Granulocytic Sarcoma (Chloroma) Presenting as Multiple Sites in Oral Cavity: Report of a Case

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Abstract

Granulocytic Sarcoma (GS), an unusual extramedullary tumor, is composed of immature granulocytic precursor cells. The intraoral occurrence of this tumor is extremely rare. Here, we report a case of GS with palatal swelling, gingival lesions in maxilla and mandible and aleukemic presentation in a 45- year- old male.

Keywords: Leukemia; Sarcoma; Myeloid; Extramedullary

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Introduction

Granulocytic Sarcoma (GS), also known as chloroma, extramedullary myeloid tumor, myeloid sarcoma, leukocytic sarcoma and myelosarcoma is defined as an extramedullary tumor mass of immature cells of myeloid lineage [1-3]. Myeloid growth factors primarily enhance leukemic proliferation [4].

The first case of GS was reported by Burn in 1811 [5]. In 1853, King used the term chloroma, because of its greenish color, to refer to GS whose tumoral cells produced myeloperoxidase with exposure to the air [6], but because this tumor is not always green, granulocytic sarcoma is a more appropriate term [2].

In the head and neck areas, GS is often seen in the soft tissues of orbit, nasal cavity and paranasal sinuses, but it can also appear in any location throughout the body including the skin, breasts, gastrointestinal, genitourinary, respiratory tracts, peripheral nerves and lymph nodes [7-10]. Uncommon sites are the jaws and lips [11]. There is a female predilection and most cases occur in childhood [11].

Although intensive chemotherapy is the main treatment choice for GS, the related death and relapse rates are the essential factors for prediction of prognosis of GS [1, 2, 12].

Recently, improving leukemia stem cell biology understanding and considering interaction of the stroma and the host response, may introduce more markers which show the value of result prediction and guide therapy [12]; for example, CD47 which is highly expressed on leukemic stem cells compared to the normal hematopoietic stem cells and microRNA expression patterns are additional markers for predicting worse survival rate [12]. Some degrees of improvement can be achieved after surgery and radiotherapy, but the prognosis of GS is poor and most patients die within months [13]. The intraoral occurrence of GS is extremely rare [14]. This report describes a case of GS which affected both jaws. It seems that only 2 cases have been reported in the literature with this appearance [14, 15].

Case Report

A 45-year-old male referred to Shahid Beheshti Maxillofacial Pathology Department with a two year history of generalized proliferative gingival maxillary lesions with palatal right side swelling and mandibular labially gingival lesions (Figure 1).

The lesions were asymptomatic, without any bleeding or purulent discharge. The right submandibular lymph node was palpable and the patient noticed this swelling after the extraction of the third molar one month prior to his visit to our department. The gingivally lesions were red and soft with irregular surfaces, and the palatal swelling had a purple-gray appearance with intact overlying mucosa (Figure 2).

Radiographic examination revealed a moderate bone loss similar to a periodontal disease.

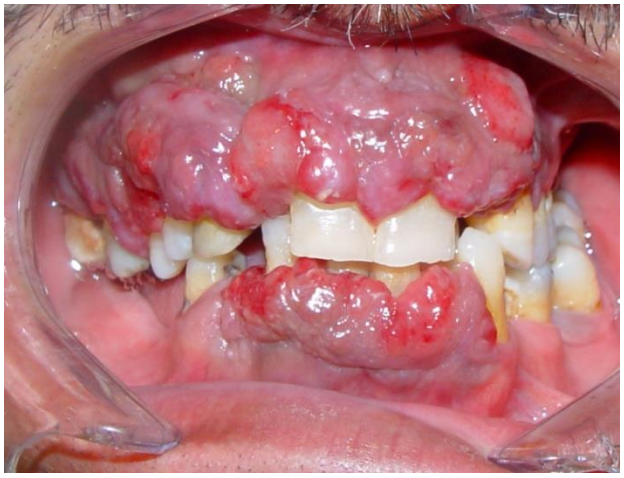

Figure 1. It shows the appearance of generalized proliferative gingival lesion in patient.

