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Case Report

A Palatal Ulcer Might Be the First Sign of Potentially Fatal Diseases - Two Case Reports

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Abstract

Background: A palatal ulcer is a non-specific clinical presentation and might be the first sign of a potentially fatal disease; thus, accurate diagnosis is challenging.

Case Summary: Here, we present two cases with palatal mucosal ulcers both located on the left side and with similar clinical appearance. Case 1 was diagnosed with pulmonary Tuberculosis (TB) and case 2 was diagnosed with Extranodal NK/T-Cell Lymphoma, nasal type (ENKTCL). Both cases responded well to systemic therapy, and the palatal ulcers completely healed without recurrence.

Conclusion: TB and ENKTCL should be included in the differential diagnosis of palatal ulcer of unknown etiology.

Keywords: Diagnosis; Extranodal NK/T Cell Lymphoma; Palatal Ulcer; Pulmonary Tuberculosis

Abbreviations

CT: Computed Tomography; CRP: C-Reactive Protein; DNA: Deoxyribonucleic Acid; EBV: Epstein-Barr Virus; ENKTCL: Extranodal NK/T Cell Lymphoma, Nasal Type; EBER: Epstein-Barr Virus Encoded RNA; ESR: Erythrocyte Sedimentation Rate; Hb: Hemoglobin; HIV: Human Immunodeficiency Virus; HE: Hematoxylin and Eosin; HE: Hematoxylin and Eosin; ISH: In Situ Hybridization; LDH: Lactate Dehydrogenase; MRI: Magnetic Resonance Imaging; NEUT#: Neutrophil Count; PET/CT: Positron Emission Tomography/Computed Tomography; RNA: Ribonucleic Acid; TB: Tuberculosis; WBC: White Blood Cell

Background

The accurate diagnosis of palatal ulcer is a challenging clinical problem due to the overlapping clinical features of various types of ulcerative lesions [1,2]. Here, we present two cases with mucosal ulcers both of which were located on the left palate and had a similar clinical appearance. It is worth noting that each of the two palatal ulcers was the initial clinical manifestation of a severe, potentially fatal disease, respectively.

Case Presentation

Case 1

A 27-year-old Chinese male patient visited the Department of Oral Medicine, Shanxi Provincial People's Hospital, China, with the chief complaint of a painful ulcer on the left palate for two weeks. He described that the palatal ulcer pain was aggravated and affected his swallowing function. His sputum had increased during the last four weeks, without significant cough. He also gradually developed a sore throat and hoarseness, and was diagnosed with pharyngitis in a local hospital. Oral amoxicillin and some traditional Chinese medicine were given, but these treatments were all ineffective. In recent weeks, the patient had intermittent fever with temperatures up to 38.8 ˚C without chills or rigors. He denied any history of infection and allergies. However, slight weight loss during the last 3 months was reported. The patient smoked 20 cigarettes a day for several years and did not have a drinking habit.

Intraoral examination revealed a large superficial mucosal ulcer involving the left hard and soft palate covered by yellow-white exudation (Figure 1A). The ulcer was irregular but its right border was the midpalatal suture, extending to the gingival area of the left maxillary molar. Initial blood investigations revealed elevated White Blood Cells (WBC (15.47 $\times 10^9$/L), neutrophils (76.1%), monocytes (15.8%), platelets (403 $\times 10^9$/L), erythrocyte sedimentation rate (ESR, 60 mm/h), and decreased hemoglobin (Hb, 116 g/L). The test results for syphilis and Human Immunodeficiency Virus (HIV) were both negative.

