



Case Report

Ghost cell odontogenic carcinoma: Role of p53 as predictor of progression

Pallavi Srivastava¹, Nidhi Anand¹, Nuzhat Husain¹

¹Department of Pathology, Dr Ram Manohar Lohia Institute of Medical Sciences Lucknow U.P, India

Keywords:

Ghost cell odontogenic carcinoma;
Ki 67 proliferation index;
p53

ABSTRACT

Ghost cell odontogenic carcinoma (GCOC) a rare malignant Odontogenic Carcinoma with an unpredictable behaviour presenting with local recurrences and distant metastases, to best of our knowledge about 38 cases have been reported in the past. This is an additional case of GCOC in a 25-year old female presented with a slow-growing mandibular swelling since 9 months with restricted jaw mobility. The CT scan showed an ill-defined osteodestructive lesion in the mandible. The histological examination confirms the diagnoses as a GCOC.

Immunohistochemical examination was performed for Ki-67 proliferation index and p53 a predictor of progression. This case was managed by wide surgical resection of tumor and reconstruction of the defect by free fibular flap. Six months follow-up period shows no signs of recurrence. GCOC is rare Odontogenic Carcinoma with unpredictable behaviour however p53 & Ki67 proliferation index can predict the progression of tumor and help in differentiation from benign precursor lesions as early diagnosis & treatment of GCOC is necessary to prevent local recurrences & distant metastases.

Correspondence:

Prof Nuzhat Husain, MD

Head of Department, Department of Pathology

Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow, U.P, India

ORCID ID: 0000-0003-1831-9063

Email: drnuzhathusain@hotmail.com



Received : July 13th 2019; Accepted : January 3rd 2020

Citation : Srivastava P, Anand N Husain N. Ghost cell odontogenic carcinoma: Role of p53 as predictor of progression. J Pathol Nep 2020;10:1673-6 DOI 10.3126/jpn.v10i1.24763

Copyright: This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

INTRODUCTION

Ghost cell odontogenic carcinoma arises as de novo or from precursor lesion like calcifying cystic odontogenic tumor, dentinogenic ghost cell tumor or calcifying odontogenic cyst.¹ The GCOC has unpredictable behaviour with local recurrences and even case with distant metastasis have been reported in literature²⁻⁴, so early diagnosis and treatment is needed along with long term follow up. We report a case of ghost cell odontogenic carcinoma in a 25 yr old female presenting with a large mass in the mandibular region since 9 months which progressively increased in size with restricted jaw mobility.



Figure 1: Imaging findings: CECT Sagittal & Coronal view showing lesion arising from left half of body of mandible (A, B). 3D-reconstruction image showing osteodestructive image extending from root of canine to molar tooth.

CASE REPORT

A 25-year-old female presented with a painful mass in the lower jaw that enlarged progressively since she had first noticed it 9 months earlier. The size increased and presented with restricted mobility of the lower jaw. Physical examination revealed a 6 x 3.5 x 0.8 cm hard, fixed mass in the mandible, extending from the left first molar to canine. The mucosa was focally ulcerated with the overlying skin appeared normal. A 1.5-cm submandibular lymph node was palpated in the left submandibular area. A Wide Local Excision (WLE) hemimandibulectomy was performed with lymph node excision & reconstruction plate placement was done. Blood tests including complete blood count, electrolytes and biochemistry were normal. Imaging studies including CT scan head & neck revealed a large osteoexpansile and osteodestructive heterogenous lesion arising from left half of body of mandible and anteriorly involving symphysis measuring 5.7 x 3.0 x 2.4

cm. Multiple internal septations were identified. Thinning as well as focal areas of cortical breach in lingual cortex with involvement of the surrounding soft tissue was also evident. The lesion surrounded the root of canine, premolar and molar tooth. Mandibular canal was also involved by the tumor. Ramus of the mandible was spared. (fig. 1A-C) A WLE hemimandibulectomy was performed and send for histopathology at other centre and was reported as mucoepidermoid carcinoma. The histopathological sections after staining with hematoxylin and eosin showed tumor comprising of island of odontogenic epithelial cells with basaloid morphology admixed with abundant ghost cells representing large polygonal epithelial cells with eosinophilic cytoplasm that have lost their nuclei but have maintained a faint outline of cellular and nuclear membrane. The intra-cytoplasmic keratin preserves the cell outline and the corresponding previous site of the nucleus and represents aberrant keratinization (fig. 2A-D). Immunohistochemistry revealed high p53 but Ki

