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Oral Granulocytic Sarcoma: A case report

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Abstract

Granulocytic sarcoma (GS) is a localized infiltrate of immature granulocytes in an extramedullary site. This lesion is most frequently associated with leukemia, but can occur associated with others myeloproliferative disorders. GS can affect virtually any part of the body, but lesions in the oral cavity are rare, with only 37 cases described.

Case Description: We present a rare case of GS in a 23-year-old female, with a prior history of acute myeloid leukemia, presenting with a solitary mandibular swelling in the region of the erupting 3rd lower left molar. After biopsy, conventional immunohistochemical stains were positive for CD45 (hematological marker) and myeloid markers, such as myeloperoxidase, and CD68, demonstrating myeloid lineage with monocytic cells differentiation, suggesting the diagnosis of GS associated to Acute Myeloid Leukemia (AML-M5).

Clinical implication: Although GS is a rare tumor in oral cavity, and its diagnosis is usually difficult, the clinician must know about its existence to make differential diagnosis.

Keywords: *Oral cavity, acute myeloid leukemia, granulocytic sarcoma, chloroma.*

Introduction

The granulocytic sarcoma (GS) is an extramedullary solid tumor composed of immature cells of granulocytic lineage (myelocytes) (1). It was first described in 1811 by Burns and King, in 1853, used the term Chloroma for the green color of the tumor when exposed to air, due to the presence of myeloperoxidase in the tumor cells (1). As this color was inconsistent and the lesion consisted of immature cells of granulocytic lineage Rappaport (1996) (2) suggested to designate this neoplasm as granulocytic sarcoma (1,3).

In 1892, Dock associated GS to leukemia (1) and more recently this tumor has been associated to myeloid leukemias and other myeloproliferative disorders, such as polycythemia vera and myeloid metaplasia (2,4), as well as in the evolution of myelodysplastic syndromes (5).

The oral involvement is considered rare and only 37 cases have been described between from 1883 and 2008 (6,7). The intraoral location is diversified and sites as the hard and soft palates, tongue, maxillary and mandibular gingival, buccal mucosa, lips, tonsils, periapical region have been affected.

Case Report

Female patient, 23 year-old, was admitted in May, 2006, at Walter Cantídio University Hospital in Federal University of Ceará, Brazil, for strong pain in the lower and upper limbs, epistaxis and metrorrhagia, associated to ecchymosis and bone pain in the retrosternal region and coxofemoral joints. The patient had fever, and blood studies evidenced thrombocytopenia and blasts could be seen in the peripheral blood. A myelogram revealed 77% of blastic infiltration, compatible with acute leukemia, suggesting, but not concluding, a hypogranular variant of the promyelocytic leukemia. The immunophenotype analysis showed to be negative for CD34, HLA-DR, CD41, CD14, CD19, CD3, and positive for CD33 and CD117. Chemotherapy was started (June 6th) with ARA-C 200mg/m² and Daunoblastin 45mg/m², at the 4th day Daunoblastin was discontinued. At the 6th day of chemotherapy methotrexate, ARA-C and dexamethasone intratechal was administrated, this combination was suspended after five cycles (16th day of chemotherapy) due to hemodynamic instability, but the systemic administration of ARA-C was continued. Cefepime and vancomycin was associated with chemotherapy to prevent infections.

On June she was referred to a dentist for evaluation, complaining of pain in the lower left hemi-arch, with the initial diagnosis of pericoronitis in the region of the erupting 3rd lower left molar. The treatment with systemic antibiotic administration and local cleaning of the oral cavity with chlorhexidine digluconate at 0.12% was not successful. The clinical picture of the patient evolved with the development of a symptomatic red

tumor injury with the approximate size of 4cm in the gingiva and alveolar mucosa in the vestibular, distal and lingual regions of the 3rd left lower molar (Figure 1). An incisional biopsy of the lesion was carried out without any complications. Due to systemic complications, the patient developed acute respiratory failure and severe sepsis. Despite broad spectrum antibiotic therapy and intensive care measures the patient died, after 2 months in hospital (38th day of chemotherapy).

Microscopic examination showed diffuse infiltration and destruction of the normal host tissue by sheets of poorly differentiated cells. The blast cells have convolutes, round or ovoid nuclei, and abundant eosinophilic cytoplasm, showing morphologic features of myelomonocytes (Figure 2). Hematoxylin-eosin staining could not disclose a conclusion and a subsequent immunohistochemistry analysis using myeloid markers such myeloperoxidase, CD117 (polyclonal antibody against carboxy terminal domain of c-Kit p 145) and CD 15 (granulocytes and Reed-Sternberg cells) was done. The panel also included haematolymphoid markers such CD45 (leucocyte-common antigen) and TdT (terminal deoxynucleotidyl transferase- T and B lymphocyte precursors), CD 68 (macrophages and histiocytes) and CD 34 (hematopoietic progenitor).

Immunohistochemistry staining was positive in blast cells and expressed strong cytoplasmatic positivity for CD 68, middle staining for CD 45 and myeloperoxidase, this was indicating infiltration of gingival tissue with monocytic cells, probably AML-M5, corroborating the observed in myelogram (Figure 3).



Fig. 1. Intra-oral view of the red tumor injury with the approximate size of 4cm in the gingiva and alveolar mucosa in the vestibular, distal and lingual regions of the 3rd left lower molar.

