

Pediatric Acute Promyelocytic Leukemia Presenting as Tongue Chloroma: Case Report

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Abstract

Chloroma is a rare extramedullary tumor consisting of immature myeloid cells. Occurring in 1%-2% of patients with Acute Myelogenous Leukemia (AML). In a significant proportion of cases, it displays myelomonocytic or pure monoblastic morphologic features, which correlate with the French-American-British (FAB) classification of AML M4 and M5 respectively. Cytogenetically, chloroma occurs in association with a variety of chromosomal abnormalities, including MLL rearrangement in V and T. Usual sites include the skin, soft tissue and lymph nodes. Tongue chloroma is extremely rare. Here we report a case of pediatric Acute Promyelocytic Leukemia (APL) presenting with tongue chloroma. Furthermore, the prevalence of myeloid sarcoma of the spine was 1.0% among all patients with acute and chronic myeloid leukemia.

Keywords: Tongue chloroma; Myeloid sarcoma; Acute promyelocytic leukemia

Introduction

Chloroma also known as Myeloid Sarcoma (MS) Granulocytic Sarcoma or Myeloblastoma is a rare extramedullary tumor consisting of immature myeloid cells occurring in 1%-2% of patients with AML [1,2]. Less commonly it occurs during the course of myelodysplastic syndrome, chronic myeloid leukemia and other myeloproliferative diseases [3]. In a significant proportion of cases it displays myelomonocytic or pure monoblastic morphologic features which correlate with the French-American-British (FAB) classification of M4 and M5 respectively [4].

Cytogenetically MS has been found to occur in association with a variety of chromosomal abnormalities including MLL rearrangement in V and T. Usual sites include the skin, soft tissue and lymph nodes. Rare cases of tongue chloroma have been previously described in adults. It is extremely rare to be associated with Acute Promyelocytic Leukemia (APL) [5]. Here we report a case of pediatric APL presenting with tongue chloroma.

Case Presentation

Patient is a three and a half year old girl referred to our cancer center with one week history of growing tongue masses and abnormal CBC. She had two masses that erupted one after the other reaching about 1.5 cm each and causing progressive dysphagia and odynophagia. On examination her upper gum was erythematous and slightly hypertrophied; the tongue was covered with whitish coat and the masses were fungating one from the center and the other from the left lateral side of the tongue as shown in Figures 1a-1c.



Figure 1: Lateral sides of the tongue A) Showing the first mass after two days of its eruption, photo taken by the family; B) Showing the masses upon referral to us after one week; C) Complete resolution of the masses after one week of induction treatment with ATRA and Idarubicin.

She had fever for one day but no bleeding or any other symptoms. Aside from the oral findings and fever of 39.4°C axillary, exam was remarkable for pallor, tachycardia upto 151 beat/minute and ejection systolic murmur. Family tried local antifungals which were not useful and after a week of the onset of symptoms she had a CBC done that revealed anemia (hemoglobin 4.6 GM/DL), leukocytosis with neutrophilia (WBC 29 K/UL, 74% neutrophils and 24% lymphocytes and 0.6% monocytes) and thrombocytopenia (platelet 32 k/UL). Blood film and bone marrow aspirate showed atypical promyelocytes with cytoplasmic granulation (Figure 2).

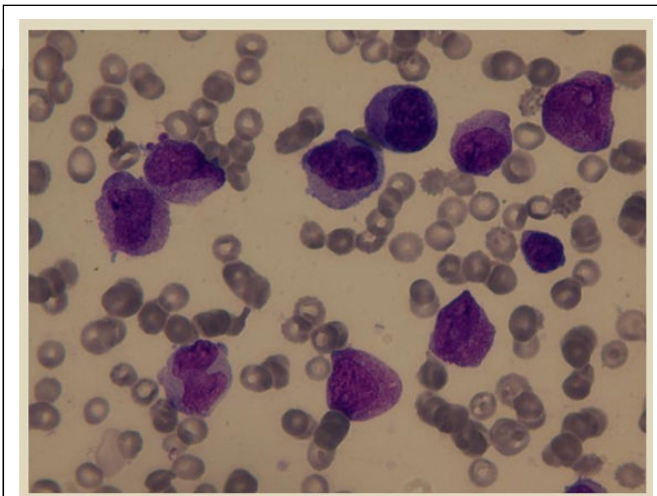


Figure 2: Bone marrow aspirate showing atypical promyelocytes with cytoplasmic granulation.

