

1 **Ceruminous Adenocarcinoma with Extensive Parotid ,Cervical and Distant Metastases –**
2 **Case Report and Review of Literature**

3

4

5 Jih-Chuan Jan, M.D.¹, Ching-Ping Wang, M.D.¹, Po-Cheung Kwan, M.D.², Shang-Heng Wu,
6 M.D.³, Hui-Fen Shu, M.D.⁴

7

8

9 From the Department of Otolaryngology-Head and Neck Surgery¹ and Pathology², Taichung
10 Veterans General Hospital, and the Department of ³Otolaryngology and ⁴Pathology,
11 Fong-Yuan Hospital, Taiwan, ROC

12 China Medical University, Taiwan

13 National Yang-Ming University, Taiwan

14

15 Address for correspondence Dr. Ching-Ping, Wang, Department of Otolaryngology, Taichung
16 Veterans General Hospital, Taichung City, Taiwan, Tel: 886-4-23592525 ext. 5401, Fax:
17 886-4-23596868, E-mail: entcpw@gmail.com

18

19 Word counts 2052

20 Abstract

21 We report a case of high-grade ceruminous adenocarcinoma in a 47-year-old male. The tumor
22 initially presented as a five millimeter nodular mass on left external auditory canal (EAC).
23 Consequently, extensive intraparotid and neck lymph nodes metastasis occurred and axillary
24 lymph nodes metastases developed several months later. To our knowledge, extensive neck
25 and distant lymph node metastasis of a patient with a ceruminous adenocarcinoma has not
26 been reported previously. We also believe that this case represents the first report of lymph
27 nodes metastasis to level V of neck and axilla from cancer of external ear canal. We present
28 our experiences in dealing with this rapidly progressing malignant tumor. The clinical features,
29 pathology, and treatment are described and relevant literatures have been reviewed.

30

31 Key words: Ceruminous gland, Adenocarcinoma, External auditory canal, Metastasis

32 Introduction

33 In general, tumors of the external auditory canal (EAC) are quite uncommon, and glandular
34 tumors comprise only a minority of these tumors. Tumors of the ceruminous gland are
35 uncommon in the external auditory canal. Ceruminous adenocarcinoma is a malignant
36 subtype of ceruminous gland neoplasm¹, which is an exceedingly rare malignancy of the
37 external auditory canal. The true incidence and biological behavior of these tumors is still
38 obscure not only owing to the rarity of these tumors but also due to ambiguous tumor
39 nomenclature. The dearth of knowledge about this disease entity leads to difficulty in
40 establishing the formulation of definitive treatment plans.

41

42 Most ceruminous adenocarcinomas behave as moderately aggressive, slow-growing tumors
43 with local invasion. Regional lymph nodes and distant metastasis are rare.^{2,3} On reviewing of
44 literatures; only one case of lung metastasis has been reported.⁴ Most recurrences are local
45 recurrence, and the recurrence rate can be quite high in spite of treatment with aggressive
46 multimodal managements. Here we present a case ceruminous adenocarcinoma that shows as
47 a 5 mm nodular lesion but with rapid progression with extensive intraparotid and neck lymph
48 nodes, including level V, metastases. We also believe that this case represents the first report
49 of lymph nodes metastasis to level V of neck and axilla from cancer of external ear canal.

50 Case report

51 A 47-year-old male, with underlying irregular hypertension medically controlled, smoked
52 cigarettes and drank socially for decades. He suffered from increased left ear discharge for
53 one month and visited a local hospital for help. On physical examination, he was found to
54 have a 5 mm sized nodular lesion arising from the anteroinferior wall of left external ear canal.
55 The left tympanic membrane and the other ear were normal. No obvious neck
56 lymphadenopathy or palpated parotid mass was found. Examination of the nose, nasopharynx,
57 oral cavity, oropharynx, larynx, and hypopharynx was unremarkable. Computerized
58 tomography (CT) scan of temporal bone demonstrated a 5 mm sized nodular lesion with soft
59 tissue density in the left external auditory canal but no sign of bone destruction or erosion
60 (Figure 1). There was no notable abnormality in the middle, inner ear or in the internal
61 auditory canal. The patient underwent a trans-canal wide excision and the histopathological
62 examination of the specimen provided a diagnosis of high-grade adenocarcinoma.
63 On histological examination, the ear canal tumor measured $5 \times 6 \text{ mm}^2$ with normal
64 ceruminous gland nearby. The tumor undermined the squamous epithelium lining the
65 external auditory canal via subepithelial invasion (Figure 2). On high-power field, the tumor
66 cells were shown as cuboidal to polygonal cells, with eosinophilic cytoplasm, and large,
67 round-to-ovoid, hyperchromatic, vesicular nuclei. The nucleoli were conspicuous. The cancer
68 cells were disposed in irregular glands or solid sheets, separated by bands of fibrous tissue.
69 (Figure 3) Focal areas of tumor invasion into lymphatic channel and epidermis were
70 demonstrated. The dense desmoplastic response in the stroma was evident.
71 Three weeks after surgery, several tender masses were found on his left neck. Then he was
72 referred to our hospital. During the hospitalization, a series of studies were arranged.
73 Otoscopic examination of the external auditory canal showed no evidence of local recurrence
74 or obvious residual tumor. A thorough search for other primary sites of adenocarcinoma,

