

ROLE OF HELICOBACTER PYLORI ERADICATION THERAPY IN THE MANAGEMENT OF RECURRENT APHTHOUS STOMATITIS: A CASE REPORT

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Abstract. Recurrent aphthous stomatitis (RAS) is one of the most frequently encountered oral mucosal lesions. The RAS is characterized by recurrent painful ulcers, which can be either single or multiple. The prevalence rate of RAS ranges from 5 to 60% among the different ethnic and socio-economic groups. To date, RAS is one of the least understood oral diseases. It causes many problems for the affected individual due to the diverse precipitating factors and recurrent nature. Prompt diagnosis and management of RAS is a challenge for clinicians. Several factors, such as nutritional deficiencies, genetic, immunological, haematological, hormonal, trauma, and stress, were identified as causal and precipitating factors. Various micro-organisms, including *Helicobacter pylori* (*H. pylori*), are believed to be associated with the development of RAS. *H. pylori* is a microaerophilic, gram-negative bacterium that colonises the gastric mucosa. Very few reports are available in the literature highlighting the association between *H. pylori* and RAS. Pain relief, fast ulcer healing increased ulcer-free period are the treatment strategies used for RAS. Identifying the causal factors helps the better management of the patients. The present case highlights the difficulties faced by a geriatric patient due to recurrent major aphthous ulcers and the successful management of the recurrent ulcers followed by *H. pylori* eradication therapy.

Key words: *Helicobacter pylori*, recurrent aphthous stomatitis, eradication therapy, laser therapy

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INTRODUCTION

Oral cavity is considered a mirror of the human body reflecting the systemic health status of an individual. The oral mucosa is prone to frequent ulcerations due to a wide variety of causes such as trauma, recurrent aphthous stomatitis, oral manifestations of systemic diseases, medications, infections and oral cancer [1, 2]. Various gastrointes-

tinal diseases such as Crohn's disease, ulcerative colitis, Gardner syndrome, Peutz-Jeghers syndrome, malabsorption conditions related to haematopoiesis, jaundice and gastric reflux diseases manifest oral mucosal changes [3].

Recurrent aphthous stomatitis (RAS) is the most common type of oral ulceration that typically occurs on the non-keratinized areas of the oral mucosal

membrane [4]. The aetiology of RAS is diverse and the diagnosis of RAS is based on the clinical history and presentation. Literature evidence enumerates a wide array of aetiologies attributed to the development of RAS. There are various local and systemic factors that have been identified to be related to the development of RAS, among them nutritional deficits, deficiency of serum iron, folic acid, vitamins B3, B12 and C [5]. *H. pylori* is a microaerophilic, gram-negative bacterium that colonises the gastric mucosa. *H. pylori* is also believed to be responsible for the development of RAS. There are very few reports available in the literature highlighting the association of *H. pylori* and RAS [6]. However, literature evidence of direct cause and effect of *H. pylori* infection and development of RAS is controversial. The present case highlights the diagnostic dilemma of recurrent major aphthous ulcers and the successful management of the recurrent ulcers by laser therapy and *H. pylori* eradication therapy.

CASE REPORT

A 67-year-old female patient reported to the department of Oral medicine and Radiology with the complaint of pain and burning sensation in her tongue since one month. She gave history of suffering from pain, burning sensation of the mouth, sore mouth, redness of the mucosa and inability to eat spicy food since 2 years. She had consulted physicians, dermatologists and dentists for the same. She underwent multiple tests in the past but she never received confirmative diagnosis and she was advised several medications which did not provide her with complete relief. History revealed that patient had developed a large painful ulcer in the tongue a year before, which was associated with burning sensation and pain. The patient had previously undergone dental consultation for the same complaint where biopsy of the lesion was performed followed by histopathological examination, which revealed moderate dysplasia with chronic non-specific inflammation. Haematological and serological reports which were performed one month back revealed negativity for the IgG antinuclear antibody and mild neutrophilia. The patient was under daily oral supplements which consisted of vitamin A in the dosage of 25,000 IU/day, omega-3 fatty acid 30 mg, vitamin E 400 IU/day, elemental zinc 50 mg, vitamin C 1,000 mg and vitamin B complex. The patient was prescribed colchicine 0.5 mg for 10 days by her physician. There was no significant previous medical history. The patient was poorly built and nourished with a history of reduced appetite. On intra-oral examination, multiple erosions of the buccal mucosa, lower lip and tongue were noted. A solitary ulcerative lesion mea-

