

Case Report

Acute Myelogenous Leukemia Presenting with Primary Oral Lesions Initially Diagnosed as Acute Necrotizing Ulcerative Gingivitis

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Abstract

We report two cases that presented to the emergency department (ED) with oral pain, fever, and malaise, with physical findings leading to the initial diagnosis of acute necrotizing ulcerative gingivitis (ANUG), also known as Vincent's angina and trench mouth. Both cases on repeat exam, not only failed to improve, but required immediate admission. Both worsened rapidly despite appropriate antibiotic therapy, and both succumbed to their illness within a few days.

In both cases, the underlying diagnosis was acute myelogenous leukemia (AML) in blast crisis. It is likely that the leukemic infiltrates seen in monocytic variants of AML contributed to the gingival morphology which lead to the misdiagnosis of ANUG.

Case Report One

A 53-year-old female presented to the ED complaining of "mouth abscesses". She had been seen two days previously by her internist and started on clindamycin. Review of systems was positive for only fevers and malaise. Vital signs were as follows: temperature 38.9° Celsius (C), heart rate of 119 beats per minute (BPM), blood pressure 200/98 millimeters (mm)Hg, respirations 20 respirations per minute (RPM), and oxygen saturation 97% on room air. Exam was remarkable for the oral findings noted in Figure 1. There was no lymphadenopathy (LAD), cachexia, ill appearance, or hepatosplenomegaly noted.



Figure 1: Severe gingival pathology with violaceous discoloration in a 53 year old female patient.

A diagnosis of ANUG with moderate dehydration was made. The patient was administered IV fluids, metronidazole, ampicillin/sulbactam, and pain control therapy. She was noted to have been tolerating oral fluids, and her symptoms and vital signs improved in the ED. The case was discussed with Oral and Maxillofacial Surgery and immediate outpatient follow was scheduled for the next day.

The patient's general appearance was unchanged from ED discharge the following day in the clinic. Vital signs showed a heart rate of 110 BPM and a temperature of 38.5 °C. During the clinic visit, a Complete Blood Count (CBC) was ordered and demonstrated a white blood count of 121,000 with 36% blasts. At this point, the patient was admitted to Hematology/Oncology service and diagnosed with AML, phenotype M5. Two days into her hospitalization the patient underwent a hypotensive cardiopulmonary arrest and resuscitative efforts failed.

Case Report Two

A 45-year-old female presented to the ED with complaints of oral pain. She had been seen four days earlier at another facility, diagnosed with "a strep infection," and treated with a course of oral sulfamethoxazole/trimethoprim (SMT/TMP) and tramadol. Review of systems was positive for isolated malaise and fevers. Vital signs recorded in the ED were within normal limits. Oral exam revealed significant gingival changes, described much like

Case Report One, Figure 1. It was further noted that she exhibited cervical, post-auricular and axillary painless lymphadenopathy. A presumptive diagnosis of ANUG was made, and doxycycline was added to her previously prescribed SMT/TMP, along with an oral narcotic for pain control.

Three days later she returned to the ED with no relief of previous symptoms, additionally complaining of chest pain and shortness of breath. Her appearance was described as “moderate distress”. Vital signs revealed relative hypotension (102/66mmHg), tachycardia (129BPM), and hypoxia (89% on room air). Her temperature was 37.2 °C. No cardiopulmonary abnormalities were noted.

Treatment was initiated for presumed pneumonia and dehydration. She received IV fluids, ceftriaxone, and azithromycin. At a later time, Vancomycin was added to her antibiotic regimen. A complete blood count CBC showed hyperleukocytosis, with predominance of blasts.

A diagnosis of AML with blast crisis was made, prompting admission to the ICU and emergent leukapheresis. Despite aggressive therapy she rapidly deteriorated over the next two days and succumbed to her illness.

Discussion

Both patients described above presented with oral manifestations that were initially diagnosed and treated as ANUG. When therapy failed, alternate diagnoses were entertained, and the underlying cause of the gingival changes was definitively identified. In both of these cases, this diagnosis was AML. Herein we present a discussion of these two entities, including the pathophysiology, presentation, and diagnosis.

Acute Necrotizing Ulcerative Gingivitis

ANUG is an acute infectious gingivitis. This entity was first described in the late 1800’s by Plaut and Vincent and recognized again in the setting of World War I soldiers, thus earning the name trench mouth (Murayama, 1994). Some of its many names include trench mouth, Vincent’s disease/ - gingivitis/ - infection/ - stomatitis/ - periodontitis/ - angina, Gilmer’s disease, and fusospirochetal gingivitis.

