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DEEP LOBE PLEOMORPHIC ADENOMA OF THE PAROTID GLAND - A CLINICOPATHOLOGICAL STUDY WITH A REVIEW OF MOLECULAR GENETICS

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ABSTRACT

Background: Pleomorphic adenoma is the most common benign tumour of the salivary glands. It usually occurs in the superficial part of the parotid gland, while tumours arising from the deep lobe are uncommon. Deep lobe tumours can be difficult to diagnose and treat because of their location and close relation to important structures like the facial nerve and parapharyngeal space. This study includes patients diagnosed with deep lobe pleomorphic adenoma at a tertiary care centre over a period of 2 years. Information was collected regarding patient history, symptoms, imaging (CT/MRI), surgical approach, and postoperative results. All cases were confirmed by histopathological examination.

Aims and Objectives: 1. To study the incidence of Deep Lobe Pleomorphic Adenoma of parotid gland lesions in patients attending ENT OPD/admitted in ENT ward in our region. 2. To evaluate the distribution in age, sex, modes of presentation of the parotid gland swellings. 3. To study histomorphology of parotid salivary gland lesions and correlate with FNAC findings.

Subjects and Methods: Patients admitted in ENT WARD/attending ENT OPD with FNAC proven Pleomorphic Adenoma parotid swellings are selected for the present study from 1st Jan 2024 to 1st January 2026. A prospective clinical study is conducted over the selected group for their age, sex, modes of presentation and their investigations. Study on various treatment modalities and their operative approach has been done.

Observation and Results: The parotid gland lesions were more common in females and in most of the cases belonged to lower socioeconomic status. The most common investigation done was Fine needle aspiration cytology. In maximum cases Superficial Parotidectomy was done. Total Conservative Morbidity was done in few cases. Morbidity with facial nerve paralysis was seen in 1 case. Facial nerve paresis was seen in 2 cases.

Conclusion: This study is a single institutional experience of 10 cases. Deep lobe pleomorphic adenoma is a rare condition that requires careful evaluation. Imaging plays an important role in diagnosis and surgical planning. Complete surgical removal with preservation of the facial nerve provides good outcomes and low chances of recurrence. Most of the patients were in fourth decade of life. Imaging, especially MRI, helped in identifying the exact size and extent of the tumour. Fine needle aspiration cytology and histopathological examination plays a crucial role in diagnosis and treatment of these cases. Management was mainly operative. No major complications or recurrence were noted during follow-up.

KEYWORDS: Pleomorphic adenoma, deep lobe parotid, parapharyngeal space, facial nerve, benign salivary tumour, case series.

INTRODUCTION

Pleomorphic adenoma is the most common salivary gland neoplasm, representing approximately 63% of all parotid gland tumours [(1)] .According to the literature, most pleomorphic adenomas arise in the superficial lobe of the parotid gland (about 90% of cases), with involvement of the deep lobe occurring in fewer than 10% of patients[(2)] .The

diagnostic evaluation and treatment planning include ultrasonography (US), magnetic resonance imaging (MRI), computed tomography (CT), and fine-needle aspiration cytology (FNAC)[3]. Fine-needle aspiration cytology (FNAC) plays a pivotal role in the preoperative evaluation of parotid gland tumours, offering a minimally invasive, cost-effective, and reliable diagnostic approach with high sensitivity and specificity. In salivary gland cytopathology, the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) is the most widely accepted and standardised grading system, providing clear diagnostic categories and associated risks of malignancy to guide clinical management. Within this system, pleomorphic adenoma the most common benign parotid tumour is classified under Category IVa (Benign Neoplasm), reflecting its characteristic cytomorphological features and low risk of malignancy[4] .Dissection near the facial nerve presents a significant challenge; therefore, total parotidectomy carries a substantially higher risk to the facial nerve compared with superficial parotidectomy[5] .Separating the facial nerve from the glandular parenchyma is the most technically demanding step of parotidectomy, and most complications arise from this process. [6]

Diagnostic Category	Risk of Malignancy	Management
1. Nondiagnostic	25%	Clinical and radiologic correlation or repeat fine-needle aspiration (FNA)
2. Nonneoplastic	10%	Clinical follow-up and radiologic correlation
3. Atypia of Undetermined Significance (AUS)	10%–35%	Repeat FNA or surgery
4. Neoplasm		Surgery or clinical follow-up
i. Benign	<5%	
ii. Salivary Gland Neoplasm of Uncertain Malignant Potential (SUMP)	35%	
5. Suspicious for Malignancy	60%	Surgery
6. Malignant	90%	Surgery