Results and Discussion

Flowcytometry was consistent with AML M3 with 67% of total peripheral blood cells positive for CD117(D), CD13, CD33, CD64, VD58 and cMPO. FISH study confirmed the presence of PML/RARA gene rearrangement in 91% of cells. Karyotyping showed 46, XX, t(15;17) (q24;q21) 46, XX confirming the diagnosis of acute promyelocytic leukemia. Coagulation studies showed prolonged PT, INR and PTT of 20 seconds, 1.74, 50.9 seconds respectively [6]. Fibrinogen was low at 140 mg/dL. Next generation sequencing for myeloid panel came back positive for TP53 exon #08 NM_000546.5:c.845G>A (alternate variant frequency 48%), KRAS exon#02 NM_033360.2:c.35G>A (alternate variant frequency 1%) and NRAS exon # 02;02.

NM_002524.4:c.34G>A; c35G>A (alternate variant frequency 4%; 12%). Biopsies were not taken from the lesions, assuming them to be chloromas. Induction treatment per standard pediatric APL therapy was started with All-Trans-Retinoic Acid (ATRA) (25 mg/m²/day divided q12 hrs on days 1-30), dexamethasone (10 mg/m²/day divided BID on days 1-5) and Idarubicin (12 mg/m² on days 1, 3 and 5) after echocardiogram showed normal heart structure and function [7,8]. During therapy, she was supported with blood products, FFP and antibiotics. No significant bleeding occurred. Patient did not develop ATRA differentiation syndrome or any other complication of treatment.

Patient showed a remarkable response to therapy with the oral lesions resolving within one week of starting Induction therapy.

Tongue chloroma is extremely rare and being associated with APL is further uncommon. A medline search of English Language literature revealed four adult reported cases. The first case was a patient with APL [5]. He was 45-year-old when he presented with tongue masses and found at the same time to have promyelocytes in the peripheral blood smear and bone marrow. Tongue biopsy was consistent with promyelocytes. ATRA 45 mg/m² and daunorubicin plus cytarabine were started. The patient developed ATRA syndrome 48 h later, with fever, pulmonary infiltrates and pleural effusions. On day 4, the patient developed worsening dysphagia with purulent oropharyngeal exudates that were postulated to be related to local differentiation of promyelocytes.

The exudates and the tongue ulcer gradually improved and had completely resolved by day 16. The patient had completed chemotherapy and remained well in a cytogenetic and molecular remission at 1-year follow-up [9]. Despite the fact that chloromas are usually associated with FAB classification of M4 and M5 subtypes, the second reported case of tongue chloroma, similar to the previous patient, showed neither of the previous morphologies. The patient was a 55-year-old male who presented with biopsy proven tongue chloroma. His bone marrow biopsy revealed AML M2 with no cytogenetic abnormalities. Patient was started on induction chemotherapy and achieved complete remission. Chloroma can herald, follow or occur with the diagnosis of primary AML. It can also be seen upon relapse. The latter was the scenario of the third reported case of a 19-year-old male with primary refractory acute myeloid leukemia who received salvage therapy with mitoxantrone and cytarabine combination [6]. He received consolidation therapy 3 months later with a matched-unrelated-donor stem-cell transplant. The disease relapsed in the Bone Marrow (BM) 9 months after the initial stem-cell transplant and was successfully treated by repeat transplant from the same donor. Ten months following repeat transplant, the patient presented with an increasing number of extramedullary sites of biopsy-proven disease relapse (i.e. cranial and peripheral nerves, tongue, abdominal wall and chest wall). Repeated biopsy of the BM and chimera study showed no morphologic evidence of leukemic infiltrate with 100% donor-cell population. He was treated with radiation therapy and gemtuzumab ozogamicin for the isolated extramedullary leukemia relapse.

Although chloromas more commonly occur with AML, they can be seen during the course of Myelodysplastic Syndrome (MDS) chronic myeloid leukemia and other myeloproliferative diseases. The fourth reported case of tongue chloroma was associated with MDS. She was a 72-year-old woman who was previously diagnosed with MDS and refractory anemia who later developed a biopsy proven tongue chloroma. She was treated with radiation therapy and responded well with tumor shrinkage and total resolution two months after the completion of therapy.

Conclusion

Although it is unlikely for APL to present with chloromas and exceedingly rare to present with tongue chloromas, still it may occur. Increased awareness of the oral cavity as a site of chloromas will result in earlier referrals to specialized oncology centers. Further microscopic examination of bone marrow smear and cytogenetic analysis plays an important role to determine the source of MS, which are also very vital for subsequent treatment.

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