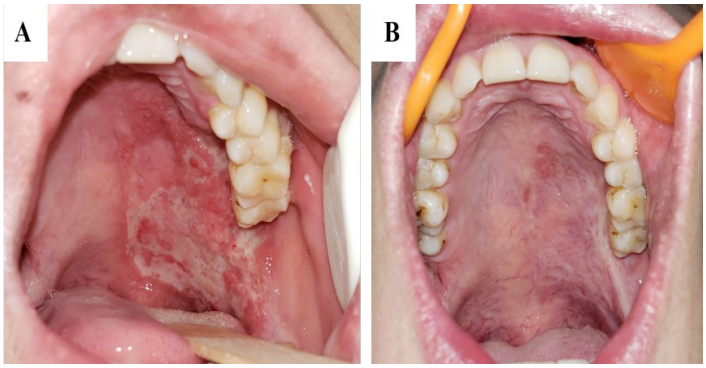

Figure 1: A: a large superficial mucosal ulcer involving the left hard and soft palate covered by yellow-white exudation in case 1. B: after receiving standard anti-tuberculosis treatment, complete resolution of the palatal ulcer with no other significant oral findings was observed in case 1.

On physical examination, the patient had a fever (body temperature 37.6 ˚C) and looked thin and weak, but without obvious cough and other symptoms at the first visit to our department. Chest X-ray revealed a compressed left thorax with elevated diaphragm (Figure 2A), an irregular high-density patchy shadow in the left upper lung, and multiple high-density nodules with blurred edges in the right lung. The superior mediastinum was widened.

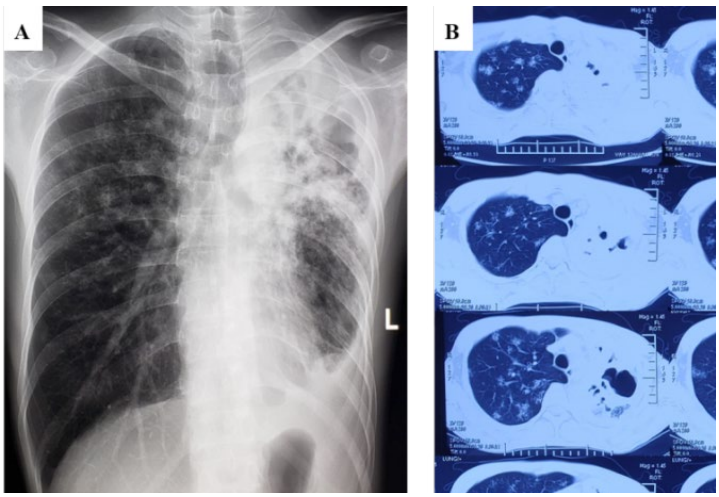

Figure 2: A: the chest X-ray in case 1 showed an irregular patchy high-density shadow in the left upper lung, and multiple nodular high-density shadows with blurred edges in the right lung. In addition, the left thorax was reduced, the left diaphragm was elevated, and the superior mediastinum was widened. B: the chest CT in case 1 showed left lung damage and the “fireworks sign” in the right lung.

Chest Computed Tomography (CT) detected the "fireworks sign", due to multiple patchy and nodular high-density shadows with blurred edges along the bronchus of the right lung. On the left side, a soft tissue shadow accompanied by a cavity formation on the upper lobe and interstitial changes in the lower lobe were detected, the pulmonary volume was reduced, and the chest was collapsed with thickening of the left pleura (Figure 2B). In addition to the imaging characteristics consistent with signs of pulmonary Tuberculosis (TB), the sputum smear for acid-fast bacilli was also strongly positive.

Based on these results, the patient was diagnosed with pulmonary TB and immediately referred to a specialist hospital for infectious diseases for further management. He subsequently received standard anti-TB treatment and obtained an excellent therapeutic response. After four months, his general condition improved significantly and complete resolution of the palatal ulcer with no other significant oral findings was observed (Figure 1B). To date, the patient has been followed for 24 months with no evidence of recurrence.

