

CYTOMORPHOLOGICAL CHARACTERISTICS OF AMELOBLASTOMA BY FINE NEEDLE ASPIRATION BIOPSY PROCEDURE CONFIRMED WITH HISTOPATHOLOGICAL EXAMINATION

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INFO ARTIKEL	ABSTRACT
Diterima 04 November 2022 Direvisi 12 Desember 2022 Disetujui 25 Desember 2022	Background: Ameloblastoma is the most common benign epithelial odontogenic tumor with malignant potential and is usually located in the jaw. It constitutes about 1-3% of all tumors and cysts of jaws. This entity has a very high recurrence rate of over 50% even after wide excision. Preoperative diagnosis of ameloblastoma can be made by fine-needle aspiration biopsy (FNAB) which is used as a guide for surgical planning. Case report: We report a case of a tumor in the mandible of a 41-year-old man with a preoperative diagnosis of ameloblastoma from a fine needle aspiration biopsy. Cytological examination of FNAB was confirmed by histopathological preparation of tumor tissue. Conclusion: The fine needle aspiration biopsy cytology is a reliable procedure for the pre-operative diagnosis of ameloblastoma. Pre-operative diagnosis of ameloblastoma can be used for planning therapy and early diagnosis of recurrence cases that can improve patient survival
Keywords Jaw; mandibular.	

Introduction

Fine Needle Aspiration Biopsy (FNAB) is a technique in which a fine needle is used to aspirate the contents of a solid or cystic lesion to produce a cellular material that is used for cytologic diagnostics. The FNAB technique is quite simple, minimally invasive with a low complication that allows rapid diagnosis, and can differentiate benign and malignant lesions with a high degree of accuracy when correlated with clinical and radiographic findings. The information obtained from the FNAB procedure is useful as a guide for surgical planning, especially in large lesions and patients with systemic disorders (Pilati et al.,

2020).

To determine the sensitivity, specificity, and accuracy of FNAB in the preoperative assessment of ameloblastoma. The authors compared the cytopathological and histopathological features so that the sensitivity, specificity, and accuracy of FNAB in the diagnosis of ameloblastoma can be compared. be determined. From this study, the sensitivity was 88.9%, specificity 100%, and accuracy 88.9% (Okoh et al., 2020).

The correlation of clinical-radiological findings helps in the evaluation of the diagnosis by FNAB. The FNAB procedure provides a simple, inexpensive, fast, and reliable

How to cite:	Dewi Safnita, Noza Hilbertina, Yessy Setiawati (2022). Cytomorphological Characteristics Of Ameloblastoma By Fine Needle Aspiration Biopsy Procedure Confirmed With Histopathological Examination. <i>Jurnal Health Sains</i> , 3(12). https://doi.org/2722-5356
E-ISSN:	2722-5356
Published by:	Ridwan Institute

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preoperative diagnosis of ameloblastoma. It can provide an early evaluation of the lesion, avoid unnecessary surgical biopsies and ensure adequate surgical excision in a planned manner (Fairweather et al., 2018).

