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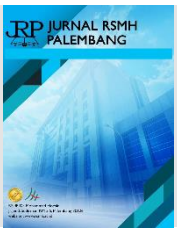

Primary Adenoid Cystic Carcinoma, Subtype of Ceruminous Adenocarcinoma in Right External Auditory Canal: A Case Report

Eka Putra Pratama[1*], Susilawati[1], Wresnindyatsih[1]

[1]Department of Anatomical Pathology, Faculty of Medicine, Universitas Sriwijaya / Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia

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Corresponding author:
Eka Putra Pratama

E-mail address:
res_sandoz@yahoo.com

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ABSTRACT

Background. Ceruminous adenocarcinoma is rare, accounting for less than 2,5% of all external auditory canal neoplasms. The tumours occur in the outer half of the external auditory canal, excluding direct extension from parotid gland. Adenoid cystic carcinoma is the most common subtypes. Adenoid cystic carcinoma needs to be distinguished from its primary origin from the salivary glands and extends to ear, because they share the same histopathology features and immunohistochemistry. Therefore, combinations of clinical features and radiology is needed to diagnose this tumour correctly. **Case description.** A female patient, 60 years old, admitted to RSMH Palembang with complaint ofyellow discharge coming out from ear. She also havehearing loss and pain since 6 months before admission to the hospital. One week later, the patient develops facial weakness with no mass on face. CT-Scan examination was performed, with the results showed that the mass in right external auditory canal and extends to the mastoid cavity, maxillary sinus wall and brain parenchym. Biopsy was performed in mastoid region and revealed tumour mass with cribriform pattern, few solid pattern, consists of bilayered neoplastic cells with inner luminal and outer abluminal cells. Immunostaining showed CK7 and CD117 positive in luminal cells, p63 positive in abluminal cells, S100 showed positivity in myoepithelial cells. **Discussion and conclusion.** Based on clinical symptoms, radiology, histopathology, and imunohistochemical staining, the mass in right mastoidis consistent with a ceruminous adenocarcinoma, adenoid cystic carcinoma subtypes, originated from external auditory canal.

1. Introduction

Ceruminous adenocarcinoma is a very rare ceruminous gland malignancy that occurs in human, accounting for less than 2,5% from all of the external auditory canal tumour and the second most common carcinoma originated from ceruminous gland. Ceruminous adenocarcinoma according to World Health Organization (WHO) 2017, can be subclassified as adenocarcinoma, adenoid cystic carcinoma and mucoepidermoid carcinoma.[1,2]

The most common symptoms that can be found in ceruminous adenocarcinoma, including mass, hearing loss, discharge or blood discharge from ear canal, pain and fascialis nerve paralysis, followed by lymphadenopathy and tinnitus. Ceruminous adenocarcinoma often locally recur, extent through regional lymph node and distant metastasis.[1]

Ceruminous glands are modified apocrine glands located in the external auditory canal. Neoplastic lesions originating from these glands are extremely rare in humans and become a ruled out diagnosis. Secondary tumors like adenoid cystic carcinoma originating from parotid gland that expands to the ear is more common and constitute the main differential diagnosis, especially for ceruminous adenocarcinoma with adenoid cystic carcinoma subtype. Due to the limitations of the anatomical location, benign and

malignant tumors in this area give similar clinical and radiological symptoms. Benign and malignant tumors in this area also have overlapping histomorphological features, which presents a challenge in establishing an accurate diagnosis and appropriate treatment options.[1] An accurate identification is needed in diagnosing seruminous adenocarcinoma both clinical and histopathological information. We report one case of ceruminous adenocarcinoma in a 60-year-old woman in the Department of Anatomical Pathology, RSUP dr. Mohammad Hoesin Palembang.

