

## Case Report

# Multiple bilateral Warthin's tumors of the parotid glands with pleomorphic adenoma: a case report

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**Abstract:** Parotid tumors of different histological types are rare. This article reports a case of multiple bilateral synchronous Warthin's tumors of the parotid glands with a simultaneous pleomorphic adenoma of the left parotid gland. The diagnosis, pathological features, pathogenesis, treatment, and prognosis of multiple primary parotid benign tumors similar to this case are discussed with reference to the relevant literature.

**Keywords:** Warthin's tumor, pleomorphic adenoma, parotid gland, multiple primary tumor

### Introduction

Pleomorphic adenoma and Warthin's tumor are the most common benign tumors of the parotid gland. Primary parotid benign tumors usually present as solitary lumps, multiple tumors presenting synchronously or metachronously are uncommon [1-3], and these primary tumors' pathological types are usually same [4]. Cases of bilateral Warthin's tumors with unilateral pleomorphic adenoma are extremely rare. We describe a case of a patient presenting with multiple bilateral synchronous Warthin's tumors of the parotid glands with a simultaneous pleomorphic adenoma of the left parotid gland.

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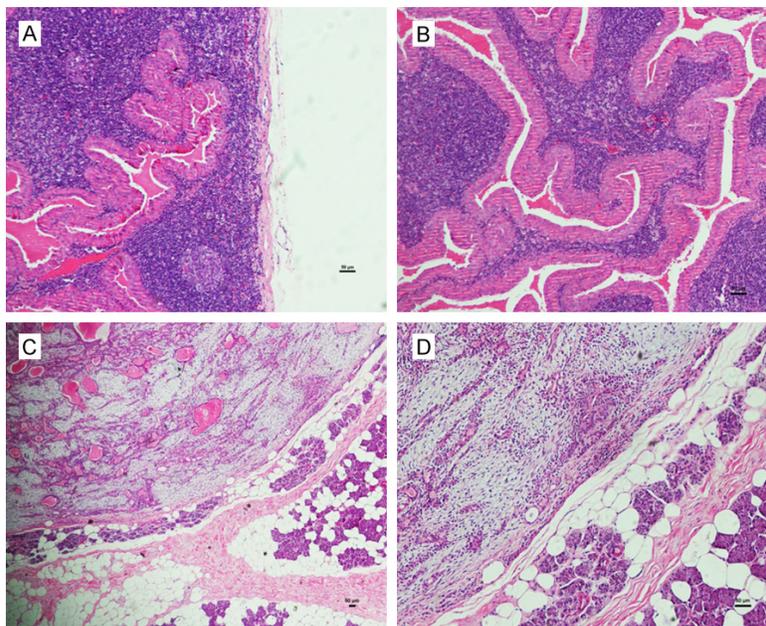
A 55-year-old man presented to West China Hospital of Stomatology in October 2017 with a 5-year history of a lump in front of his left earlobe. The patient complained that the mass was the size of a fava bean which grew slowly. He had recently noticed a new lump behind the left angle of his mandible 2 months before his visit. He had a habit of heavy smoking, about 25 cigarettes/day, for at least 30 years. Enhanced computed tomography (CT) revealed two well-circumscribed lesions that apparently strengthened with clear boundaries out of the surrounding tissue in the superficial lobe of the

left parotid gland. The density of the lesions is increased and homogeneous. They were about 22 mm and 15 mm in diameter. CT images also revealed a small lesion in the right parotid gland. Multiple space-occupying lesions of the parotid glands were considered (**Figure 1**). Examination: two ellipsoid-shaped lumps could be touched in the left parotid region. The anterior one was hard and its surface caused a slight nodular feeling. The posterior one was soft and had a smooth surface. Both of the lumps were movable to a certain extent and revealed no tenderness. In the right parotid gland, the nodule was too small and could not be clearly touched. The color and temperature of the skin was normal. Each branch of facial nerve and the duct of parotid gland showed no obvious abnormalities. Clinical diagnosis: bilateral tumor of the parotid gland (Warthin's tumor was suspected). The patient was in good condition and denied systematic medical history. Heart, lung, spleen and other vital organs did not detect significant positive signs, limbs activity was good, with no deformity. Preoperative examinations were completed. Surgical treatment for the tumor in the right parotid gland was not considered since it was less than 10 mm in diameter, it demands for regular examination and review. The left parotid gland including the masses was resected completely on

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**Figure 1.** Enhanced CT scan of the parotid gland. A. Two high density lesions were seen in the left parotid gland. Mild Homogeneous enhancement was seen in both tumors. B. The posterior one was 22 mm in diameter. C. The anterior one was 15 mm in diameter.