Case 2

A 45-year-old previously healthy Chinese female patient presented to the hospital with a large palatal ulcer for 2 weeks, which had worsened over the previous few days. She had intermittent fever without any apparent cause for three months, which was accompanied by fatigue, chills, sore throat, sweating and weight loss. Other signs and symptoms were denied. When examined in a local hospital, she was diagnosed with leukopenia and anemia based on the results of blood tests, and she received corresponding treatments to raise the leukocyte count, correct anemia and anti-infection. However, her condition did not improve and her symptoms persisted. She was referred to a higher-level hospital two months ago. She was thought to have TB and received anti-TB treatment combined with symptomatic supportive treatment. The fever initially improved, but relapsed after two weeks, and was then even more aggravated. These treatments failed and the patient's condition deteriorated. Two weeks ago, an ulcerative lesion on the left palate in the oral cavity was noted. Topical steroid treatment, including both inhaled and gargled corticosteroids were administered for several days, but the palatal ulcer increased in size, which affected her chewing and swallowing. Hence, the patient was referred to our department for further investigations. She had no history of smoking, drinking alcohol or drug abuse and had previously been in good health. Nasal symptoms such as nasal congestion and epistaxis were absent.

A thorough oral examination was immediately performed. A large superficial ulcer without bony destruction and palatal perforation was detected on the left palate (Figure 3A). The right border of the ulcer reached the midpalatal suture and did not involve the right palate. A fixed bridge restoration was observed between the left maxillary canine and the first molar. Several residual crowns and roots were also found in the oral cavity. The patient had a slight fever (body temperature 37.2 ˚C), and felt weak and faint.

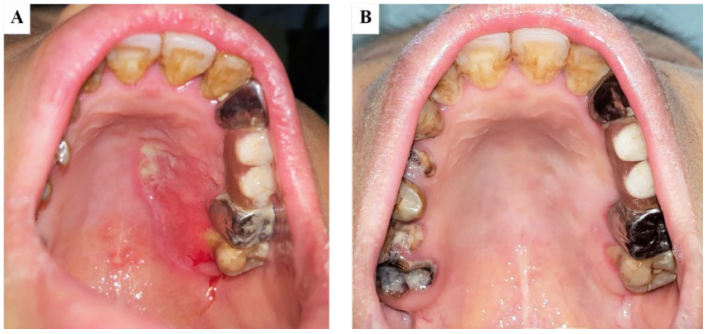

Figure 3: A: A large superficial ulcer without bony destruction and palatal perforation was detected on the left palate in case 2. B: The palatal ulcer was healed completely after four weeks of chemotherapy without relapse.

Laboratory examinations revealed leukopenia (WBC 2.4×10^9/L, normal range 4-10 $\times10^9$/L; neutrophil count of 1.42×10^9/L, normal range 2-7 $\times10^9$/L), and anemia (Hb 97 g/L, normal range 110-150 g/L). ESR was slightly elevated (24 mm/h, normal range 0-20 mm/h), but C-Reactive Protein (CRP) and Lactate Dehydrogenase (LDH) were within the normal range. The detection of HIV, syphilis and antinuclear antibody spectrum were all negative. Blood culture results were also negative. No other abnormalities were detected in the TB-related tests. Her chest X-ray was unremarkable. Cranial CT revealed ethmoid sinus inflammation without any obvious mass lesions. Abdominal ultrasound showed slight splenomegaly and left upper abdominal nodules (accessory spleen or enlarged lymph nodes could not be excluded). The results of bone marrow aspiration appeared normal. A biopsy of the palatal ulcer was performed and sent for histopathological examination. Hematoxylin and Eosin (HE) staining showed chronic inflammation of the palatal mucosa, the formation of ulceration and erosion, and diffuse or focal lymphocytic infiltration in the lamina propria (Figure 4A).