Figure 1: Milan grading for reporting salivary gland cytopathology [7]

Over the last two decades, considerable advances have been made in understanding the molecular pathogenesis of pleomorphic adenoma. Cytogenetic and molecular studies have demonstrated recurrent chromosomal rearrangements involving chromosome 8q12 and chromosome 12q13–15, leading to activation of the proto-oncogene PLAG1 and the architectural transcription factor HMGA2, respectively. These genetic alterations represent early oncogenic events that promote abnormal cellular proliferation and impaired differentiation within salivary gland tissue. Additional molecular abnormalities involving FGFR1, CTNNB1, MDM2, and other signalling pathways have also been reported, highlighting the complex genetic landscape of pleomorphic adenoma and its potential progression to carcinoma ex pleomorphic adenoma.

Despite increasing knowledge of the molecular biology of pleomorphic adenoma, published literature specifically addressing the clinicopathological spectrum of deep lobe lesions remains limited. Furthermore, few reports integrate detailed clinical findings, radiological characteristics, histopathology, and current molecular genetic concepts into a single comprehensive analysis.

REVIEW OF LITERATURE:

Pleomorphic adenoma is the most common benign tumour of the parotid gland, accounting for the majority of salivary gland neoplasms [1,7]. Most of these tumours arise from the superficial lobe, while deep lobe involvement is relatively uncommon and seen in less than 10% of cases [1,2]. Deep lobe pleomorphic adenomas are clinically significant due to their tendency to extend into the parapharyngeal space, which may present as an intraoral bulge and lead to delayed diagnosis [1,7]. These tumours typically present as slow-growing and painless swellings, and symptoms like rapid growth, pain, or facial nerve involvement are uncommon and may indicate malignant change [7]. Imaging plays an essential role in diagnosis and surgical planning. MRI is considered the most reliable modality for evaluating deep lobe tumours and their extension into surrounding spaces [1,3]. Advanced imaging techniques such as multiparametric ultrasound can also aid in the evaluation of salivary gland tumours in selected cases [3]. Fine needle aspiration cytology (FNAC) is widely used for preoperative diagnosis as it is minimally invasive and provides reasonably accurate results, although its accuracy depends on sampling and tumour location [4]. Surgical excision remains the treatment of choice for pleomorphic adenoma, with different approaches such as superficial parotidectomy, extracapsular dissection, and combined approaches depending on tumour extent [2,6]. Tumours involving the deep lobe and parapharyngeal space often require combined transparotid and transcervical approaches for complete removal [1]. Preservation of the facial

nerve is crucial during surgery, as it is closely related to the parotid gland, and its identification and dissection represent the most challenging part of the procedure [5,6]. Despite being benign, pleomorphic adenoma has a risk of recurrence, particularly if the tumour capsule is ruptured or excision is incomplete [8]. There is also a small risk of malignant transformation in long-standing or recurrent cases, emphasizing the importance of complete surgical removal [8]. Overall, the literature suggests that accurate imaging, proper surgical planning, and complete excision with facial nerve preservation result in favourable outcomes and low recurrence rates [1,8].

SUBJECTS AND METHOD

Patients admitted in ENT WARD/attending ENT OPD, in a tertiary care centre in Western UP with FNAC proven Pleomorphic Adenoma Parotid are selected for the present study over a period of 2 years from 1st Jan 2024 to 1st January 2026.

A prospective clinical study is conducted over the selected group for their age, sex, modes of presentation and their investigations. Study on various treatment modalities and their operative approach has been done. Written informed consent was obtained from all patients.

Inclusion criteria

1. All patients willing to participate in the same duration with parotid swellings.
2. Parotid lesions diagnosed as Deep Lobe Pleomorphic adenoma Parotid based on FNAC findings.
3. Lesions that were not concomitant with other lesions such as infections.

Exclusion criteria

1. Any neurological or psychiatric illness; altered sensorium; patients with any other major medical disorders like DM, blood disorders, hypertension, acute and chronic liver and kidney disease
2. Pregnant and breast feeding females

Sample Size

All patients who presented to ENT OPD with Deep Lobe Pleomorphic Adenoma parotid in the given duration and who are willing to participate have been taken in sample size.

CASES:

Case 1

A 45-year-old male presented with a swelling over the right side of his face, which he had noticed for the past 2 years. The swelling had increased slowly in size over time. There was no associated pain, facial asymmetry, or difficulty in swallowing. On clinical examination, a firm and non-tender mass was felt in the right parotid region [Figure 1].