75 including gastroscopy, colonoscopy, CT scan of lung, and whole body PET scan revealed
76 negative for other malignancy. Another CT of head and neck showed several ring-like
77 enhancing nodular lesions with a central necrosis over left parotid gland, carotid space and
78 posterior triangle of left neck (Figure 4). Fine needle aspiration of level V lymph node of the
79 left neck yielded a suspected metastatic adenocarcinoma. The patient underwent a left total
80 parotidectomy with facial nerve preservation and left radical neck dissection. The pathology
81 reported a high grade metastatic adenocarcinoma. Tumor metastasized to intraparotid lymph
82 nodes (4/5), and to cervical lymph nodes (level I: 6/6, level II: 23/24, level III: 16/16, level IV
83 15/15, level V: 14/14) with extranodal invasion. Nearly all the intra-parotid and cervical
84 lymph nodes were violated by cancer cells, which were histologically compatible with
85 previous EAC tumor. The presence of extranodal invasion was found

86

87 Neoadjuvant chemoradiation was administered post-operatively with 5-FU, MTX,
88 Epirubicin, and Cisplatin in divided 12 doses and radiation with 7000 cGy in 35 fractions.
89 Unfortunately, a lump was palpated over his left axilla 6 months later after completion of
90 chemoradiation. Excisional biopsy of axillary lymph nodes revealed high grade metastatic
91 adenocarcinoma. After discussion with the patient and his family, he was transferred back to a
92 local hospital for palliative treatment.

93 Discussion

94 Malignant tumors arising from the glandular structures of the external auditory canal are rare.
95 On reviewing of literatures, several origins of EAC adenocarcinomas have been reported,
96 including ceruminous gland², sebaceous gland⁵, direct invasion from parotid gland⁶, and
97 distant metastasis from other glandular tissues.⁷⁻⁹ We believe that this case is a tumor of
98 ceruminous adenocarcinoma. First of all, the tumor was located deep in the cartilaginous
99 segment of the EAC; this corresponds to the distribution of the ceruminous glands rather than
100 sebaceous glands.¹⁰ On pathological view, the normal glandular structures of specimen show
101 no resemblance to the sebaceous gland. Secondly, the tumor presented ear canal mass as an
102 initial symptom. The CT scan and physical examination did not show a lesion within the
103 parotid gland. Several weeks later, another CT scan of head and neck demonstrated multiple
104 nodular lesions located in the parotid gland but with an intact external ear canal wall. These
105 pictures are not compatible with a parotid cancer with ear canal invasion. On pathologically
106 reviewing the parotid specimen, the diseases are in intraparotid lymph nodes rather than
107 parenchyma of gland. Thirdly, although several authors have reported ear canal tumors as a
108 distant metastatic cancer⁷⁻⁹, there is not any evidence of other primary sites for
109 adenocarcinoma during one year follow-up period. We conclude that the ear canal tumor
110 should be a primary ceruminous adenocarcinoma.

111
112 Most ceruminous adenocarcinomas behave as moderately aggressive, slow-growing tumors
113 with local invasion. Regional lymph nodes and distant metastasis are rare.³ This case shows a
114 rapid course of disease progression via neck lymph node metastasis rather than by local tissue
115 infiltration or destruction. Ceruminous adenocarcinoma may occur in any grade depending on
116 the degree of cytological and architectural atypia.¹¹ The ability of malignant neoplasms to
117 invade adjacent normal tissues is fundamental to the neoplastic process. On pathologic view,

118 the tumor cells show high-grade malignancy and evidences of lymphatic permeations, focal
119 invasion into epidermis and desmoplastic responses. Desmoplastic responses are results of a
120 complex interaction between the host and invading neoplasm, comprising fibroblasts, various
121 inflammatory cells, proliferating vascular structures, as well as normal parenchymal cells
122 undergoing atrophy at the invasive edge. These may explain the circumstances of extensive
123 lymph nodes metastases; even though the primary lesion is quite small.

