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Granulocytic Sarcoma of Mandible: A Case Report

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Abstract:
Granulocytic sarcoma (GS) is a localized infiltrate of immature granulocytes in an extramedullary site. It is generally associated with leukemia. However, it can also occur in other myeloproliferative disorders. While it can impact any part of the body, its manifestation in the oral cavity is rare. This study presents a rare case of GS affecting the oral cavity of a male, 29 years in age and with a history of paresthesia. We performed a segmental mandibulectomy as treatment and then recommended chemotherapy post-histopathological evaluation. The surgical outcomes were satisfactory as the patient remained in remission for 10 months.
Keywords: *chloroma, granulocytic sarcoma, maxillofacial surgery, myeloid sarcoma, oral surgery*

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I. Introduction

Granulocytic sarcoma (GS) or myeloid sarcoma is an extramedullary solid tumor made up of immature cells ofgranulocyticlineageormyelocytes.[1]GSisalocalizedinfiltrateofimmaturegranulocytesinanextramedullarysite, superficially resembling sarcoma.[2]Burns (1811)[3] was the first to identify this condition. Subsequently, King (1853)[4] namedit'chloroma'basedonthegreencolorexhibitedbythetumor,andattributabletotheexistenceofmyeloperoxidase enzymes in the immature myeloid cells.[2]GS is often found in people suffering from acute myeloproliferative disorders orchronicleukemia.[5]Itisaprobablesignofblasttransformationinchronicmyeloidleukemiaorprecedeacutemyeloid leukemia.[5]Thisrareentitycanoccuratanyage;however,itismainlyobservedinpeoplebelow15yearsofage.[6]

Rappaport (1996)[7] named this neoplasm as GS as the lesion consisted of immature cells of granulocytic lineage. Further, its color too was inconsistent.[1,8] GS is often observed in the evolution of myelodysplastic syndromes,[10]myeloid leukemias and other myeloproliferative disorders, for instance, myeloid metaplasia and polycythemia vera.[7,9] However, there is very little mention of the oral involvement in literature.[11,12]Interestingly, The majority of GS instances are identified in people who have already been diagnosed with leukemiaor who are likely to develop the disease in the future.[2]Although the incidence of GS is less frequent in oral and maxillofacial region, it should not be disregarded altogether.[13] The present study contributes a rare case of GS in oral cavity to the extant literature. The case is about a male patient who was 29 years of age and with a history of paresthesia. He exhibited symptoms of GS. His participation in the study was voluntary. All relevant information of the case was appropriately documented after due approval from the institutional ethics committee.

II. CaseReport

A male patient, 29 years-old, reported to Guru Nanak Institute of Dental Sciences & Research (GNIDSR), Kolkata, India. His chief complain was the swelling he had been experiencing on the lower left side of the lower face. Till about 8 months prior to this hospital visit, he had been feeling absolutely fine and with no cause for concern. In June2020, hebegan to feel paresthesia on the left side of the lower jaw region. He visited a local dentist who prescribed him medications, and advised an orthopantomogram of mandible. A procedure was performed on 21th July, 2020, to extractthe affectedtooth36. About 10 to 20 days later, the patient developeda swelling intraorally in that region. The dentist prescribed more medicines, and advised another orthopantomogram of mandible. However, the swelling continued to increase. The patient then visited a homeopathic doctor who prescribed him homeopathic medicine. When this too proved unsuccessful, he came to GNIDSR for consultation.

General examination during his first visit revealed that he had normal pulse rate, blood pressure, respiration rate, and SP02 level. He also exhibited complete absence of pallor, edema, cyanosis, clubbing, and icterus. However, he had facial asymmetry, and the extraoral examination identified an approx. 3*4 cm2 bony hard non-tender swelling ontheleft side along the lower border of themandible withoutskin fixicity and no extra-oral discharging sinus (refer to Figure 1a). Paresthesia was present on the left side of lower jaw and lip region. Onpalpation, ipsilateral level Ibwas found to have palpable lymph nodes of less than 3cm, that were non-tender, soft-to-firm in nature, and not fixed to the

underlying structure. The lymph nodes at ipsilateral levels I, III, IV and Vwere not found palpable and non-tender. Theintraoral examination identified an approximately 3*2 cm2bony- hard swelling extending from distal surface of 33 to distal surface of 37. An expansion of the buccal cortex was noticed. There was intra oral pus discharge from the sulcus of 35 (refer to Figure 1b). Radiological examination was then conducted on 13th November, 2020, the results of which showed an osteolytic lesion extending from distal surface of 34 to distal surface of 37, bony destruction up to 1cm of the lower border, scalloping of the border, and the presence of bony septa (refer to Figures 1c and 1d). Based on the clinical, lab and radiographic findings, we initially diagnosed osteomyelitis. Accordingly, we followed a surgical protocol of segmental resection with a submandibular approach.

