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Central papillary cystadenocarcinoma of the mandible: A case report and review of the literature

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ABSTRACT

INTRODUCTION: Central papillary cystadenocarcinoma of the jaw is an extremely rare tumor with only three previously reported cases in the English literature. This tumor is a histologically low-grade cancer, affecting more commonly in the mandible than in the maxilla.
PRESENTATION OF CASE: A 65-year-old woman presented with a two months history of a rapidly growing, painless mass of the right ascending ramus of the mandible. The pathologic report from incisional biopsy was a papillary cystic tumor with a differential diagnosis of cystadenoma versus cystadenocarcinoma. Segmental mandibulectomy, parotidectomy and submandibular gland resection were performed. The final pathology was intraosseous papillary cystadenocarcinoma.
DISCUSSION: Clinical features of central papillary cystadenocarcinoma of the mandible mimic an odontogenic lesion and metastatic bone disease, careful review of radiograph and pathology should be done. Surgical excision with wide margins is the appropriate treatment. Postoperative radiation therapy should be considered in histologically aggressive or high-stage tumor.
CONCLUSION: This is the fourth case of central papillary cystadenocarcinoma of the mandible in the English literature. Although it is usually a low-grade cancer, en bloc resection with adjuvant postoperative radiotherapy in a high-stage disease, and long-term follow-up allow the patient to have a favorable prognosis.

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1. Introduction

Malignant salivary gland neoplasms that occur primarily in the mandible are rare, with most of them being mucoepidermoid carcinoma.[1,2] Papillary cystadenocarcinoma of the salivary gland is uncommonly found[3] and when it originates intraosseously in the mandible, only three cases have been previously reported.[2,4,5] Histologically, the tumor is characterized by a predominantly cystic and invasive growth pattern with a papillary component and defined as a low-grade malignant glandular tumor.[3,6] The radiologic finding consists of a unilocular or multilocular radiolucency mandibular lesion which mimics an odontogenic lesion and metastatic bone disease.[2,4] The authors report the fourth case, and discuss clinical features and management of central papillary cystadenocarcinoma of the mandible.

2. Presentation of case

A 65-year-old woman presented with a two months history of a rapidly growing, painless mass of the right face without trismus, facial or trigeminal neuropathy, or other neck mass. Her history included controlled hypertension and a left thyroid lobectomy for toxic adenoma several years ago. Physical examination revealed a hard consistency mass about 7 cm × 7.5 cm over the right mandibular ramus (Fig. 1). Fine needle aspiration biopsy (FNAB) was performed but the result was unsatisfactory. Computed tomography scan showed a large multilocular low density area at the ascending ramus of the mandible attached to the parotid gland and an ill-defined border between submandibular gland and the mass (Fig. 2). An open incisional biopsy was performed and the pathological report was a papillary cystic tumor with a differential diagnosis of cystadenoma versus cystadenocarcinoma.

Segmental mandibulectomy, parotidectomy and submandibular gland resection were performed (Fig. 3). Neck dissection was not performed because no lymphadenopathy was detected in CT scan. The final pathology was intraosseous papillary cystadenocarcinoma of the mandible with both major salivary glands being normal tissue. Microscopically, the tumor contained multiple cystic

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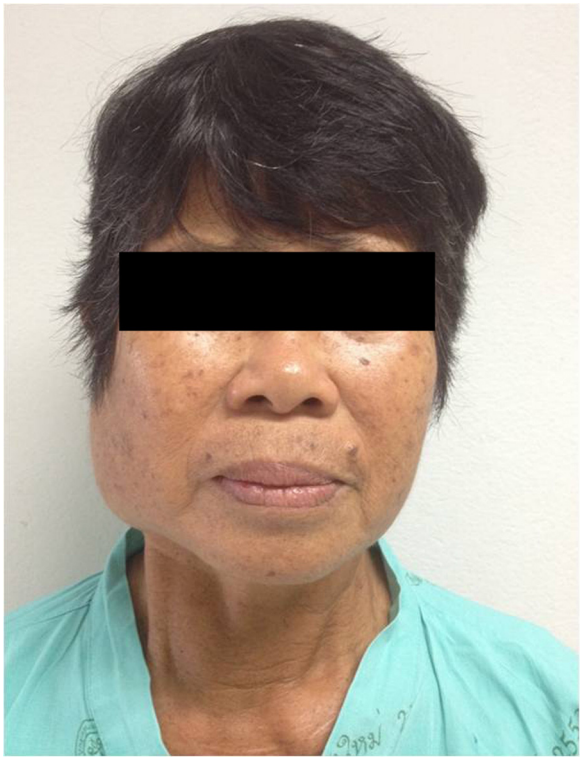