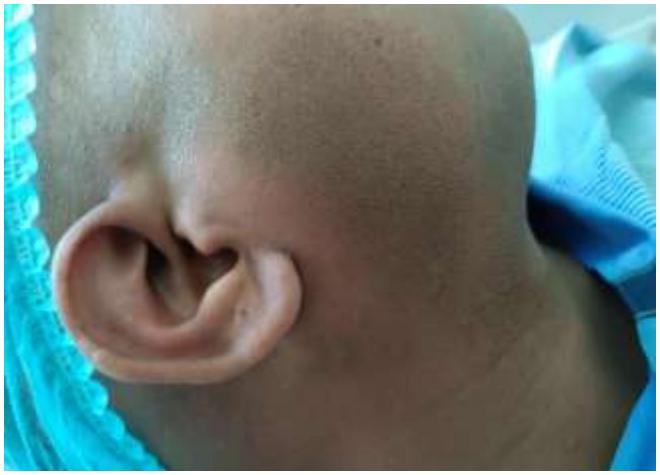

Figure 1 – Preoperative Picture Showing Swelling in Right Parotid Region

Facial nerve function was intact, with no evidence of weakness. CT SCAN of Neck revealed a diffuse mass arising from the deep lobe of the right parotid gland, extending into the parapharyngeal space [FIGURE 2].

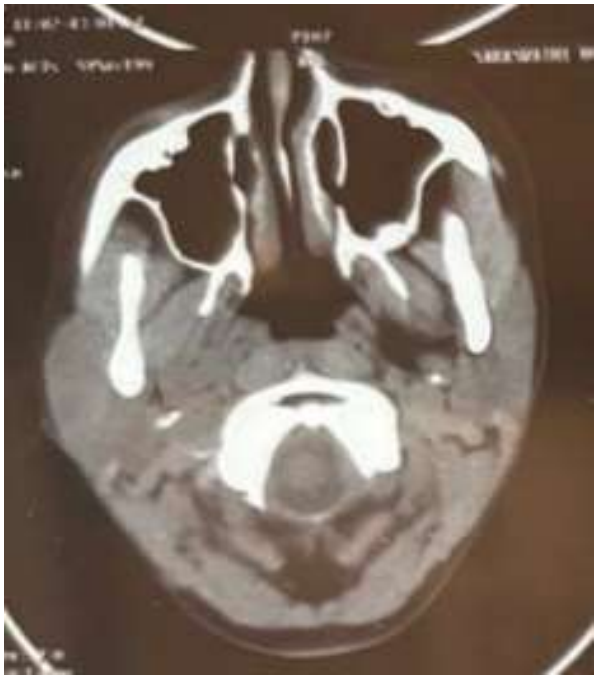

Figure 2 – NCCT Scan Neck Demonstrating a Diffuse Lesion in Right Lobe of Parotid

Fine needle aspiration cytology (FNAC) findings were suggestive of pleomorphic adenoma. The patient underwent complete surgical removal of the tumour via transparotid approach. The facial nerve was carefully identified and preserved during the procedure [Figure 3a, 3b].