2. Case Report

A 60-year-old woman presented with smelly yellowish discharge from right ear canal since two years ago. The discharge is greenish yellow, smelly, accompanied by ear pain and hearing loss. There were no complaints about tinnitus, fever, runny nose, painful swallowing and difficulty swallowing. The patient went to the doctor and was given an ear drops, the complaint was reduced.Since the last six months, complaints of discharge from the ear have recurred, also with headaches. The discharge is greenish yellow, smelly, accompanied by ear pain and hearing loss. The patient then went to an ENT doctor and was advised to do a CT-Scan examination. The patient was referred to the RSUP dr. Mohammad Hoesin Palembang for further management. Audiometry examination showed a sensorineural deafness of very severe degrees in right ear. CT-Scan showed a mass in right external auditory canal with destruction of the tymphanic segment of the basic sphenoid wing forming the right temporomandibular joint, extending to the right cerebral temporal parenchyma of the right inferior gyrus and the posterior maxillary sinus wall of the right nasal cavity (Figure 1).

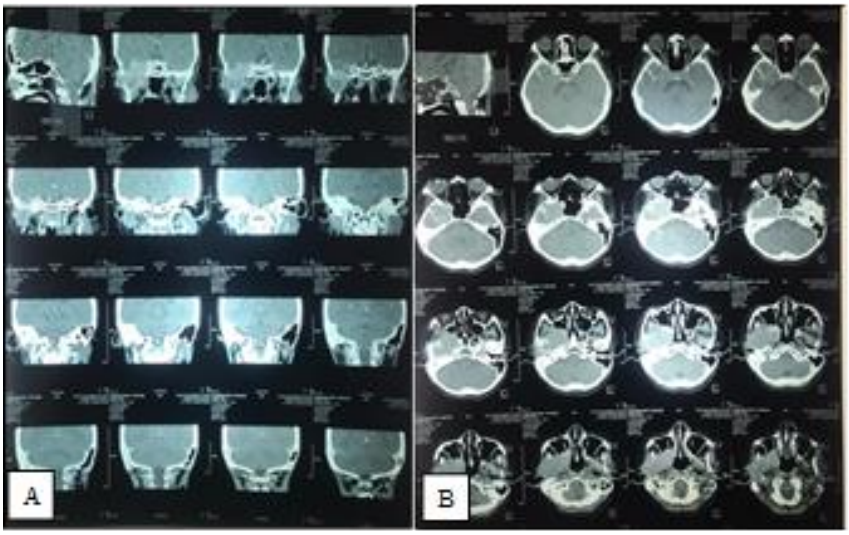


Figure 1. Mastoid CT-Scan. CT-Scan showed a mass in right external auditory canal with destruction of the tymphanic segment (A) Coronal section. (B) Axial Section.

Small biopsy was done in the mastoid region and microscopic examination showed fragmented tissue. The tumor mass forms a tubular and cribriform structures, with the lumen containing a basophilic amorphous mass, some of which also form a solid structure. The mass of the tumor consists of neoplastic cells arranged in a bilayer (luminal and abluminal cells) in the form of epithelial and myoepithelial cells, the N/C ratio is increased, with round-oval nucleus, fine chromatin, hyperchromatic, some with small nucleoli visible, eosinophilic cytoplasm, surrounded by fibroconnective tissue stroma, with inflammatory cells including lymphocytes and plasma cells. Perineural invasion cannot be assessed in this small biopsy. Immunohistochemistry confirmed the presence of two

distinct cell populations. The luminal cells expressed cytokeratin 7 and CD117, while abluminal cells expressed S100 protein and p63. Based on these clinical features, radiology, histopathological and immunohistochemical findings, the diagnosis of ceruminous adenocarcinoma with adenoid cystic carcinoma subtypes was established. (figure 2 and 3)

