Case Report

Primary intraoral granulocytic sarcoma: A rare case presenting as generalized gingival enlargement

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Abstract

Granulocytic sarcoma (GS) is an extremely rare condition involving infiltration of myeloblasts or immature myeloid cells in an extramedullary site. It is also known as chloroma, myeloid sarcoma or extramedullary myeloid tumor. It usually occurs concomitantly with acute myelogenous leukemia or with the onset of blastic phase of chronic myelogenous leukemia. On rare occasions, it evolves even before the onset of leukemias, and when it precedes leukemias without any overt signs, it is referred to as the primary type. Although GSs can involve any body part, localization in the oral cavity is extremely rare. The recognition of this rare primary entity is important because early aggressive chemotherapy can cause regression of the tumor and improve survival. Here, we report a rare case of GS in a nonleukemic 62-year-old female who presented with generalized gingival enlargement involving both maxilla and mandible.

Key Words: Generalized gingival enlargement, granulocytic sarcoma, myeloid sarcoma

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INTRODUCTION

Granulocytic sarcoma (GS) is a rare solid tumor composed of primitive precursors of the granulocytic series of white blood cells that include myeloblasts, promyelocytes and myelocytes occurring in an extramedullary site. It is also known as chloroma, GS or extramedullary myeloid tumor. It was first described in 1811 by Burns and later termed Chloroma in 1853 because some typical forms of GS gave a characteristic green color caused by the enzymatic reaction of myeloperoxidase (MPO) in the tumor cells. Subsequently, it was appropriately termed GS because of the tumor cells' origin from the granulocytic lineage.[1-3]

GS usually occurs concurrently along with the course of an acute or chronic myeloid leukemia or with other types of myeloproliferative disorders[4] or may be the first manifestation of a relapse or infrequently may precede leukemias by months to years.[5]

Although GS can occur at any extramedullary site, its occurrence in the oral cavity is an extremely rare event with only 45 cases being reported. The involvement sites in the oral cavity are highly variable and it has been reported to affect the hard and soft palates, gingivae, buccal mucosa, lips, tonsils and tongue.[6-8] Although oral manifestation of this disease has been reported, its presentation in the gingiva as a generalized gingival enlargement involving both the upper and lower jaws in a nonleukemic patient has not been reported in the literature.

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Hence, we report an extremely rare clinical presentation of intraoral GS presenting in the upper and lower jaws as a generalized gingival enlargement in an aleukemic patient.

CASE REPORT

A 62-year-old female patient reported to the Dental Hospital, Department of Oral Pathology with a 4-month history of gingival enlargement and bilateral tender submandibular lymph node enlargement. Clinical intraoral examination revealed a generalized maxillary and mandibular gingival enlargement involving the facial and the lingual gingiva, firm in consistency and covering two-thirds of the teeth [Figure 1]. The lesions were asymptomatic, without any bleeding or purulent discharge. Teeth present showed generalized attrition and Grade 3 mobility in relation to 37 and 47 and were tender on percussion. Extraoral examination revealed bilateral tender, mobile submandibular lymph nodes. A thorough medical history revealed a 10-year history of hypertension and was on medications. Panoramic X-ray revealed generalized bone loss pattern and severe alveolar bone resorption in relation to 37 and 47 resembling floating teeth. It also revealed a diffusely bordered radiolucency in the periapical area of left maxillary lateral incisor and right maxillary second molar [Figure 2]. Complete hematological and biochemical investigations were all within normal limits except for an elevated erythrocyte sedimentation rate.

The clinical differential diagnosis included drug-induced gingival enlargement because of the 10-year history of antihypertensives and idiopathic gingival enlargement. Because of the underlying bony changes, inflammatory gingival enlargement was considered, but as the enlargement was firm in consistency, an inflammatory etiology was ruled out.

Considering the history and the generalized nature of presentation, an incisional biopsy was planned for and subsequently, a biopsy was done from the mandibular anterior facial gingiva and submitted for histological evaluation [Figure 3]. Satisfactory hemostasis was achieved after the biopsy procedure, and 7-day postbiopsy healing was uneventful.

