Title:

Pleomorphic Adenoma in an 85-Year-Old Female Patient with Right Mandibular Swelling- A Case study.

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Outlines

Introduction:

Pleomorphic adenoma is a common benign tumor of the salivary glands that can occur in various locations in the head and neck region, including the parotid gland. This case study presents the case of an 85-year-old female patient with right mandibular swelling, which was diagnosed as pleomorphic adenoma. The introduction section provides an overview of the incidence, etiology, significance, and the role of ultrasound in the diagnosis of pleomorphic adenoma.

Incidence:

Pleomorphic adenoma usually appears in middle-aged people as a palpable slowly growing mass. It is the most common benign salivary gland tumour in adults (70–80% of all benign tumours of the major salivary glands) and the third most common in the paediatric population (Thoeny, 2007).

When all salivary gland tumours are considered, the incidence has been reported to range annually from 0.4 to 13.5 cases/100,000 population with peaks and troughs of disease in defined populations (Bjørndal et al. 2011). National cancer registries have estimated that the incidence of malignant major salivary gland cancers (parotid and submandibular glands) in England 1990–2006 was between 0.7 and $0.8/10^6$ population/annum (Price et al., 2010), but because of a quirk in coding, cancers of the minor salivary glands were excluded and grouped instead with cancer of the oral cavity. To our knowledge, no official record is kept of

benign disease of the salivary glands, and apart from one study (Bradley, 2001), the true incidence of salivary neoplasms remains unclear.

From Reviewed literatures (Thoeny, 2007, Kalwaniya et al., 2023), there is slight female predilection to pleomorphic adenomas.

Most pleomorphic adenomas (84%) occur in the parotid gland, followed by 8% in the submandibular gland, 6.5% in the minor salivary glands, and only 0.5% in the sublingual glands, highlighting the predominant involvement of the parotid gland in this benign tumour of the salivary glands (Thoeny, 2007).

Etiology:

The etiology of pleomorphic adenoma is unknown, but the incidence of this tumor has been increasing in the last 15-20 years in relation to the exposure of radiation (Bokhari and Greene, 2020). In a pilot case–control analysis by Zheng et al. (2004), the study postulates that gamma radiation is a risk factor in both malignant and benign salivary gland tumours, but the exact mechanism remain unknown; consequently, patients treated with radiotherapy, workers occupationally exposed to ionising radiation, or populations exposed to nuclear incidents or terrorists events are at high risk of developing radiation- related salivary gland tumours (Zheng et al., 2004). The above study also highlighted the high sensitivity of salivary gland to irradiation.

Another study suggests that oncogenic simian virus (SV40) may play a role in the onset or progression of pleomorphic adenoma (Gündüz et al., 2018).

Significance:

A case study on pleomorphic adenoma holds significant importance in the field of medical research and patient care. Pleomorphic adenoma is the most common benign salivary gland tumor, and studying cases provides valuable insights into its diagnosis, treatment, and management. Through a detailed examination of patient history, clinical presentation, diagnostic imaging, histopathological analysis, and treatment outcomes, a case study allows healthcare professionals to gain a deeper understanding of various presentation and diagnosis of salivary gland tumours. By sharing and analysing such cases, medical practitioners can enhance their knowledge, improve diagnostic accuracy, optimize treatment strategies, and ultimately contribute to better patient outcomes in the management of pleomorphic adenoma.

Ultrasound Role:

Ultrasound plays a crucial role in the diagnosis and management of pleomorphic adenoma, a common benign tumor of the salivary glands. With its non-invasive nature and real-time imaging capabilities, ultrasound is instrumental in assessing the size, location, and characteristics of the tumor. It helps in differentiating pleomorphic adenoma from other salivary gland lesions, guiding the selection of appropriate treatment approaches. Additionally, ultrasound aids in planning surgical interventions by providing precise anatomical details and assisting in the identification of important structures to avoid damage during excision. Moreover, ultrasound can be used for post-treatment surveillance, monitoring tumor recurrence, and assessing treatment outcomes. Its versatility and effectiveness make ultrasound an indispensable tool in the comprehensive diagnosis and management of pleomorphic adenoma.

