**Atypical presentation of leukemia**

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**BACKGROUND**

- Chronic myelomonocytic leukemia (CMML) is a malignant hematopoietic stem cell disorder with overlapping features of myelodysplastic syndrome (MDS) and myeloproliferative neoplasm (MPN).
- Seen in older adults, median age of 65-75 year, predominantly males
- The estimated incidence of CMML is about 3 cases per 100,000 persons per year
- The most patient with CMML have genetic mutations occurring in the TET2, SRSF2, ASXL1 or RAS genes, but clonal cytogenetic abnormalities can be found in up to 30% of patients
- The most common cytogenetic abnormalities seen in CMML are rearrangements or deletions of chromosome 7 and trisomy 8.
- CMML is most aggressive type of myeloid leukemias
- Expected median overall survival is about 30 months
- About 15-30% people with CMML go on to develop acute myeloid leukemia

**CLINICAL COURSE**

Patient is an 81 year old male with past medical history of heart failure with preserved ejection fraction and aortic arch dissection status post aortic arch repair about 3 years ago who presented to primary care resident clinic with 2 painful tongue lesions (see image below) for about 5 days. He remembered biting his tongue before these lesions appeared. He was not on chemotherapy or immunomodulating agents. He does not have history or family history of autoimmune disease. Due to history of smoking (quit 1982), there was concern for malignancy (oral squamous cell carcinoma). He was prescribed lidocaine gel for pain relief and ENT referral was placed for possible biopsy.

Patient presented to ENT office but now has lesions on both sides of the tongue. He was diagnosed with hepatic stomatitis and valtrex and prednisone taper was prescribed. No biopsy was done at this time as it was thought to due to viral eruption. His tongue lesions resolved but recurred and went to see ENT and he was again prescribed valtrex and prednisone taper. No biopsy was done this time. He was seen again by ENT for third recurrence and biopsy was done. Per note, biopsy was normal (no pathology report found in the electronic medical record).

About a month later, patient presented to the emergency department with hematocrit requiring massive transfusion. The colonoscopy showed diverticulitis and ulcer at the sigmoid colon. There was an abnormal cellular population noted on the CBC. The peripheral smear had the morphological findings consistent with myelodysplastic/myeloproliferative process (such as CMML). He was discharged with outpatient hematology/oncology referral. He was seen by oral surgeon outpatient after discharge and diagnosed with traumatic ulcerative granuloma with stronal eosinophilia and repeat biopsy was done. The patient was prescribed dexamethasone rinse.

Before he could follow up with hematology/oncology outpatient, he presented back to the emergency department with hematocrit requiring massive transfusion. The hematology/oncology recommend repeating peripheral smear and bone marrow biopsy. The repeat peripheral smear showed monocytosis, neutropenia, borderline thrombocytopenia and no dysplasia. The bone marrow biopsy showed acute myeloid leukemia (36 blasts- see bone marrow pathology images below), trilineage dysplasia, normal karyotype, negative FISH. Hematology determined that he is not a candidate for bone marrow transplant. Since he had cytopenia, hypomethylating agents (Azacitadine + Venetoclax) were recommended. The oral lesions were treated with dexamethasone rinse and cutaneous lesions with clobetasol ointment. The patient was also placed on steroid taper as it probably helped with lesions in the past. Unfortunately, patient continued to decline and went on hospice.

**BRIEF SUMMARY OF CASE**

- We present the case of an older adult with multiple oral lesions, cutaneous lesions and gastrointestinal bleed due to leukemic infiltration.
- Peripheral smear concerning for myelodysplastic/myeloproliferative process (such as CMML).
- Bone marrow biopsy showed acute leukemia transformation.
- This case is made to consider leukemia in patients with oral/cutaneous lesions or gastrointestinal bleed.

**LEARNING OBJECTIVES**

- The oral/cutaneous lesions could be the first manifestation of serious systemic disease
- Consider further work up in patients with multiple ulcerations.
- CMML is most aggressive type of myeloid leukemia with poor prognosis and higher rate of acute leukemia transformation

**DISCUSSION**

There are many etiologies of oral ulcer and most are benign. The initial concern for this patient was oral and oropharyngeal cell carcinoma as patient had history of smoking but then diagnosed with hepatitis B antibodies and chronic ulcerative granulomas with stronal eosinophilia. The traumatic ulcerative lesions with stronal eosinophilia can affect all ages and usually secondary to trauma from biting, ill-fitting dentures or broken fillings. Our patient did not have dentures or broken fillings. He never had this type of lesions before and it would be unusual to suddenly start having oral lesions from biting his tongue and plus his lesions progressed to involve the buccal mucosa. There have been case reports of Behçet disease and Behçet like disease in MDS. The Behçet disease was on the differential diagnosis when was was hospitalized, however, Behçet disease usually presents in age 20-40 and our patient does not fit into this age group. The crohn’s disease was also on differential diagnosis, however, the patient likely had a higher chance of having ulceration in multiple location (oral, GI tract, skin) due to leukemia infiltration based on peripheral smear rather than the Crohn’s disease. The presence of skin infiltration is often associated with disease progression (transformation to acute leukemia) and poor prognosis. This patient had monosomy 5 with blasts in initial peripheral smear which is caused by chronic myelomonocytic leukemia (CMML). The bone marrow biopsy after few months showed acute leukemia transformation (M5 blasts with trilineage dysplasia). He has normal karyotype and fluorescence in situ hybridization (FISH) assay result came back normal (negative for BCR-ABL1 fusion). Our patient met all the diagnostic criteria for CMML.

The 2016 World Health Organization (WHO) diagnostic Criteria for CMML include all the following:

- Persistent (≥3 months) peripheral blood mononucleosis; absolute monocyte count >1000/microL and greater than 10 percent of the entire white blood cell differential
- Not meeting WHO criteria for BCR-ABL1 positive chronic myeloid leukemia, primary myelofibrosis, polycythemia vera, or essential thrombocythemia
- ≥20 percent myeloblasts + monoblasts + promonocytes in peripheral blood and bone marrow
- Dysplastic changes in one or more myeloid lineages. If myelodysplastic changes are absent or minimal, the diagnosis of CMML can be made if the above three criteria are met and:
- An acquired clonal cytogenetic (or mutational abnormality) is present in bone marrow cells or
- Persistent mononucleosis for ≥3 months and all other causes of mononucleosis have been excluded

The signs and symptoms of CMML are non-specific but if there is leukemic infiltration it tends to be found in the spleen, liver, lymph nodes and skin (often nodular). Less frequently the oropharynx is involved and it usually causes gingival hypertrophy. The leukemia can rarely involve gastrointestinal tract like this patient. There only have been few case reports of leukemic involvement of the gastrointestinal tract.

**CONCLUSION**

- This case was challenging given the presentation of uncommon symptoms for a disease that is seen infrequently.
- CMML occur in the male elderly population. This diagnosis should be considered if there are concerns for a possible autoimmune disease since Behçet disease given that there can be leukemic infiltration to the oropharynx and GI mucosa.

**REFERENCES**

15. Special thanks to OMERF photography lab for providing bone marrow pathology images.