suring around 1.3 x 1.1 cm in size was noted on the left lateral border of the tongue with an erythematous appearance. On palpation, the lesion was soft in consistency and tender, without induration (Figure 1).



Fig. 1. Clinical presentation of the major aphthous ulcer in the tongue

Missing teeth were presented with the maxillary right and left second premolar, mandibular left first and second molar, mandibular right first molar; root stumps were presented with the maxillary right first premolar, maxillary left second molar and mandibular right second premolar. Dentinal caries was noticed with the maxillary left first premolar, mandibular left first premolar and mandibular right second molar. The maxillary left first molar was supra-erupted, with sharp cusp impinging on the lesion. A provisional diagnosis of major aphthous ulcer on the left lateral border of the tongue was given. The differential diagnoses considered were traumatic ulcer and chronic non-healing ulcer of the tongue. Extraction of the offending tooth was carried out and topical corticosteroid therapy (0.1% triamcinolone acetonide) local application thrice daily for a period of 14 days was suggested. Chlorhexidine gluconate 0.2% mouthwash was also prescribed and the patient was re-examined after 14 days. Complete regression of the tongue lesion was noted after 14 days (Figure 2).



Fig. 2. Healed tongue lesion post administration of topical corticosteroid therapy

In her recall visit patient reported with multiple painful ulcerations of variable sizes in the lower labial mucosa and the tongue. The lower lip lesion was associated with swelling in the left side of the lip. The ulcers exhibited yellowish slough in the floor, with erythematous halo (Figure 3).



Fig. 3. Clinical presentation demonstrating the recurrent ulcers

The recurrent aphthous ulcers in the lower lip and the right side of tongue were treated with laser photobiomodulation therapy using the Epic X (BIOLASE) diode laser with the parameters 0.7-1.0 W in continuous wave (aphthous ulcer mode), in a non-contact manner for 30-45 seconds; each of the aphthous ulcers was irradiated three times at a distance of 1-3 mm. Topical corticosteroids and benzydamine mouthwash were prescribed for a period of 7 days. The patient was referred to the Department of Gastroenterology for further evaluation and to rule out inflammatory bowel disease. Oesophago-gastroduodenoscopy was performed which revealed antral gastritis (Figure 4).

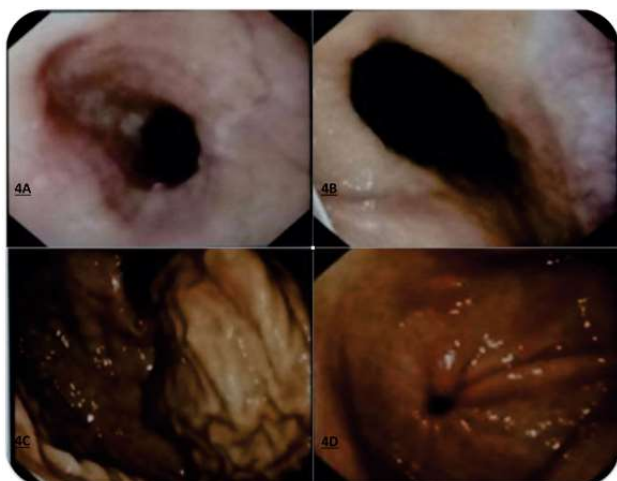


Fig. 4. Oesophago-gastroduodenoscopy demonstrating the antral gastritis

Biopsy of the antral mucosa demonstrated Rapid Urease Test positivity representing *H. pylori* infection. Colonoscopy which was performed to rule out ulcerative colitis revealed normal colonic mucosal study with small internal haemorrhoids (Figure 5).

