Case 1
An 18-year-old female reported to the Department of Oral Medicine with the complaints of oral ulcers on the tip of tongue and buccal mucosa for last 1 week. There was no history of previous episodes of oral ulceration or weight loss. Mild fever, malaise, and stomach upset accompanied the ulcers. Her submandibular lymph nodes were palpable and tender bilaterally and she exhibited extreme pallor. Intraoral examination showed the presence of several ulcers on the tip of tongue, buccal mucosa, and gingiva [Figure 1]. The ulcers were irregular and surrounded by reddish blue hemorrhagic periphery. There was mild enlargement of interdental gingiva in maxillary and mandibular anterior teeth. There was no bleeding on probing and plaque and calculus were minimal. In this case, aphthous stomatitis and HIV associated oral ulcers were considered as differential diagnosis. Acute necrotizing ulcerative gingivitis and stomatitis which presents with gingival necrosis and punched out ulceration was also considered as a differential diagnosis. The irregular shape and presence of reddish blue periphery around the ulcers prompted us for the investigations. Hematological investigations revealed anemia (Hb-7.8 g%), high leukocyte count (34,900 mm$^3$) and low platelet count (25,000 mm$^3$). Peripheral blood smear showed multiple atypical myeloid blast cells suggestive of AML [Figure 2]. The patient was referred to an oncologist for further management.

Case 2
A 25-year-old male reported with the complaint of swelling in gum since 1 month. There was history of weakness, weight loss, and fever for 4–5 days. History of epilepsy, hypertension or any long-term medication was negative. Physical examination revealed extreme pallor. Intraoral examination showed the presence of several ulcers on the tip of tongue, buccal mucosa, and gingiva [Figure 1]. The ulcers were irregular in consistency, pale pink and devoid of stippling. There was mild enlargement of interdental gingiva in the anterior region [Figure 3]. Differential diagnosis of inflammatory gingival hyperplasia was considered. However, local factors like plaque and calculus were not proportional to the severity of the disease and there was no bleeding on probing. Drug induced gingival enlargement, due to phenytoin, nifedipine and cyclosporine was also ruled out by history. The above clinical presentation led to a provisional diagnosis of gingival enlargement due to leukemia which was further confirmed by hematological examination and peripheral smear. Blood investigations revealed severely decreased hemoglobin level (5 g%). Other blood investigations showed markedly increased leukocyte count (65,000 mm$^3$), reduced platelet count (25,000 mm$^3$), and reduced RBC count (1.69 million mm$^3$). Peripheral blood
smear showed evidence of multiple immature myeloid blast cells indicative of AML. [Figure 4] The patient was referred to a hematologic oncologist for further treatment.

Leukemia is a neoplastic disease characterized by excessive proliferation of immature white blood cells and their precursors. The malignant immature white blood cells increase in number at the expense of the bone marrow cells resulting in decrease in the number of erythrocytes causing anemia, weakness, fatigue, and pallor. Decreased platelets cause bleeding and petechiae. The decreased normal mature granulocyte number makes the patients prone to viral, bacterial and fungal infections and septicemia. The leukemic cell population also has the propensity to invade extramedullary tissues and its presence as leukemic infiltrates has been reported in the kidneys, lungs, bowels, breasts, testes, eyes, meninges, lymph nodes, liver, prostate, skin, and oral cavity.

Oral manifestations have been observed in 15–80% of leukemic cases and more commonly seen in acute (65%) than in chronic leukemia (30%). Acute leukemia is often associated with oral mucosal pallor, petechiae, ecchymoses, bleeding, ulceration, gingival enlargement, trismus, mental nerve neuropathy (“numb chin syndrome”), facial palsy, and infections. Enlargements of mucosa, gingiva, or masticatory muscles can occur due to direct infiltration by malignant leukocytes.[1–3]

There are only few reports of oral ulceration as first manifestation of leukemia. Dean[4] and Alizerai[5] et al. have reported oral ulceration with necrotic slough and erythematous periphery on gingival margin as first sign of AML. Oral ulceration in leukemia may be due to neutropenia and anemia. Gingival hyperplasia of marginal, attached, and interdental gingiva occurs may to infiltration of gingival tissues by neoplastic leukemic cells.

Oral lesions may sometimes be the first and only manifestation of potentially fatal conditions like leukemia. Such oral mucosal lesions are likely to be encountered by dermatologists, otolaryngologists, dental surgeons, general, and oral physicians. Awareness of clinical manifestations of systemic diseases can play a vital role in early diagnosis and referral for proper
treatment and potential complications of hemorrhage, necrosis, and infection can be avoided. Thus, oral lesions with atypical manifestations should be considered as important criteria for diagnosis of this occult hematological malignancy.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

References
1. Hiraki A, Nakamura S, Abe K, Takenoshita Y, Horinouchi Y, Shinohara M, et al. Numb chin syndrome as an initial symptom of acute lymphocytic leukemia: report of three cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997;83:555-61.
2. Dean AK, Ferguson JW, Marvan IS. Acute leukemia presenting as oral ulceration to a dental emergency service. Aust Dent J 2003;48:195-7.
3. Bodey GP. Oral complications of myeloproliferative disease. J Postgrad Med 1971;49:115-21.
4. Katz J, Peretz B. Trismus in a 6 year old child: A manifestation of leukemia. J Clin Pediatr Dent 2002;26:337-9.
5. Alirezaei S, Bakhshi M, Taheri J, Mafi A, Moghaddas O. Oral ulcerations as the first manifestations of acute leukemia. A case report. Open J of Stoma 2013;3:507-9.

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