On gross examination, the excised material showed a central grayish-white nonspecific soft tissue material. H&E sections revealed dense cellular infiltrate of pleomorphic cells just beneath the epithelium exhibiting moderate cytoplasm and round to oval-shaped polymorphic nuclei with inconspicuous nucleoli [Figures 4 and 5]. A histological differential diagnosis included a high-grade non-Hodgkins lymphoma, anaplastic large cell lymphoma and lymphoblastic leukemia. However, since the tumor cells' phenotype was not characteristic for a diagnosis to be made, an immunohistochemical analysis with a panel of antibodies was planned for further characterization of the lesion. Tumor cells demonstrated a positive reaction to CD43 [Figure 6] and strong positive reaction to MPO [Figure 7] monoclonal antibodies; whereas, they were negative to CD3, CD20, CD79, ALK and Tdt monoclonal antibodies. Based on the above histological and immunohistochemical findings, a diagnosis of GS was made.

A prompt referral was made to the specialty cancer center, and a complete hematological workup was done. Repeated peripheral blood films and the bone marrow aspirate were all negative for the cytologic evidence of acute leukemia. Since the blood and bone marrow findings did not reveal any leukemic findings; a final diagnosis of the primary extramedullary myeloid tumor was made. The patient was referred to cancer specialty hospital for further management.

DISCUSSION

GS is an extramedullary localized tumor mass composed of immature cells of the granulocytic lineage. Although GS can occur virtually anywhere in the body, intraoral GS is rare and can occur in the palate, the gingiva and the buccal mucosa. A structured search of GS in the PubMed online from 1981 to 2014 revealed only 45 cases

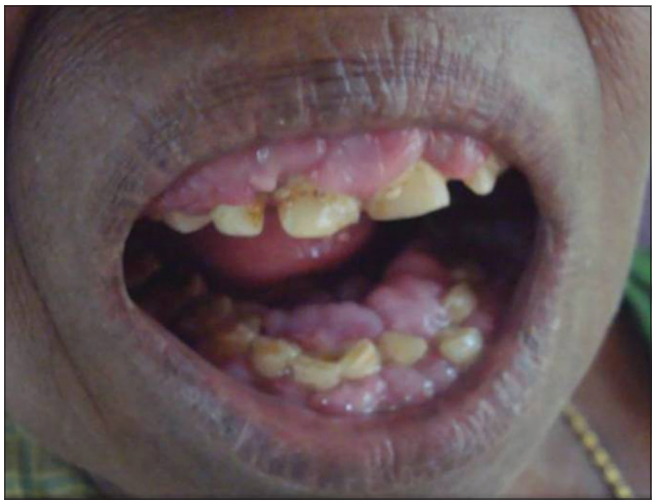

Figure 1: Intraoral clinical appearance of granulocytic sarcoma, presenting as maxillary and mandibular gingival enlargement

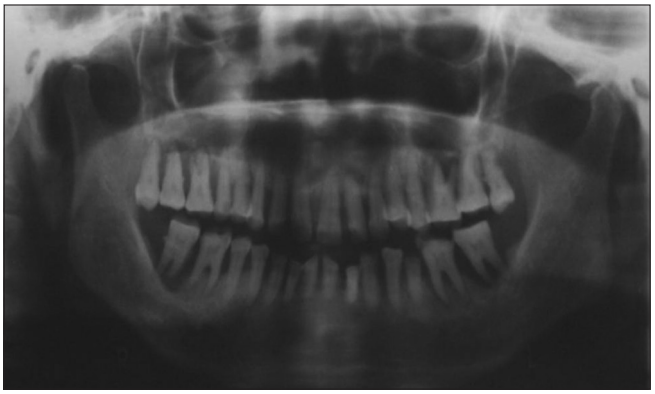

Figure 2: Panoramic X-ray showing generalized bone loss and severe bone resorption in relation to 37 and 47