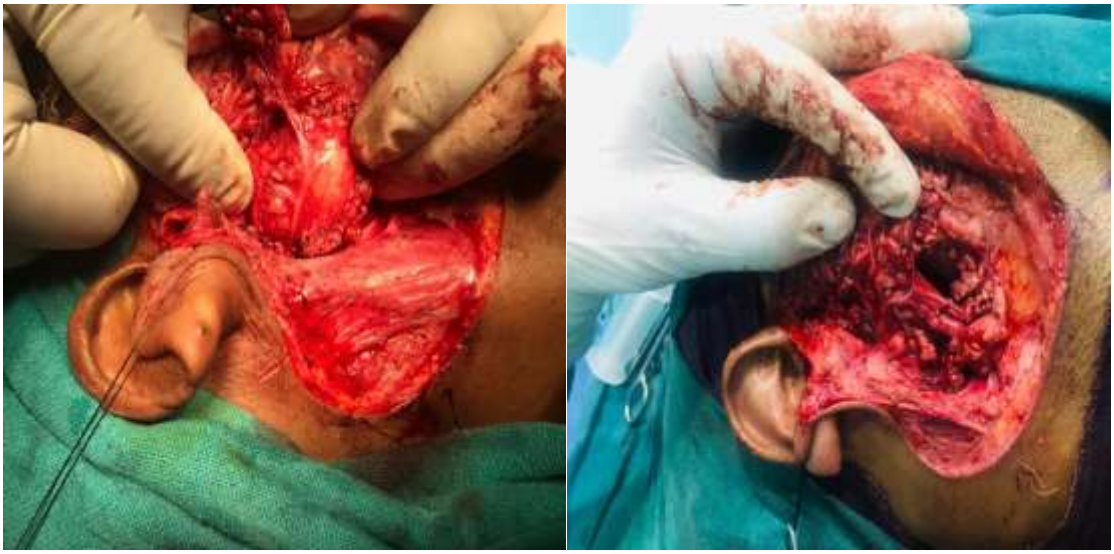

Figure 3a - Intraoperative Picture Figure 3b (After Removal)

The tumour was excised in total without any spillage [Figure 4].

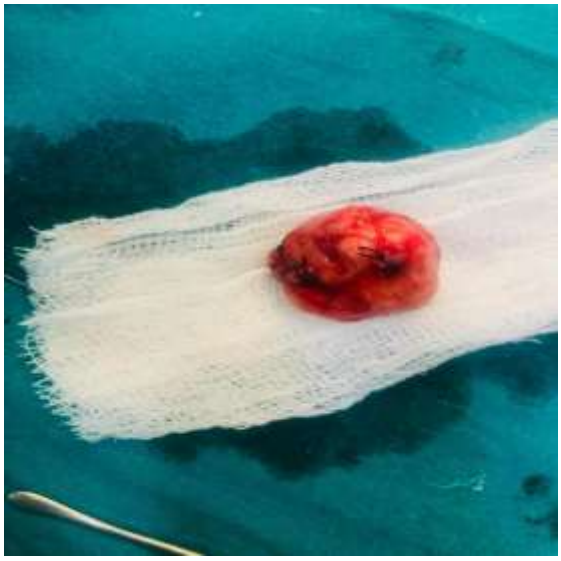

Figure 4 – Excised Specimen

Histopathological analysis confirmed the diagnosis of pleomorphic adenoma [Figure 5].

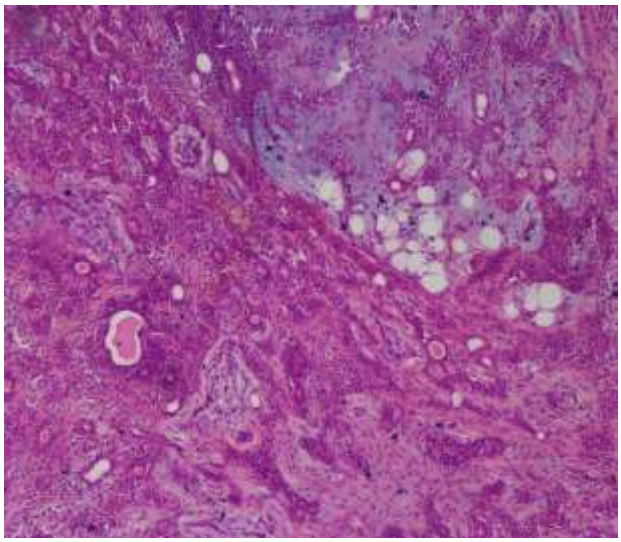

Figure 5 – Microphotograph Showing Areas of Epithelial and Myopithelial Differentiation

In the postoperative period, the patient developed mild facial nerve weakness (House-Brackmann Grade II), which resolved completely within 6 weeks. There was no evidence of recurrence on follow-up**.**

Case 2

A 38-year-old female presented with a swelling in the left upper neck for 1.5 years. She also complained of a sensation of fullness in the throat but had no difficulty in swallowing or breathing. On examination, a firm swelling was present below the angle of the mandible on the left side [Figure 6].

