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Granulocytic sarcoma of the oral cavity in a chronic myeloid leukemia patient: An unusual presentation

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Abstract
Intraoral granulocytic sarcoma is an unusual manifestation of chronic or acute leukemia. The oral manifestations often involve enlargements of the gingival and mucosal tissue from direct leukemic cell infiltration. Only 38 cases have been reported in scientific literature to date. We present the case of a 47 year-old female who was diagnosed with chronic myeloid leukemia (CML) in December 2006. She was referred to a dentist for further evaluation, revealing generalized gingival overgrowth as well as periodontal, apical disease, and bleeding of the gums. An oral biopsy was performed and histological features revealed immature blast-like cells.

Key words: *Sarcoma, oral manifestation, myeloid leukemia.*

Introduction
Granulocytic sarcoma (GS), also known as extramedullary myeloid tumor or chloroma, is a rare solid tumor composed of immature cells of the granulocyte series, which occur in an extramedullary site (1). GS is most frequently found in acute and chronic leukemia patients and can precede acute myeloid leukemia and the blast crisis stage of chronic myeloid leukemia. This tumor most often occurs in the subperiosteal bone structure and soft tissue, but can also be found in the skin, lymph nodes, bone, orbit and eye, bronchi, pericardium, peritoneum, gastrointestinal tract, kidney, reproductive organs, breast, and bladder. Although oral manifestations of AML are common and often involve enlargements of the gingiva and mucosal tissue from direct leukemic cell infiltration, involvement of GS is, however, rare and only 38 cases have been reported in scientific literature to date (1,2).

Therefore, this paper presents a rare case of intraoral granulocytic sarcoma in the upper and lower jaws during a blastic crisis stage of chronic myeloid leukemia with the aim of providing clinicians with more knowledge about the pathology in order to improve the management of affected patients.

Case Report
A 47 year-old female patient was suffering from chronic myeloid leukemia (CML) Ph+, diagnosed in December 2006 by bone marrow biopsy and myelogram. She was referred to a dentist for further evaluation in August 2007. A physical examination revealed generalized gingival overgrowth (Fig. 1), periodontal and apical

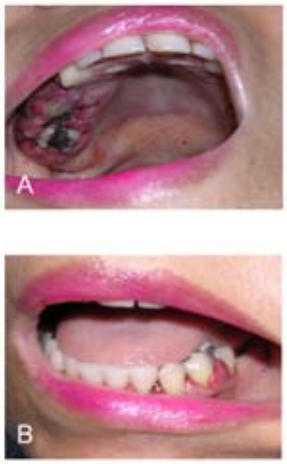

Fig. 1. A and B: Clinical manifestations in oral mucosa.

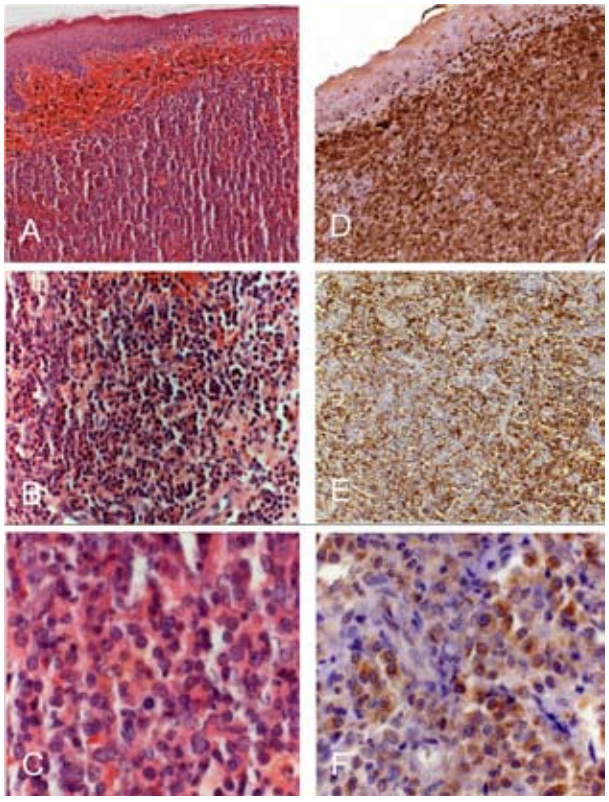

Fig. 2. A. Diffuse infiltrate with monomorphous immature-like cells (hematoxilin and eosin staining, 40x). B: Partial substitution of connective tissue by leukemic cells (100x). C: Infiltrate cells with large size and round-to-oval shape and mild to moderate basophilic cytoplasm without granules (200x). D,E: Tumor cells showed strongly positive reaction to lysozyme and myeloperoxidase (MPO) stain (40x) F: Neoplastic cells are positive for TdT (terminal deoxynucleotidyl transferase).

