

## A chronic oral ulcerative eruption



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### CLINICAL PRESENTATION

A 38-year-old, white, male patient, who worked as a brick-layer, was referred for evaluation of multiple linear painful ulcers with erythematous borders, extending to a painless small nodule in the buccal mucosa. The patient reported intense and intermittent burning sensation and pain in the right buccal mucosa, which had started suddenly about a month earlier, causing difficulty in swallowing. After 2 weeks without relief, he sought aid at an emergency service, where he was treated with antibiotics for 7 days without success. Subsequently, the patient was referred to our specialized service in oral diagnosis.

Intraoral clinical examination showed that the ulcerative lesion only affected the labial and posterior regions of the right buccal mucosa (Figure 1). At the end of the linear ulcer, there was a small nodule that was slightly perceptible only when the posterior region of the right buccal mucosa was palpated. There were no other nodules or ulcerative lesions throughout the mouth, either on other areas of the mucosa or skin. In addition, the patient considered himself a healthy man with no other complaints besides the persistent oral ulcerations. A detailed review of his systems and past health history revealed noncontributory past as well as current medical history.

### DIFFERENTIAL DIAGNOSIS

On the basis of the clinical aspects, the following hypotheses were considered: reactive lesion, ulcers caused by infections/infestations and immune-mediated systemic conditions.

#### Reactive lesion

Traumatic ulcers are some of the most common lesions that may occur at any site in the oral mucosa. They present as shallow or deep ulcers, depending on the cause of trauma. Generally, traumatic lesions are self-limiting after the causal (underlying) factor is eliminated, with total remission occurring in a maximum of 15 days. However, some cases can last longer, particularly with persistence

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Fig. 1. Clinical aspect observed at the moment of clinical diagnosis showing multiple linear ulcers with erythematous border and nodular volume at the end of the line (white arrow).

of the causal agent. Even though common, trauma was not considered in this case because of the peculiar clinical aspects of the ulcer, duration of evolution, and lack of a history of trauma.<sup>1</sup>

#### Infectious ulcer/infestation

Oral ulcerative lesions may occur as a result of viral infectious processes. The most common ulcers in adults are mainly caused by herpes virus and enterovirus. Herpes simplex virus (HSV) infection was considered in a differential diagnosis. It is caused by HSV-1 and HSV-2, with HSV-1 being the most common in oral infections. HSV infection may manifest clinically as primary herpetic gingivostomatitis or recurrent infection. Primary HSV infection is more common in children and unusual in adolescents and adults. Acute gingivitis, vesicles, and ulcers in the oral mucosa may be present as the primary form, and vesicles and ulcers are observed as recurrent herpes. The lesions of HSV infection are usually self-limiting, disappearing in approximately 15 days.<sup>2</sup> Although there was some clinical similarity, HSV infection was ruled out particularly because of the disease course in the current case.

Herpes zoster, which is a viral disease caused by reactivation of varicella zoster virus, was also considered. Classically, the affected individual is infected earlier in life, with the infection manifesting as chickenpox. Later, viral reactivation may occur through manifestation of herpes zoster. The main risk factor is immunosuppression

caused by advanced age, treatment with cytotoxic drugs, radiation, presence of malignancies, and alcohol abuse. Painful shallow ulcers may occur in any intraoral region innervated by the maxillary and mandibular branches.<sup>3</sup> In this case, although the linear ulcers were unilateral, the patient was an immunocompetent young adult. Furthermore, he had no recollection of having had chickenpox in his childhood or of experiencing pain or any vesicles before the present ulcers, and hence herpes zoster was ruled out.

Coxsackie virus infections are more common in children and cause vesicles that break rapidly, forming ulcers in the oral mucosa; the ulcers are usually accompanied by systemic symptoms, such as fever, diarrhea, myalgia, and vomiting. The most well-known presentation is hand, foot, and mouth disease, in which lesions are present in these three locations. The disease is usually self-limiting, with remission of ulcers in 1 week.<sup>4</sup> Although it was a diagnostic possibility, the patient's age, the duration of his ulcers, and the absence of lesions at other locations made Coxsackie virus infection a less likely option.