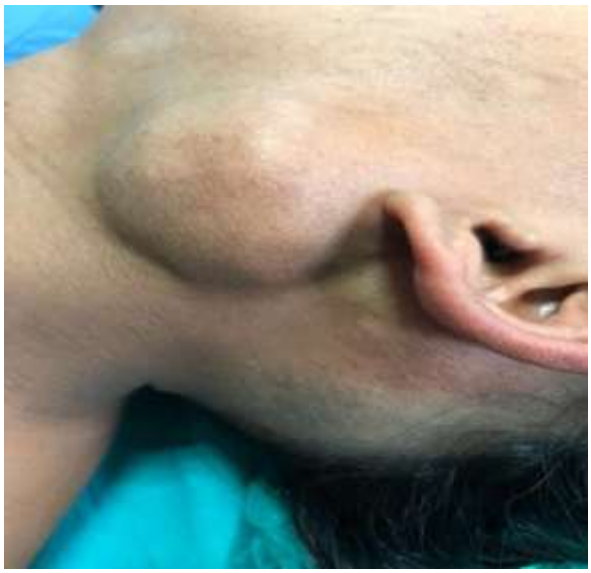

Figure 6 – Preoperative Picture Showing Swelling in Left Parotid Region

Facial nerve function was intact. CT SCAN Neck revealed a diffuse mass arising from the deep lobe of the right parotid gland extending medially into the parapharyngeal space [Figure 7].

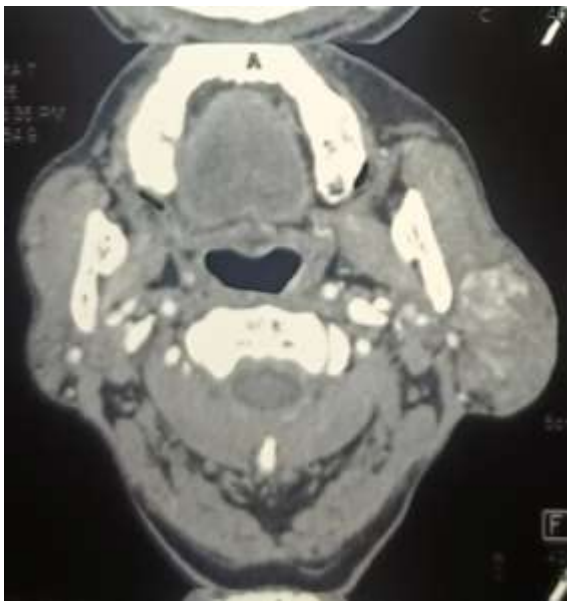

Figure 7- NCCT Scan Neck Demonstrating A Diffuse Lesion In Left Parotid Gland

FNAC findings were consistent with pleomorphic adenoma. The tumour was excised through transparotid approach. The mass was carefully dissected and removed in toto. The facial nerve was preserved throughout the procedure [Figure 8].

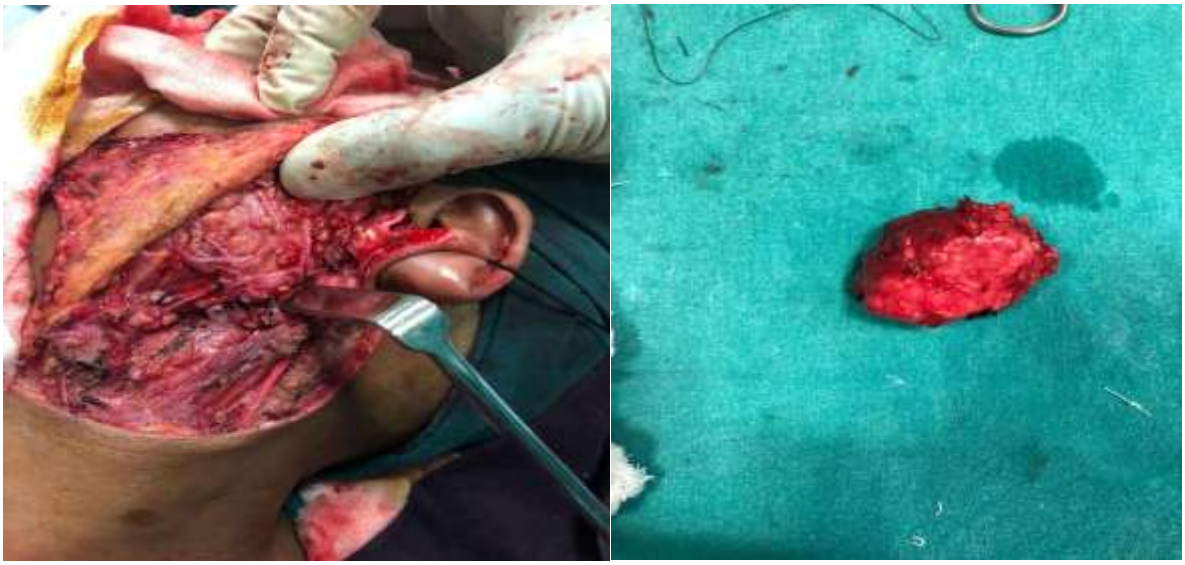

Figure 8 A - Intraoperative Picture Figure 8 B- Excised Specimen

Histopathology confirmed pleomorphic adenoma [Figure 9].