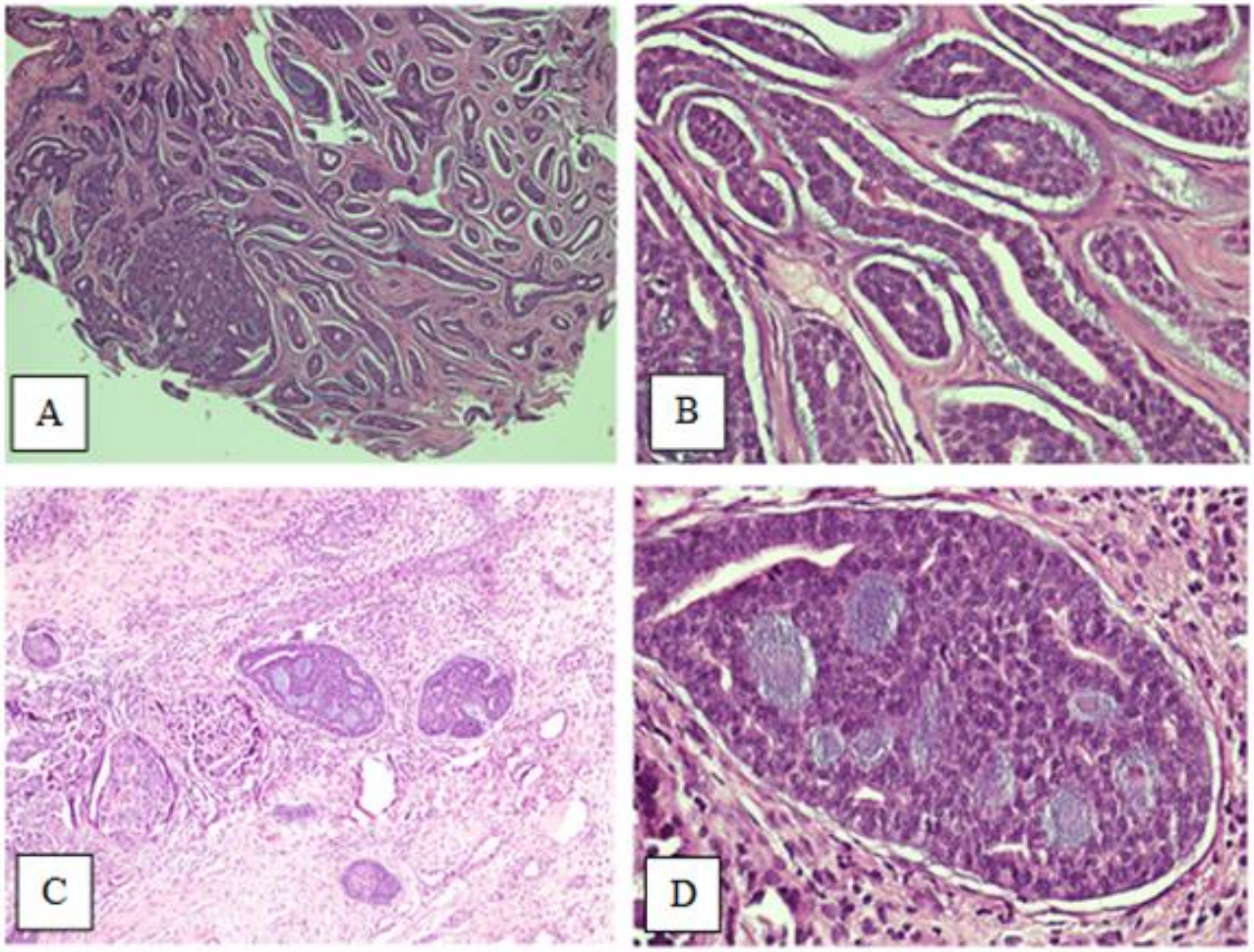
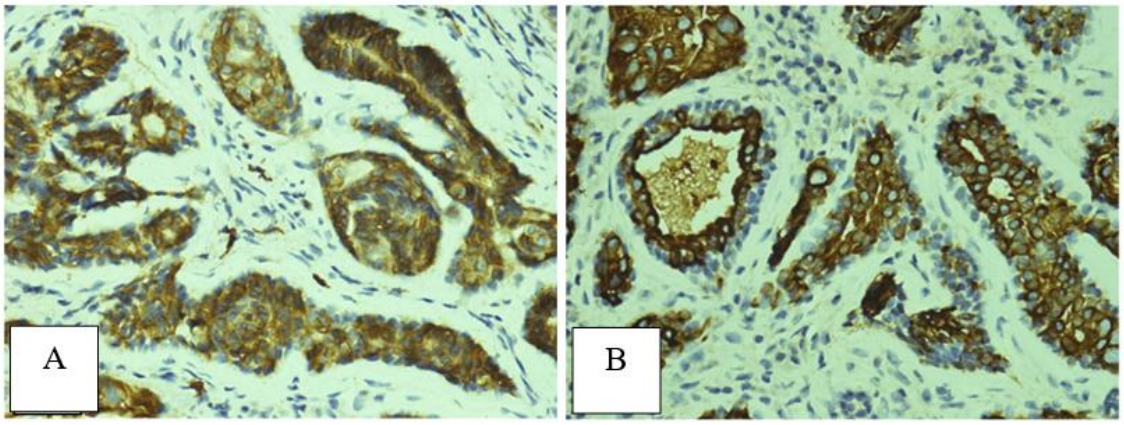