Ulcers caused by parasitic oral infestations are not common, but they were considered because of the patient's occupation, which probably made him more susceptible to infestation by parasitic larvae. Humans are infected by parasites, such as helminths, through the ingestion of larvae or infected eggs or by penetration of larvae into the oral mucosa or skin. Oral infestations are rare and have a broad clinical presentation, varying from a painless solitary nodule to itching white tracks/ulcers surrounded by erythema. Systemic symptoms vary, depending on the degree of infestation, the species of the parasite, and the response of the host, and can generate abdominal pain and diarrhea.<sup>5</sup> Although the patient was systemically asymptomatic and the clinical presentations of oral parasitic infestations are variable, the present case had similar aspects, such as asymptomatic nodules and ulcerations. Because of this, oral parasitic infestation was a strong diagnostic possibility.

### Oral manifestation of systemic disease

Oral ulcers may represent a spectrum of systemic diseases, usually related to inflammatory processes. Vesiculobullous diseases present vesicles that break and become painful ulcers in mucosae and skin. Pemphigus vulgaris is the most common vesiculobullous disease with oral presentation. It is an uncommon chronic autoimmune disease, more prevalent in women in the fifth decade of life.<sup>6</sup> Although pemphigus vulgaris can cause chronic oral ulcers, the current clinical appearance was not similar to oral pemphigus lesions, and the patient's demographic profile was not what is expected in pemphigus vulgaris.

Other possible differential diagnoses included oral manifestations of gastrointestinal (GI) disorders.

Pyostomatitis vegetans is a rare chronic mucocutaneous condition that is strongly associated with ulcerative colitis or Crohn disease. It is characterized by numerous pustules of white-yellowish content, with an erythematous and edematous base that may break or coalesce, giving a "snail track" appearance. Pyostomatitis vegetans occurs mainly on the tongue, lips, gingiva, tonsillar pillars, buccal mucosa, and soft and hard palates. Generally, the patients can experience fever, submandibular adenopathy, and pain, which are highly variable symptoms that are not necessarily related to the extension and size of the ulcers. In addition, patients with GI disorders, such as Crohn's disease, ulcerative colitis and celiac disease, may present with linear ulcers in the mouth. GI disorders characteristically produce systemic symptoms, such as chronic diarrhea and abdominal pain.<sup>7</sup> The clinical characteristics of GI disorders are similar to those of the case reported here. However, the fact that the patient did not have any systemic changes refuted this important diagnostic hypothesis of oral manifestation of GI disorders.

### DIAGNOSIS AND MANAGEMENT

Although the linear ulcer was an important part of the lesion in the present case, it was essential to pay attention to the nodule at the end of the ulcer. On the basis of our past experience,<sup>8</sup> we know that persistent, burning, linear ulcers associated with a nodule at the end of the ulcers is highly suggestive of larva migrans. Therefore, an excisional biopsy of the nodule was performed under cover of local anesthesia.

The histopathologic analysis revealed circular parasitic inclusions located within the lower portion of the epithelium, with inflammation in the underlying connective tissue. The microscopic spectrum was compatible with a nematode infection (Figure 2).

On the basis of the clinical and histopathologic aspects of this case, thiabendazole was prescribed at a dose of 25 mg/kg twice a day for 4 days.

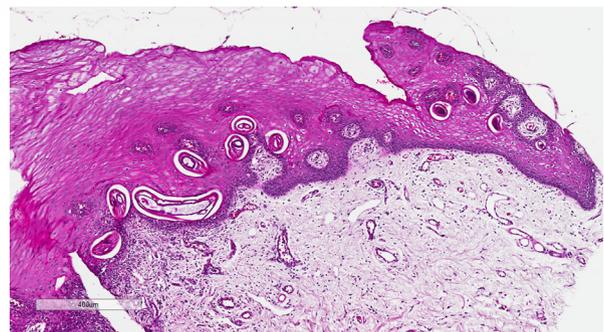


Fig. 2. Histopathologic examination revealed parasitic inclusions in the epithelial tissue. A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM04683.

The patient returned after 1 week, confirming use of the medication exactly as prescribed (taken only for 4 days). He had no symptoms, and total remission of the oral lesions was evident. The patient reported that the burning sensation had disappeared on the second day of medication and that he did not experience any adverse systemic effects of the medication.