Figure 1. Pre-operative photographs. (a) extraoral examination, (b) intraoral examination, (c) CECT shows osteolytic lesion extending from 35 to 37, (d) CECT shows destruction of both buccal and lingual cortex of left side of mandible

The patient underwent a segmental mandibulectomy on 5th January, 2021, from 33 to 38 region (refer to Figure2a),followedbyReconplatereconstruction(refertoFigure2b).Wethensentthespecimen(refertoFigure 2c) for histopathological evaluation using hematoxylin and eosinstaining.

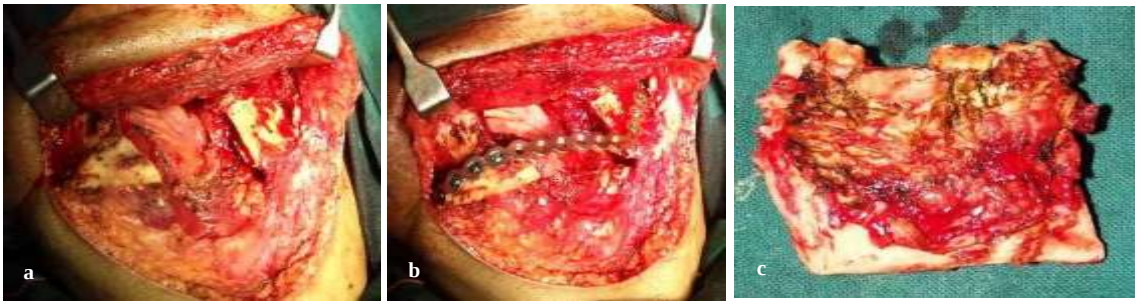

Figure 2. Per-operative photographs. (a) segmented mandible, (b) Recon plate reconstruction, (c) specimen

The test revealed small pieces of fibro-collagenous tissue infiltrated by nests and trabeculae of intermediate size mononuclear cells having dispersed nuclear chromatin and irregular nuclear margin (refer to Figure 3). The surrounding stroma showed infiltration by heterogenous population of cells – eosinophils, lymphoid cells, and histocytes. Eosinophilic myeloid precursors were also seen. For the final diagnosis, we performed immunohistochemistry. The tumor cells tested positive for Myeloperoxidase and CD15 (refer to Figures 4).