Fig. 1. A 65-year-old woman with a hard consistency mass at right mandible.

cavities with papillary projection. The neoplastic ducts infiltrate into the bone and surrounding skeletal muscle. The lining epithelia are mostly single layer of cuboidal cells with mild cellular and nuclear pleomorphism. The mitotic activity is low. The necrosis and perineural invasion is not present (Fig. 4).

The tumor cells are immunoreactive for CK7, CK19 and CEA but not for CDX-1, CK20, CA-125 and TTF-1.

The diagnosis was central papillary cystadenocarcinoma of the mandible. Post-operative radiotherapy with a total dose of 66 Gy (2 Gy per fraction) at the primary site and upper neck (levels I–III) was administered because of the large tumor size with cortical bone erosion although the surgical margins were negative and perineural invasion and high grade features were absent.

One year after surgery and ten months post-radiation therapy, the patient has no tumor recurrence both at the primary and neck (Fig. 5).

3. Discussion

Papillary cystadenocarcinoma of the salivary gland described by the WHO in 1991 is extremely rare.[3,7] The tumor is also called malignant papillary cystadenoma, atypical type of adenocarcinoma, low-grade papillary adenocarcinoma, and mucous-producing adenopapillary carcinoma.[3,8] This tumor is more commonly found in the major salivary glands (65%) and most often occurs in the parotid gland (95%).[6] The minor salivary glands involved by the tumor are found in the lip, buccal mucosa, palate, tongue and retromolar trigone.[6] Tumor histology is characterized by a cyst and papillary endocystic projection and defined as a low-grade glandular tumor with an indolent behavior.[3,6] However, the presence of intense nuclear and cellular pleomorphism and numerous mitosis with a rapidly progressive clinical course indicate a high-grade malignant tumor.[3]

Central or primary malignant salivary gland neoplasm of the jaw is a rare neoplasm arising intraosseously.[1,4,5,9] The tumor is