Figure 2. Microscopic examination. (A) The tumor is made of tubular and cribriform structures (H/E x40). (B) Tubular structures lined by bilayered cells (H/E x400). (C) Cribriform structures (H/E x40). (D) Cribriform structures lined by bilayered cells (H/E x400)



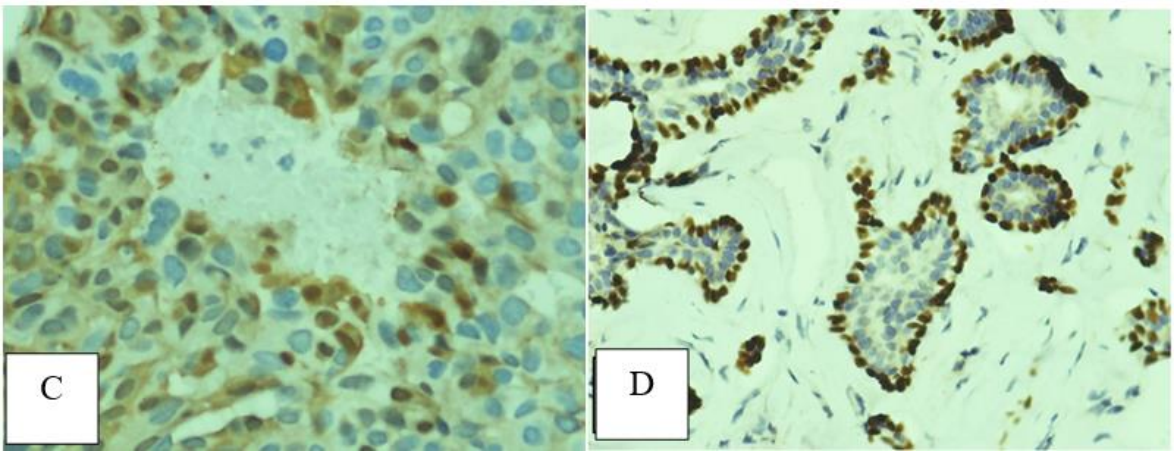


Figure 3. Immunohistochemical findings. (A) Immunostain for CK7 cytoplasm positivity in luminal cells. (B) Immunostain for CD117 cytoplasm positivity in luminal cells. (C) Immunostain for S100 focal positivity. (D) Immunostain for p63 nuclear positivity in abluminal cells.

3. Discussion

The ear can be divided into three regions or compartments which include: outer ear, middle ear with temporal bone and inner ear. The outer ear consists of the auricle, external auditory canal (or meatus) and tympanic membrane at the medial end of the auditory canal. The middle ear consists of an ossicle that sends vibrations received from the tympanic membrane on the outer ear, the eustachian tube that connects the middle ear to the nasopharynx, and the middle ear cavity in the form of an air cavity in the temporal bone. The inner ear consists of the cochlea which acts as a hearing receptor, the semicircular canal contains endolymph fluid which functions to maintain the balance of the body and the utricular saculus which contains nerve cells.[3]

Histologically, the auricle is a cutaneous structure lined by keratinizing squamous complex epithelium with the dermis contain skin adnexal structures including hair follicles, sebaceous glands and eccrine sweat glands. In addition, there are modified apocrine glands called ceruminous glands in the outer third of the external auditory canal,which replace eccrine glands in the auricular dermis. Ceruminous glands produce cerumen and are lined by cuboidal cells in the luminal with eosinophilic cytoplasm, which often contain brownish yellow granular pigments. These cells have secretory apical snouts in their luminal parts. The abluminal part linedby flattened myoepithelial cells. The ducts of the ceruminal glands lead to the hair follicles.[3]