While acknowledging the high sensitivity and specificity of ultrasound imaging in the diagnosis of pleomorphic adenoma, CT/MRI imaging has been recorded to play key roles, especially in areas of hard palate pleomorphic adenoma with associated assessment of the cortical outline (Kakimoto et al., 2009, Patigaroo et al., 2014).

CASE HISTORY

Clinical Examination:

An 85-year-old female patient presented to my ultrasound clinic with GP referral indication of right mandibular swelling (slow growing ? cause).

On clinical examination, a non-tender, firm, and not hot mass measuring approximately 2cm in diameter is palpable in the right mandibular region. The overlying skin appears normal, and there are no signs of inflammation. The patient has normal oral hygiene and no dental abnormalities. No palpable lymph nodes are noted in the neck, and there are no other abnormalities on examination.

Diagnostic Workup:

1. **Ultrasound Scan and findings:** The ultrasound scan of the salivary glands reveals a well-defined, mildly hypoechoic, heterogeneous, and hypervascularised mass with posterior acoustic enhancement, seen within the superficial lobe of the right parotid gland; features indicative of a pleomorphic adenoma.

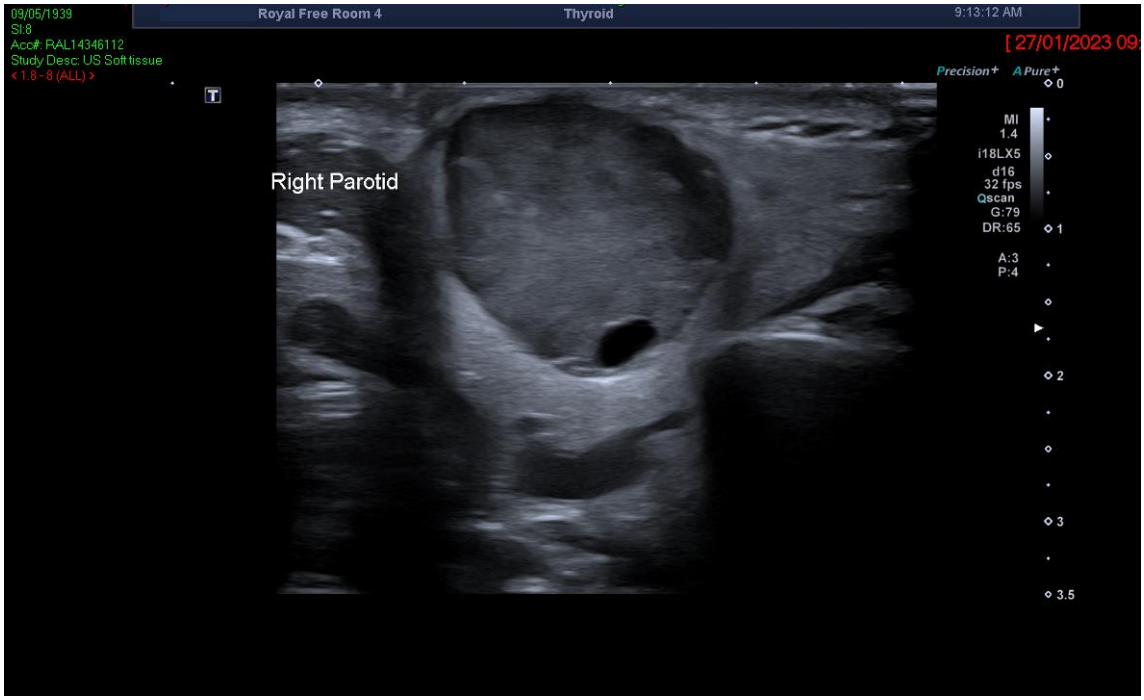

Fig. 1: A well-defined lobulated hypoechoic lesion with small anechoic cystic changes is noted within the superficial lobe of the right parotid gland. Note the posterior acoustic enhancement.