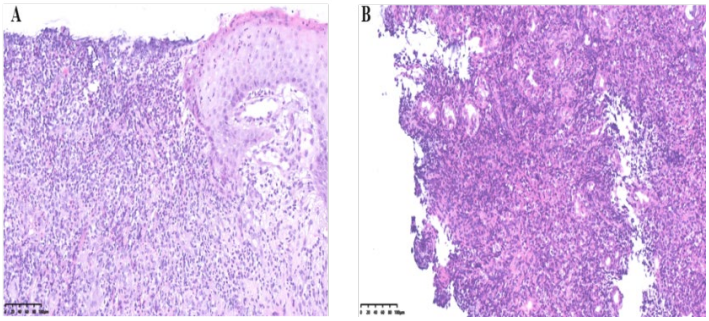

Figure 4: Histopathological features of case 2 (HE staining, ×200). A: The palatal ulcer. HE staining showed chronic inflammation of the palatal mucosa, the formation of ulceration and erosion, diffuse or focal lymphocytic infiltration in the lamina propria. B: The mucosa of the left lateral nasal septum. HE staining showed a diffuse infiltration of polymorphic neoplastic cells.

Both imaging and pathological findings were considered non-specific and did not provide useful diagnostic clues. Considering the patient's severe and deteriorating general condition, further examinations were immediately performed. Repeated biopsy of the palatal ulcer was recommended, but was not accepted by the patient and her family. After consultation with a hematologist, Positron Emission Tomography/Computed Tomography (PET/CT) was performed. Hypermetabolic lesions were detected at the mucosal thickening of the left hard palate, inferior part of the left ethmoid sinus, left inferior turbinate and left lateral wall of the nasal septum (Figure 5). Extranodal NK/T-Cell Lymphoma, nasal type (ENKTCL) was highly suspected based on the results of PET/CT and the patient's clinical symptoms. A biopsy of the mucosa of the left lateral nasal septum was strongly recommended and was finally accepted by the patient. The second biopsy was performed by an otolaryngologist for further pathological diagnosis. HE staining showed diffuse infiltration of polymorphic neoplastic cells (Figure 4B). Immunohistochemical analysis was then performed. The neoplastic cells were positive for cytoplasmic CD3 ($CD3\varepsilon^+$), $CD56^+$, cytotoxic granule-associated protein (Granzyme B), $CD8^+$ and negative for CD 20. The positive rate of KI-67, which is a cell proliferation marker, was over 80%. *In Situ* Hybridization (ISH) showed that the cells were strongly positive for Epstein-Barr virus encoded RNA (EBER). Serological detection of EBV DNA was also positive. The final diagnosis of ENKTCL was confirmed.

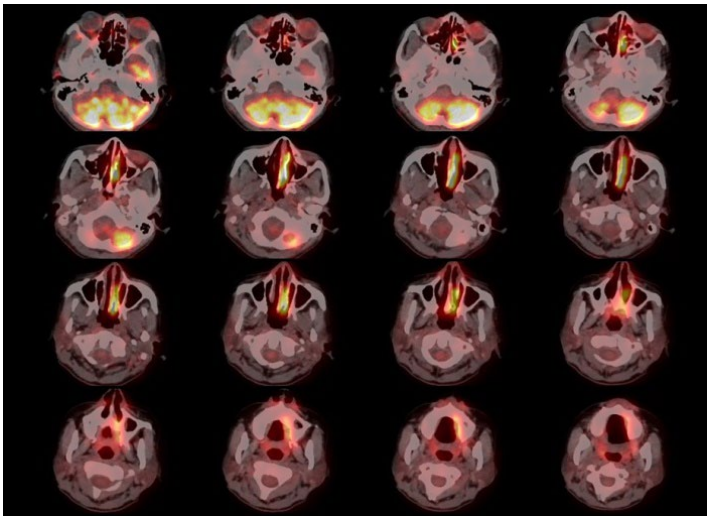

Figure 5: In case 2, hypermetabolic lesions were detected by PET/CT at the mucosal thickening of the left hard palatal, inferior part of the left ethmoid sinus, left inferior turbinate and left lateral wall of the nasal septum.