**Figure 2.** Observation of pathological section: A. The tumor composed of glandular duct and lymphoid stroma (HE  $\times$  40). B. The epithelium consisted of two layers of cells. The inner layer was columnar epithelial cells containing eosinophilic granule and the outer layer is flat-shaped cells with small size. Tumor interstitium was reactive lymphoid tissue (HE  $\times$  100). C. The tumor was pleomorphic showing the glandular epithelium and myoepithelial epithelium. Two kinds of epithelium formed a double tubular structure, myoepithelial cells distributed in the myxoid regions (HE  $\times$  40). D. Local capsule was infiltrated (HE  $\times$  100).

October 18th, 2017. At surgical exploration of the left parotid region, it was difficult to identify the facial nerve stem directly due to abundant fibrous tissue. Therefore an ante grade approach was chosen by dissection from the peripheral branches and a total parotidectomy was performed. Facial nerve stem and facial nerve branches were protected well by anatomical preservation. Intraoperative frozen section analysis revealed that the anterior tumor was con-

sistent with pleomorphic adenoma with focal infiltration of its capsule. The posterior tumor was consistent with Warthin's tumor.

Postoperative histological examination: superficial lobe of the left parotid gland. General observation: a piece of gland and lesions measuring 60 mm  $\times$  50 mm  $\times$  40 mm. The posterior encapsulated mass measuring 20 mm  $\times$  15 mm  $\times$  15 mm with a dark brown cutting face. Pathology observation: the tumor composed of glandular duct and lymphoid stroma. The tumor was composed of a lymphoid matrix containing epithelium-lined cystic space. The epithelium was tall and eosinophilic with a discontinuous layer of small cells at the base. Histological diagnosis: Warthin's tumor. The size of the anterior tumor was about 12 mm  $\times$  10 mm  $\times$  10 mm, and

the cutting surface was gray and white. Pathology observation: dominant epithelial components intermingled with chondroid, myxoid and fibrous stroma. The structure was pleomorphic showing the glandular epithelium and myoepithelial epithelium. Two kinds of epithelium formed a double tubular structure, myoepithelial cells distributed in the myxoid regions. The tumor infiltrated local capsule. Histological diagnosis: pleomorphic tumor (**Figure 2**).

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**Table 1.** Primary parotid gland benign tumors of different pathological types

Author	Age	Sex	Histology
Gaynor et al. (1976) [7]	63	M	Warthin's tumor and pleomorphic adenoma
Herbst et al. (1984) [8]	54	F	Dermal-type basal cell adenoma and dermal cylindroma
Banik et al. (1985) [9]	75	M	Non-Hodgkin's lymphoma adenolymphoma
Banik et al. (1985) [9]	76	M	Non-Hodgkin's lymphoma arising in Warthin's tumor
Goh et al. (1989) [10]	80	M	Cystic basal cell adenoma and Warthin's tumor
Toida et al. (1990) [11]	76	F	Warthin's tumor and pleomorphic adenoma
Dreyer et al. (1993) [12]	67	F	Warthin's tumor and sebaceous lymphadenoma
Lefor et al. (1993) [13]	/	F	Warthin's tumor and pleomorphic adenoma
Slavin et al. (1995) [14]	84	M	Warthin's tumor and myoepithelioma
Seifert and Donath (1996) [15]	/	/	Basal cell adenoma and canalicular adenoma (hybrid tumours)
Seifert and Donath (1996) [15]	/	/	Warthin's tumour and sebaceous adenoma (hybrid tumours)
Hosokawa et al. (1997) [16]	82	M	Warthin's tumor and pleomorphic adenoma
Chow and Chow (1997) [17]	53	M	Pleomorphic adenoma and tubular basal cell adenoma
Araki and Sakaguchi (2004) [18]	/	/	Warthin's tumor and oncocytoma
Richmon et al. (2004) [19]	/	M	Facial nerve schwannoma and monomorphic adenoma
Herce-López et al. (2009) [20]	55	F	Warthin's tumor and pleomorphic adenoma
McCormick et al. (2009) [21]	71	M	Warthin's tumor and pleomorphic adenoma
Scheller et al. (2012) [22]	46	M	Sebaceous lymphadenoma and membranous basal cell adenoma
Liu et al. (2013) [23]	78	M	Warthin's tumor and Hodgkin's lymphoma
Di Napoli et al. (2015) [24]	73	M	Warthin's tumor and Hodgkin's lymphoma
Andrews et al. (2015) [25]	55	M	pleomorphic adenomas and basal cell adenoma
Gvozdzan et al. (2015) [26]	54	F	Warthin's tumor and basal cell adenoma