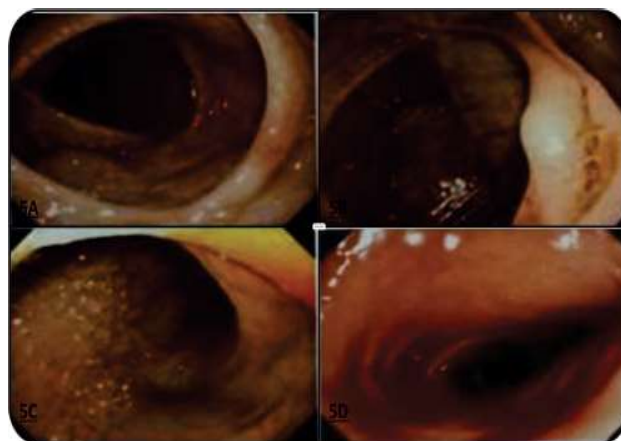


Fig. 5. Colonoscopy demonstrating the normal colonic mucosa

The patient was treated with *H. pylori* eradication therapy, the Sompraz HP kit 3-0-3, which is a combination of amoxicillin, clarithromycin and esomeprazole. She was prescribed itopride hydrochloride (Ganaton 50 mg tablets, 1-1-1) and *Bacillus coagulans*, *Lactobacillus*, *Bifidobacterium* and fructooligosaccharides (Lactogut capsules, 1-0-1) for a period of 14 days. Intra-oral examination was carried out post 14 days from *H. pylori* eradication therapy, which revealed successful healing and regression of the oral lesions (Figure 6). The patient was kept under follow-up and no new lesions were reported 6 months following the *H. pylori* eradication therapy.



Fig. 6. Clinical presentation post *H. pylori* eradication therapy and laser therapy

DISCUSSION

Recurrent aphthous stomatitis was first described by Johann von Mikulicz-Radecki in 1898. There are three types of RAS, namely the minor, major and herpetiform ulcers. RAS is characterised by repeated emergence of one or more ulcers and erosions in varying oral sub sites. RAS is a chronic oral mucosal inflammatory and ulcerative condition which is typi-

cally characterised by repeated ulcerations of non-keratinised mucosa. The oral mucosal ulcerations and erosions in RAS are typically surrounded by an erythematous halo [7]. RAS is regarded as one of the most widespread oral mucosal diseases, with a prevalence of about 2% of the global population [7, 8].

In the present report, major aphthous ulcer was diagnosed in a 67-year-old female. According to the report of Diaz et al. [9], major aphthous ulcers are reported to be more common in the age group of 35-59 years, whereas minor and herpetiform ulcers are more common in the age group of 19-34 years. Although RAS is associated with a diverse range of aetiological factors, various micro-organisms including viruses, bacteria, and genetic vulnerability have also been considered as aetiological factors apart from the major factors [8]. Decrease in the levels of oral *Streptococcus salivarius* and increase in the *Acinetobacter johnsonii* were associated with the occurrence of RAS lesions [10]. *H. pylori* infection has also been implicated in the disease pathogenesis of RAS [11].

Helicobacter pylori is a gram-negative, S-shaped bacterium that has been associated with duodenal ulcers and gastritis. *H. pylori* has been reported to be present in high density in dental plaque [12]. Apart from the gastric mucosa, oral mucosa also serves as an alternative reservoir for the micro-organism. However, the direct relationship of *H. pylori* infection in the pathogenesis of RAS is still under research [13]. It is also known that both RAS and peptic ulcers related with *H. pylori* are immunologically mediated ulcerative lesions, with probable association with anaemia. Similarities exist in the histological characteristics of gastric ulcers and oral aphthous ulcers which respond to treatment with broad-spectrum antibiotics [14]. Few studies available in the literature have confirmed the association of *H. pylori* with RAS by the identification of *H. pylori* in the oral lesional tissue using the polymerase chain reaction. According to the literature evidences, *H. pylori* DNA

was detected in 2-38.9% of the recurrent aphthous lesions [6, 12].