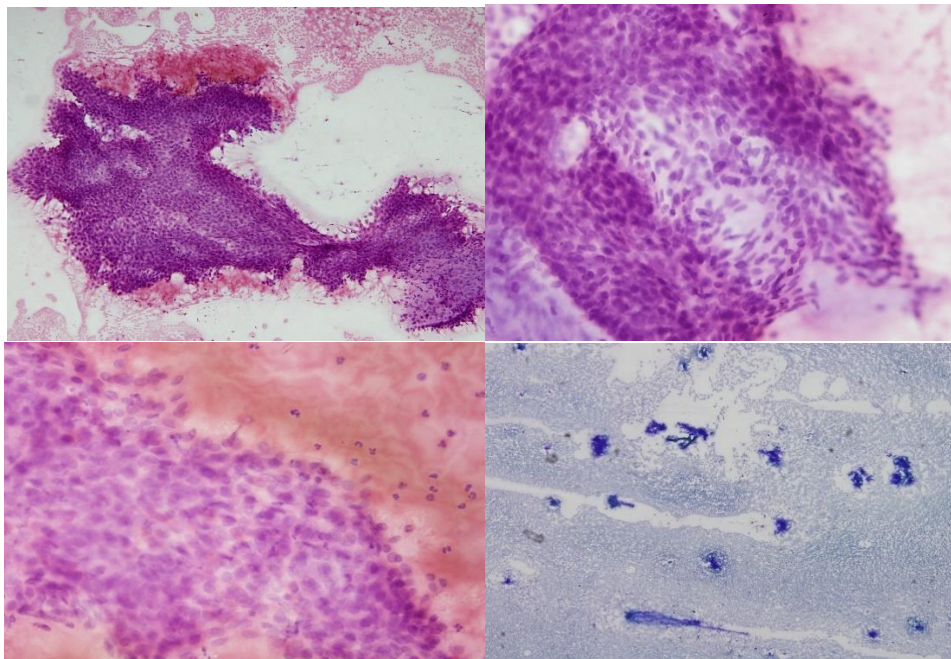
Case Report

A 41-year-old male patient presented with the chief complaint of swelling, painless over the left side of the mandible for 16 years, and progressive increasing swelling, pain, and often bleeds over the last 2 months. The patient was diagnosed with suggestive ameloblastoma by physical and radiograph examination. A fine needle aspiration biopsy procedure was recommended for the swelling. Past medical history revealed the patient had swelling in the same site in 2005. The patient had surgery in 2006 with a diagnosis of a dental cyst. The patient underwent a head CT scan with the results of a hypodense lesion on the left mandibular bone with cortical thinning and

destruction of the left mandibular bone.

Physical examination revealed a swelling in the left side of the mandible measuring 5x4x3 cm, firm, fixed, and the overlying skin was normal. The fine needle aspiration biopsy was performed and the bloody aspirated material was smeared on slides glass for air-dried smears were stained with may-Grunwald-Giemsa and alcohol-fixed smears with Hematoxylin-Eosin stain.

On microscopic cytologic, the smears showed the cellular smear consisting of cohesive clusters of tumor cells which are round to oval with dense chromatin, and slightly monomorphic nuclei. The lymphocytes and polymorphonuclear leucocytes are also found in the background. Based on the following cytological features consistent with the diagnosis of ameloblastoma (Figure 1A-F). Histopathological examination of tumor tissue is required to confirm the diagnosis.



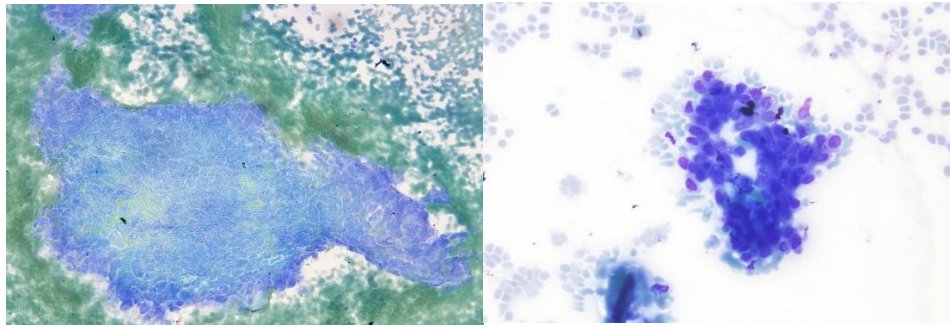


Figure 1. FNAB cytology examination. Groups of cells with round-oval nuclei, slightly monomorphic, hyperchromatic (A:100x), peripheral palisading (B:400x), and lymphocyte and polymorphonuclear leukocyte distribution (C: 400x) in HE staining. Cellular material (D: 40x, E: 200x, F: 400x) in May Grunwald Giemsa staining

The patient underwent a hemimandibulectomy for the removal of the tumor and reconstruction. A histopathological examination of the tumor was performed. On macroscopic examination of the mandibular tumor tissue (figure 2A) showed brownish-white tissue, rubbery, and bone-like structure size was 10x6x5 cm. The cross-section shows one brownish-white mass with a diameter of 5.5 cm.