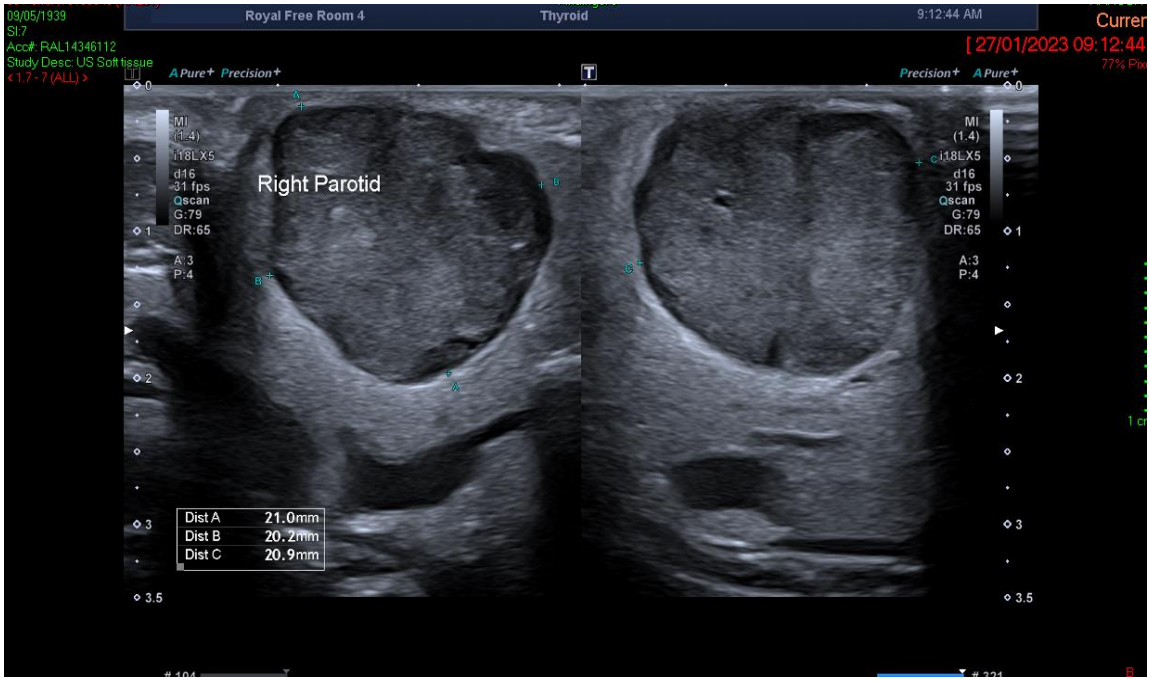

Fig 2: Long and short axis view of the right parotid pleomorphic adenoma measured 2.1cm in maximum size.