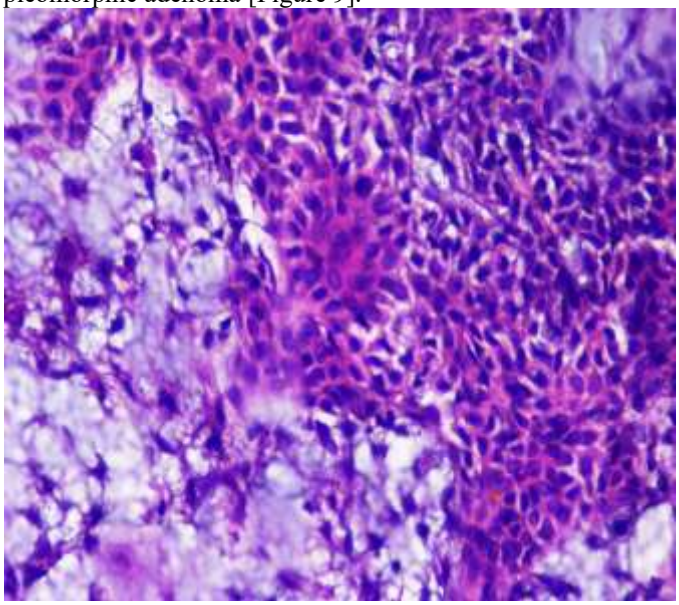

Figure 9 - Microphotograph Showing Areas of Epithelial and Myopithelial Differentiation Scattered Within Myxoid Stroma

The postoperative period was uneventful, with no facial nerve deficit. The patient remained disease-free during follow-up.

Case 3

A 52-year-old Female presented with a slowly enlarging swelling in the left parotid region for 3 years. There was no history of pain, rapid growth, or facial nerve involvement. Clinical examination showed a firm, non-tender mass in the left parotid area [Figure 10].

Figure 10 – Preoperative Picture Showing Swelling in Left Parotid Region

Intraoral examination did not reveal a significant bulge. Facial nerve function was normal. NCCT SCAN NECK demonstrated a deep lobe parotid tumour without significant parapharyngeal extension [Figure 11].

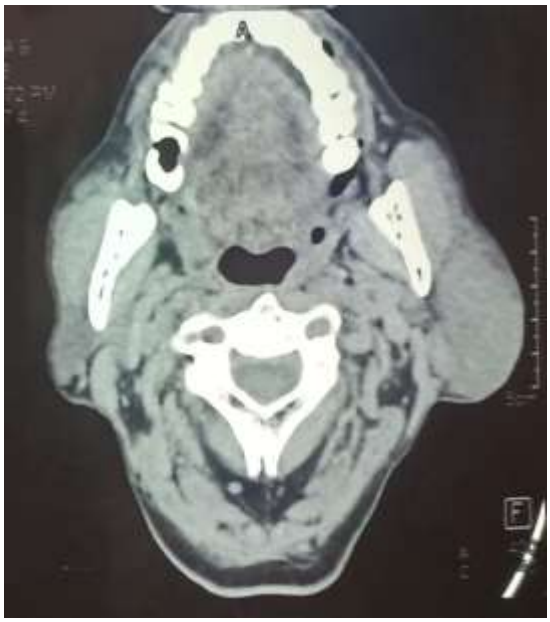

Figure 11 – NCCT Scan Neck Demonstrating a Significant Lesion in Left Parotid Gland

FNAC suggested pleomorphic adenoma. The patient underwent Total conservative parotidectomy with deep lobe tumour excision via a transparotid approach. The facial nerve was identified and preserved [Figure 12A, 12 B].

Figure 12a - Intraoperative Picture Figure 12 B- Excised Specimen

The tumour was removed completely. Histopathological examination confirmed pleomorphic adenoma [Figure 13].