On microscopic examination revealed connective tissue stroma containing the proliferation of odontogenic cells forming a plexiform structure and islands with the edges lined with columnar epithelium arranged in palisading (figure 2B-F). The stellate reticulum cells are arranged in the middle layer. There are some cells with squamous metaplasia, formation cyst, and bone trabecula also found. The histopathological diagnosis is conventional ameloblastoma.

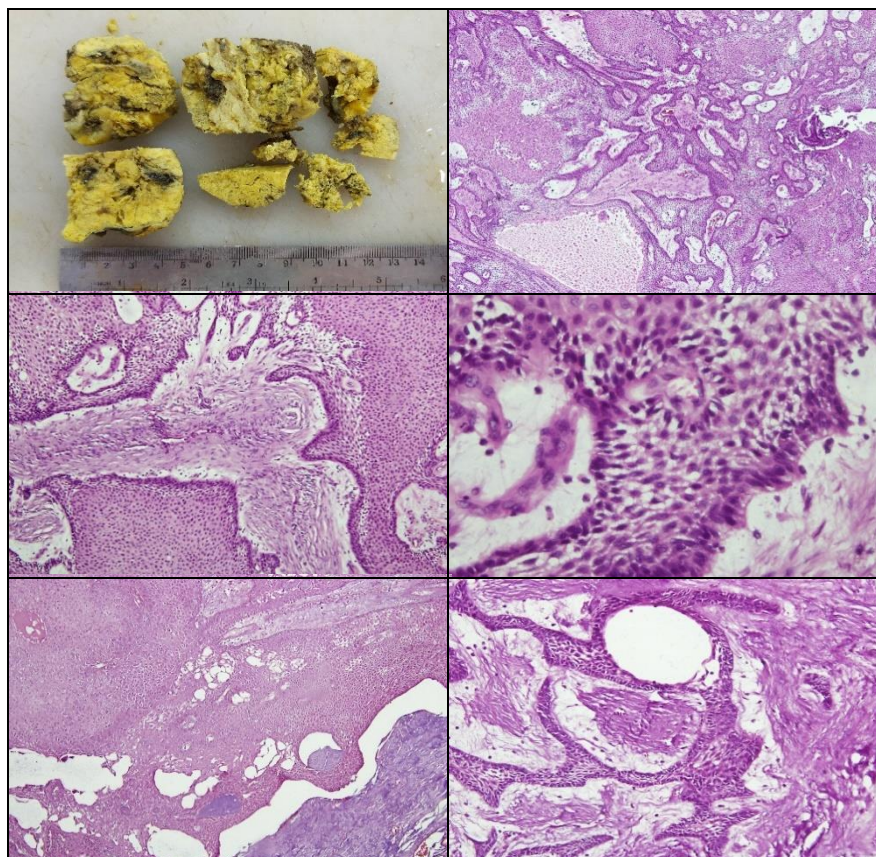


Figure 2. Histopathological examination. Macroscopic appearance (A). The microscopic examination showed the proliferation of odontogenic cells that form plexiform structures and islands (B: HE, 40x) and the cells are arranged in palisade at the periphery (C: HE, 200x). The odontogenic cells are seen arranged in plexiform structure and nests between bone tissue (E, F: HE, 200x).

Result and Discussion

Ameloblastoma is the most common benign odontogenic tumor arising from odontogenic epithelium. They are locally aggressive epithelial odontogenic neoplasm. The patient presents with swelling in the mandibular region, slowly growing, painless, often progressive increasing swelling that can be destructive and multilocular. (Zaidi et al., 2021) Reported two cases of ameloblastoma in which the patient presents with swelling in the jaw from 2 years to 5 years. In this case the patient presents with painless swelling in the mandibular region since 16 years ago. The swelling is slowly growing, and progressively increasing swelling over the last two months. The patient history of a dental cyst 16 years ago and had surgery.