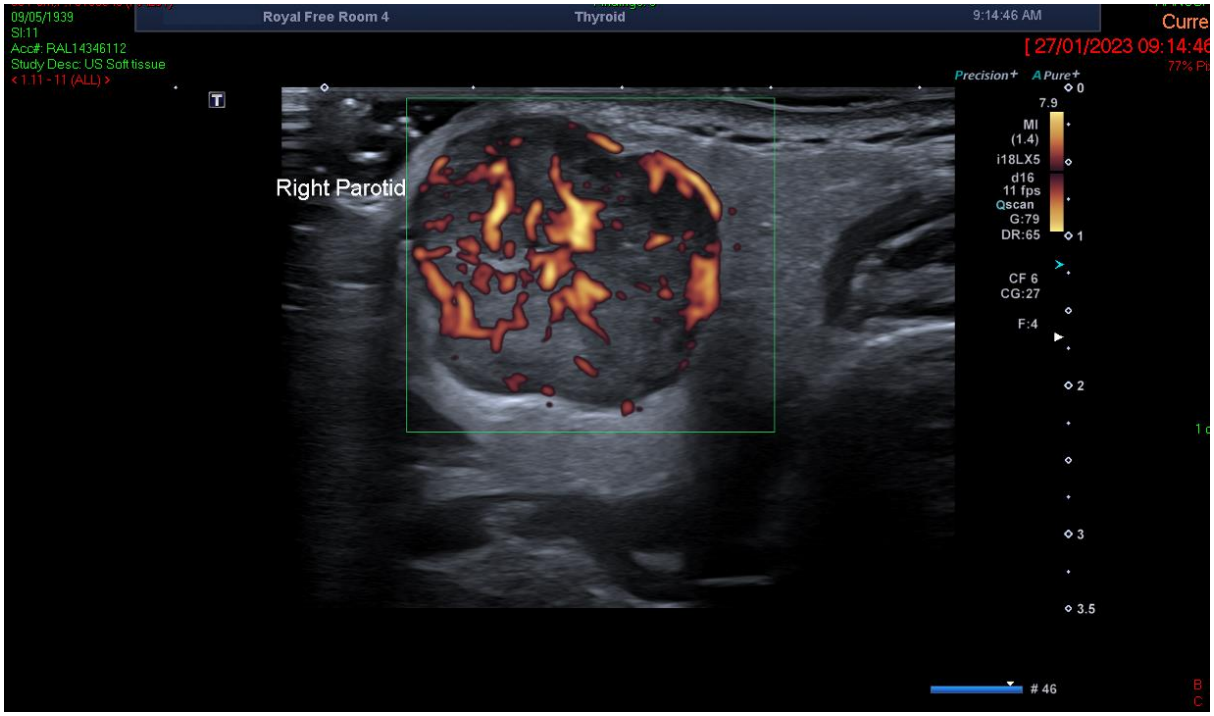

Fig 3: The right parotid pleomorphic adenoma demonstrates increased vascularity (hyperaemia) on power doppler interrogation.

Fig 4: There is active arterial flow noted on colour doppler and pulsed wave doppler assessment (to distinguish cases of twinkle artefacts as seen in sebaceous/ epidermal inclusion cyst).

2. **Ultrasound scan recommendation**: Specialist referral plus Fine needle aspiration was recommended for further evaluation (this is based on local protocol/guidelines at Royal Free Hospital NHS Foundation Trust (See Appendix A)

3. **Fine Needle Aspiration (FNA)**: A fine needle aspiration (FNA) of the suspected pleomorphic adenoma was performed by one of the radiologists at Royal free Hospital. Cytology samples were obtained and sent to the Cytology unit of the Trust. The FNA shows a mixture of epithelial and myoepithelial cells, which is consistent with a pleomorphic adenoma. Based on the clinical presentation, imaging findings, and cytological examination, a decision is made to proceed with surgical excision of the mandibular mass. The excised specimen is to be sent for histopathological examination.
4. **Treatment and Follow-up**: The patient undergoes a partial mandibular resection with removal of the mass. The surgery is performed by an experienced oral and maxillofacial surgeon at royal free hospital London, and there are no complications during the procedure. The excised specimen is sent for histopathological examination, which confirms the diagnosis of pleomorphic adenoma and indicates complete excision with clear margins. Postoperatively, the patient recovers well without any major complications. She is advised to continue regular follow-up visits with her oral and maxillofacial surgeon for monitoring and to detect any recurrence early. She is also counselled on the importance of maintaining good oral hygiene and seeking prompt medical attention if she notices any new symptoms or changes in the surgical area.

Discussion:

Ultrasound diagnosis of pleomorphic adenoma:

The sensitivity and specificity of ultrasound in the diagnosis of pleomorphic adenomas varies widely between studies. This is likely due to differences in study design, patient population, ultrasound technique, and operator experience. Despite this variability, the overall pooled accuracy of ultrasound in the diagnosis of pleomorphic adenomas was high, at 84% (sensitivity, 82%; specificity, 86%) (Bialek et al, 2003). This is also supported by Miao et al. (2015) in his article on differentiating between Warthin tumour and pleomorphic adenoma with ultrasound sensitivity, specificity, and accuracy at 69.8%, 81.1%, and 75% respectively, while excluding masses with ≥50% macroscopic cystic structures (Miao et al., 2015).