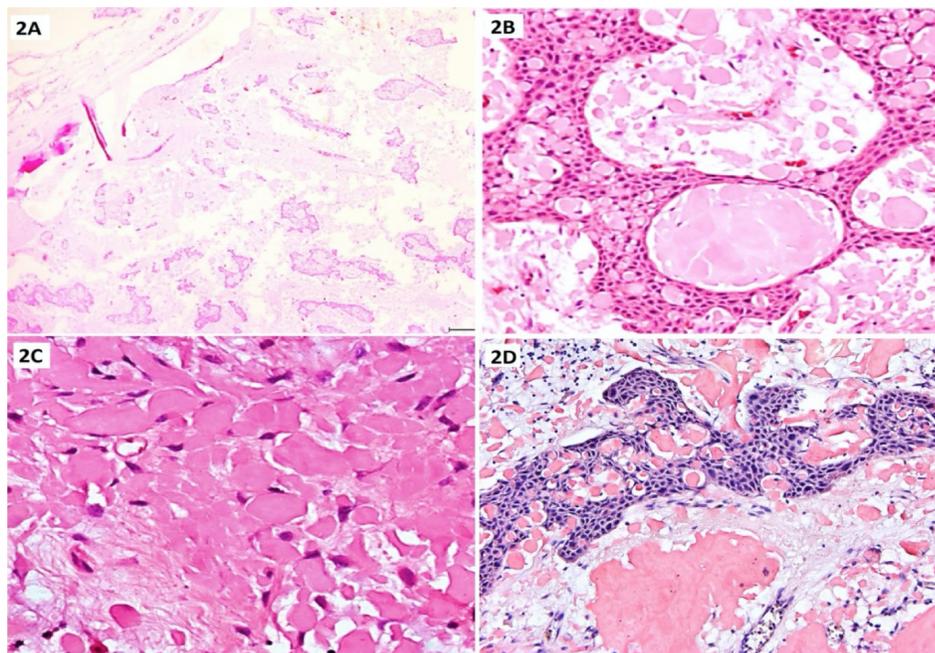


Figure 2: Histopathology findings: An osteodestructive lesion [A] with tumor comprising of island of odontogenic epithelial cells with basaloid morphology admixed with abundant ghost cells [B,C]. Congo red stain: Negative in ghost cells[D] [HE stain; X20 (A) X100 (B,D) and X 200 (C)].

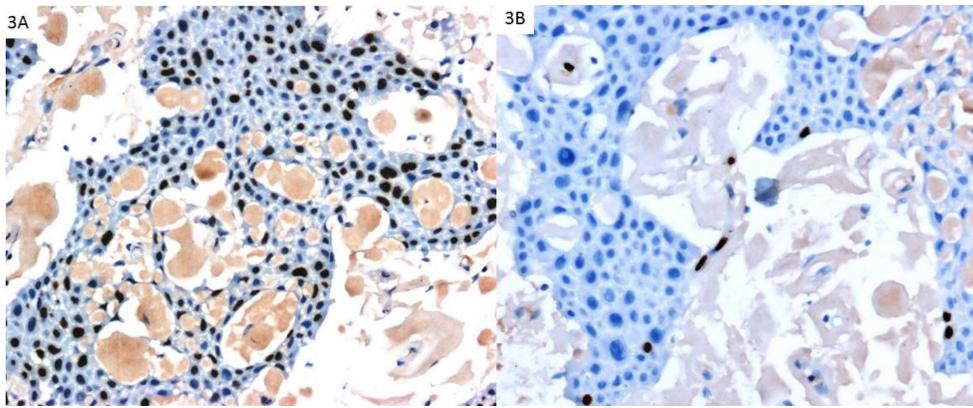


Figure 3: Immunohistochemistry findings: A) p53 expression (~80%) B) Ki67 proliferation index (~5%). (X 20).

67 index was 5% in tumor. (fig. 3A-B) A diagnosis of GCOC was made on the basis of the clinico-radiological, histopathological, and immunohistochemical findings. The following differential diagnosis were considered including Ameloblastic carcinoma, Calcifying cystic odontogenic tumor & Calcifying epithelial odontogenic carcinoma. The postoperative period was uneventful, after a follow up of one year; there were no signs of local recurrence or distant metastasis.

DISCUSSION

GCOC was first described by Gorlin et al followed by Ikemura et al, they reported the first case of GCOC arising from calcifying odontogenic cyst.^{5,6} There are three theories regarding the origin of GCOC, first arising from benign cyst like Calcifying Odontogenic Cyst or Dentogenic Ghost cell tumor, secondly the tumor arising from other Odontogenic Carcinomas and lastly the tumors arising *denovo*.³ There is wide age range from 13 to 86 years,³ with most cases arising from maxilla followed by mandible, among 38 cases about 14 cases were seen arising from mandible as in our case. The carcinoma has unpredictable clinical course with 5 year survival rate was estimated about 70%, 6 with high rate of local recurrence, 17 cases among 38 cases presenting with local recurrence and 3 cases with distant metastasis have also been reported with lung being the common site of distant metastasis. Due to limited number of cases documented, not much is known about the treatment but all the cases underwent wide local excision due to high rate of local recurrences but radiotherapy was not found to be effective, as in oral squamous cell carcinoma. Role of chemotherapy is not known. In one of the case reports by Ahmed S et al reported the first case of paediatric GCOC treated by multimodal approach which included wide local excision followed by chemotherapy, radiotherapy and immunotherapy and followed patient for 14 months after therapy, the patient responded to the treatment with no signs