The patient was then referred to the Department of Hematology. Following eight cycles of chemotherapy (PGemOx regimen), the patient achieved complete remission. The palatal ulcer healed completely after four weeks of chemotherapy without relapse (Figure 3B). The patient has been closely followed up, and shows no evidence of recurrence and her general condition remains good. Re-examination of PET-CT showed no evidence of hypermetabolic lesions.

Discussion and Conclusions

The diagnosis of palatal ulcer is a clinical problem, especially in cases where the lesions are limited solely to the palate and without involvement of the skin and other parts of the oral cavity [2]. Although palatal ulcers may look similar clinically, their causes can vary considerably, ranging from developmental abnormalities (e.g. cleft palate) to infections (e.g. fungal or herpes simplex), inflammation (e.g. aphthous stomatitis), immune-mediated disorders (e.g. lupus erythematous), iatrogenic causes (e.g. tooth extraction) and malignant tumors (e.g. squamous cell carcinoma), which makes accurate diagnosis quite challenging [1-3].

Here, we report two cases with a left palatal ulcer and similar clinical manifestations, but different underlying causes. One was due to progressive pulmonary TB and the other was due to ENKTCL. TB is a life-threatening infectious disease caused by a Mycobacterium tuberculosis complex and has been a worldwide health problem for centuries. In recent decades, the prevalence of TB has started to increase, it has been estimated that one-fourth to one-third of the world's population have latent TB and millions of people die each year due to this infection [4]. Oral TB lesions are uncommon and nonspecific in their clinical presentation [5]. Most of these lesions are secondary to pulmonary TB. The most likely route of self-inoculation involves the pathogenic organisms being carried in the sputum and entering the mucosal tissue through a small break in the surface. It is also possible that the organisms are carried by the hematogenous route, deposited in the submucosa and subsequently proliferate and ulcerate the overlying mucosa [6,7]. A typical lesion is an irregular, superficial or deep, painful ulcer, involving mainly the tongue and labial mucosa in middle-aged and elderly patients [5-7]. Here, the patient with secondary TB was a young male with the first sign of a large irregular ulcer on the palate, which has rarely been reported.

ENKTCL is a rare and aggressive type of Non-Hodgkin lymphoma [8-10]. The prognosis of ENKTCL is poor and the 5-year survival rate was reported to be less than 40% [11]. Although the predominant site is the nasal cavity, ENKTCL, previously described as a lethal midline granuloma and midline malignant reticulosis [12], can often involve the oral cavity [13,14]. The definitive diagnosis of ENKTCL is often difficult and may be considerably delayed due to the high rate of misdiagnosis [11,15]. In case 2, the initial oral biopsy and cranial CT revealed only nonspecific inflammation and did not provide useful diagnostic information.

The use of PET/CT played an important role in helping to avoid misdiagnosis. The valuable role of PET/CT in the diagnosis, staging, prognosis and treatment evaluation of NK/T cell lymphoma has been well documented [16,17]. It has been suggested that PET/CT could be used as a standard imaging modality for NK/T cell lymphoma [18]. The present case also supported PET/CT as a promising tool for diagnosing ENKTCL, and it might be useful when added to the routine diagnostic process for ENKTCL.

The oral cavity is a mirror of general health and may serve as an early warning system for certain diseases [19,20]. It is worth noting that palatal ulcers might be the first visible sign of potentially fatal diseases before systemic symptoms become apparent, which was also demonstrated by the cases presented here. As early and accurate diagnosis is vitally important for patient survival, dentists should be aware of the possible oral lesions of these systemic diseases. A comprehensive review suggested two straightforward approaches to diagnose these disorders. As illustrated in the charts, one approach is based on the site of involvement, the other is based on the course of the disease, the onset and number of oral ulcers [2]. It is also the responsibility of dentists to timely refer these patients to appropriate physicians. As shown by previous studies and our report, TB and ENKTCL should be included in the differential diagnosis of refractory palatal ulcers in the oral cavity that fail to respond to conventional therapy [7,14].