124 To date, no specific data is available on cervical lymph node metastasis patterns for these
125 tumors. Concerning the anatomic relationship, the routes of lymphatic drainage should be to
126 the nodes anterior, posterior, and inferior to the auricle, with the inferior nodes draining to the
127 subparotid and subdigastric nodes. On other high grade malignancies of EAC, such as
128 squamous cell carcinomas, lymph nodes metastases are commonly seen in parotid, level II
129 and III.³ On reviewing previously reports of regional spray pattern of external ear
130 malignancies, there is no case showing metastasis to the posterior triangle nodes.¹² Our case
131 showed extensive lymph nodes metastasis from parotid to level II to V. Consequently, we
132 recommend that whenever neck dissection is considered for external ear malignancy, level V
133 neck dissection may be considered

134 The treatment modality of ceruminous adenocarcinoma is not yet well-established. Combined
135 surgery and irradiation is advocated by most authors presently. Hicks, in survey of the
136 literature, advocated wide en bloc excision of the EAC, surrounding bone and associated
137 cartilage, mastoid, middle ear, parotid and contingent muscle, lymphatics and nerve structure
138 with preservation of the facial nerve for tumors involving the EAC.¹³ When the patient was
139 transferred to our hospital, he did not show any evidence of residual tumor in EAC but with
140 extensive parotid and cervical lymph nodes involvement. After full discussion with the patient
141 and physicians of head and neck oncology, we decide to treat the primary site of EAC with
142 chemoradiation rather than extensive surgery. There is no local or regional recurrences after 1

143 year follow up. The role of chemotherapy in ceruminous adenocarcinomas has not yet been
144 evaluated. In our case, the chemotherapy of 5-FU, MTX, Epirubicin, and Cisplatin did not
145 prevent the patient from distant metastasis.

146 The actual long-term disease-free survival rates after such aggressive multimodal therapies
147 are not clear at present; further experience after treatment will provide further information for
148 long-term disease control.

149

150 Reference

- 151 1. Wetli CV, Pardo V, Millard M, et al. Tumors of the ceruminous gland. *Cancer*
152 1972;29:1169-78.
- 153 2. Soon SL, Bullock M, Prince ME. Ceruminous adenocarcinoma: a rare tumour of the
154 external auditory canal. *J Otolaryngol* 2001;30 (6) 373-7
- 155 3. Joseph Chang CY, Cheung SW. Tumors of the Ear and Temporal Bone. Auditory canal:
156 glandular tumors. Philadelphia: Lippincott WW, 2000
- 157 4. Turner HA, Carter H, Neptune WB. Pulmonary metastases from ceruminous
158 adenocarcinoma (cylindroma) of external auditory canal. *Cancer*. 1971
159 Sep;28(3):775-80.
- 160 5. Ray J, Schofield JB, Shotton JC, Al-Ayoubi A. Rapid invading sebaceous carcinoma of
161 the external auditory canal. *J Laryngol Otol*. 1999 Jun;113(6):578-80
- 162 6. Choi JY, Choi EC, Lee HK, Yoo JB, Kim SG, Lee WS. Mode of parotid involvement in
163 external auditory canal carcinoma *J Laryngol Otol*. 2003 Dec; 117 (12): 951-4
- 164 7. Michaelson PG, Lowry TR. Metastatic renal cell carcinoma presenting in the external
165 auditory canal. *Otolaryngol Head Neck Surg*. 2005 Dec;133(6):979-80.
- 166 8. Cumberworth VL, Friedmann I, Glover GW. Late metastasis of breast carcinoma to the
167 external auditory canal. *J Laryngol Otol*. 1994 Sep;108(9):808-10. Review.
- 168 9. Carson HJ, Krivit JS, Eilers SG. Metastasis of colonic adenocarcinoma to the external ear
169 canal: an unusual case with a complex-pattern of disease progression. *Ear Nose Throat J*.
170 2005 Jan;84(1):36-8.
- 171 10. Main T, Lim D. The human external auditory canal, secretory system--an ultrastructural
172 study. *Laryngoscope*. 1976 Aug;86(8):1164-76.
- 173 11. Mills RG, Douglas-Jones T, Williams RG. 'Ceruminoma'—a defunct diagnosis. *J*

- 174 Laryngol Otol. 1995 Mar;109(3):180-8.
- 175 12. Lee D,Nash M,Har-El G. Regional spread of auricular and periauricular cutaneous
176 malignancies. Laryngoscope. 1996 Aug;106(8):998-1001
- 177 13. Hicks GW. Tumors arising from the glandular structures of the external auditory canal.
178 Laryngoscope. 1983 Mar;93(3):326-40.

179

180 Figure 1. Axial CT revealing a $5 \times 6 \text{ mm}^2$ mass over left external ear canal.

181 Figure 2. External auditory canal tumor, low-power view. The tumor was mainly situated in
182 the subepithelium with bulging into the external auditory canal. Note the normal glandular
183 structure in the upper left-hand corner. (Hematoxylin and eosin stain, $\times 10$)

184 Figure 3. Malignant cell exhibiting cellular atypia, nuclear pleomorphism, and eosinophilic
185 cytoplasm. The tumor cells were arranged in an irregular glandular pattern. (Hematoxylin and
186 eosin stain, × 400)

187 Figure 4. Axial CT showing multiple ring-like enhancing nodular lesions with a central low
188 density over left parotid gland and multiple enlarged lymph nodes with central necrosis over
189 the carotid space and posterior triangle of the left neck.