In the present case, major aphthous ulcers were associated with antral gastritis and *H. pylori* infection. The report of Dowsett S.A. and Kowolik M.J. highlights that about 90% of the adult population in developing countries are infected with *H. pylori* [15]. According to the observations of Maleki et al. [16], patients who had *H. pylori*-associated RAS exhibited more severe symptoms than those who had non-*H. pylori*-associated RAS. This finding suggests that *H. pylori* infection may worsen the clinical presentation and course of the ulcers.

A systematic review conducted by Rao L.N. et al. concluded that eradication of *H. pylori* can be effective in the management of recurrent aphthous stomatitis [17]. Karaca S. et al. conducted a prospective study to investigate the association between RAS and *H. pylori* in 23 patients and the effect of eradication therapy on recurrence. They concluded that recurrence was reduced with *H. pylori* eradication therapy after one year of follow-up. Our patient also did not report with any recurrence after the 6-month follow-up [18].

The authors conducted a literature search for the reported cases using the following search terminologies: recurrent aphthous stomatitis, *Helicobacter pylori*, eradication therapy, in the PubMed database from 2012 to 2022. Only two articles mentioned in detail about *H. pylori*-associated RAS and the eradication therapy protocol and follow-up [19, 20]. The results obtained are presented in Table 1.

In the present case, the patient had a long clinical course of the ulcerative lesions associated with pain. The lesions subsided on administration of topical steroid therapy but there was significant recurrence within three months of the initial treatment. However, the lesions responded well to laser therapy along with *H. pylori* eradication therapy. A systematic review by Vale F.A. et al. reports low level laser therapy to be beneficial in symptomatic treatment of RAS along

Table 1. Cases with RAS and *H. pylori* eradication therapy reported in the PubMed database from 2012 to 2022

Study No.	Author	No. of cases	Age	Gender	Treatment	Follow-up	Result
1.	Gao et al. [2021] [19]	1	49 years	Female	Quadruple therapy [Proton pump inhibitor, tetracycline, metronidazole, bismuth subsalicylate]	5 months	Eradication of <i>H. pylori</i> Resolution of RAS
2.	Tas et al. [2012] [20]	46 patients 16 with negative <i>H. pylori</i> infection 30 with positive <i>H. pylori</i> infection	Mean age- 38.00 ± 12.73 years	19 female 11 male	Triple therapy [Amoxicillin 1,000mg BID, clarithromycin 500 mg BID, lansoprazole 30 mg BID for 14days] Additional 2-month-intake of lansoprazole 30 mg once daily]	3 months 6 months	18 patients Eradication of <i>H. pylori</i> RAS decreased in eradicated group. 60% of success rate

with acceleration of the healing period [21]. The triple medicinal regimen is considered as one of the successful method of *H. pylori* eradication [13]. According to the literature reports, *H. pylori* eradication therapy in RAS patients is positively associated with increase in the levels of serum vitamin B12 [22]. The eradication of *H. pylori* in the stomach may promote relief of RAS symptoms and healing of oral ulcers, and even prevent the occurrence of RAS [13]. In the present case, the patient was kept under long-term follow-up and no new lesion was detected 6 months after the *H. pylori* eradication therapy.

CONCLUSION

The present case focuses on the prompt diagnosis and management of recurrent major aphthous ulcers. The successful eradication of *H. pylori* by pharmacologic therapy and the improvement in patient's oral health condition is highlighted in the report. However, the association of RAS with *H. pylori* infection is controversial and requires further long-term prospective studies to establish a strong relationship of *H. pylori* in the pathogenesis of RAS.

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