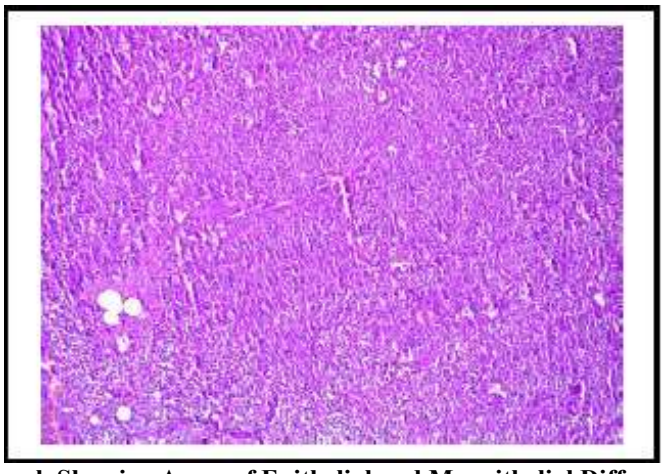

Figure 13 - Microphotograph Showing Areas of Epithelial and Myopithelial Differentiation Scattered Within Myxoid Stroma

The patient had no postoperative complications and showed no signs of recurrence on follow-up.

RESULTS AND OBSERVATIONS

The present study was done in the department of E. N. T - HNS for duration of 2 years from 1st JAN 2024 – 1st JAN 2026. During this period 10 cases were admitted in the department/attended ENT OPD. The results and observations are made according to the following tables & charts.

Table 1 - Age Distribution

Age Distribution	No. of Cases	Percentage
1 -10 YRS	0	0
11 – 20 YRS	0	0
21 -30 YRS	2	20%
31 – 40 YRS	4	40%
41 – 50 YRS	3	30%
51 – 60 YRS	1	10%

The present study shows commonest age group as the fourth decade followed by fifth decade. The youngest patient was 27 years of age and the oldest was 58 years of age

Table 2 - Sex Distribution

Sex	No. of Cases	Percentage
Male	4	40%
Female	6	60%

They were seen to be more common in females with 60%

CLINICAL PRESENTATION

Table 3 - Mode of Presentation

Mode Of Presentation	No. of cases	Percentage
Pre Auricular Unilateral Firm Swelling	8	80%
Cystic Swelling	2	20%

The commonest presentation was preauricular unilateral firm swelling (80%).

Table 4 - Investigations

Type of Investigation	No. of Cases	Percentage
Fnac	10	100%
Usg Neck	6	60%
Ct Scan Neck	10	100%
Histopathology	10	100%

In the present study among the investigations, FNAC and CECT SCAN NECK were important and were done in most of the cases of parotid gland swellings.

Table 5 -Mode of Treatment – out of 10 parotid cases,

Operative Approach	No. of Cases	Percentage
Superficial Parotidectomy	6	60%
Total Parotidectomy	4	40%

Table 6 - Complications

Type of Complication	No. of Cases	Percentage
Facial Nerve Paralysis	1	10%
Neck Hematoma	1	10%
Infection	1	10%

In the present study we have encountered a few complications also. They were treated conservatively.

Follow Up: Our cases were followed up after 2 weeks and 1 month of discharge from hospital.

DISCUSSION

Pleomorphic adenoma is the most common benign tumour of the parotid gland. However, tumours arising from the deep lobe are less common and may extend into the parapharyngeal space, making diagnosis more difficult [1,7]. In our series, two patients had tumours extending into the parapharyngeal space and presented with an intraoral bulge, while one case was limited to the deep lobe without significant extension.

These tumours usually grow slowly and are painless, which was seen in all our patients [7]. Symptoms like pain, rapid increase in size, or facial nerve weakness are uncommon in benign tumours and may suggest malignancy[12]. None of our patients had facial nerve involvement before surgery.

Imaging plays an important role in identifying the tumour and planning surgery[11,12]. MRI is especially helpful in showing the exact location and extent of the tumour[9,10]. Newer techniques like multiparametric ultrasound can also help in evaluating salivary gland tumours in selected cases [3]. In our study, MRI clearly showed deep lobe involvement and parapharyngeal extension.

FNAC is commonly used for the preoperative diagnosis of parotid tumours. It is a simple and useful test, although its accuracy may vary depending on the tumour location and sampling [4]. In all our cases, FNAC suggested pleomorphic adenoma, which was later confirmed on histopathology.

The greatest advance in understanding pleomorphic adenoma has been the identification of recurrent chromosomal rearrangements involving PLAG1 and HMGA2. Cytogenetic studies have shown that more than half of pleomorphic adenomas harbour chromosomal abnormalities involving 8q12, resulting in activation of the PLAG1 proto-oncogene, whereas approximately 10–15% demonstrate rearrangements involving 12q13–15, leading to overexpression of HMGA2. These alterations are considered early oncogenic events and represent the molecular hallmark of pleomorphic adenoma.