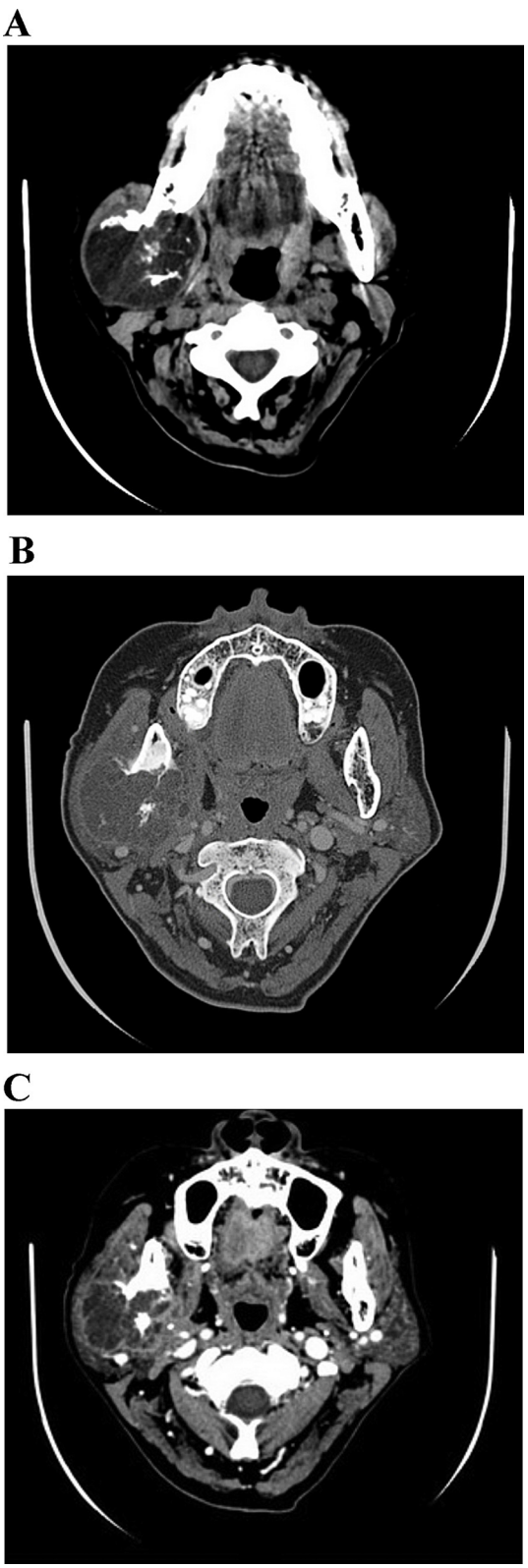

Fig. 2. Axial non-contrast enhanced CT scan of the mandibular ramus shows a circumscribed margin, multilocular cystic mass at the right side with internal coarse, irregular calcifications (A). Bone window image reveals a very thin bone around the expansile mass (B). The tumor has contact surface with the right parotid gland and caused lateral displacement of the gland in a contrast enhanced film (C).

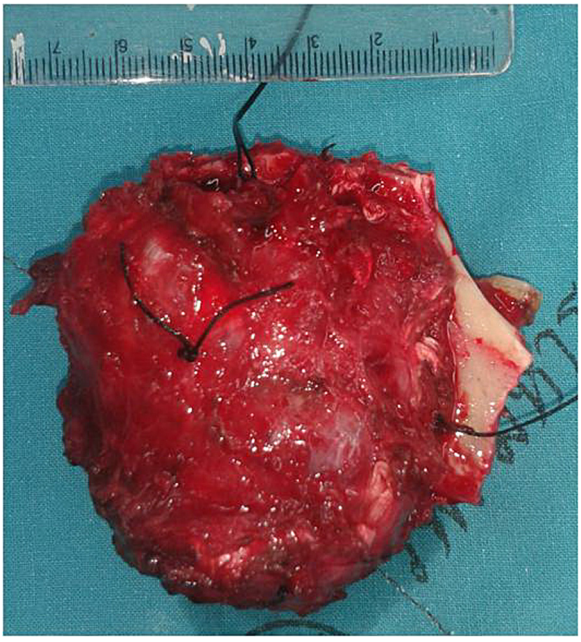

Fig. 3. Surgical specimen (tumor at ascending ramus of the mandible).

found more commonly in the mandible than in the maxilla[1] and comprises less than 0.4% of all salivary gland carcinomas.[9] Ectopic salivary gland tissue has been reported in a wide variety of locations, including the skin of the neck, the thyroid, the pituitary, the mastoid, the middle ear, the maxilla, and the mandible.[1,9] Neoplasm of the heterotopic salivary tissue is rare and most reported cases are in the upper cervical lymph node and in the mandible.[9]

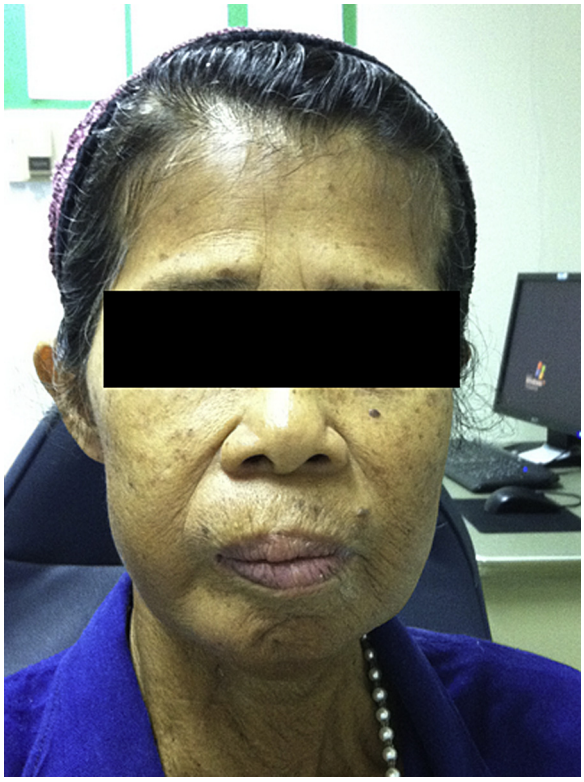

Fig. 5. Picture of the patient 1 year after surgery.