### Discussion

Currently, a defined time period prior to the designation as a metachronous lesion has not been established. Ethunandan [5] used an interval of 6 months in their study to define it. In this case, it took a long time (approximately 58 months) to discover the tumor in the posterior part of the parotid gland, after the tumor found in the anterior part. As a result, it was considered a synchronous lesions on both parts (anterior and posterior of the left parotid gland), and also, metachronous lesions on both sides (left and right parotid glands). According to another Yu's [6] statistics, multiple tumors makes up 3.4% of all the tumors of parotid gland with males outnumber females by 0.3-4.9 on average, where metachronous ones could account for 30%. It could also be read in Ethunandan's [8] statistics that metachronous tumors accounted for 20% of multiple tumors and were all bilateral in distribution. He concluded that 83% metachronous tumors were of the same histological type and Warthin's tumor is the most common metachronous tumor (50%). We can come to realize that bilateral Warthin's tumors with a pleomorphic adenoma is extremely rare.

Primary parotid gland benign tumors of different pathological types are rare. Synchronous bilateral parotid gland tumors are extremely rare. 22 cases reported in English were found at literature search in the databases PubMed and Medline using the following Mesh headings: Parotid Benign Tumor and Multiple Primary, Case Report (**Table 1**). To the best of our knowledge, this is the second patient with multiple bilateral Warthin's tumors and a pleomorphic adenoma of the parotid glands.

The pathogenesis of multiple parotid tumors still remains uncertain. As for pleomorphic adenomas, currently, the most remarkable risk factor is the history of radiation exposure [27]. Research shows that 40%-70% of pleomorphic adenomas have concern with the ectopic expression of gene HMGA2 (12q13-15) [28] or PLAG1 (8q12) [29]. For the Warthin's tumor, there is a wide recognition that the history of heavy smoking is a risk factor. Although the pathogenesis of Warthin tumor is controversial, some researchers consider that it results from the entrance of epithelial cells of oral mucosa into lymph node in parotid gland during the time of embryogenesis. Such theory can explain

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how Warthin's tumor occurs in parotid lymph node, parotid gland and superior cervical tissue. Other researchers consider it immune response of lymphoid component against epithelium instead of the exposure of tumor cells in lymphoid tissue [30-32].

Such auxiliary examinations as B-ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) are deemed common in diagnosing parotid gland tumors. However, to obtain a more accurate diagnosing result, rich experience and comprehensive understanding of the sufferer's medical history are necessary. But imaging tests are unreliable when diagnosing a co-existence of tumors with different histological types. MRI scan is a good choice of diagnosing parotid gland tumors because of its remarkable identifying ability towards soft tissue. For instance, pleomorphic adenomas usually reflect round like and are enveloped by a layer of smooth surface [33], with bright signal areas on the T2-weighted images and prompts low-intensity edges where the envelope exists [34]. Ultrasound guided fine needle aspiration cytology (Ultrasound-guided FNAC) is considered as a relatively simple examination of which the accuracy of identifying the benign tumors with the malignant tumors can reach to 85%-97% [35]. But it's diagnostic sensitivity towards the parotid disease sensitivity is not high. Pre-operative physical examinations, especially palpation is significant in the diagnosis of parotid tumor. The difficulty arises when diagnosing tumors from the deep lobe of parotid gland.

Resection stands in the first place when dealing with multiple parotid gland tumors. Ethundan M [5] believes such benign multiple tumors basically happening in the superficial parotid should be adopted palpation during operation and superficial parotidectomy owing to the difficulty of precisely judging the number of tumors and their pathological types before operation. Whether to adopt the surgical method of parotidectomy of total lobe should be decided by the position and features of the tumor.

In this case, the intraoperative frozen biopsy hints that the enclosed mass and its envelop in the anterior part of left superficial parotid gland are under focal infiltration, requiring left parotidectomy. Nerve-related symptoms and Frey syndrome haven't been found in the patient

after the surgery. Therefore, when there are occupying lesions in bilateral parotid gland with clear boundaries and good mobility, we should first consider diagnosis of Warthin's tumor. For treatment, operation on unilateral parotid region should be done first with multiple neoplastic nodules. Intraoperative frozen biopsy is necessary and the margin and extent of the surgery can be determined according to the result. Through this, the radical treatment for parotid tumors with different histological types will not be mistaken or neglected, especially the co-existence of some borderline tumors and malignant ones. Also, regular follow-up after the operation is needed.

### Conclusion

The current case represents, to the best of our knowledge, the second documented instance of multiple bilateral Warthin's tumors and a pleomorphic adenoma of the parotid glands.

It is necessary for us to accumulate more cases and to establish a long-time follow-up database to achieve a deeper indication of the pathogenesis of multiple parotid tumors. On this foundation we can discover more precise diagnostic schemes to evaluate the most proper surgical margin. Ultimately, we can reduce the recurrence rate and in the meantime, reduce the incidence rate of complications after the operation.

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### Disclosure of conflict of interest

None.

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