To provide more valuable diagnostic clues for atypical oral ulcers, the possibility of systemic involvement should be considered. Moreover, the patient's relevant medical history should be carefully reviewed and concurrent systemic symptoms should be explored and identified. For example, both cases reported here had a long history of intermittent fever of unknown cause, which should arouse suspicion of underlying systemic diseases. Other noteworthy symptoms include chills, weight loss, fatigue, epistaxis, abdominal pain, diarrhea and persistent cough. Based on the patient's condition, a comprehensive clinical investigation, including laboratory tests and imaging examinations, such as complete blood count, ESR, HIV, syphilis, oral microbiological culture, chest X-ray or CT and nasal CT, should be performed. When necessary, examination of immune function, gastrointestinal endoscopy, bone marrow biopsy and PET/CT should also be undertaken to determine the cause of disease.

It has been suggested that tissue biopsy is essential for the definitive diagnosis of chronic oral ulcer, especially if not responsive to traditional therapies [21]. However, the limitations of biopsy technique have been discussed [22,23]. In particular, it has been suggested that standard biopsy procedures need to be modified if the patient has severe or poorly controlled systemic diseases [23]. Dentists are at high risk of M. tuberculosis infection through close contact with patients and the aerosol produced during dental treatment [24]. In case 1, after the diagnosis of progressive pulmonary TB was made, an oral biopsy was not undertaken to reduce the risk of hospital acquired infection. Following treatment of pulmonary TB, the palatal ulcer completely healed and no recurrence was observed in the follow-up period, which also confirmed that the etiology of this palatal ulcer was TB. In case 2, an oral biopsy was performed but the pathological findings were discordant with the final diagnosis. Based on these two cases, we suggest that an oral biopsy and the interpretation of the pathological findings, especially in atypical or refractory palatal ulcers, should be done cautiously. The patient's medical history, general symptoms or necessary laboratory and radiological examinations should also be considered carefully.

In conclusion, a palatal ulcer is a non-specific clinical presentation and might be the first sign of potentially fatal diseases; thus, accurate diagnosis is challenging. This report aims to emphasize that, although rare, TB and ENKTCL should be included in the differential diagnosis of palatal ulcer of unknown etiology.

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Authors' Contributions

ZB, YG and YS examined and diagnosed these cases. ZB and NC designed and wrote this case report. HB performed the pathological examinations. All authors revised the manuscript. All authors have read and approved the manuscript.

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Availability of data and materials

All necessary data are included in this published study. More data and details are available from the author upon reasonable request.

Ethics approval and consent to participate

The case report and related examinations were all approved by the Medical Ethics Committee of Shanxi Provincial People's Hospital (NO. 201902). Informed consent was obtained from the patients and their families.

Consent for publication

Written informed consents were obtained from the patients for publication of this case report and any accompanying images. A copy of the written consent is available for review from the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