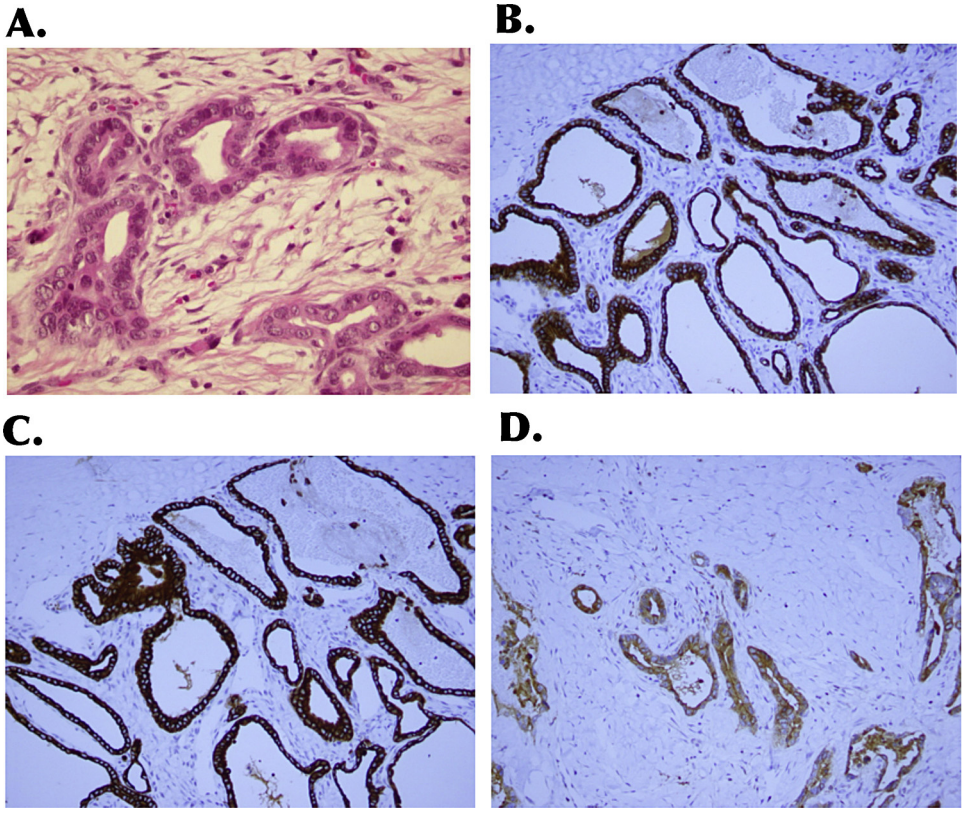

Fig. 4. Histopathology of the tumor shows cystic cavities lined with single layer of cuboidal cells with mild nuclear pleomorphism. (A) (H&E stain, 400× magnification). The tumor's immunohistochemical stainings are positive for CK7 (B), CK19 (C) and CEA (D)

The pathogenesis of salivary gland tumor arising centrally within the mandible has been proposed as (1) entrapment of salivary tissue from the major or minor salivary glands within bone during embryonic development, (2) aberrant induction of salivary tissue from the dental lamina epithelium during embryonic development, (3) metaplastic transformation of mucous secreting cells in odontogenic cyst epithelium, or (4) entrapment of minor salivary glands from chronic osteomyelitis.[1,2,10,11]

The most frequent manifestation of the patient is a swelling of the mandible followed by bony pain or tooth pain, trismus, paresthesia of the lip, mobile teeth and drainage.[1,2]

Unilocular or multilocular radiolucency in a radiograph is characteristic of a central bone lesion,[1,2] although it has been reported that most lesions with unilocular destruction were malignant changes in odontogenic cysts, and most lesions with multilocular destruction were intraosseous salivary gland carcinomas.[9]

The histology of a central salivary gland neoplasm in the mandible is identical to that of its salivary gland counterparts and usually does not pose diagnostic difficulties.[9] The principal differential diagnosis for this disease is metastasis from another primary carcinoma and cystic odontogenic lesion.[1,2,9] The presence of intermediate cells and multilocular destruction would favor the diagnosis of central salivary gland malignancy.[9]

