (RTX), omeprazole, and vonoprazane? Was the patient also receiving glucocorticoids, nonsteroidal anti-inflammatory drugs, antidepressants, neuroleptics, anxiolytics, antibiotics, aspirin, paracetamol, diclofenac, bisphosphonates, warfarin, antihypertensives, quinidine, glimepiride, tiropramide, or chemotherapeutic agents, all of which can potentially cause esophagitis [3]? Did she have a history of thoracic radiation therapy? Esomeprazole can also cause gastrointestinal side effects [4]. What analgesics was she taking? Was bendamustine considered as a possible cause of the esophagitis [5]? Knowledge of concomitant medications is crucial, as ulcerative esophagitis can be caused by interactions between different substances and not just by a single drug.

Thirdly, no imaging, in particular no contrast-enhanced magnetic resonance imaging of the mediastinum, was performed to assess whether the lymphoma had spread into the mediastinum or whether the mediastinal lymph nodes were enlarged. It is also not mentioned whether there was focal hyperactivity in the mediastinum on fluorodeoxyglucose positron emission tomography (FDG-PET).

Fourth, the index patient had isolated ulcerative esophagitis, but no lesions or symptoms in other gastrointestinal segments. Since gastrointestinal side effects of RTX usually involve the intestine, it is unusual for the esophagus to be affected in isolation without intestinal involvement. Intestinal manifestations of RTX side effects include diarrhea, abdominal pain, blood in the stool, mucosal ulceration, and histologically confirmed active inflammation [6]. It would therefore be important to know whether the index patient underwent a colonoscopy and whether it was unremarkable.

Fifth, the course of the illness is not adequately documented [1]. The report should state after how many weeks of bendamustine plus RTX the combination was switched to RTX as monotherapy, how long she received RTX as monotherapy, and how long after the onset of esophageal symptoms the RTX administration was discontinued.

The sixth point is that it is unclear why the RTX therapy was not discontinued earlier, approximately five months after its initiation. It is equally unclear why omeprazole was not administered upon the initial endoscopic diagnosis of esophagitis, rather than only after the presence of ulcerative esophagitis with bleeding.

In summary, the case report has several limitations that should be considered before drawing a final conclusion. Before RTX is suspected as the cause of the ulcerative esophagitis, all other possible causes must be carefully ruled out.

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