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Growth rate characteristics of Warthin's tumours of the parotid gland☆

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Abstract. The aim of this study was to evaluate growth characteristics of parotid gland Warthin's tumours. The medical records of 134 patients who had a cytological or histopathological diagnosis of Warthin's tumour between 1997 and 2013, at a single tertiary care centre, were reviewed retrospectively. Thirteen of these patients underwent observation with 30 serial computed tomography or magnetic resonance imaging scans of the head and neck, with 24 Warthin's lesions identified. The mean length of time between scans was 882 days, and mean initial and final sizes per lesion were 3.9 cm^3 and 5.6 cm^3, respectively. Average growth of these lesions was 8% per year (95% confidence interval −27% to 43%; range −148% to 460%; median −8%), and was highly variable (standard deviation 96%). Age over 75 years was associated with slower growth ($P = 0.03$), but gender, smoking status, multifocality, bilaterality versus unilaterality, and initial size did not correlate with the growth rate. Warthin's tumours appear to have an approximate average doubling time of 9 years, but can have a wide range of growth rates, with many cases showing a reduction in size. Either conservative management or surgical resection could be supported by these data, depending on the current size of the tumour, appearance, symptoms, and the age, health, and wishes of the patient.

Keywords: Warthin's tumour; papillary cystadenoma lymphomatosum; parotid; growth rate; surgery; observation; imaging.

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Warthin's tumours are the second most common benign lesions of the parotid gland, accounting for 14–30% of all parotid tumors.[1] They are commonly associated with male smokers, although some studies have found an increasing incidence in women.[1–3] Previous studies have shown that up to 94% of patients with Warthin's tumour have a history of tobacco use.[1,4] Warthin's tumour can be unifocal or multifocal and when multifocal can be synchronous or metachronous. While it is difficult to diagnose a multifocal Warthin's tumour, the reported incidence of multifocality is up to 50%. In addition, 4–7.5% of Warthin's tumours are bilateral.[5] Multifocal lesions are not necessarily associated with unilateral or bilateral disease.[6]

Management options for Warthin's tumour include surgery, especially when the lesions are symptomatic or cosmetically concerning, or observation. The 2014 guidelines of the National Comprehensive Cancer Network (NCCN) for Cancers of the Head and Neck for a diagnosis of a clinically benign head and neck tumour recommend 'follow-up as

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clinically indicated'.[7] There is some debate about whether surgery or observation is most appropriate for Warthin's tumour.[8] When advising patients about treatment options and determining clinically appropriate follow-up, it would be useful to know the general characteristic growth rate of this tumour. While commonly described as 'slow-growing', the authors are aware of no published data showing the growth rate characteristics of Warthin's tumour. The aim of this retrospective review was to provide a better characterization of the rate of growth of parotid gland Warthin's tumours.

Materials and methods

After ethical approval was obtained from the institutional committee on human research, a database was collected from the medical records of a single tertiary care centre. This included 134 patients with a cytological or histological diagnosis of Warthin's tumour between the years 1997 and 2013. The database was queried for pertinent patient information including smoking status, laterality, multifocality, age, surgical pathology results, and the availability of head and neck cross-sectional imaging studies (computed tomography (CT) and/or magnetic resonance imaging (MRI)). Patients were eligible for this study if they had at least two serial CT and/or MRI studies available to measure the rate of growth. For three scans, outside reports were detailed enough to use reported measurements even though the scans themselves were not available.

Warthin's tumours have a heterogeneous appearance with solid and cystic components on CT and MRI, as they are more likely to have cystic elements than other salivary gland tumours. They have well demarcated margins (also seen with the other benign salivary gland tumours) and can be quite vascular.

Occasionally, high T1 signal intensity on MRI can be seen within segments of the tumour, related to focal accumulation of cholesterol crystals or intralesional haemorrhage. The contrast enhancement is also heterogeneous.

None of these imaging findings is considered pathognomonic for Warthin's tumour. However, bilateral salivary gland well-circumscribed heterogeneous density (on CT) or signal intensity (on MRI) lesions with cystic changes suggest the diagnosis. For the purposes of radiographic analysis in this study, in patients for whom at least one lesion was a cytology-proven Warthin's tumour, all other parotid lesions with similar imaging characteristics consistent with Warthin's tumour were assumed also to be Warthin's tumours.