Ceruminous adenocarcinoma is a malignant tumor originating from the ceruminous glands in the external auditory canal. Ceruminous adenocarcinoma is a rare tumor, occurring in <2.5% of all external auditory canal tumors. Females are more frequently affected, with a female to male ratio of 1.5: 1. The mean age of affected patients is 50 years (range 21 to 92 years), as the case for benign tumors.[1,2,4,5]

Adenoid cystic carcinoma is the most common variant of ceruminous adenocarcinoma. It is twice as common as other variants of ceruminous adenocarcinoma. Undetermined ceruminous adenocarcinoma or NOS is the second most common variant of ceruminous adenocarcinoma. Mucoepidermoid carcinoma is the rarest variant of ceruminous adenocarcinoma and only a few cases that have been reported in the literature.[1,4]

The cause of cerumucinous adenocarcinoma is unknown, but the adenoid cystic carcinoma variant are usually occurs in the result of a genetic disorder with chromosome translocation t(6; 9), which causes fusion of the MYB-NFIB gene, and this disorder is the same as adenoid cystic carcinoma of the salivary glands. The genetic data for adenocarcinoma or

mucoepidermoid carcinoma variants have not been found yet.[2,6]

The most common symptom of ceruminous adenocarcinoma with adenoid cystic variant is usually ear pain, followed by hearing loss and ear discharge (otorrhea). In addition, chronic or recurrent otitis externa can also be found, bleeding, tinnitus, vertigo and nerve symptoms in the form of facial nerve paralysis and paraesthesia, without a mass in the parotid gland, to exclude the primary adenoid cystic carcinoma originating from parotid gland. The tumor massranges from 0.5 to 3.0 cm in size, with an average diameter of 1.55 cm. Deep infiltration of the surrounding connective tissue with destruction of bone and invasion of nerve vessels is common. On radiological examination, computed tomography scan (CT-Scan) and magnetic resonance imaging (MRI) can help determining tumor infiltration to the surrounding connective tissue. Expansion into the infratemporal fossa and invasion of the parotid gland may also be seen.Some studies showed thatCT-Scan examination can help distinguished between ceruminous adenocarcinoma adenoid cystic carcinoma variant anda primary parotid adenoid cystic carcinoma. CT Scan examination of primary parotid adenoid cystic carcinoma showed a stylomastoid foramen erosion and fascialis canal enlarged on the temporal bone[1,4,7,8]

Macroscopic examination of the tumor is usually an exophytic mass, ulcerated, polypoid or round in shape.[9] Surface ulceration can also be found in benign tumors. Ulceration itself is not specific for cases of malignancy.[4]

The histopathological features of ceruminous adenocarcinoma with adenoid cystic carcinoma subtype is similar to that of the salivary gland, which is a mass of tumor that is not encapsulated with infiltration of tumor cells into the surrounding connective tissue.[1] The tumor consists of abluminal cells in the form of modified basaloid or myoepithelial cells, which is the dominant cell type, the cytoplasm is scant, eosinophilic cytoplasm, some with clear cytoplasm, angular to oval nucleus, uniform, hyperchromatic, indistinct nucleoli and unclear cell boundaries. Luminal cells are usually scattered among basaloid cells and are difficult to identify, usually characterized by a round nucleus and eosinophilic cytoplasm. Tumor cells are usually arranged in a pattern of tubular nests or cribriforms of varying sizes and there is an amorphous mass of material trapped in the lumen. Myxoid or mucinous changes are common. Tumor cells can also form solid patterns, which is associated with a worse prognosis. Tumor necrosis and pleomorphic cells are usually rare. Perineural invasion is frequent and can be multifocal. Some histopathologic features that correlate with an increased risk of recurrence and poor prognosis include: solid tumor pattern, bone invasion, perineural invasion and margin resection that is still positive.[9-13]

Immunohistochemical markers on both basal cells and luminal cells are usually positive for cytokeratin and epithelial membrane antigen (EMA) markers. Luminal cells are positive for CD117, cytokeratin 7 and 19, whereas myoepithelial cells usually express S100, p63, smooth muscle actin (SMA) and CK5/6. Cytokeratin staining is usually less reactive in abluminal cells than luminal cells. Histochemical mucicarmine and periodic acid schiff (PAS) staining with diastase can be used to see the presence of intracytoplasmic mucin in variants of mucoepidermoid carcinoma.[1,2,4,8]