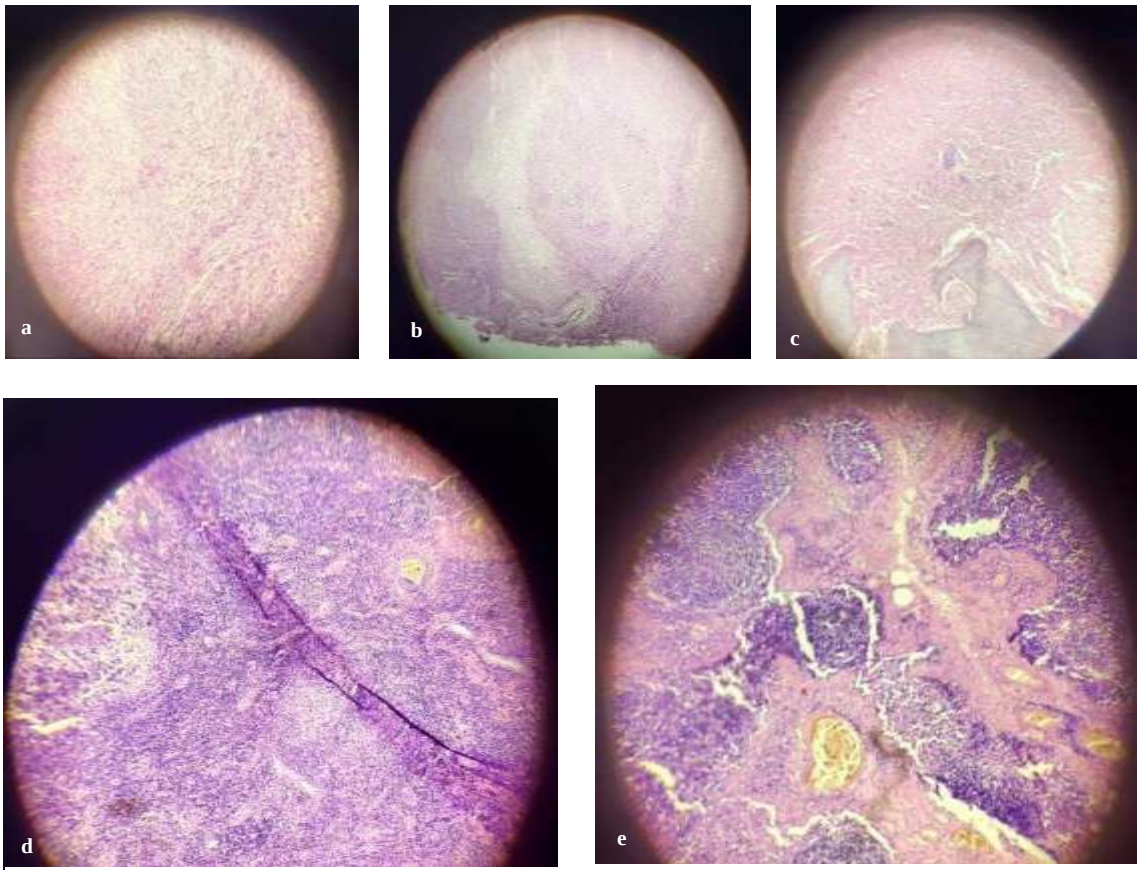

Figure 3. Histopathological examinations. (a) Round cells and hypercellular areas visible, (b) Large atypical blast cells resembling myeloid cells, (c) Large atypical blast cells with areas of hemorrhage, (d) Sheet like proliferation of myeloid cells, (e) Islands of proliferative myeloid cells with dispersed RBC and surrounding matrix of collagen fibers

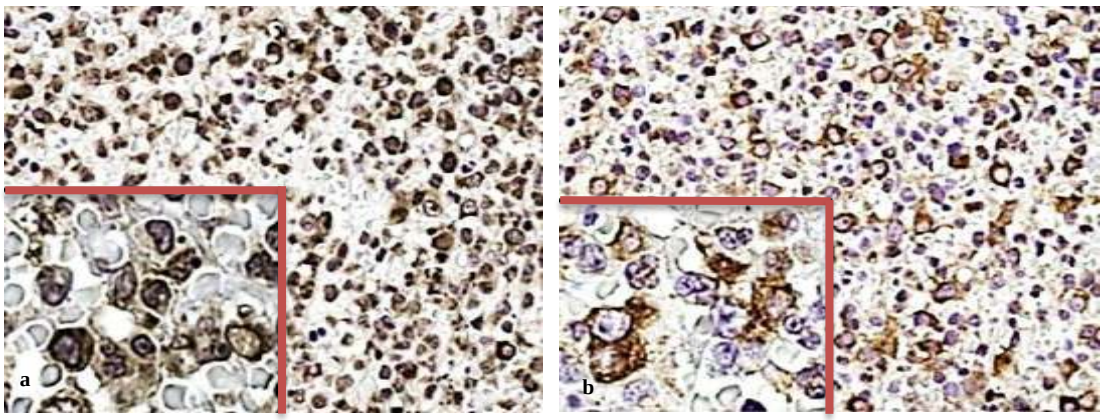

Figure 4. Histological and immunohistochemical findings (IHC stain, x400) (IHC stain, x1000). (a) Strong immunoreactivity to the marker CD68, (b) Tumor cells strongly positive for myeloperoxidase

The lesional cells expressed lysozyme and CD68 was negative for CD45, CD30, CD20, CD3, Pax-5, TdT and CD34. These results supported the diagnosis of GS. The patient was then advised to undergo chemotherapy. A whole-body scan was done using Positron Emission Tomography and Computed Tomography (PET-CT) (refer to Figures 5). The PET-CT scan showed (i) metabolically active soft tissue congestions at the siteofleftsegmentalmandibulectomy,whichweretobeobservedclosely;and(ii)non-fluorodeoxyglucose-avid bilateral neck lymph nodes, which were to be observed for futuredevelopment.