References

1. Fitzpatrick SG, Cohen DM, Clark AN (2019) Ulcerated Lesions of the Oral Mucosa: Clinical and Histologic Review. Head Neck Pathol 13: 91-102.
2. Sardana K, Bansal S (2014) Palatal ulceration. Clin Dermatol 32: 827-838.
3. Bruce AJ, Dabade TS, Burkemper NM (2015) Diagnosing oral ulcers. JAAPA 28: 1-10.
4. Cohen A, Mathiasen VD, Schön T, Wejse C (2019) The global prevalence of latent tuberculosis: a systematic review and meta-analysis. Eur Respir J 54: 1900655.
5. Krawiecka E, Szponar E (2015) Tuberculosis of the oral cavity: an uncommon but still a live issue. Postepy Dermatol Alergol 32: 302-306.
6. Erbaycu AE, Taymaz Z, Tuksavul F, Afrashi A, Güçlü SZ (2007) What happens when oral tuberculosis is not treated? Monaldi Arch Chest Dis 67: 116-118.
7. Sharma S, Bajpai J, Pathak PK, Pradhan A, Singh P, et al. (2019) Oral tuberculosis - Current concepts. J Family Med Prim Care 8: 1308-1312.
8. Haverkos BM, Pan Z, Gru AA, Freud AG, Rabinovitch R, et al. (2016) Extranodal NK/T Cell Lymphoma, Nasal Type (ENKTL-NT): An Update on Epidemiology, Clinical Presentation, and Natural History in North American and European Cases. Curr Hematol Malig Rep 11: 514-527.
9. Al-Hakeem DA, Fedele S, Carlos R, Porter S (2007) Extranodal NK/T-cell lymphoma, nasal type. Oral Oncol 43: 4-14.
10. Haverkos BM, Coleman C, Gru AA, Pan Z, Brammer J, et al. (2017) Emerging insights on the pathogenesis and treatment of Extranodal NK/T Cell Lymphomas (ENKTL). Discov Med 23: 189-199.
11. Wu X, Li P, Zhao J, Yang X, Wang F, et al. (2008) A clinical study of 115 patients with extranodal natural killer/T-cell lymphoma, nasal type. Clin Oncol (R Coll Radiol) 20: 619-625.
12. Metgud RS, Doshi JJ, Gaurkhede S, Dongre R, Karle R (2011) Extranodal NK/T-cell lymphoma, nasal type (angiocentric T-cell lymphoma): A review about the terminology. J Oral Maxillofac Pathol 15: 96-100.
13. Meng W, Zhou Y, Zhang H, Jiang L, Wang Z, et al. (2010) Nasal-type NK/T-cell lymphoma with palatal ulcer as the earliest clinical manifestation: a case report with literature review. Pathol Oncol Res 16: 133-137.
14. Jabbari Azad F, Delavarian Z, Hatami M, Rahimi H, Abdolvahed MR (2017) Extranodal NK/T Cell Lymphoma with Destruction of the Uvulae: A Case Report. Iran J Otorhinolaryngol 29: 101-108.
15. Yanagi H, Nakamura Y, Takagi D, Kubota K (2012) Extranodal natural killer/T-cell lymphoma: a diagnostic dilemma. Rhinology 50: 325-331.
16. Zhou X, Lu K, Geng L, Li X, Jiang Y, et al. (2014) Utility of PET/CT in the diagnosis and staging of extranodal natural killer/T-cell lymphoma: a systematic review and meta-analysis. Medicine (Baltimore) 93: e258.
17. Dong GH, Li Y, Wan HF, He CY, Yang L, et al. (2018) Value of PET/CT in the prognosis of extranodal NK/T cell lymphoma. Zhonghua Yi Xue Za Zhi 98: 1256-1260.
18. Tse E, Kwong YL (2017) The diagnosis and management of NK/T-cell lymphomas. J Hematol Oncol 10: 85.
19. Chi AC, Neville BW, Krayer JW, Gonsalves WC (2010) Oral manifestations of systemic disease. Am Fam Physician 82: 1381-1388.
20. Islam NM, Bhattacharyya I, Cohen DM (2011) Common oral manifestations of systemic disease. Otolaryngol Clin North Am 44: 161-182.
21. Kumaraswamy KL, Vidhya M, Rao PK, Mukunda A (2012) Oral biopsy: oral pathologist's perspective. J Cancer Res Ther 8: 192-198.
22. Chen S, Forman M, Sadow PM, August M (2016) The Diagnostic Accuracy of Incisional Biopsy in the Oral Cavity. J Oral Maxillofac Surg 74: 959-964.
23. Avon SL, Klieb HB (2012) Oral soft-tissue biopsy: an overview. J Can Dent Assoc 78: c75.
24. Kamala R, Sinha A, Srivastava A, Srivastava S (2011) Primary tuberculosis of the oral cavity. Indian J Dent Res 22: 835-838.