Laboratory test results were normal, so the patient's diagnosis was stated as inflammatory and reactive hyperplastic lesions.

The patient's teeth were extracted. Only 2 maxillary central incisors were preserved for esthetic. Tissues needed for histopathologic evaluation were obtained from the gingivectomy of gingivally proliferative masses and with a full thickness flap from the palatal swelling.

Soft tissue specimens were fixed in 10% neutral buffered formalin and embedded in paraffin blocks. For standard pathological examination, the sections were prepared with H&E stain.

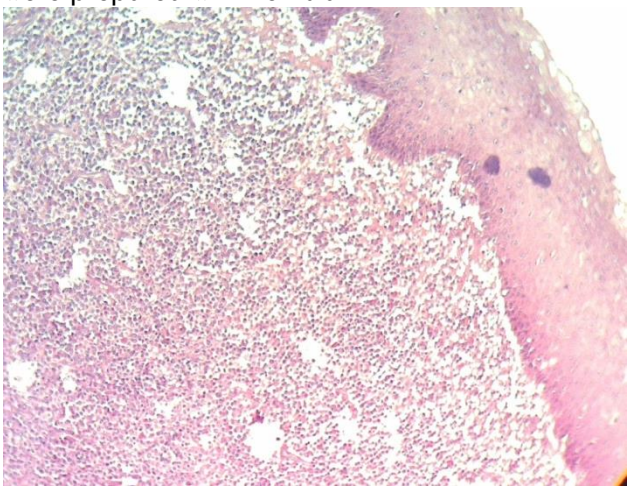

Figure 3. It shows histological specimen showing a dense cellular infiltration in the stroma just beneath the epithelium.
HE stains .Original object lens magnification 4x.

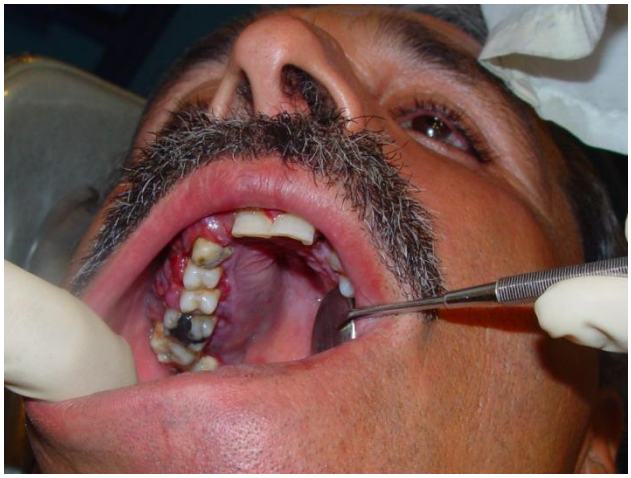

Figure 2. It shows the palatal right side swelling with intact overlying mucosa.

The slides of both gingival and palatal specimens showed a dense cellular infiltration under the epithelial layer in deeper portions.
The cells were mononuclear which showed pleomorphism with moderately amount of cytoplasm and round to oval nucleus with prominent nucleoli. These cells did not have a characteristic phenotype. Therefore, a series of differential diagnosis such as large cell lymphoma, plasmacytoma, poorly differentiated carcinoma and lymphoblastic leukemia was suggested (Figure 3-4).

For the final diagnosis, a panel of antibodies was applied using the Immunohistochemistry (IHC) method. The tumor cells were diffusely positive with

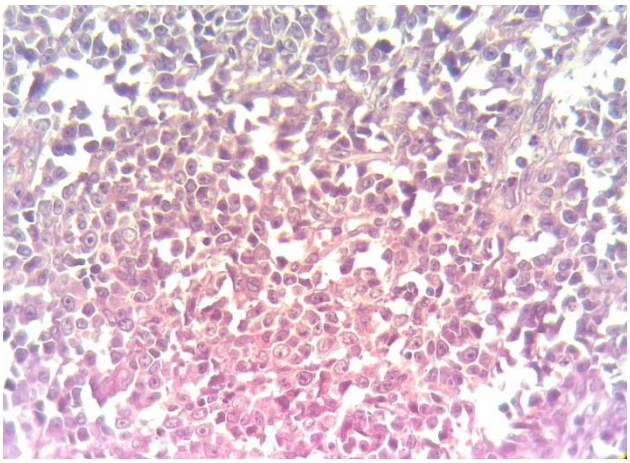

Figure 4. It shows larger magnification demonstrates cells and nuclei characteristics: mononuclear cells with moderately amount of cytoplasm and round to oval nucleus with prominent nucleoli. Original object lens magnification 40 x.