of local recurrence and distant metastasis.⁷

The clinical and radiographic finding are not diagnostic of GCOC, however on radiography the lesion appears as mixed radiopaque or radiolucent lesion with bone destruction and ill-defined borders⁸, in the present case the lesion was heterogenous osteodestructive with ill-defined borders extending from canine to first molar. Histopathology is required for definite diagnosis the findings includes island of odontogenic epithelial cells admixed with ghost cells, there are various theories regarding the nature and formation of ghost cells, Hong et al reviewed and re-evaluated ninety two cases of calcifying odontogenic cyst & proposed that the ghost cells are result of ischemia induced squamous metaplasia of odontogenic epithelium while Roh et al detected vitronectin receptors and tartaric acid resistant phosphatase in ghost cells and the cause of bone resorption in GCOC due to release of cytokines.^{9,10} Immunohistochemical markers including p53 is required for distinguishing benign cyst from carcinoma, with over expression of p53 in GCOC as compared to benign cyst¹¹ and Ki67 along with MMP 9 also used to predict the disease progression.¹² Our case showed overexpression of p53 expression (~80%) with low Ki67 proliferation index (~5%) which represents low rate of progression. In one case report by Bose P et al had documented multiple changes in SHH pathway and APC mutation associated with the GCOC, but due to rarity of the tumor there are limited molecular studies.¹³

CONCLUSIONS

In conclusion early diagnosis of GCOC is important due to high rate of local recurrence and few case of distant metastasis have also been documented in literature. The knowledge of the benign precursor lesions of GCOC is necessary as they may undergo malignant transformation. Immunohistochemistry marker including p53 and Ki-

67 proliferation index is necessary for diagnosis and predicting the rate of tumor progression..

Conflict of Interest: None

REFERENCES

1. Ledesma-Montes C, Gorlin RJ, Shear M, PraeTorius F et al. International collaborative study on ghost cell odontogenic tumours: calcifying cystic odontogenic tumour, dentinogenic ghost cell tumour and ghost cell odontogenic carcinoma. *J Oral Pathol Med* 2008;37:302-8. [Crossref](#)
2. Ellis GL, Shmookler BM. Aggressive (malignant?) epithelial odontogenic ghost cell tumor. *Oral Surg Oral Med Oral Pathol* 1986;61:471-8. [Crossref](#)
3. Cheng Y, Long X, Li X, Bian Z, Chen X, Yang X. Clinical and radiological features of odontogenic ghost cell carcinoma: review of the literature and report of four new cases. *DentomaxillofacRadiol* 2004;33:152-7. [Crossref](#)
4. Grodjesk JE, Dolinsky HB, Schneider LC, Dolinsky EH, Doyle JL. Odontogenic ghost cell carcinoma. *Oral Surg Oral Med Oral Pathol* 1987;63:576-81. [Crossref](#)
5. Gorlin RJ, Pindborg JJ, Odont, Clausen FP, Vickers RA. The calcifying odontogenic cyst-a possible analogue of the cutaneous calcifying epithelioma of Malherbe. An analysis of fifteen cases. *Oral Surg Oral Med Oral Pathol* 1962;15:1235-43. [Crossref](#)
6. Ikemura K, Horie A, Tashiro H, Nandate M. Simultaneous occurrence of a calcifying odontogenic cyst and its malignant transformation. *Cancer* 1985;56:2861-4. [Crossref](#)
7. Ahmed S, Watanabe M, deMello D, Daniels T. Pediatric Metastatic Odontogenic Ghost Cell Carcinoma: A Multimodal Treatment Approach. *Rare Tumors*. 2015;7(2):73-75. [Crossref](#)
8. Kim HJ, Choi SK, Lee CJ, Such CH. Aggressive epithelial odontogenic ghost cell tumor in the mandible: CT and MR imaging findings. *AJNR Am J Neuroradiol*. 2001;22:175-9. [Website](#)
9. Hong SP, Ellis GL, Hartman KS. Calcifying odontogenic cyst. A review of ninety-two cases with reevaluation of their nature as cysts or neoplasms, the nature of ghost cells, and subclassification. *Oral Surg Oral Med Oral Pathol* 1991;72:56-64. [Crossref](#)
10. Roh GS, Jeon BT, Park BW, Kim DR, Hah YS, Kim JH, et al. Ghost cell odontogenic carcinoma of the mandible: A case report demonstrating expression of tartrate-resistant acid phosphatase (TRAP) and vitronectin receptor. *J CraniomaxillofacSurg* 2008;36:419-23. [Crossref](#)
11. Corso G Del, ML Tardio, DB Gissi. Ki 67 and p53 expression in ghost cell odontogenic carcinoma: a case report and literature review. *Oral MaxillofacSurg* 2015;19:85-9. [Crossref](#)
12. Zhu ZY, Chu ZG, Chen Y, Zhang WP, Lv D, Geng N, Yang MZ. Ghost cell odontogenic carcinoma arising from calcifying cystic odontogenic tumor: a case report. *Korean J Pathol* 2012;46:478-82. [Crossref](#)
13. Bose P, Pleasance ED, Jones M, Shen Y et al. Integrative genomic analysis of ghost cell odontogenic carcinoma. *Oral Oncol*. 2015;51:e71-5. [Crossref](#)