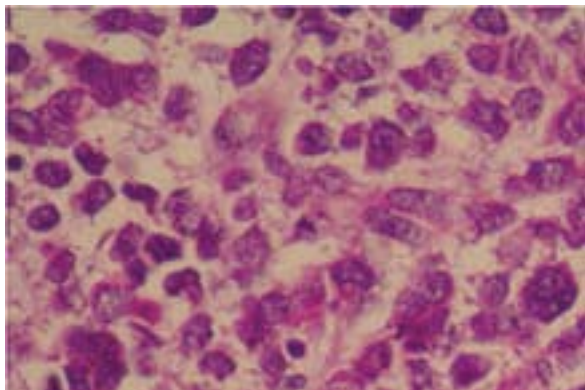


Fig. 2. Photomicrograph of the gingival lesion revealed diffuse infiltration and destruction of the normal host tissue by sheets of poorly differentiated cells, with convoluted nuclei, dense and acidophilic cytoplasm. Nuclear pleomorphism and mitotic activity, including abnormal mitoses is present. (Hematoxylin and eosin stain) and original magnification 400X.

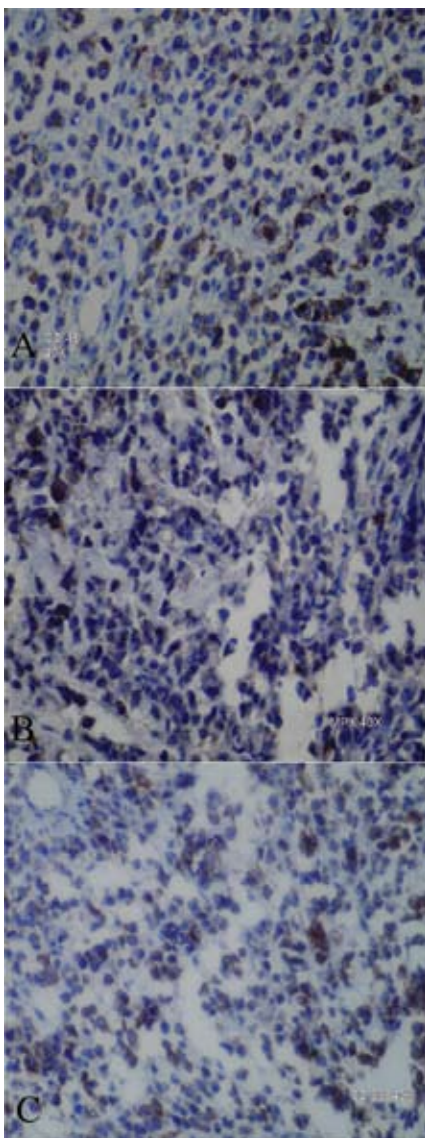


Fig. 3. Photomicrograph of the immunohistochemistry study. A: Middle cytoplasmatic positivity for CD45. B: Moderate positivity for MPX. C: Strong cytoplasmatic positivity for CD68. (Original magnification 400X).

Discussion

GS is a neoplasm composed of progenitor cells of granulocytic lineage. It is believed that GS begins in the bone marrow and reaches the subperiosteal through haversian channels. Once the subperiosteal is reached, the tumor can spread to other parts of the body. The region of head and neck is affected in 12 to 43% of the cases (8).

The intraoral GS is rare, and it is frequently associated to AML. From 37 cases described in the literature, 23 were associated to the AML (6). AML-M4 and AML-M5 were the most involved types (9). The GS can appear months or years before the AML manifests, during the course of the illness or represent a leukemia relapse or remission (6).

Oral GS occur in a wide age spectrum, ranging from 1 to 89 years of age, affecting both males and females with slight propensity for female gender, in the ratio of 4:3. The tumor may develop in the palate, mandible, gingiva, lips, intra-alveolar space, tongue, tonsils, buccal mucosa (6,7).

The clinical characteristics reported are quite varied. Most of the authors reported a strong tissue increase, with the mucosa remaining intact and the color varying among brown, black, red and pale-gray (6). It may be symptomatic (10) or asymptomatic (11). Some GS can be confused with reactive lesions (12). The involvement of the periapical region of a tooth was reported (13), as well as the lesion in the dental alveolus after the tooth extraction (10).

The GS diagnosis is usually difficult, mainly when it is the first sign of myeloid leukemias, or it does not present the green color (14). The differential diagnosis must include reactive lesions (12), benign neoplasms and malignant neoplasms, such as sarcomas, lymphomas, epidermoid carcinomas and metastasis of other neoplasms (1,13). The incisional biopsy is required for histopathologic and immunohistochemical analysis in order to clarify the diagnosis.

The morphology of this tumor is quite variable. Some cases show a diffuse infiltration of cells that may include all the stages of myeloid differentiation being easy to recognize the eosinophilic myelocytes. Nonetheless, other neoplasms indicate the presence of blastic cells, with little or no granulocytic differentiation (8,15). Due to poor myeloblastic differentiation the histopathological diagnosis by hematoxylin and eosin staining (H&E) can be difficult, and errors are common in the diagnosis (1).

In order to refine and confirm the morphologic differential diagnosis, the immunohistochemistry is indispensable. In our case, hematological origin was confirmed by the positivity for CD45, the myeloid lineage was identified by the positivity of myeloperoxidase and CD68. The intense scoring for CD68 showed the lesion consisted mainly of monocytic cells. Therefore, based on the data presented, we conclude that the gingival lesion was compatible with GS, with monocytic cells, possibly related to an AML - M5.

Conclusion

The granulocytic sarcoma is a rare neoplasm in the region of the oral cavity and it is frequently confused with other tumors. The diagnosis of the GS is always challenging for both the physician and the pathologist, mainly when it is not associated to the myeloid leukemia, when it is necessary to differentiate it from other malignant tumors, such as the lymphomas. The careful morphological analysis and the staining by immunohistochemistry are vital for establishing the diagnosis. Even though a lesion is rare in the oral cavity, its occurrence may never be ignored.

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