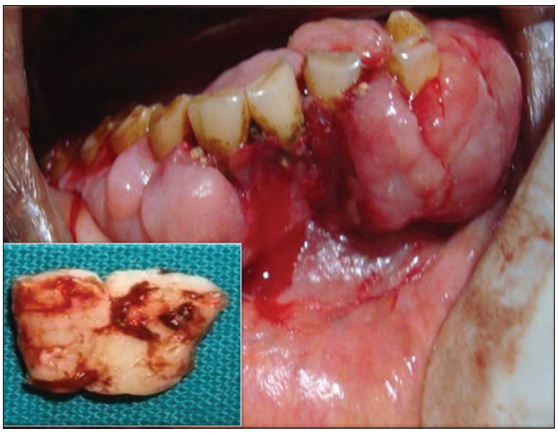

Figure 3: Incisional biopsy from the mandibular anterior facial gingiva

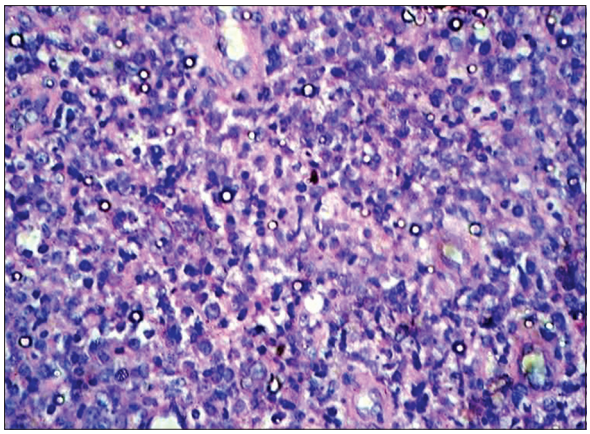

Figure 4: Histology revealing dense cellular infiltrate of pleomorphic cells exhibiting moderate cytoplasm (H&E stain, ×100)

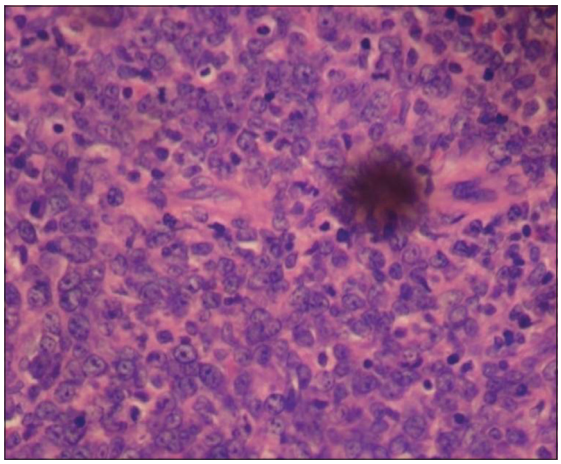

Figure 5: Histology revealing dense cellular infiltrate of pleomorphic cells exhibiting moderate cytoplasm and round to oval polymorphic nuclei with inconspicuous nucleoli (H&E stain, ×400)

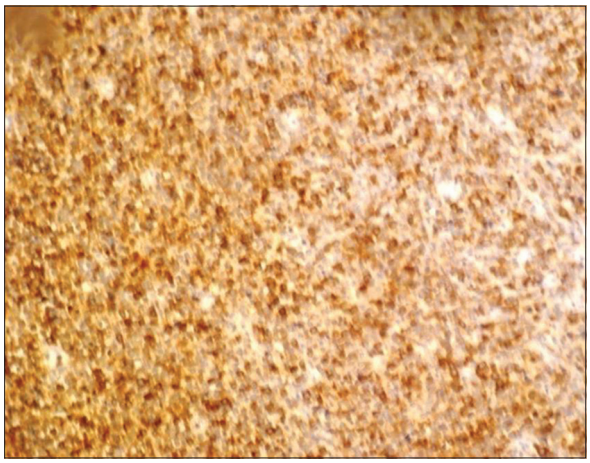

Figure 6: Immunohistochemistry showing the tumor cells having strong positive reaction to CD43 (IHC stain, ×100)

of intraoral GS. However, most of the cases involved just one site and presented clinically either as a mass or mucosal ulceration. The occurrence of intraoral GS as multiple masses involving multiple sites is extremely rare with only two reported cases in which the tumor involved both the maxilla and the mandibular gingivae.

The clinical course of GS can be varied and can occur in three possible clinical situations: In association with AML, in association with chronic myeloproliferative disorders or as a predecessor to AML.[9] The majority of GS have occurred in patients with known leukemia or in whom leukemias eventually developed. However, the occurrence of lesions before the onset of overt disease is rare, and when it does so, most cases proceed to overt leukemia within 2–4 years. However, uncommonly, cases without progression have also been described.[10-12] Although GS has reportedly occurred in nonleukemic patients, there are only two reported cases of intraoral GS in nonleukemic cases.