Odontogenic tumors derived from epithelial, ectomesenchyme, and mesenchymal elements of the tooth-forming apparatus, constitute a heterogeneous group of lesions exclusively found within the jaw bones. It may arise from remnants of tooth-forming components, such as rests of the dental lamina, developing enamel organ, and the epithelial lining of odontogenic (dentigerous) cysts, or possibly from the basal epithelial cells of the oral mucosa (Hendra et al., 2020).

Ameloblastoma usually occurs in the third to fifth decades of life with a peak in the fourth decade. In developing countries, the incidence is reported at a younger age (Hendra et al., 2020). The patient in this case with a history of a dental cyst at 26 years old, then the second lesion in the same site enlarged at the age of 41 years.

The genetic and molecular features of ameloblastoma are still poorly understood. As ameloblastoma is characterized by slow growth, its development may initiate in childhood. The similarities between these odontogenic tumors and the tissues found under tooth development in childhood make it

difficult to distinguish them histologically. Therefore, a better understanding of the histological structures during tooth development is warranted. The fact that the posterior end of the dental lamina proliferates continuously, and that aberrant tooth germs most often are found in this region has been proposed as the statement for why ameloblastoma occurs most frequently at the angle of the mandible. This also may explain the high incidence of ameloblastoma associated with impacted lower third molar, as this region receives significant irritation (Fan et al., 2015).

The stimuli and specific kind of irritation, that cause the developmental epithelium to develop into ameloblastoma, demand further investigation, as these may be the direct cause of the neoplasm. Gene expression profiling, to identify the candidate genes that may be involved in the origination of ameloblastoma, needs to be further studied. The expression of the genes, about human tooth development, requires also further investigation (Fan et al., 2015).

Most cases of ameloblastoma are asymptomatic and are found on radiological examination. Radiographic characteristics of ameloblastoma generally show radiolucent, unilocular, or multilocular cystic lesions with a “bubble soap” appearance, cortical thinning or destruction, local invasion, and root resorption. The CT scan showed cortical damage and soft tissue involvement due to tumor cell infiltration, especially in the cancellous portion of the bone cortex (Aloua et al., 2021). The patient in this case underwent a head CT scan with a hypodense lesion on the left mandibular bone with cortical thinning and destruction of the left mandibular bone.

Ameloblastoma has a high recurrence rate after surgery (up to 50% of cases) and is therefore placed in the borderline tumor category rather than the benign tumor category.

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Long-term follow-up is required in ameloblastoma patients who have undergone surgery (Zheng et al., 2019). The research by Ling Bi et al reported patients under 50 years old has a high recurrence of ameloblastoma than patient over 50 years old. Maxilla-origin ameloblastoma had a higher tendency to relapse because tumor cells could extend beyond the radiographic margin in the cancellous bone at an average of 4,5 mm, even up to 8 mm. Since the cortical bone of the maxilla is thinner than the mandible. It is easier for tumor cells to infiltrate into the cortical bone and even earlier to extend into adjacent soft tissue (Bi et al., 2021).

The patient in this case had a history of dental cysts 16 years ago and had undergone surgery, but the results of the anatomical pathology examination were not obtained. From the patient's medical history, it can be estimated if the jaw swelling experienced by the patient is a recurrence of the previous lesson.

The FNAB procedure can be performed to establish a pre-operative diagnosis of ameloblastoma. Ameloblastoma is destructive, inherently making it easier to penetrate the needle during an FNAB procedure. In daily practice, ameloblastoma is rarely aspirated and their cytologic findings are still poorly documented in the literature (Okoh et al., 2020).

Cytological characteristics of ameloblastoma include basaloid cells or epithelial cells resembling ameloblasts with nuclei arranged palisade at the periphery and in the middle consisting of cells resembling stellate reticulum cells. The presence of squamous differentiation can be seen and this finding was reported by (Zaidi et al., 2021);(Gupta et al., 2018).

On FNAB cytology examination, in this case, showed a cellular smear consisting of scattered and clustered epithelial cells with round-oval nuclei, slightly monomorphic, hyperchromatic. There was an infiltration of lymphocytes and PMN leukocytes. The microscopic appearance can be found in ameloblastoma and confirmed by histopathological examination of tumor tissue diagnosed as ameloblastoma.