One study by Bialek et al (2003) on the effectiveness of ultrasound in diagnosing and distinguishing pleomorphic adenomas among 88 patients with tumors in the preauricular, submandibular, or cheek areas. Among these patients, 24 were confirmed to have pleomorphic adenomas. Ultrasound demonstrated a high accuracy of 96% in distinguishing between benign and malignant lesions, and an 84% accuracy in predicting pleomorphic adenomas. Ultrasound-guided fine-needle aspiration biopsy was performed on 15 of 22 primary pleomorphic adenoma cases, revealing histopathologic heterogeneity in 73% of cases. The findings highlight the value of modern ultrasound as a reliable method for precise localization, measurement, and structural assessment of tumors in these areas, potentially serving as the primary diagnostic tool or guiding biopsy.

Another study by Zajkowski et al. (2000) aimed to identify distinctive ultrasonographic features of pleomorphic adenomas and Warthin's tumors (adenolymphoma). The researchers analysed 31 ultrasound examinations of 20

pleomorphic adenomas and 10 Warthin's tumors in 28 patients, confirming all cases through biopsy or histopathology. Ultrasound criteria included borders, shape, echogenicity, structure, and presence of irregular anechoic areas within the tumor. Results showed that all lesions were hypoechoic, with 80.6% having well-defined borders. Pleomorphic adenomas often displayed a lobulated shape (55%), while Warthin's tumors varied between lobulated, oval, and irregular. The study concluded that ultrasonography is a valuable method for evaluating these tumors, and certain sonographic patterns might suggest the tumour's nature.

In a similar study by Yuan et al., (2009), the researchers analysed 19 pleomorphic adenomas and 29 Warthin's tumors, evaluating features such as size, echotexture, boundary, shape on gray-scale imaging, and vascularity using colour Doppler ultrasound. Results showed that all tumor types (Warthin's (WT) tumour and pleomorphic adenomas (PA)) were hypoechoic, with predominantly central blood flow in most cases (WT- 58.6%, PA- 42.1%). Pleomorphic adenomas often exhibited lobulated margins (PA- 84.2%, WT- 51.7%), while anechoic cystic components were more prevalent in Warthin's tumors (WT- 44.8%, PA- 5.3%). The study concluded that gray-scale ultrasonography is valuable for evaluating and distinguishing these tumors, with limited additional diagnostic information provided by colour Doppler ultrasound. Rong et al., 2014 concur with the submissions of the above researchers when they stated that lobulated outline is more frequent in pleomorphic adenoma relative to Warthin's tumour.

In view of the above reviewed literatures, it is evident that ultrasound plays key role in diagnosis of pleomorphic adenoma; however, more diagnostic accuracy with fine needle aspiration and/tissue biopsy is essential.

As would be for certain head and neck pathologies, the role of cross-sectional imaging cannot be excluded. Its multi-sectional advantages are essential in salivary gland evaluation. Research by Mikaszewski et al. (2017) reported significantly higher sensitivity and specificity- 95.8% sensitivity and 93%

specificity—in the diagnosis of pleomorphic adenoma through MRI imaging; and as can be seen in our further review in this case study, MRI plays key roles in assessment of recurrent parotid pleomorphic adenoma.

Vascularity in Diagnosis:

While some articles (Yuan et al.,2009; Zajkowski et al., 2000) place limited diagnostic value on the vascularity of benign parotid lesion, some articles (Dumitriu et al, 2010; Jiang, L.P., 2020) have reported hypervascularisation of pleomorphic adenoma as one of its minor sonographic features. According to research by Jiang (2020), Colour Doppler ultrasonography showed no significant differences in PSV between tumors, significantly less adenolymphomas had Grade 0-1 vascularity compared to pleomorphic adenomas, and the RI was significantly lower in adenolymphomas compared to pleomorphic adenomas and malignant tumors. He concluded that colour Doppler ultrasonography may have utility in the differential diagnosis of pleomorphic adenomas from adenolymphomas but is limited in its ability to differentiate pleomorphic adenomas and adenolymphomas from malignant tumors (Jiang, 2020).