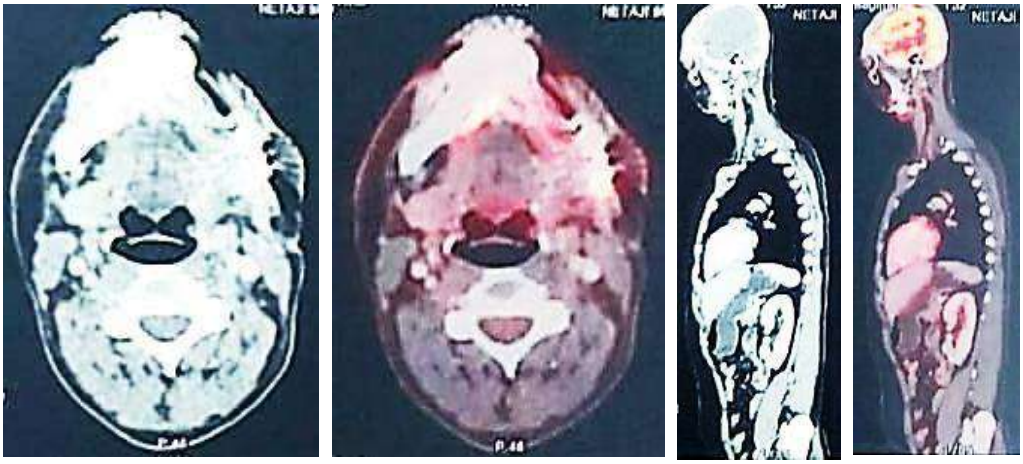

Figure 5. Post-operative PET-CT scan

Malignant cells were not found in the bone marrow aspiration, and laboratory tests indicated moderate anisocytosis, and normo- to macro-cytosis with mild hypochromia in this case. The ultimate diagnosis was intraoralprimaryGSbasedonimmunohistochemistryandbonemarrowaspirationdata,aswellasmorphological characteristics. The chemotherapy regimen comprised of Daunorubicin 60mg/m^2 IV in first three days and CytarabineArabinoside100mg/m^2continuousIVinfusionforthefirstsevendays.Thepatientexperiencedcanker sores (Grade II), minor nausea and vomiting, throughout treatment. Hence, Granisetron 1mg and Voriconazole were injected during first seven days. The patient had undergone a 3+7 inductions ofchemotherapy.

TheclinicalmanifestationsofisolatedGSinoralandmaxillofacialregionarenotuniformandvaryfrom case to case.[14] The lesion is often ignored when it is in the form of single or scattered nodules, or plaques that don't cause any discomfort.[15,16] Hyperplasia and localized or generalized gingival swelling due to GS is similar to drug-induced gingival hyperplasia[17], periapical periodontitis[18], epulis[17], an abscess.[19-21] A delay in diagnosis can occur when periodontal disease imaging findings and symptoms occur concurrently as relevant medical and medicationhistories.[14]Similarswellingandpaintosialadenitisarefoundincasesof GSinvolvingsalivaryglands show.[22,23]Inthefaceofnon-specificclinicalmanifestations,biopsyistheonlymeanstoprovidedefinitediagnosis of oral and maxillofacial GS. From a morphological standpoint, granulocytic or monocytic cells are key component of well-differentiated GS. Immature GS, on the other hand, has various blastic cells. Prior research recommends the application of immunohistochemistry analysis to differentiate GS from a variety of adenocarcinoma histiocytic sarcoma, blastic plasmacytoid dendritic cell neoplasm, Hodgkin lymphoma, lymphoblastic leukemia, non-Ewing's sarcoma, and undifferentiatedcarcinoma.[14]

III. Discussion

Primary GS is very rare condition finding occurrence in approximately two per million people. Oral primary GS generallyfindsmanifestationin areddishtobrownishulceratedsurfaceonapainfulswellingornodule.[24]GScan appearinthreeclinicalsituations:inpatientswithchronicmyeloidleukemiaorotherchronicmyeloproliferative conditions as an indication of blast transformation; in patients with previous or current acute myeloid leukemia; and in people who are otherwise well.[25] For patients without leukemia, GS is often a prelude to acute myeloid leukemia.[20]Astudyreportedthat13outof15patientsdiagnosedwithGSlaterdevelopedacutemyeloidleukemia within 10.5 months on an average, whereas the duration ranges from 1 to 49 months.[20] However some reports showingcontraryfindingsinthatnotallcasesofprimaryGSleadtoacutemyeloidleukemia.[26]Similarly,nineof 12individualswithchronicmyeloidleukemiawerefoundtohaveGSislinkedtoblasttransformation..[25]GScan, therefore, be an ominous sign for people with chronic myeloid leukemia and those who are otherwise disease-free.[20]