Ameloblastoma does not grow as a uniform solid mass but contains several cystic spaces so the FNAB procedure has the advantage of being an additional pre-operative diagnostic tool in cases of ameloblastoma,

sampling can be done in many places and deeper aspects of the tumor can be sampled which can help in a more accurate diagnosis. This is difficult to do in the incision biopsy (Okoh et al., 2020);(Kaliemoorthy et al., 2013)

Research conducted by (Okoh et al., 2020), suggested that the cytological diagnosis of ameloblastoma from FNAB specimens consisted of benign basaloid cells. This is correlated with research by (Kaliemoorthy et al., 2013). in 15 cases of ameloblastoma diagnosed from FNAB confirmed by histopathological examination of tumor tissue with a diagnosis of ameloblastoma. In this study, the results showed that the sensitivity of FNAB in the diagnosis of ameloblastoma was 86.6% which was by the study conducted by Gunhan O with a sensitivity of 100% and the study of Ucok et al. with a sensitivity of 93.5%. There were no false positive intraosseous jaw lesions diagnosed as ameloblastoma by FNAB. Therefore, the specificity of FNAB in diagnosing ameloblastoma was found to be 100%. (Okoh et al., 2020);(Kaliemoorthy et al., 2013).

The differential diagnosis of ameloblastoma in FNAB is ameloblastic fibroma, a primary intraosseous tumor. Both showed a predominance of basaloid cells with tumor cells arranged in the palisade at the periphery. However, ameloblastic fibroma has more stromal fragments than ameloblastoma. Another differential diagnosis is another basaloid cell tumor involving the jaw. Other neoplasm that also shows basaloid cell cytomorphology in FNAB can be found in salivary gland neoplasms, including pleomorphic adenoma, basal cell adenoma, adenoid cystic carcinoma, basal cell adenocarcinoma (Bibbo & Hoda, 1998);(Cantley, 2019).

Sometimes, aspiration from cystic ameloblastoma may have a paucity of characteristic basaloid cells, the presence of polymorphs, and foamy macrophages which leads to difficulty in diagnosis. In this case, ameloblastoma should be differentiated from other benign cystic lesions of the jaw including odontogenic keratocysts and dentigerous cysts. Odontogenic keratocysts show anucleate and nucleate squamous cells having central pyknotic nuclei in keratinous background. Dentigerous cysts provide straw-colored fluid containing few squamous cells and foamy macrophages. The trimodal populations of

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basaloid, stellate, and squamous cells are characteristic to differentiate ameloblastoma from these cysts (Gupta et al., 2018).

Several other intraosseous malignant lesions such as lymphoma, primary intraosseous squamous cell carcinoma, mucoepidermoid carcinoma, small cell carcinoma, and ameloblastic carcinoma showing features of basaloid cells should be

ameloblastomas, primary intraosseous squamous cell carcinoma would have malignant features. Mucoepidermoid carcinoma shows mucous cells, intermediate cells, and epidermoid cells in a mucoid background. Unlike, ameloblastoma, ameloblastic carcinoma shows high cellularity, nuclear pleomorphism, prominent nucleoli, abnormal mitoses, and necrosis (Gupta et al.,

Differential Diagnosis	Cytomorphological	Pitfalls	Comments
Basal cell adenoma	Smears are cellular show small cluster of branching cords composed of small uniform cells with round or oval nuclei; individual cells appear as naked nuclei or have a scant amount of cytoplasm; sparse homogenous background material.	Characteristic basaloid cells, and location in mandible region.	Unlike ameloblastoma cells.
Basal cell adenocarcinoma	Shows packed groups of ovoid to spindle shaped, basaloid epithelial cells in solid, trabecular and membranous arrangements	Characteristic basaloid cells	The elongated, spindled nuclei of the basaloid cells in basal cell adenocarcinoma are a distinctive features. Diagnosis is often dependent on histologic confirmation
Adenoid cystic carcinoma	Spherical aggregates, rosette-like groups, papillary or solid fragments of cancer cells; small uniform cohesive cancer cells with minimal cytoplasm and distinct nucleoli; dispersed naked nuclei common; magenta-stained hyaline mucoid globules, cylinders of homogenous acellular material (May-Grunwald-Giemsa)	Location in mandible region and pattern of tumor cells.	Unlike ameloblastoma.