antibodies against LCA, negative with CD20, CD3 and CD79a and positive with C-kit. Therefore, according to the IHC results in combination with morphological features, the final diagnosis was made as granulocytic sarcoma.

The patient was then referred to the Hematology Department. Bone marrow biopsy and bone marrow aspiration were negative for malignant cells, and the laboratory tests revealed only an increase in the monocyte population.

The treatment protocol was 5 courses of induction chemotherapy with cytarabine, idarubici and doxorubicin and adjuvant whole brain radiotherapy.

During the chemotherapy, the patient had neutropenia and thrombocytopenia. Although we tried to manage the complications, the clinical outcome became worse, and the patient died after a heart attack 10 months post diagnosis.

Discussion

Granulocytic Sarcoma is a tumor -like collection of immature myeloid precursor cells [7]. In 1892, Dock found an association between granulocytic sarcoma and leukemia for the first time [16, 17].

Clinically granulocytic sarcoma may occur in three categories: In a patient previously known to have Acute Myeloid Leukemia (AML); as a sign of blast transformation in a patient with Chronic Myeloid Leukemia (CML), or other chronic myeloproliferative disorders; in a patient who was previously well [18].

Nearly 40 cases of intraoral GS have been reported from 1883 up to now. Involvement of oral tissue without detectable evidence of leukemic cells in peripheral blood and bone marrow was observed in 14 cases [6, 19-30]; and only two patients had both Jaws involvement [13, 14].

The highly invasive and aggressive clinical behavior of GS might be explained by the findings of Kabayashi et al. [31, 32]. In one study, they found the capability of GS-derived cell line to bind both the bone marrow and the skin fibroblast, which resulted in the formation of extramedulary myeloid tumor [31].

Gingival tissues due to expression of endothelial adhesion molecules, which may increase leukocyte infiltration, are more susceptible to leukemic cell invasion [7, 8, 16]. However, the association of AML with gingival occurrence of GS is extremely rare [14].

Diagnosis of GS in a patient with known myeloid leukemia is not difficult. However, when presented as an isolated entity, like our case, it may be clinically misdiagnosed as an inflammatory lesion such a Pyogenic Granuloma (PG), Peripheral Giant Cell Granuloma (PGCG), gingival or periodontal abscess. This may lead to surgical procedures such as gingivectomy; however, the management of GS is different. The diagnosis of GS is based on both histopathologic and IHC methods. Positive staining for CD45 is needed to confirm the hematological origin. In the next step, one or more myeloid markers such as myeloperoxidase, lysozyme, CD13, CD14, CD33, CD34, CD68 or C-Kit should be positive [2]. In the present case, tumoral cells were stained positively with C-Kit.

In patients without evidence of leukemia, antileukemic chemotherapy regime upon the initial diagnosis of GS is associated with a lower probability of AML development [33], but the overall survival rate of patients with intraoral GS is poor [18]. According to the literature, only four patients survived more than 3 years [14].

Therefore, regular therapies such as treatment with combining growth factors and pharmacologic differentiating agents [4], and assessing appropriate allograft procedures in the remission period [12] may be of importance.

Conclusion

Because GS may be seen before the diagnosis of leukemia, or it could be presented without bone marrow involvement (the same as our case), it is advisable to include GS in the differential diagnosis of severe gingival hyperplasia.

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Conflict of Interest

The authors have no conflict of interest in this study.

Authors' Contribution

Fatemeh Mashhadi-Abbas and Neda Kargahi designed and wrote this report, Mohammad Moshref and Ali Lotfi have been done excisional biopsy and collected the data .All authors read and approved the final manuscript.

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