

## Case Report

# Cystic Cellular Pleomorphic Adenoma Cytologically Mimicking Metastatic Papillary Thyroid Carcinoma: A Case Report and Review of the Literature

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**Abstract**

Pleomorphic adenomas are benign salivary gland tumors most commonly found in the parotid gland. We present an unusual case of a lateral neck pleomorphic adenoma with cystic and cellular features that was originally misdiagnosed as metastatic papillary thyroid carcinoma (PTC) on fine needle aspiration biopsy. To our knowledge, only two cases of pleomorphic adenoma have been misdiagnosed as thyroid carcinoma, and no cases of pleomorphic adenoma have mimicked PTC cytologically. This case demonstrates the importance of combining radiologic, clinical, and histopathologic information, as well as the usage of cell block and immunohistochemical stains, to correctly determine the diagnosis of pleomorphic adenoma.

**ABBREVIATIONS**

PA: Pleomorphic Adenoma; PTC: Papillary Thyroid Carcinoma; FNA: Fine Needle Aspirations

**INTRODUCTION**

Pleomorphic adenomas (PA) represent the most common benign salivary neoplasm, generally presenting as painless masses with characteristic radiologic and pathologic features [1]. PAs are classified by the amount of epithelial and myoepithelial cells, as well as chondromyxoid stromal components [2]. Cellular and cystic variants of PA are rare [2,3].

The parotid gland is the most common site for PA. While extra-parotid PAs have been reported, these tumors are difficult to diagnose clinically due to their unusual location [4].

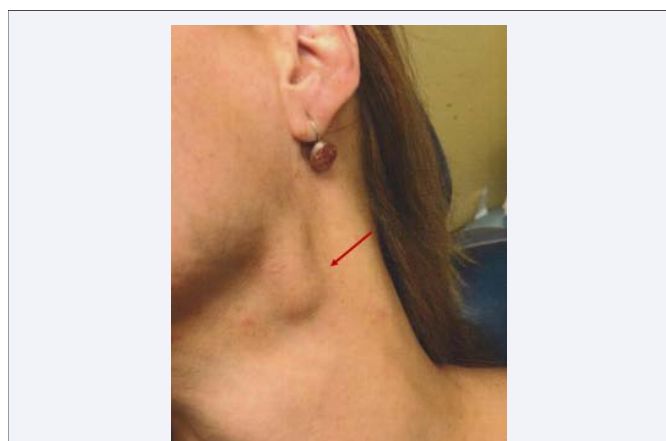
Here, we report an unusual case of cystic cellular PA of the lateral neck originally misdiagnosed as metastatic papillary thyroid carcinoma (PTC) on fine needle aspiration (FNA) biopsy by an outside institution. The case presented here demonstrates the importance of multidisciplinary collaboration and understanding of the clinical, radiological, and cytopathological features of PA. Furthermore, the use of a cell block and immunohistochemical staining (IHC) can help narrow the differential and determine the correct diagnosis.

**CASE PRESENTATION**

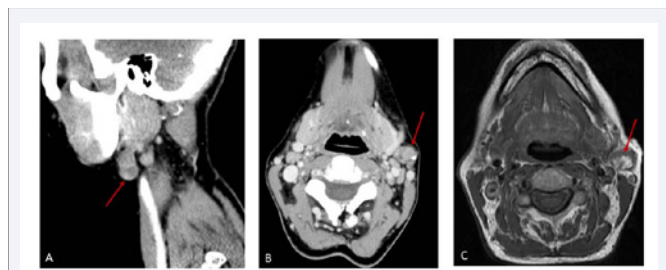
A 50-year-old female with a ten year history of multinodular goiter presented with a palpable mass on the left side of her neck located inferior to the parotid gland and lateral to the submandibular gland (Figure 1). CT imaging with contrast

revealed enlarged nodes in the left lateral compartment showing areas of calcification, avid enhancement, and cystic type change (Figure 2A,2B). The initial clinicoradiographic diagnosis was cervical lymphadenopathy of uncertain origin, with a differential diagnosis of metastatic thyroid cancer, other neoplastic processes and inflammatory diseases. The patient underwent FNA biopsy of the lateral lymph node at an outside institution, which was interpreted as positive for metastatic PTC.