diseases, and bleeding gums. The patient was given clinical treatment to control dental and gingival infectious foci and an incisional biopsy of the oral mass was performed under local anesthesia. An histological examination, using hematoxylin and eosin, showed a diffuse infiltrate with a monomorphous population of immature blast-like cells. The cells were large in size and round-to-oval in shape, and the cytoplasm was mild to moderately basophilic without granules. Also, the cells had an increased nuclear-to-cytoplasmatic ratio and nuclei were round with fine chromatin. Rare mitotic figures were observed but eosinophilic myelocytes were not seen. Connective tissue showed a partial substitution by leukemic mass with immature cells (Fig. 2–A, B and C). The specimen was immunohistochemically positive for lysozyme (Fig. 2–D), myeloperoxidase (MPO) (Fig. 2-E) and TdT (terminal deoxynucleotidyl transferase (Fig. 2-F). No reactivity to lymphoid antigens, such as CD3 and CD20, was observed (data not shown). Three months after being diagnosed with GS, the patient died.

Discussion

Intraoral GS is a rare manifestation of chronic or acute leukemia and can involve any site of the oral cavity. There are 38 reported cases of intraoral GS in the PubMed database between 1970 and 2009 (1,3,4). In the vast majority of these reports, GS has occurred in patients with diagnosed leukemia, although in a few cases the oral cavity was the first site of underlying disease (5). In summary, three out of 38 cases of intra oral GS occurred in CML patients and just one involved upper and lower jaws. This report presents an additional case that involved the upper and lower jaw and which was secondary to a CML blastic crisis. Although the diagnosis of CML had been previously established, the oral cavity biopsy was performed to confirm the diagnosis of the tumor.

Oral manifestation of malignant myeloid precursors is very rare, and it is important to establish a differential diagnosis with malignant lymphoid tumors when they present as the primary manifestation. Menasce et al. suggested in 1999 (6), an immunohistochemistry panel to exclude malignant lymphoma from extra-medullar myelogenous infiltration (EMMI), including myeloid markers (myeloperoxidase and lysozyme) together with other B- and T- lineage markers. Although the differential diagnosis was performed using lymphoid markers (CD3 and CD20), the history of concurrent leukemia led to the diagnosis of oral GS. In addition, in this case, B-cell and T-cell lymphoma were excluded by negative stains for CD3 and CD20.

This diagnosis was confirmed by positivity for myeloid markers (myeloperoxidase, lysozyme and TdT). The sensitivity of immunohistochemistry for identifying the

morphology of neoplastic cells was studied by Alexiev in 2007 (7), who concluded that CD43 and lysozyme, as well as MPO and CD117, were the most sensitive markers for large number of neoplastic cells and myeloid differentiation, respectively. In this study, lysozyme and MPO were used to ensure consistent positivity for these markers, which reflected the degree of neoplastic and myeloid differentiation of the cells. MPO is localized in the primary granules of myeloid cells and is synthesized early in the differentiation, thereby serving as an important marker for myeloid lineage (8). MPO allows one to distinguish between AML and acute lymphoblastic leukemia in which blast cells are negative to this marker (9-11). The use of a large immunohistochemistry panel has been suggested by most authors when making a diffe-rential diagnosis between GS and lymphoid as well as other myeloid tumors (6-8). However, a concise immunohistochemistry panel including CD20, CD43, CD68, and MPO can successfully identify the majority of extramedullary myeloid tumors (12). In line with clinical information that exists on the blast crisis stage of CML, a concise immunohistochemistry panel was carried out to further diagnose GS in the oral mucosa. These findings showed that the strong specificity of myeloid mar-kers (Tdt, lizosyme and MPO) and the lack of expression of lymphoid markers CD3 and CD20 seem to be sufficient to distinguish GS from lymphoid tumors.

GS rarely precedes the onset of AML, and when it occurs, data from scientific literature suggest that chemotherapy at this stage may delay the onset of AML by 36 months compared with 6 months for non-chemotherapy patients (13). The oral mucosa may be an indication of such local events, and therefore a correct clinical and histological early diagnosis of GS is important in order to initiate early chemotherapy.

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