also excluded. Lymphoma cells may also resemble the basaloid cells of ameloblastoma; however, lymphoglandular bodies are also seen, but not in ameloblastoma. Unlike

2018);(Anitha, 2020);(Perez-Ordenez & Marchese, 2013). Differential diagnoses of ameloblastoma are shown in

Table 1.
Differential diagnosis of ameloblastoma (Gupta et al., 2018);(Bibbo & Hoda, 1998);(Anitha, 2020)

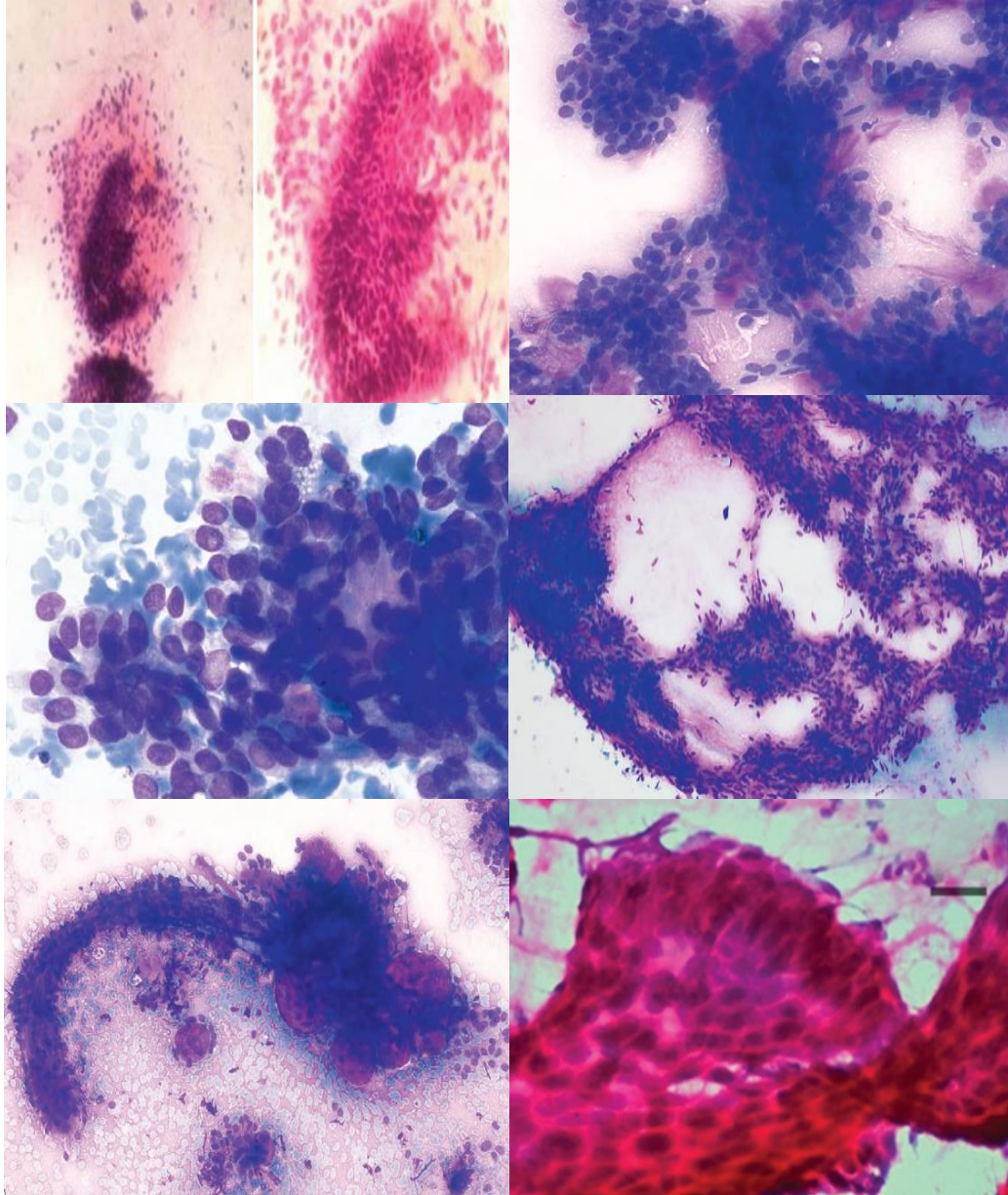
Differential Diagnosis	Cytomorphological	Pitfalls	Comments
Odontogenic keratocyst	show anucleate and nucleate squamous cells having central pyknotic nuclei in keratinous background	Sometimes, aspiration from cystic ameloblastoma may have a paucity of characteristic basaloid cells, the presence of polymorphs and foamy macrophages which leads to difficulty in diagnosis.	The trimodal populations of basaloid, stellate, and squamous cells are characteristic to differentiate ameloblastoma from these cysts
Dentigerous cyst	provide straw-colored fluid containing few squamous cells and foamy macrophages		
Lymphoma	Monotonous population of atypical lymphoid cells; intermediate-size cells with a large round nucleus, finely stippled chromatin, occasional small nuclei; small rim of basophilic cytoplasm with an occasional small cytoplasmic vacuole.	may also resemble the basaloid cells of ameloblastoma;	Unlike ameloblastoma cells.
Primary intraosseous squamous cell carcinoma	Malignant features of squamous cells.	intraosseous malignant lesions	Unlike ameloblastoma shows benign lesion
Mucoepidermoid carcinoma	shows mucous cells, intermediate cells, and epidermoid cells in a mucoid background	Characteristic basaloid cells	There is no mucous cells, intermediate cells.
Ameloblastic carcinoma	shows high cellularity, nuclear pleomorphism, prominent nucleoli, abnormal mitoses, and necrosis	Characteristic basaloid cells	Unlike ameloblastoma shows benign lesion
Ameloblastic fibroma	Predominant basaloid cells with peripheral palisading of tumor cells.	Characteristic basaloid cells	Basaloid cells with more stromal fragments than ameloblastoma
Pleomorphic adenoma	Shows fibrillary, and chondromyxoid stroma; myoepithelial cells of ovoid to plasmacytoid type; epithelial cells with uniform forming ducts or small sheets; clusters and single cells gradually merging with the mucoid mesenchymal elements.	Location in mandible region.	Fibrillar chondromyxoid stroma or mature chondroid substance, and globoid structures typical pleomorphic adenoma.