To the best of our knowledge, there are no cases of intraoral GS reported in multiple locations in a nonleukemic setting. Thus, the present case is only the first intraoral case reported which presented as a generalized gingival enlargement involving both the maxilla and mandible in a nonleukemic patient.

The diagnosis of GS may be difficult when it occurs in the oral cavity, especially with no history of hematological disorders or peripheral blood or bone marrow involvement. Moreover, when such innocuous appearing lesions are confronted in the gingiva, a high percentage of the chances is that these lesions are diagnosed as periodontal abscesses, pyogenic granuloma, carcinoma or malignant lymphomas. Moreover, on rare occasions, when they clinically manifest as generalized gingival enlargements, with an underlying medical condition as in the present case, they are misdiagnosed as drug-induced gingival enlargements.[13]

Although histologically, GS presents with sheets of relatively monomorphic intermediate to large size polyhedral cells with irregular nuclear contours, vesicular chromatin, variably prominent nucleoli and frequent mitotic figures, diagnosis of it is complicated by the inconsistency of its morphologic features.[14,15] Many a times, they may be misdiagnosed as

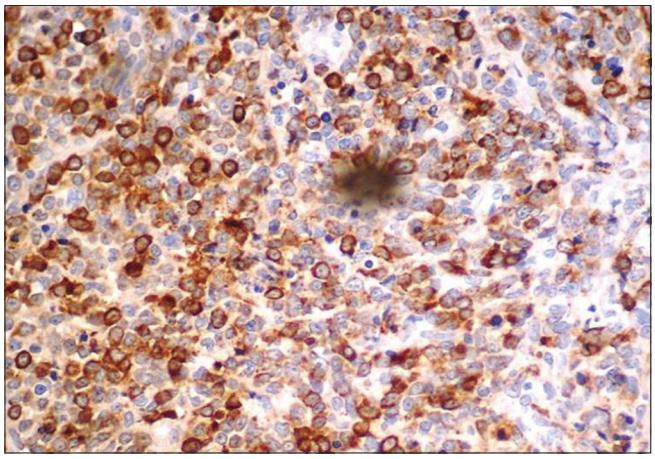

Figure 7: Immunohistochemistry showing the tumor cells having strong positive reaction to myeloperoxidase (IHC stain, ×400)

malignant lymphomas or lymphoblastic leukemia as it happened in the present case. In such cases, immunohistochemical studies may help in characterizing the lesions and in reaching a definitive diagnosis.

These inconsistent histological findings prompted us to consider a panel of immunohistochemical markers for characterization of the tumor. The panel of antibodies included were CD3, CD20, CD43, CD79, ALK and Tdt. A T-cell lymphoma was ruled out as CD3 was negative. B-cell lymphomas were ruled out as CD20 and CD79 were negative. A negative ALK excluded anaplastic large cell lymphoma. A negative TdT practically excluded lymphoblastic leukemias. The tumor was only positive for CD43 and with no reactivity to the lymphoid antigens; a possibility of a GS was raised and was further confirmed by its strong positivity for MPO.

Despite advances in treatment modalities and sincere attempt to improve the quality of life, leukemias still remain a life-threatening disease with no remarkable improvement in prognosis and survival with an estimated 24,090 deaths out of the estimated 52,380 number of new cases in 2014 with a 5-year survival rate of only 52.7% of all forms of leukemias.[16]

However, Cheng *et al.* concluded that the survival rate of GS is only 30.8%, and the survival rate of primary GS (50%) is higher than GS associated with malignancy (22.2%).[17] Although there is no standard protocol for the treatment of GS, it is imperative that these primary lesions are diagnosed in their initial stages and an early start of antileukemic therapy would promise a longer survival for these patients who are mostly young.

To conclude, intraoral primary GS is an unusual tumor with nonspecific clinical and pathologic features. The general dentist in the dental practice is frequently presented with such oral pathological lesions that are ambiguous in clinical presentation and behavior. Very often, the dentist is faced with the challenge of making a decision to commence treatment as desired by the patient or pursue further investigation to rule out more potentially morbid diagnosis. Such a cautious stance by the dentist can be possible only if the suspicion index for potentially life-threatening lesions is high in the differential list. Alternatively, these clinical situations necessitate the services of an expert that would obviate the chance of missing a diagnosis.

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Conflicts of interest

There are no conflicts of interest.

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