Ceruminous adenocarcinoma is usually a rare tumor. Because they are rare, they are often become an excluded diagnosis. Benign and malignant tumors originating from the ceruminous glands have overlapping clinical and morphological features. Therefore, the differential diagnosis of ceruminous adenocarcinoma, namely ceruminous gland adenoma and ceruminosa pleomorphic adenoma in the case of benign ceruminous gland tumors. In addition, it can also be in the form of tumors originating from the epidermal, external auditory canal, middle ear and mastoid, namely cylindromas, basal cell carcinoma and squamous cell carcinoma. Extension of the salivary tumor from the parotid gland and other

variants of ceruminous adenocarcinoma may also be considered. Radiological features play a role in an accurate diagnosis.[1] It should be noted that small biopsies can also lead to misinterpretation. Most of the samples are usually small and fragmented. Therefore, data regarding tumor infiltration can be useful in determining malignant cases. Perineural invasion and lymphovascular invasion are extremely difficult to detect on small biopsy specimens. If it is found, it will be a great help in determining the malignant nature of the tumor.[4]

The similarity in the microscopic picture of ceruminous adenoma and ceruminous gland adenocarcinoma is a glandular structure covered by two layers of epithelium. However, in adenomas, the ceruminous glands are usually arranged in lobulated clusters and can be papillary, solid or cystic patterns. The luminal cells show a broad eosinophilic cytoplasm with scattered yellow-brown cytoplasmic pigments. Cell atypia is usually mild and there is no atypical mitotic activity, necrosis, perineural or lymphovascular invasion. The macroscopic appearance is usually well defined but not encapsulated. Ceruminous pleomorphic adenoma usually shows irregular proliferation of tubuloglandular structures lined by two layers of epithelium. The stroma is usually hypocellular, consisting of either a mucoid matrix or a chondromiksoid. The lipomatous component of the mesenchymal is usually rare. Clinical symptoms between malignant and benign tumors are usually the same, namely in the form of discharge, ear pain and hearing loss. However, the duration of symptoms is usually longer in benign tumors and there is no facial nerve paralysis. Radiological features of benign tumors usually do not show destruction of the ear canal and infiltration into the surrounding structures.[1]

Ceruminous adenocarcinoma often has local recurrences and can spread to regional or systemic lymph nodes. Ceruminous adenocarcinoma with a variant of adenoid cystic carcinoma has a better prognosis than the other variants, with a survability of 8 to 10 years, compared with 1.5 to 4.7 years in the other variants. Adenoid cystic carcinoma often recur despite adequate therapy, with a recurrence rate of more than 40% in patients. Distant metastases were found in 27% of cases and the lungs were the most common location, followed by brain and bones.[1,4,7,14]

Ceruminous adenocarcinoma often expands to the middle ear, mastoid and temporal bones. Therefore, it is necessary to do a wide resection covering the osseous part of the external auditory canal with a tymphanomastoidectomy. Large or recurrent tumors require radical mastoidectomy and total parotidectomy. Intracranial extension requires excision involving part of the dura. Adjuvant radiation therapy is indicated for large tumors, high-grade carcinomas and tumors that have recurred.1,4 Several analyzes have shown that patients undergoing radiation therapy have increased survability, some also showing no significant change. Chemotherapy is not a commonly used therapeutic modality. Therapy using VMAT can reduce neurological symptoms. Follow-up is needed to identify local, regional, distant recurrences and is associated with the choice of appropriate therapy.[1,4,15]

Ceruminous adenocarcinoma is a very rare malignant tumor. The adenoid cystic variant has a clinical and microscopic appearance that is almost similar to parotid primary. In addition, this tumor also has a differential diagnosis with other malignant tumors at the same anatomical location or adjacent locations. Therefore, data of tumor invasion on radiological examination, a combination of clinical symptoms, microscopic, radiological and immunohistochemical features to differentiate it from other tumours.

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