Pathologic examination of the tumor specimen and imaging study should be reviewed to exclude the possibility of any connection with the nearby mucosa and salivary gland.[9] Histology and immunostaining are useful for differentiating the disease from odontogenic, osteogenic and metastatic lesions. The criteria for the diagnosis of the central origin of salivary gland malignancy in the mandibles have been introduced as (1) radiographic evidence of primary central bone destruction, (2) absence of any primary lesion in the major or minor salivary glands, (3) clinical and histological exclusion of a metastasis or an odontogenic lesion, and (4) histologic confirmation of the typical architectural and morphologic features of malignant salivary gland tumors.[1,2,11,12]

Li et al.[2] summarized 197 cases of central malignant salivary gland tumors of the jaw and stated that mucoepidermoid carcinomas were the most common histology (68.5%) followed by adenoid cystic carcinomas (16.2%), adenocarcinomas, NOS (5.0%), acinic cell carcinoma (4.6%), carcinoma ex pleomorphic adenoma (4.1%), and epithelial-myoepithelial carcinoma (1.5%).

A staging system for central malignant salivary gland tumor was established by Brookstone and Huvos in 1992 based on the condition of overlying bone. Stage I is indicated by lesions with intact cortical bone and overlying periosteum without signs of cortical expansion. In Stage II lesions are surrounded by intact cortical bone with some degree of expansion. Stage III is characterized by lesions with cortical perforation, breakdown of the overlying periosteum or nodal metastasis.[1]

The appropriate treatment of the primary tumor is en bloc resection, including marginal mandibulectomy and segmental mandibulectomy based on preoperative (clinical and radiologic) findings and intraoperative evaluation [2] and the authors suggest a 1–1.5 cm margin of bone resection. Neck dissection is necessary when evidence of any metastatic cervical lymph node involvement is present.[2,11] Adjuvant radiotherapy and chemotherapy have been reported in cases with perineural invasion, inadequate surgical margin, large tumor, rupture of cortical plate, and soft tissue invasion.[2,11]

Following a literature review of central papillary cystadenocarcinoma of the mandible, three cases have been previously reported.[2,4,5] The summary of four cases, including ours, listed all patients as female. Most presented with painful swelling of the mandible. Surgery was the primary therapy which was either partial mandibular resection/marginal mandibulectomy or segmental mandibulectomy. Neck dissection was performed in a case with lymphadenopathy. One case reported tumor recurrence after a segmental mandibulectomy which likely reflected an advanced stage of the disease[2] (Table 1). Our case, a large tumor at the mandibular ramus (stage III, Brookstone and Huvos's classification) underwent segmental mandibulectomy and resection of submandibular and parotid glands because the tumor approached these structures. Radiation therapy was administered postoperatively due to large tumor volume and erosion of cortical bone plate even though pathology reported free surgical margins and normal submandibular and parotid glands. There has been no evidence of tumor recurrence after one year of follow-up.

4. Conclusion

Central papillary cystadenocarcinoma of the mandible is a low-grade malignant tumor. Clinical, radiographic and histopathologic examinations should be carefully reviewed to differentiate this neoplasm from other possible diseases. The tumor's prognosis is still unsettled. Surgical excision with wide margins is the appropriate treatment, while adjuvant radiotherapy should be considered in histologically aggressive or high stage tumor. Prolonged clinical observation is mandatory.

Conflict of interest

None of the authors have any conflicts of interest to disclose.

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Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Table 1
Summary of central papillary cystadenocarcinoma of the mandible.

Author, year	Age (yrs)	Gender	Location	Signs/symptoms	Treatment	Follow-up
Johnston et al., 2006	73	F	Angle	Jaw pain, Resorbed tooth	Curettage then marginal mandibulectomy	NA
Li et al., 2008	56	F	Ramus	Painless swelling	Hemimandibulectomy	Recur in 8 mo
Takei et al., 2012	64	F	Body	Painful swelling	Partial resection of mandible Supreomohyoid neck dissection	No recurrence in 26 mo
Present report	65	F	Ramus	Painless swelling	Segmental mandibulectomy Parotidectomy Submandibular gland resection Postoperative radiotherapy	No recurrence in 1 yr

Author contributions

Dr. Chonticha Srivanitchapoom and Dr. Pichit Sittitrai were involved in writing the paper, data collection and preparing the literature review. Processing and histologic analyses was done by Dr. Pongsak Mahanupab. All authors approved the final version of the manuscript.

Key learning points

- Central papillary cystadenocarcinoma of the mandible can mimic an odontogenic lesion and metastatic bone disease.
- En bloc resection with adjuvant postoperative radiotherapy is the treatment.

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