Case Report

Carcinoma in a gigantic preexisting pleomorphic adenoma

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ABSTRACT

Carcinoma ex pleomorphic adenoma (CEPA) is a rare malignancy arising from a primary or recurrent pleomorphic adenoma. Peak incidence is seen in octogenarian females. Delay in diagnosis of CEPA can be attributed to patients negligence owing to a mild nature of symptoms. CEPA is an aggressive tumor occurring mainly is major salivary glands such as parotid and submandibular glands.

Key words: Carcinogenesis, carcinoma ex pleomorphic adenoma, genes

INTRODUCTION

The most frequent type of malignant salivary gland tumors is adenoid cystic carcinoma, followed by adenocarcinoma and carcinoma ex pleomorphic adenoma (CEPA).[1] CEPA is defined as carcinoma arising (CA) from a primary or recurrent pleomorphic adenoma (PA).[2,3] It is a relatively rare malignancy, which constitutes approximately 3.6% of all salivary gland neoplasms, 6.2% of all mixed tumors and 11.2% of all malignant neoplasms of salivary glands.[2] Prevalence is 56 cases/million and yearly incidence is 0.17 tumors per million persons.[2] Peak age of incidence is sixth to eighth decades of life with slight female preponderance.[2] The macroscopic features that suggest malignant transformation in PA include poorly defined and/or infiltrative tumor margins, the presence of foci of hemorrhage, and necrosis.[1] Difficulty in clinical and pathological diagnosis as well as patients' negligence for seeking treatment makes CEPA a rare but important entity. Herein we discuss a case of 85-year-old female with long standing (20 years) parotid swelling, presenting with a recently developed pain in the swelling which proved out to be CEPA after histological examination. We shall also discuss about the clinical, pathological and molecular perspective along with the causes of delay in treatment.

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CASE REPORT

An 85-year-old lady presented with the complaint of swelling on the right side of the face for more than 20 years. Swelling initially was about 1 cm × 1 cm in size and noticed just below the ear lobule. It was gradually increasing in size until 2 months when it showed exponential growth in size. Since then she also developed pain in the swelling which was sudden in onset, dull aching, continuous in nature and used to get relieved with analgesics. Pain was associated with a sudden increase in the size of swelling by about 20%.

On clinical examination, a mass of size 22 cm × 10 cm × 10 cm was found over right parotid area, extending up to midline below the chin, hanging up to 8 cm below the right clavicle. Ear lobe was raised upwards. Surface was irregular and bosselated with variegated consistency (firm and cystic). Skin over the swelling was normal in shine and texture except at the lower end where congested veins were present. No signs of facial nerve palsy were found [Figure 1].

Preoperative fine needle aspiration cytology (FNAC) revealed PA. Computed tomography (CT) scan revealed a large, heterogeneously enhancing solid and cystic mass arising from right parotid gland with maintained surrounding fat planes, with no obvious evidence of infiltration into adjacent tissues and the parapharyngeal space was maintained.

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The tumor was excised under general anesthesia. Lazy "S" incision along with the creation of skin flaps to provide sufficient tissue for closure were done. Skin flaps from the surface of the tumor were raised. Facial nerve was found to be embedded within the tumor mass. Lower branches of the facial nerve were divided, and tumor was removed en bloc [Figure 2]. Primary closure was done with a negative suction drain placed in the wound. Postoperatively, facial nerve palsy was evident, which was treated symptomatically [Figure 3].

Macroscopically the tumor measured 20 cm × 10 cm × 8 cm. On cut section, large lobulated, globular mass with cystic and myxoid degeneration filled with mucoid material and areas of hemorrhage measuring 19 cm × 9 cm × 4 cm were present.

Microscopically sections revealed partially encapsulated tumor composed of solid nests of large pleomorphic malignant epithelial cells with central vesicular nuclei and prominent nucleoli. There were cords and nests of benign epithelial cells enveloped by mantle of myoepithelial cells, in the amphophillic chondromyxoid stroma. At some places, chondroid metaplasia was also seen. Mitotic count was low.

DISCUSSION

Malignant PA is of three types: (1) First is a benign PA, which metastasizes as benign PA. (2) Second type is a carcinosarcoma. (3) Third, the most common type, CEPA develops in association with a benign primary or recurrent PA and accounts for most of the reported cases of malignant PA.[1]

Carcinoma ex pleomorphic adenoma is an aggressive tumor with high overall mortality, occurring mainly is major salivary glands such as parotid and submandibular glands. It mainly occurs in sixth to eighth decades of life, predominantly in females. Most common presenting symptom is a slow growing firm parotid mass. Many a times, it can be asymptomatic as most cancers are not widely invasive and may present like PAs.[4,5] Facial palsy may or may not be present.[5] In the study by Olsen and Lewis facial nerve involvement was present in approximately one-third of patients.[5] Skin ulceration, tumor fungation, skin fixation, palpable lymphadenopathy, dysphagia,[3,5] swollen jaw, dental pain and loss of vitality[6] are some other symptoms that may be associated. Pain with rapid enlargement of tumor points toward malignancy.[5]

The risk of malignant transformation in PAs is 1.9–23.3%[7] which increases with long duration, recurrences, advanced age and location in major salivary gland.[8] Risk of malignancy increases from 1.6% in tumors of duration < 5 years, to 9.5% for those with a history of >15 years.[9]

On molecular basis, development of CEPA follows the model of carcinogenesis with loss of heterozygosity at chromosomes 8q (most common), then 12q and finally at 17p[10] associated with mutation in tumor suppressor genes like p53 and p21.[11-13] Various studies support dysregulation of COX-2 gene[14] and role of cell adhesion molecules (CAM) like E-cadherin, neural-CAM and beta catenin[15-18] in the development of CEPA.

