

# Hyalinizing clear cell carcinoma arising in recurrent pleomorphic adenoma of parotid gland

K Mardi, J Sharma

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## Abstract

Hyalinizing clear cell carcinoma (HCCC) is a neoplasm that predominantly affects the oral cavity in adult females. The tumor cells show a characteristically clear cytoplasm and the stroma has areas of hyalinization. We report the first case of hyalinizing clear cell carcinoma arising in a recurrent pleomorphic adenoma of the parotid gland in a 44 year-old female. The tumor cells were positive for cytokeratin and were negative for SMA, S-100 protein.

## INTRODUCTION

Hyalinizing clear cell carcinoma (HCCC) is a neoplasm that predominantly affects the oral cavity in adult females<sub>1</sub>. It is considered to be a low-grade indolent neoplasm, because of rare recurrence and metastasis. Their occurrence in parotid gland is uncommon and HCCC arising from a pleomorphic adenoma of the parotid gland has not been reported so far.

## CASE REPORT

A 44 year-old male presented with recurrent swelling in the left preauricular region. He had a history of parotid mass about 20 years earlier that was excised and reported as pleomorphic adenoma. Since then the tumor had recurred twice in the same place and had been excised again with the diagnosis of pleomorphic adenoma.

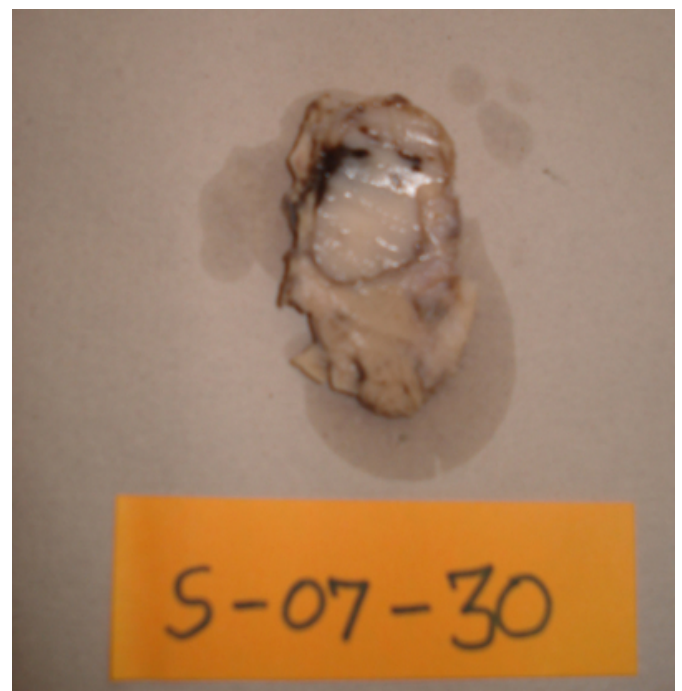
On clinical examination, there was a 4x3 cm, well-defined, nontender, firm, mobile growth in the left preauricular region. Clinical possibility of recurrent pleomorphic adenoma was considered and a superficial parotidectomy was conducted.

Pathologic findings: On gross examination the specimen measured 6x4.5x1cm. Cut section showed a 2.8x2cm, grey to white lesion with slightly irregular margins. Surrounding parotid parenchyma was within normal limits (Fig1). Microscopic examination showed sheets, cords and nests of round to polygonal tumor cells with abundant clear cytoplasm, separated by stroma showing areas of hyalinization (Fig 2&3). These clear cells showed centrally located vesicular nuclei, inconspicuous nucleoli and slightly

irregular nuclear membranes. Mitotic figures were less than 1 per 10 high power fields (HPF). Few residual areas of pleomorphic adenoma were also present (Fig4). The tumor cells were negative with PAS, mucicarmine and Sudan black stains. Immunohistochemically, these cells were positive for cytokeratin and were negative for SMA and S-100 protein. A definite diagnosis of HCCC arising in recurrent pleomorphic adenoma was rendered (carcinoma e-pleomorphic adenoma).