## DISCUSSION

The life cycle of nematodes begins with the eggs of larvae that are found in the host's feces and that grow and develop in soil until reaching maturation (filariform larvae). They infect the definitive host through penetration of skin.<sup>9</sup> *Ancylostoma braziliense* and *Ancylostoma caninum* are the most common species, and dogs and cats are their natural hosts. Humans are infected by skin contact with contaminated soil or sand containing filariform larvae.<sup>10</sup> Cutaneous larva migrans is a skin infection caused by percutaneous penetration of nematode larvae and by larval migration to the epidermis, resulting in the typical clinical appearance.<sup>11</sup> Although common in skin, oral larva migrans is rare, with few reports in the English-language literature.<sup>8,12-17</sup> The current report presents the second case in our oral diagnosis service, encountered after an interval of 23 years, which corroborates the rarity of larva migrans oral manifestations.<sup>8</sup> This can be explained by the rarity of contaminated soil or sand reaching the mouth. However, as described in our current report, individuals who are engaged in outside activities or jobs, and presences of animals are vulnerable to infection, especially when lacking basic hygiene conditions. Our patient reported that during his work as a bricklayer, he would drink water using his hands after direct contact with sand.

The filariform larvae migrate in no particular direction in the epidermis because they cannot mature in the human host.<sup>9</sup> This causes an inflammatory reaction, with the typical clinical appearance of a serpiginous erythematous lesion known as a "creeping eruption."<sup>10</sup> Itching is often very intense and may be caused by movements of the larvae in the epidermis as well as by their release of proinflammatory enzymes, such as hyaluronidase and metalloprotease.<sup>18,19</sup> Our patient exhibited a clinical pattern similar to that described in the literature, with multiple linear ulcers with erythematous border, causing pain and pruritus, which make it difficult to eat. Interestingly, the patient reported that the itching "walked" through the mouth, which can be explained by tissue destruction caused by migration of the larva.

Another important aspect is that although the clinical appearance is very distinctive, the diagnosis of oral lesions can take some time, particularly because clinicians are not familiar with this entity. The current patient had previously sought nonspecialized medical treatment

and had been treated with antibiotics without success. After 30 days, he was referred to our service.

Generally, the diagnosis is based on the clinical appearance of the lesion. However, a biopsy and histopathologic analysis can help confirm the diagnosis through direct visualization of migrating larvae.<sup>5</sup> However, some authors claim that histopathologic confirmation and removal of larvae are not usually attempted because the migrating larvae are difficult to locate.<sup>20,21</sup> Histologically, the larvae are 0.5 mm thick and up to 10 mm long and are typically confined to the deep epidermis because the parasite lacks collagenases, which are required to penetrate the basement membrane.<sup>21</sup> On the basis of past experience,<sup>8</sup> we know that the biopsy should be performed directly on the nodule at the end of the serpiginous path because this is the probable lodging place of the larva. Biopsy performed at the path of the larvae will probably show nonspecific ulcerations and associated inflammatory infiltrate because of the tissue destruction caused by larval migration. In the present case, a single excisional biopsy of the nodule was performed. The larva was observed in the deep epithelial layer but did not go beyond the limit of the basal layer. Inflammatory infiltrate was observed between epithelial cells (exocytosis), arranged in the form of microabscesses, and underlying connective tissue.

Although described as a self-limiting lesion, some cases of larva migrans exhibit multiple lesions, an exacerbated clinical aspect, and a long evolution, with reports of persistent infestations lasting up to 2 years.<sup>22</sup> Moreover, there are records of maturation of *A. caninum* in the intestines of humans, indicating the possibility of ingestion of larvae.<sup>9,23</sup> Therefore, treatment with anthelmintics is recommended for alleviation of symptoms and to reduce the risk of recurrence and secondary bacterial infection.<sup>24</sup> Cutaneous larva migrans can be treated topically with thiabendazole 10% and freezing. Oral treatment can be performed with thiabendazole, albendazole, and ivermectin.<sup>25</sup>

With regard to the treatment of oral larva migrans, there is a case report that used only biopsy as a treatment, without the use of anthelmintic medication.<sup>17</sup> The current patient was also treated with oral thiabendazole because of his symptoms and the duration and extent of the lesions. Although systemic manifestations are not expected, because in most of cases larvae cannot mature in humans, we chose to prescribe oral medication as a preventive measure for possible ingestion of larvae. After 2 days, the burning sensation disappeared. In addition, no adverse changes were observed, as in our first case.<sup>8</sup>

## CONCLUSIONS

In summary, occurrence of larva migrans is common in skin but is rare in the oral mucosa, with few reports published in the English-language literature. Therefore, it is

important to recognize the peculiar clinical features of oral larva migrans, although they are very similar to those of its cutaneous counterpart.

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