Pathologists at the study institution reviewed and confirmed the fine needle aspiration (FNA) cytology of Warthin's tumour for all patients who were included in this study. The final pathology was determined only in those patients who underwent surgical resection.

Each lesion was assessed for size change by two methods: (1) Using three perpendicular measurements, an ideal ellipsoid volume was calculated using the equation $(4/3)\pi abc$, where a, b, and c are the perpendicular radii of the shape. For example, if the measured perpendicular diameters were 1 cm, 2 cm, and 3 cm, the volume of the ideal ellipsoid would be calculated using $(4/3)\pi(1/2)(2/2)(3/2)$. (2) The single largest dimension in the anterior–posterior, medial–lateral, or cranio-caudal planes was measured for each lesion. A single neuroradiologist (A.U.) performed the tumour measurements at the time of the study analysis.

The rate of growth was calculated as a percentage change in volume or length, respectively, divided by the number of days between imaging studies. Measurements from CT and MRI scans were used interchangeably. When three or more scans were available, growth was measured between the first scan and each subsequent scan. For the purposes of analysis, every data point was weighted equally unless indicated otherwise.

Potential influences on the growth rate, including gender, multifocality, laterality, smoking status, and age, were investigated using the two-tailed Student's t-test. The potential influences of the size of the initial lesion on growth rate were assessed using a Pearson correlation. A statistically significant level of evidence was defined as $P < 0.05$. All calculations were done using Microsoft Excel.

Results

Of the initial 134 patients, 70 (52%) were excluded for having no imaging studies available. Forty-three (32%) were excluded because only one evaluable CT or MRI was available. Eight (6%) were excluded for having ultrasound studies only (and no CT/MRI). Thirteen out of 134 patients (10%) with 24 Warthin's tumour lesions in the parotid gland(s) met the inclusion criterion by having two or more evaluable CT or MRI. The growth rate characteristics of these 24 presumed Warthin's tumour lesions were examined retrospectively using a total of 30 imaging studies, which yielded 55 data points. Three patients had serial CT only, four had serial MRI only, and six had a mixture of both imaging modalities. Each patient had two to four evaluable imaging studies. Five patients (38%) had bilateral disease, and five (38%) had multifocal tumours. Two patients (15%) had unilateral multifocal disease, while three patients (23%) had multifocal tumours that were also bilateral. Of the 11 patients for whom smoking history was available, nine (82%) were smokers. Nine of the 13 patients (69%) were men. The average age at the time of the first scan was 67 years (range 51–83 years). No additional metachronous lesions developed on repeat scans. Table 1 lists patient characteristics, along with the average growth of all lesions for each patient.

Three patients (23%) underwent a unilateral parotidectomy after having serial imaging. One patient underwent a unilateral parotidectomy before serial imaging was completed; the contralateral side was included in this analysis. One patient's imaging was for unilateral recurrence after bilateral parotidectomy.

For 11 patients, FNA biopsies were done either after or more than 4 months before any imaging was completed. For patients 2 and 7, the initial images were taken 15 and 8 days, respectively, after FNA biopsies.

For the volume (cm^3) measurement analysis, the mean initial and final sizes per lesion were 3.9 cm^3 (range 0.2–15.1 cm^3) and 5.6 cm^3 (range 0.2–29.2 cm^3), respectively. The unweighted mean length of time between scans was 989 days (range 182–2436 days). With these measurements, the mean rate of volumetric growth per lesion was 8% per year (95% confidence interval −27% to 43%; range −148% to 460%; median −8%). The average volumetric growth per year, using data from the first and last scans only, was 0.71 cm^3 per year.

This volume-based mean growth rate estimates an approximate doubling of volume every 9 years for the study sample. However, the growth measurements were highly variable (standard deviation (SD) 96%), with two lesions (8%) doubling in size within 1 year and 13 (54%) shrinking over the time between the first and last scans. Seven of 13 patients (54%) had at least one shrinking lesion. Of these, five had multiple lesions. Three of these five patients (60%) had multiple lesions that only decreased in size over time. The average volumetric shrinkage for lesions that decreased in size was 33% per year (range −148% to −1.2%). Variability in the growth rate among multifocal lesions

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