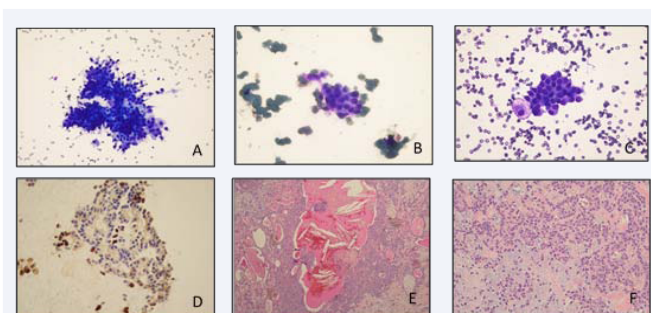
Based on this outside diagnosis, the patient was referred to our hospital for a total thyroidectomy and lateral neck dissection. Review of the outside cytology slides showed low grade neoplastic cells with moderately enlarged nuclei and moderate cytoplasm in the background of numerous macrophages, mimicking metastatic PTC. However, due to a lack of evidence of primary PTC in the thyroid, a repeat FNA was performed for cell block and IHC studies. FNA of the mass was morphologically identical to the outside biopsy and showed cystic fluid with macrophages and slightly complex sheets of neoplastic cells showing moderate enlarged nuclei, mild pleomorphism, and increased Nuclear: Cytoplasmic ratio (Figure 3A-C). No stromal component was identified. The cell block showed neoplastic cells with medium, round, dark nuclei forming a glandular structure.



**Figure 1** Patient presented with a palpable mass on the left side of her neck. Neck mass is inferior to the parotid gland and lateral to the submandibular gland.



**Figure 2** A,B: Sagittal and axial CT soft tissue neck with contrast demonstrate an exophytic soft tissue abutting the left parotid tail showing areas of calcification, avid enhancement, and cystic type change that extends to left level II nodal chain expected location. C: Axial spin echo T1 weighted MRI image shows hyperintensity within the known left neck mass in the left level IIa nodal chain suspect for hemorrhagic byproducts.



**Figure 3** A,B: DQ stain showing cells with a slightly complex, papillary architecture with mild pleomorphism and increased N:C ratio, mimicking the morphology seen in metastatic papillary thyroid carcinoma (DQ, x200, x400). C: DQ stain from a different patient with a known diagnosis of metastatic papillary thyroid carcinoma, used as a control (DQ, x400). D: p63 immunostaining on the cell block showing positive nuclear staining in myoepithelial cells and negative nuclear staining in neoplastic cells (x400). E: Low-power microphotography of the resected specimen showing a cystic space with abundant foamy macrophages and adjoining cellular, glandular areas (hematoxylin-eosin, x40). F: Intermediate-power microphotography of the resected specimen showing epithelial and myxoid-stromal component (hematoxylin-eosin, x200). DQ, (Diff-Quik®); N:C, (N, nuclear: C, cytoplasmic).

IHC studies performed on the cell block sections showed no staining for TTF-1, Thyroglobulin, p40, ER, GATA3 or Calcitonin. Two populations of myoepithelial cells and neoplastic epithelial cells were identified, and the glandular structures were negative for p63 and surrounded by scanty p63 positive cells (Figure 3D). Based on these IHC stains, metastatic PTC was ruled out and PA was confirmed.

Given these incongruent FNA results, the patient underwent further radiographic imaging including PET/CT and MRI. The PET/CT results could not identify a definite primary tumor site, and there was no evidence of focal hypermetabolism within the thyroid. On MRI, an oblong mass (3.0 cm x 1.9 cm) was visualized at the left parotid tail (Figure 2C). In comparison with previous imaging two months prior, the mass had grown in size. Due to the absence of a clear fat plane between the superior border of the mass and the left parotid tail parenchyma, a parotid origin of either a primary malignancy or acute disease of an intra-parotid lymph node was then suggested as the revised diagnosis.

