

Methamphetamine-induced widespread oral ulcerations

Metamfetamin ilişkili yaygın oral ülserler

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Dear editor,

3,4-methylenedioxymethamphetamine (MDMA), known as ecstasy, is a hallucinogen and stimulant illicit drug. Besides the systemic effects of this drug are well documented¹, it can also present with a range of oral side effects such as xerostomia, bruxism, dental erosion, and ulcers.² Oral ulcerations due to MDMA abuse can be severe and widespread. We would like to raise awareness about this kind of ulcers may be associated with ecstasy use, and it should be included in the differential diagnosis.

A 38-year-old male patient presented to our outpatient clinic with complaints of one year history of multiple oral ulcerations and intense pain. According to the patient, the first lesion emerged from the left half of the tongue and ulcerated over time. Eventually, similar ulcerations spread to various parts of the oral mucosa.

The patient's notable past medical history included tonsillectomy operation, pilonidal sinus surgery, gastritis, panic disorder and mood disorder. He was on lansoprazole, venlafaxine, and lithium medication at the time of presentation. Family history was insignificant. While questioning patient's

habits, he admitted smoking for 20 years, using cannabis for 15 years and then, "Ecstasy" (3, 4 methylenedioxymethamphetamine, MDMA) for the last one year.

Oral examination revealed widespread ulceration that destroys the left half of the tongue and multiple perforations located on bilateral buccal mucosa, the floor of the mouth and gingival ulcers. (Fig. 1) Furthermore, the patient described severe pain associated with oral lesions. The patient did not show any extraoral finding.

Numerous biopsies had been performed at different times. Examination of the previous biopsies revealed ulcerative areas containing inflammatory cell infiltrate and fibrine deposition surrounded by epithelial hyperplasia. In the subepithelial area, there was preponderance of plasma cell infiltrate and fibrosis, possibly due to previous biopsies. (Fig. 2) Thus, autoimmune diseases and neoplasias were excluded. Additional stainings for EBV, CMV, syphilis and fungal infections were negative. Immunofluorescence assay was also negative.

Key words: methamphetamine, MDMA, ecstasy, oral, mucosa, ulceration

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Fig. 1a. There is massive tissue loss affecting left half of the tongue; **1b.** Perforation on the right buccal mucosa; **1c.** Perforation located on the left side of oral mucosa.

Imaging studies such as MRI, CT, PET-FDG, Ultrasound of maxillofacial structures and related body segments showed no significant findings.

Anti-HIV ELISA test and syphilis serology were negative. HBV and HCV serologies were also negative. Bacterial and fungal cultures from lesions showed no causative agents. Interferon gamma release assay (IGRA) for tuberculosis tested negative. The patient's history of recurrent aphthous ulcer was negative and no additional finding was found in assessments for Behçet's disease. The antinuclear antibody panel (ANA) was positive at 1:80 serum dilution, and extractable nuclear antigen (ENA) panel was negative. Serum immunoelectrophoresis showed no paraprotein bands. Serum Immunoglobulin (Ig) levels were normal. Up-to-date toxicology panel was negative.

Initially, benzydamine, chlorhexidine and corticosteroid mouthwashes treatments had been commenced. Afterwards, he had been treated with systemic antibiotic treatments including ornidazole, ampicillin/sulbactam, and benzathine penicillin G 2.4 million units three times weekly for suspected syphilis infection, without improvement. Intravenous methylprednisolone, colchicine, and hyperbaric oxygen therapy were also among the treatments that were prescribed and they had been ineffective.

All possible causes had been eliminated, and clinical picture was attributed to MDMA use. Ulceration is one of the reported oral mucosa effects of MDMA. To our knowledge, there are only a few cases involving oral mucosal ulcerations related to MDMA abuse in the literature^{1,3-5} To the best of our knowledge, there have been no previous reports of severe and widespread oral involvement comparable to our patient. There are several factors that may explain the severity of the lesions such as frequency of the abuse, application method and interaction between MDMA and other drugs used by the patient, as these can potentiate the adverse effects.

Our patient has been using Venlafaxine, a selective noradrenaline reuptake inhibitor (SNRI), for seven years due to panic disorder. Additionally, he has been diagnosed with mood disorder and has been used lithium for last six months. Brazier et al.¹ state an example of interaction between MDMA and selective serotonin reuptake inhibitor (SSRI) antidepressants. SSRIs are competitive inhibitors of MDMA hepatic metabolism at the debrisoquine hydroxylase (CYP2D6) enzyme stage, and thus they can increase the adverse effect of MDMA. Considering that our patient had been using Venlafaxine for seven years, which also inhibits the same enzyme stage, this condition may be one of the explaining factors of widespread ulcerations.

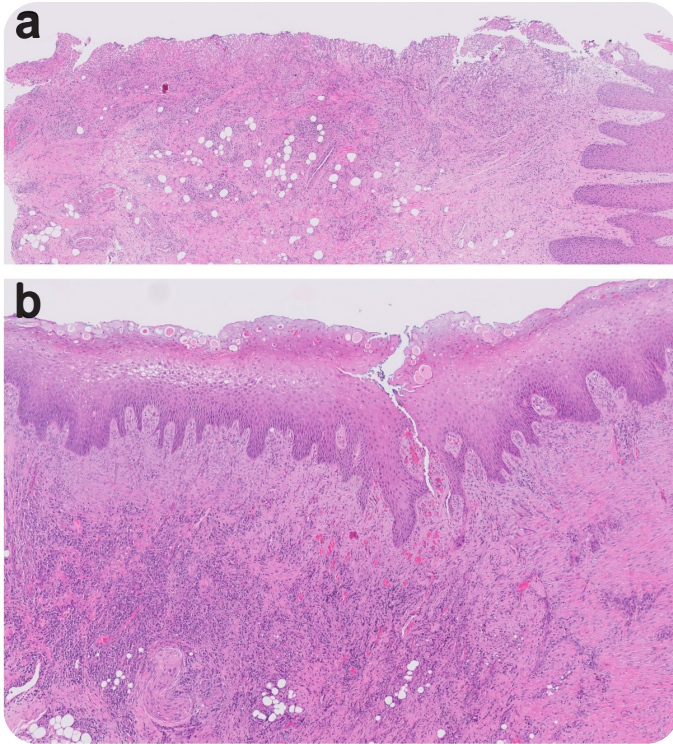


Fig. 2a. Base of the ulcer containing inflammatory cell infiltrate and fibrine deposition, surrounded by epithelial hyperplasia (HE x100); **2b.** Preponderance of plasma cell infiltrate and adjacent fibrosis in the subepithelial area (HE x200).

Lithium was not considered as a primary factor since the patient had been using it for only six months and there is no clear relationship in the literature in terms of increasing the effect of MDMA, to our knowledge.

In conclusion, presentation of unusual and widespread oral ulcerations may be related with the MDMA use and clinicians should have a high index of suspicion. We would like to highlight that MDMA abuse should be included in the differential diagnosis list for widespread oral ulcerative lesions with tissue loss.

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