OralprimaryGScanbeaccuratelydiagnosedwithhistopathologicalandimmunohistochemicalanalysis (Hu et al. 2020)[24.] Occasionally, it may be diagnosed in other myeloproliferative diseases such as myeloid metaplasia, polycythemia vera, and hyper eosinophilia.[27] However, imaging assessments and plain-film radiographic examinations may have their limitations, particularly in identifying soft tissue tumors.[28] Treatment of and prognosis for intraoral GS depend on the medical history of the patient and the clinical presentations. For instance, Xie et al. (2006)[29] treated an intraoral GS with history of chronic myelogenous leukemia with Gleevec, which led to a complete remission. In line with clinical information about the blast crisis stage of chronic myelogenous leukemia, a concise immunohistochemistry panel may be performed to further diagnose GS in the oral mucosa.[30]

GS has been scrutinized in extensive literature reviews.[13,31,32] However, our literature review brought to light only eight cases[33-40] that were similar to the subject of our study (refer to Table 1). Chemotherapy, radiotherapy, or surgical excision are among the contemporary treatments for GS.[31] Our study demonstrates the need to adopt a surgical approach following prior research.[33,41]

Table 1: Granulocytic sarcoma cases in mandible

Study	Age, sex	Location	Clinical features	Diagnosis	Treatment	Progression	Outcome
Conran et al. (1982)[33]	2/F	Mandible - R	Swelling on right lower mandible	HE	CT+RT	_	Alive & Well/ 16 months
Reichard (1984)[34]	35/F	Mandible - R	Brownish tumor	CS - chloracetate esterase	Surgery + CT	AML8	Died of disease /13 months
Timmis et al. (1986)[35]	52/M	Mandible retromolar	Mass sessile non-tender, firm	HSHS - chloroacetate esterase; IHC - CD14, HLA	CT	_	Cardio pulmonary arrest
Stack & Ridley (1993)[36]	70/M	Mandible - R	Firm, mucosa intact	HSHS - chloroacetate esterase; IHC – antilysozomalimmunoperoxidase	CT	CML24	Died of disease / 1 month
Jordon (2002)[37]	62/F	Mandible apical	Periapical granuloma and chronic abscess	IHC - MPO, CD43, CD15	CT	MML2	Died of disease /10
Qiu (2010)[38]	16/F	Condyle - L	Preauricular swelling, restricted mouth open	IHC - MPO	Surgery + CT	_	No record
Colovic (2011)[39]	55/F	Mandible - L	Large mucosal tissue swelling	IHC - CD117, CD45, CD68, lysozyme	CT	_	Died of sepsis
Sengupta (2016)[40]	2/M	Mandible - L	Firm to hard, circumscribed, mildly tender swelling	IHC - CD45, CD68, lysozyme	CT	_	Alive & well
Present case (2023)	29/M	Mandible - L	Bony hard mass	IHC – MPO, CD15 lysozyme, CD68	Surgery + CT	AML	Died of disease/ 10 months

Note: CS=cytochemical staining, F=female, HE=histologic examination, HE= histochemical staining, IHC=immunohistochemistry, L=left, M=male, MPO=Myeloperoxidase, R=right.

IV. Conclusion

This study presents a rare case of GS in a 29-year-old male, with a history of paresthesia. He exhibited a bony hardmassontheleftsideofthemandiblefromthe34to37regions.Weperformedasegmentalmandibulectomy from 33 to 38 regions, and followed it up with Recon plate reconstruction. The patient underwent 3+7 induction chemotherapy, and survived for 10 months. Our institutional record shows that this is the first case in which surgery was performed for GS with such rare radiological and clinical features. The single case may not be sufficientforaconcreteconclusion;however,thesurgicaloutcomesweresatisfactory.Therefore,futureresearch in similar cases and with longer follow-up periods can confirm the effectiveness of ourmethod.

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