The patient subsequently underwent a superficial left parotidectomy with facial nerve dissection and left level 2 neck dissection. Final pathology revealed a 3 cm tumor composed of cystic areas lined by low cuboidal epithelial cells, macrophages, and a biphasic population of cellular epithelial cells and myoepithelial cells (Figure 3E). The epithelial cells were glandular in nature with medium hyperchromatic nuclei, similar to the morphology seen in the cell block and scanty stromal component comprised of myxoid and chondroid areas (Figure 3F). A diagnosis of PA was made. The patient tolerated the procedure well and was discharged later that day. The patient's postoperative course was unremarkable.

## DISCUSSION

Pleomorphic adenomas represent the most common benign

salivary gland tumor (70-80%) [1]. The parotid gland is the most common site of PA (90%), followed by the minor salivary glands in the soft palate [5,6]. PAs most often present in patients between the ages of 30 and 60 with an increased incidence in females [1].

PAs tend to grow slowly and present as painless masses. Diagnosis is generally made through biopsy and radiographic evaluation. On CT, PAs present as homogenous soft tissue masses and may display calcification [1]. Necrosis may be observed in large PAs, while homogeneous prominent enhancement is more common in smaller masses [1]. On MRI, smaller masses generally appear well-circumscribed, while larger masses may appear heterogeneous. PAs generally appear hypoechoic on ultrasound [1].

While FNA can be useful in the diagnosis of parotid tumors, reported accuracy rates for parotid FNAs range from 79 to 98%, partly due to the many different neoplasms and inflammatory lesions arising in the parotid gland [7]. On FNA, PAs generally display ductal epithelial cells, chondromyxoid matrix, and myoepithelial cells, which may be plasmacytoid or spindled [8]. They are characterized by a mixing of epithelial, mucoid, myxoid, and chondroid components [9].

Extracellular stroma is often a defining feature in the cytopathology of PA [10]. However, cellular PAs do arise and predominantly consist of epithelial cells with a lack of stroma. Cytologically, cellular PAs are similar in appearance to carcinoma ex pleomorphic adenoma, adenoid cystic carcinoma, basal cell carcinoma, basal cell adenoma, and polymorphous low-grade adenocarcinoma [10]. Occasionally, cases of parotid PA may undergo cystic degeneration [11]. Such cystic characteristics may complicate the diagnosis, as these lesions can be easily confused with mucoepidermoid carcinoma, carcinoma ex pleomorphic adenoma, or squamous cell carcinoma, among others [3,12]. The case presented here is the first case of PA simultaneously demonstrating both cellular and cystic features.

For complex samples, immunohistochemical (IHC) staining may supplement FNA results in determining an accurate diagnosis. IHC staining of PAs is typically positive for keratin, GFAP, and S-100 [13]. Conversely, IHC staining of PTC is typically positive for TTF-1, thyroglobulin, and Galectin-3 [14,15]. In this case, the use of IHC stains eliminated the initial diagnosis of metastatic PTC and confirmed the diagnosis of PA.

Although rare, there have been cases of extra-parotid PAs mimicking thyroid neoplasms (Table 1). In two cases, the PA was misdiagnosed as thyroid carcinoma based on imaging, yet histopathological evaluation revealed the correct diagnosis of PA [16,17]. However, the false diagnosis of PTC in our case was assigned based on initial FNA cytology and imaging, which revealed areas of calcification, avid enhancement, and cystic type change. The PA was thereby deemed to exhibit radiographic features similar to that of metastatic PTC. However, had an MRI been obtained earlier, the tumor's relation to the parotid gland would have been established, leading to the correct diagnosis of PA. To our knowledge, this is the first reported case of PA that mimicked PTC both cytologically and radiologically.

In the case presented here, a cystic cellular PA mimicked

metastatic PTC on initial imaging and FNA biopsy, leading to a preliminary misdiagnosis. This case highlights the importance of combining radiologic, clinical, and cytopathologic information, as well as the usage of cell block and immunohistochemical stains in order to determine an accurate diagnosis [18-20].

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## CONFLICT OF INTEREST

Dr. Urken is the Medical Advisor of the THANC Foundation.

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