

## Case Report

# Carcinoma ex pleomorphic adenoma: Diagnostic dilemma and treatment protocol

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### Abstract

Carcinoma ex pleomorphic adenoma (CXPA) is a carcinoma arising from a primary or recurrent benign pleomorphic adenoma. It often poses a diagnostic challenge to clinicians and pathologists. The entity is difficult to diagnose preoperatively. Pathological assessment is the gold standard for making the diagnosis. Treatment for CXPA often involves an ablative surgical procedure, which may be followed by radiotherapy. We report a case of a 65-year-old lady with a history of recurrent swelling in the left preauricular region and a history of surgery 10 years back, in the same region. Preoperatively, a diagnosis of pleomorphic adenoma of the parotid gland metastasizing to the cervical lymph node was made, but postoperatively it was reported as CXPA adenoma of the parotid gland. A radical parotidectomy involving en bloc resection of the facial nerve along with deep and superficial lobes of the parotid was performed followed by radiotherapy. The fact that pleomorphic adenomas are classified as benign tumors should not overshadow the wide range of biological behaviors associated with these tumors. On account of the potential for malignant transformation, surgical treatment must be properly performed. Surgery followed by radiotherapy should be considered as the standard care for a patient with carcinoma ex pleomorphic adenoma.

**Key words:** Carcinoma ex pleomorphic adenoma, parotidectomy, parotid carcinoma

### INTRODUCTION

Primary parotid carcinomas are uncommon and generate considerable interest because of their histological variability, grade of malignancy, and clinical behavior. Parotid malignancies are relatively rare, accounting for 1-3% of all head and neck cancers.<sup>[1]</sup> A pleomorphic adenoma is the most common parotid neoplasm, accounting for about 50% of all parotid tumors.<sup>[2]</sup> Carcinoma ex pleomorphic adenoma (CXPA) is defined as a carcinoma arising from a primary (*de novo*) or recurrent benign pleomorphic adenoma.<sup>[3,4]</sup> CXPA has been named as carcinoma ex mixed tumor, carcinoma ex adenoma, and carcinoma ex benign pleomorphic adenoma.<sup>[3]</sup> Carcinoma ex pleomorphic adenoma is a rare, aggressive, poorly understood malignancy, which usually occurs in the salivary glands and accounts for most reported cases of

malignant mixed tumors. They mainly affect patients in their sixth to eighth decades of life, have a slight male sex predominance,<sup>[5]</sup> and they mostly involve the 'major' salivary glands. In CXPA, an epithelial malignancy develops in association with a primary or recurrent benign pleomorphic adenoma.

The pathogenesis of CXPA is not well-understood. Two hypotheses are mentioned: These tumors are malignant from the onset or a carcinomatous transformation of a mixed tumor occurs.<sup>[6]</sup> The incidence of CXPA accounts for 5 to 25 percent of primary parotid carcinomas.<sup>[2,7]</sup> Misdiagnosis is not rare, as the residual pleomorphic adenoma component may be small, and therefore missed, on histological analysis. The most common clinical presentation of CXPA is of a firm mass in the parotid gland. The proportion of the adenoma and carcinoma components determine the macroscopic features of this neoplasm. The entity is difficult to diagnose preoperatively. Pathological assessment is the gold standard for

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making the diagnosis. Treatment for CXPA often involves an ablative surgical procedure, which may be followed by radiotherapy. Overall, patients with CXPA have a poor prognosis. Accurate diagnosis and aggressive surgical management of patients presenting with CXPA can increase their survival rates.<sup>[8]</sup>

## CASE REPORT

A 65-year-old lady reported to our Department of Oral and Maxillofacial Surgery with a chief complaint of swelling in the left preauricular region since six months. The swelling was first small and then gradually increased in size and was not associated with pain [Figure 1]. She gave a history of surgery in the left parotid region, which was done about 10 years prior, but we could not get the details as she had misplaced the previous records.

On inspection, there was deformation of the left parotid gland region by a mass measuring about 5.8 × 4.9 cm in dimension. The patient did not present with facial palsy or ear sensory disturbances. The classical sign of parotid swelling, which was elevation of the left ear lobe, was present.

On palpation, the swelling was firm in consistency, fixed to the deep planes, and the superficial skin was normal, with no ulceration. In the cervical region level, the I, II, and III region lymph nodes were hard in consistency and fixed, the largest measuring about 3.5 × 2.3 cm in dimension. The level V region lymph nodes were palpable and mobile. Preoperative chest and vertebral radiographs and ultrasonography (USG) of the breast and ovaries were performed, to rule out metastasis. All the three scans showed no distant metastasis. A preoperative CT scan was taken, with contrast, which showed a heterogeneous ill-defined lesion, seen in superficial part of the left parotid gland, with few areas of low-density necrosis. A contrast CT showed heterogeneous enhancement, which did not enhance further on delayed images.