Treatment and Recurrence:

The optimal treatment for pleomorphic adenoma is superficial or total parotidectomy with facial nerve preservation, which results in local control rates of 95% or higher. Radiotherapy (RT) is useful to obtain local control in patients with positive margins, unresectable tumors, and multifocal recurrences after prior resection (Mendenhall et al, 2008) .

Steven et al. (1982) and Chang et al. (1985) agrees with the above treatment recommendations, stating surgery as the mainstream for treatment of pleomorphic adenoma. The above treatment recommendations agree with NICE (National Institute for health and Care Excellence) guidelines and most local policies in the National Health Service, United Kingdom.

The risk of recurrence of pleomorphic adenoma is generally associated with inadequate surgical procedure, which could have been spillage of tumor or breach of tumor capsule (Almeslet, A.S., 2020).

The follow-up of parotid pleomorphic adenomas (RPAs) poses challenges, especially when relying solely on ultrasonography, as observed in the study by Redaelli de Zinis et al. (2008). Routine ultrasonography accounted for only 12.1% of RPA diagnoses, with most patients presenting due to parotid swelling. The recurrent nature of RPAs, often multinodular, reinforces pathogenetic hypotheses related to incomplete excision or tumor spillage during initial surgery. MRI emerges as a superior tool for delineating RPA extension, portraying its multinodular nature and potential deep-lobe or parapharyngeal involvement. Despite nonspecific signal and enhancement characteristics, MRI aids in assessing the residual parotid gland after prior surgeries. However, its limitations in identifying all nodules highlight the need for careful clinical and microscopic evaluation. Managing RPAs involves tailored approaches, considering observation, individualized surgery, potential facial nerve resection, and postoperative radiotherapy. Regular ultrasonography remains crucial for lifetime follow-up, while MRI is selectively recommended for cases with deep-lobe or parapharyngeal involvement, emphasizing a comprehensive and personalized management strategy (Redaelli de Zinis et al., 2008).

In a similar study of recurrent parotid pleomorphic adenoma, Witt et al. (2015) supported the adoption of magnetic resonance imaging as the choice for assessing pleomorphic adenoma recurrence.

Conclusion:

In conclusion, ultrasound is a valuable imaging modality for the diagnosis of pleomorphic adenomas, the most common benign tumor of the salivary glands. It is a non-invasive, cost-effective, and widely available imaging technique that provides real-time imaging, making it suitable for initial evaluation of salivary gland masses.

Overall, ultrasound demonstrates high sensitivity in detecting pleomorphic adenomas, but its accuracy may be limited by operator experience and the size of the tumor. Small tumors may be challenging to detect on ultrasound, and the operator's experience and expertise in evaluating salivary gland masses can impact the accuracy of the diagnosis. Therefore, it is essential to have experienced radiologists or sonographers who are familiar with the ultrasound characteristics of pleomorphic adenomas and other salivary gland lesions to obtain accurate results.

In the case study of an 85-year-old female presenting with a right mandibular swelling, non-tender, not hot, and ultrasound features showing a well-defined, lobulated, oval, hypoechoic, and soft tissue mass with posterior acoustic enhancement, noted within the superficial lobe of the right parotid gland, the ultrasound findings are consistent with pleomorphic adenoma. A definite diagnosis was confirmed through histopathological examination after surgical excision of the mass.

Ultrasound can provide valuable information about the location, size, shape, and internal characteristics of pleomorphic adenomas, aiding in the planning of further management and surgical intervention. It can also help differentiate pleomorphic adenomas from other salivary gland lesions, such as malignant tumors or inflammatory conditions. However, it is important to note that ultrasound alone may not be sufficient for a conclusive diagnosis, and other

imaging procedures, such as fine-needle aspiration cytology (FNAC) or magnetic resonance imaging (MRI), may be needed for further evaluation or follow up in certain cases.

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Appendix (RFL)

A: Management algorithm