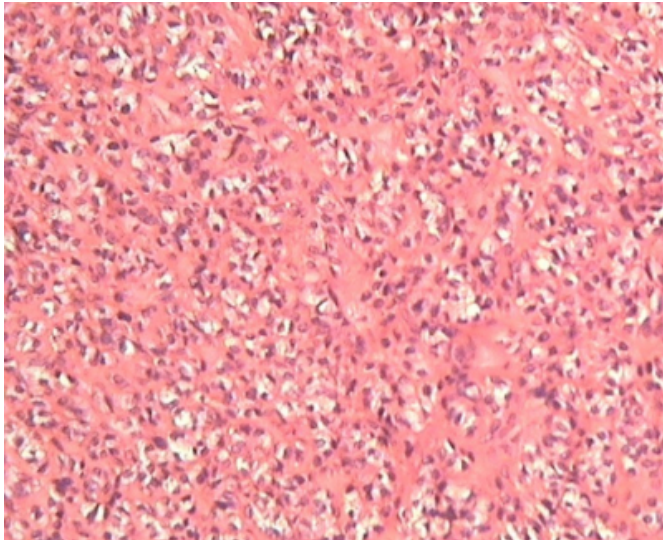
## Figure 1

Figure 1: Gross photograph showing a well-circumscribed, grey-white tumor in the parotid parenchyma.



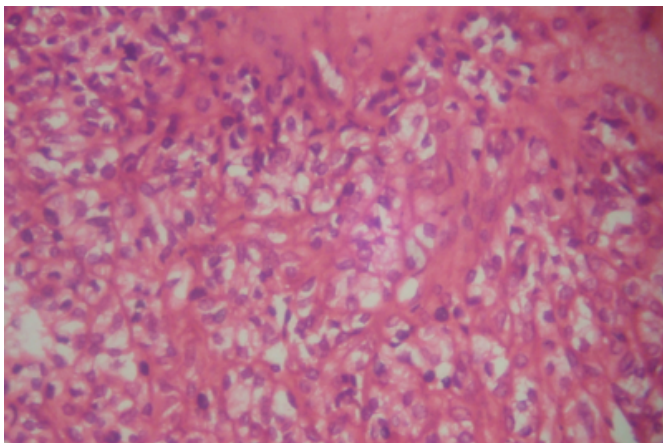
**Figure 2**

Figure 2: Photomicrograph showing sheets of clear cells separated by hyalinized stroma (H&E, 10x)



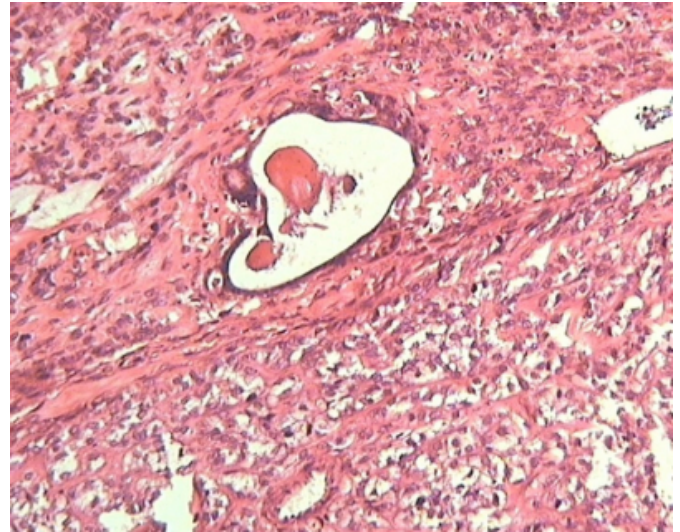
**Figure 3**

Figure 3: Higher magnification showing tumor cells separated by hyalinized stroma (H&E, 40x)



**Figure 4**

Figure 4: Photomicrograph showing residual areas of pleomorphic adenoma along with the clear cells (H&E, 10x)



## DISCUSSION

Clear cell carcinoma, NOS, is a rare form of salivary gland tumor and involves mostly minor salivary glands, especially those of the palate. Only 4 cases of clear cell carcinoma arising in pleomorphic adenoma have been reported so far, 2 in submandibular glands and 2 in a minor salivary gland of the palate<sup>2,3,4,5</sup>. We report the first case of hyalinizing clear cell carcinoma arising in recurrent pleomorphic adenoma.