PLAG1 encodes a zinc-finger transcription factor that is normally expressed during embryogenesis but is largely silent in mature salivary tissue. Chromosomal translocations place PLAG1 under the control of active promoter regions of partner genes, resulting in inappropriate overexpression. Increased PLAG1 activity subsequently stimulates several downstream growth-promoting pathways, particularly the IGF2 signalling pathway, enhancing cellular proliferation and tumour development. Recent molecular studies have further demonstrated that HMGA2 functions upstream of PLAG1 and contributes to activation of the HMGA2–PLAG1–IGF2 axis, providing a unifying mechanism for tumour initiation and growth.

HMGA2 is an architectural transcription factor involved in chromatin remodelling and regulation of gene expression during embryonic development. In adult tissues, HMGA2 expression is minimal; however, chromosomal rearrangements restore its expression in pleomorphic adenoma, promoting cellular proliferation and inhibiting terminal differentiation. Although PLAG1 and HMGA2 abnormalities are mutually exclusive in many tumours, both alterations ultimately activate overlapping oncogenic pathways responsible for tumour growth.

Several additional fusion partners have been identified, including CTNNB1, FGFR1, LIFR, CHCHD7, and TCEA1, all of which contribute to promoter swapping and aberrant PLAG1 activation. These discoveries explain the remarkable histological diversity of pleomorphic adenoma despite a relatively limited number of driver genetic events. They also highlight that pleomorphic adenoma is a genetically defined neoplasm rather than merely a morphologically heterogeneous tumour.

Molecular markers and malignant transformation. Although pleomorphic adenoma is benign, incomplete excision and prolonged tumour duration increase the risk of recurrence and carcinoma ex pleomorphic adenoma. Malignant transformation is believed to occur through a multistep accumulation of additional molecular alterations beyond PLAG1 and HMGA2 activation. Loss of heterozygosity involving chromosomes 8q, 12q, and 17p, together with abnormalities of TP53, MDM2, HER2, EGFR, and PI3K/AKT signalling pathways, has been implicated in progression towards carcinoma ex pleomorphic adenoma. Recent evidence suggests that PLAG1 and HMGA2 continue to serve as useful molecular markers even after malignant transformation because they help establish the pre-existing pleomorphic adenoma origin of these carcinomas.

Surgery is the main treatment for pleomorphic adenoma [6]. The choice of surgical approach depends on the size and extent of the tumour. In our cases, a combined transparotid and transcervical approach was used for larger tumours with parapharyngeal extension, while other cases were managed with either a transcervical or transparotid approach[9,10]. Different techniques, such as superficial parotidectomy and extracapsular dissection, have been described in the literature [2,6].

Preservation of the facial nerve is very important during parotid surgery. A good understanding of facial nerve anatomy helps in reducing complications [5]. In our series, the facial nerve was preserved in all cases. One patient developed temporary facial weakness, which recovered completely within a few weeks.

Another important aspect is the risk of recurrence and malignant transformation. Although pleomorphic adenoma is a benign tumour, there is a small risk of recurrence, especially if the tumour capsule is breached during surgery [8]. Factors such as deep lobe location, large tumour size, and close relation to the facial nerve may increase the difficulty of surgery and the risk of recurrence [8,11]. In our series, careful surgical technique and complete excision helped prevent recurrence.

Complete removal of the tumour without rupture is essential to prevent recurrence [1]. In our study, all tumours were removed completely, and no recurrence was seen during follow-up. This shows that proper surgical technique can give good outcomes with minimal complications.

CONCLUSION

Deep lobe pleomorphic adenoma is a rare parotid tumour that may present with subtle clinical findings and parapharyngeal extension. MRI is essential for diagnosis and surgical planning, while FNAC supports preoperative evaluation. Complete surgical excision with preservation of the facial nerve remains the treatment of choice. With careful technique, outcomes are excellent, and recurrence is uncommon.

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Author's Contribution: AK- Definition of intellectual content, Literature survey, Prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation; GS- Concept, design, clinical protocol, data collection; AK, GS- Design of study, manuscript preparation; SS, YK- Manuscript editing, review and article submission; AK, GS- Manuscript Revision; MS, CK- Literature survey, Coordination and Manuscript revision

Consent: Written informed consent has been taken by the patient
Ethical Approval: The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from all patients or guardians prior to enrolment.
Statistical Analysis: Data were analysed using descriptive statistics. Categorical variables were expressed as frequencies and percentages.

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