Gross appearance is greyish-blue and transparent to yellowish if PA component is dominant, with areas of necrosis and hemorrhage if the dominant component is malignant.[2,5,19] Microscopically the tumors may be noninvasive, minimally invasive and invasive on the basis of invasion of carcinomatous component outside the fibrous capsule.[20,21] Malignant component may be adenocarcinoma not otherwise specified (most commonly), adenoid cystic carcinoma, mucoepidermoid carcinoma or salivary duct carcinoma type.[7,19,22,23]

Histological examination is a gold standard for diagnosis. FNAC, commonly used for diagnosis preoperatively,

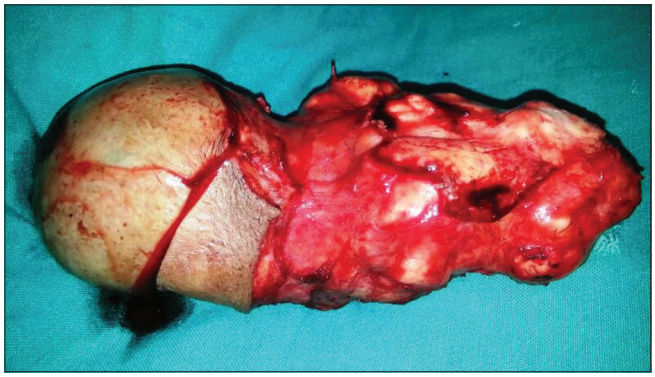

Figure 1: Completely excised tumor

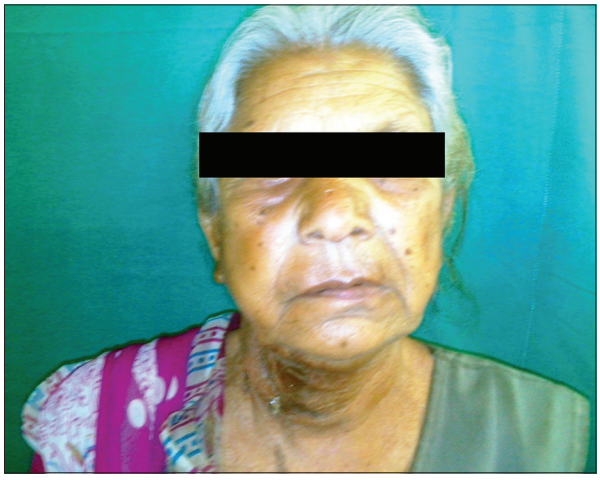

Figure 2: Postoperative appearance with obvious facial nerve palsy on the affected side

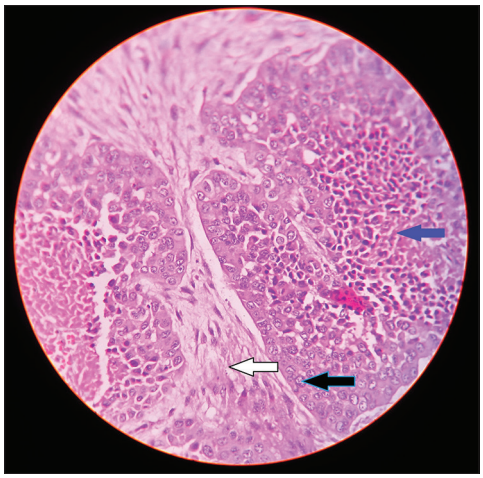

Figure 3: Black arrow - Infiltration of the glandular elements by malignant cells with prominent nucleoli. White arrow - Stroma of the parotid gland showing infiltration by malignant cells. Blue arrow - Pyknotic/dead cells

shows a low sensitivity.[3,7] Combination of FNAC, ultrasonography, CT-scan and magnetic resonance imaging should be used as none of these modalities are of high accuracy when used alone.[24]

Treatment for CEPA is parotidectomy (superficial, total or radical, based on invasiveness of tumor and involvement of adjacent structures like facial nerve, mandible or mastoid). Superficial parotidectomy is done for CEPA localized to the superficial lobe of the parotid gland. Total parotidectomy involves the resection of both the deep and superficial lobes of the parotid, in cases of invasive cancers, with an attempt to preserve the facial nerve. Radical parotidectomy, in cases of facial nerve involvement by the tumor, involves en bloc resection of the tumor along with the facial nerve. Postoperatively chemo-radiotherapy is given. However, there is limited literature on the effectiveness of chemotherapy in the management of CEPA.[3,22] Neck dissection may or may not be done depending upon presence or absence of metastasis to cervical lymph nodes.[3,5]

Removal of the specimen may be followed by an immediate reconstructive surgery if required. Sural nerve grafting may be performed in cases where facial nerve has been removed. However, this is not undertaken in the case of longstanding preoperative facial nerve palsy. Rarely, radial forearm free flap, a sternomastoid flap or a cervical rotation flap is performed. According to Gnepp, the 5 years survival rates of the patients of CEPA ranges from 25% to 65%.[2]

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