Fine needle aspiration cytology (FNAC) of the parotid gland swelling, from the level V lymph node region, was performed, which showed cells in clusters and singly scattered, round to oval cells, with a pleomorphic vesicular nucleus, prominent nucleoli, and scanty cytoplasm. The background showed necrosis mixed with blood. The Level V lymph node showed numerous aggregates of ductal epithelial cells, showing cellular pleomorphism and hyperchromatic nuclei. Few spindle cells were also seen. Considering the patient's clinical symptoms a total parotidectomy with extended

supraomohyoid neck dissection was planned, with preservation of the facial nerve [Figures 2 and 3]. However, the frozen sections revealed intravascular and intraneural involvement, hence, a radical parotidectomy, involving en bloc resection of the facial nerve along with the deep and superficial lobes of the parotid and an extended supraomohyoid neck dissection, was performed [Figures 4 and 5].

The patient was advised postoperative radiotherapy of 46Gy radiation, in 23 fractions, once daily, five days/week. The postoperative histopathological report suggested CXPA of the parotid gland with tumor infiltration in the submandibular gland, and level III and V lymph nodes showing tumor infiltration [Figure 6].

## DISCUSSION

Pleomorphic adenoma is the most common benign tumor that affects the salivary glands and occurs in 60-70% of the cases. Pleomorphic adenoma is characterized by proliferation of the epithelial-mesenchymal tissue of the salivary gland. Occasionally, a pleomorphic adenoma may undergo malignant transformation resulting in CXPA or carcinosarcoma, respectively. CXPA is an infrequent aggressive malignancy. Regional metastasis is common and mortality is high. This type of tumor is difficult to diagnose, as the mixed tumor component is often small and overlooked, and the malignant component may be difficult to classify.

The exact pathogenesis of CXPA remains controversial. Gerughty *et al.*,<sup>[9]</sup> believed that these tumors were malignant from the onset, as 60% of the patients in their series were initially seen without a history of a pre-existing tumor. The study by Beahrs *et al.*,<sup>[10]</sup> suggested that a carcinomatous transformation of a benign mixed tumor occurred because the median age of onset for a benign mixed tumor was 10 years younger than that for CXPA, and most patients were initially seen with a history of a mass present for many years (average duration, 23.3 years), with a sudden growth and new symptoms. Spiro *et al.*,<sup>[11]</sup> found that a third of their patients were aware of a lesion for at least 10 years. Eneroth and Zetterberg<sup>[12]</sup> observed that mixed tumors that had been present for longer than five years showed a tetraploid population of cells, similar to that found in CXPA. This suggested that as mixed tumors grew, the cells could undergo a transformation that could induce a carcinomatous component. The increased preoperative duration of a PA increased the risk of malignant transformation into a CXPA. In Gnepp's review,<sup>[3]</sup> the cancer had a mean lead up time of 23.3 years, with half the patients aware of the swelling for about two to three

years. Although the time from the onset of symptoms until diagnosis varied dramatically from one month to 52 years, more recent literature showed a mean lead up time of nine years, with half the patients being

aware of a painless mass for less than one year.<sup>[13,14]</sup>

As the presenting symptoms are quite similar to those presenting with benign PA, it is important



**Figure 1:** Preoperative frontal view



**Figure 2:** Opsite applied



**Figure 3:** Exposure of the parotid gland by the modified Blair incision



**Figure 4:** Parotidectomy done



**Figure 5:** Excised specimen



**Figure 6:** Postoperative frontal view

that clinicians maintain a high level of clinical suspicion, which can be challenging, considering the rarity of this cancer. The histological features of CXPA are: Capsule invasion, hemorrhage, and necrosis alternating with areas presenting classical features of pleomorphic adenoma.<sup>[15]</sup> Recent studies have shown that the most frequently encountered histological types in CXPA are: Highly malignant adenocarcinoma or undifferentiated carcinoma, although many other types have been found such as squamous cell carcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, papillary carcinoma, and terminal duct carcinoma,<sup>[13]</sup> CXPA treatment is surgical parotidectomy, with neck dissection. Some authors<sup>[16,17]</sup> recommend surgery and postoperative radiotherapy. Features associated with an unfavorable prognosis include: High tumor grade, large size, soft tissue invasion, perineural invasion, and lymph node metastases. According to LiVolsi and Perzin,<sup>[17]</sup> the extent of tumor infiltration beyond the capsule is the most reliable prognostic marker. CXPA metastasizes exclusively as a carcinoma. Distant metastases occur more frequently than regional metastases. Distant metastases seem to show a particular affinity for lung and bone, especially the vertebral column.<sup>[18]</sup>

## CONCLUSION

Carcinoma ex pleomorphic adenoma is an uncommon entity, with significantly clinical and pathological relevance. It is important to be aware of the disease, as it is difficult to be diagnosed both clinically and pathologically. The fact that pleomorphic adenoma is classified as a benign tumor must not overshadow the wide range of biological behaviors associated with these tumors. On account of the potential for malignant transformation, radical surgical treatment must be performed. Surgery followed by radiotherapy must be considered as the standard of care for a patient with carcinoma ex pleomorphic adenoma.

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