The differential diagnosis of lesions with prominent clear cells involving the parotid gland is extensive and includes clear cell myoepithelial carcinoma, clear cell epithelial-myoeplithelial carcinoma, hyalinizing clear cell carcinoma, clear cell variant of acinic cell carcinoma and oncocytoma, mucoepidermoid carcinoma, and metastatic lesions especially carcinomas from kidney and thyroid, and from balloon cell melanomas. In clear cell epithelial-myoeplithelial carcinomas, the clear cells are usually part of myoeplithelial component and form a mantle around an inner layer of small cuboidal epithelial cells; this dimorphic pattern can be highlighted immunohistochemically. Hyalinizing clear cell carcinoma shows groups and trabeculae of polygonal, glycogen-rich cells separated by dense collagen bands. These cells are immunohistochemically positive for cytokeratins, but are usually negative for myoeplithelial markers (s-100 and smooth muscle actin). Clear cell myoeplithelial carcinoma shows sheets of clear cells sometimes admixed with spindle shaped and other myoeplithelial cells. These cells are positive for cytokeratins, s-100 and actin (rrSMA). The tumor cells are also positive for glycogen. Clear-cell variants of acinic

cell carcinoma are usually never pure and cells with periodic acid Schiff positive and diastase resistant cytoplasmic zymogen granules are also present. Sebaceous neoplasms are positive for fat stains and clear cell mucoepidermoid carcinomas show positivity for mucin. Metastatic renal cell carcinomas are positive for both fat and glycogen and immunohistochemically positive for vimentin and CD10. Additionally, they can be best excluded by imaging the kidneys. There are some malignant salivary gland tumors composed of clear cells that cannot be placed in to any of these categories and for which the descriptive term “clear cell carcinoma, NOS” is used. Some of them are accompanied by a fibrohyaline stroma and hence are called as “hyalinizing clear cell carcinoma”.

Clear cell carcinoma of the minor salivary gland with prominent stromal hyalinization has been reported under various names, and is included under the generic term of “clear cell carcinoma, NOS, in the WHO classification. Almost all of those cases had about 2-cm swelling in the oral cavity and behaved as a low-grade neoplasm. These cells are positive for cytokeratin and negative for S100 protein and smooth muscle actin. Thus this immunohistochemical pattern differentiates it from other salivary gland tumors having a predominantly clear cell component and also indicates that HCCC is composed only of epithelial cells. In 1994, Milchgrub, et al. studied eleven cases of similar type and proposed the term “hyalinizing clear cell carcinoma”. This neoplasm was thought to be low-grade in nature and was proposed to arise from epithelial cells. Initially, Batsakis et al.,<sup>6</sup> refuted its low-grade behavior and its epithelial origin. However, others<sup>7,8</sup> disagreed with him and HCCC has been accepted as a low-grade malignancy that arises purely from

epithelial cells.

Because of the lack of awareness, HCCC is often misdiagnosed as poorly differentiated carcinoma, squamous cell carcinoma, acinic cell carcinoma, mucoepidermoid carcinoma and epithelial-myoepithelial carcinoma. HCCC behaves as a low-grade neoplasm. Only occasional cases have presented metastasis. This low-grade neoplasm could be treated by a wide excision, though further case studies and long-term follow-up would be necessary to document it.

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**Author Information**

**Kavita Mardi, M.D, DNB**

Assistant Professor, Dept. of Pathology, Indira Gandhi Medical College, Shimla

**Jaishree Sharma, M.D.**

Professor and Head, Dept. of Pathology, Indira Gandhi Medical College, Shimla