Pathophysiology

A number of factors affecting immune function and opportunistic bacteria predispose patients to ANUG. They include malnutrition, sleep deprivation, emotional stress, poor oral hygiene, drug induced agranulocytosis, chemotherapy, and systemic disease. HIV is the single most important predisposing factor in developed countries (Rajandram, 2006).

Physical signs of ANUG range from oral ulcers to orofacial gangrene, also known as noma or cancrum oris (Enwonwu,

2006). It is most often seen in the setting of immunocompromised hosts, opportunistic bacteria including spirochetes, and anaerobic subgingival flora. In rare cases, *Aspergillus* species can cause disease destroying the free margin, dental crest, and interdental papillae (Khouri, 2003).

Clinical Presentation

ANUG presents with local pain, gingival ulceration, bleeding, metallic taste, and malaise. ANUG may also present with pseudomembrane formation, halitosis, fever, and lymphadenopathy. Necrosis causes ulcerations covered with a grayish-yellow pseudomembranes that when wiped away leave a bleeding ulcerated surface (Murayama, 1994).

Diagnosis and Initial Treatment

Treatment of the oral lesions involves the identification and treatment of underlying cause in addition to initiation of antibiotic therapy. As ANUG may be the first clinical sign of systemic disease, a complete lab work up is warranted. This should include a CBC with differential, metabolic profile, and HIV serology (Murayama 1994 and Enwonwu 2006). Bacterial control may be achieved with IV metronidazole, penicillin, oral debridement, daily chlorhexidine digluconate (0.12-0.2%), and hydrogen peroxide mouthwashes (Murayama 1994 and Enwonwu 2006). Pain may be controlled with oral opiates, benzydamine hydrochloride spray, and lidocaine gel (Buchanan 2006). Severe cases may prompt admission (Enwonwu 2008). Key treatments are correction of dehydration and electrolyte imbalance, and enteral nutrition when eating is impaired by pain. A dental or oral maxillary facial surgery consultation may be warranted.

Acute Myelogenous Leukemia

AML is a disorder of the hemopoietic progenitor cells. It is the most common myeloid leukemia with the median age at presentation in the eighth decade of life. Survival rate, especially in the elderly, remain dismal. Almost two thirds of young patients and 90% of older patients succumb to their disease (Rowe, 2010). Risk factors for developing AML include exposure to ionizing radiation (nuclear industry workers, atomic bomb exposure, and those involved in extensive flying), benzene (found in cigarettes), and cytotoxic chemotherapy (Estey, 2006).

Pathophysiology

All hematopoietic cells stem from a pool of pluripotent cells within the bone marrow. This pluripotent cell pool gives rise to two common stem cells lineages: lymphoid and myeloid. The myeloid stem cell is responsible for differentiation of monocytes, granulocytes, erythrocytes and megakaryocytes.

Clinical Presentations

AML results in inability of the cells to differentiate normally

and maintain proliferate appropriately. Each of the involved cell lines may be affected to varying degrees. Patients with AML will present with disorders of infection (WBC), bleeding (RBC or platelet), or organ infiltration from cell mass. Patients may also present with symptoms ranging from subtle manifestations (fever, malaise, and bone pain) to more severe symptoms like sepsis, shock, and death.

Diagnosis and Treatment

Diagnosis is suggested by the presence of blast cells in the peripheral smear. A bone marrow aspirate is needed to confirm and classify the type of AML according to WHO. The diagnosis of AML requires the presence of 20% blasts, subsequently shown to be of myeloid origin (Estey, 2006). There are two phases of therapy, the first is aimed at complete remission (CR), and the second is aimed at prolongation of CR, if it is achieved. Since 2003, progress has been made in elucidation of the molecular pathogenesis of AML allowing for therapy to target disease associated molecular defects (Dohner, 2009). Current therapy strategies include chemotherapy, cytotoxin-linked antibody therapy, stem cell transplantation, and supportive care for the disease complications. These include antibiotics, red cell or platelet transfusions, and growth factors (Dohner, 2009).

Conclusions

When a presumptive diagnosis of ANUG is made, it is imperative that the clinician maintain a high index of suspicion for a more serious underlying illness. Included in these illnesses are those resulting in an immunocompromised state, such as HIV, cancer, malnutrition, and neutropenia.

If a patient diagnosed with uncomplicated ANUG fails to improve despite aggressive oral hygiene and antibiotics where warranted, further investigation must be started emergently. Systemic signs and symptoms necessitate further efforts to elucidate the underlying pathology and rapidly initiate appropriate therapy aimed towards the inciting pathologic process.

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