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E-ISSN: 2722-5356

Published by: Ridwan Institute

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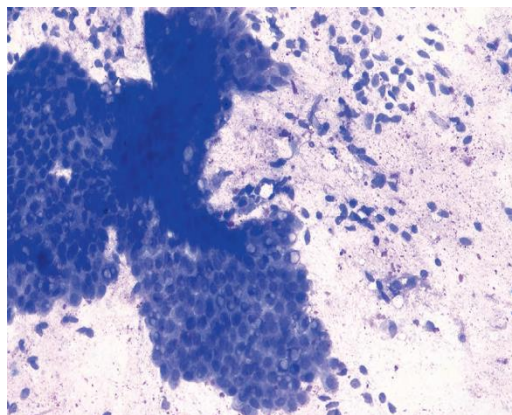


Figure 3. Cytomorphological differential diagnosis of ameloblastoma. (A) Ameloblastic fibroma. (B) Pleomorphic adenoma, MGG, xMP. (C) Basal cell adenoma, MGG, xHP. (D) Basal cell adenocarcinoma, Diff-Quick, x200. (E) Adenoid cystic carcinoma, MGG, xLP. (F) Ameloblastic carcinoma, HE, x100. (G) Mucoepidermoid carcinoma, MGG, xMP).^{10,12-14}

The correlation of clinicopathological, the diagnosis of FNAB ameloblastoma and ruling out the differential diagnosis. Preoperative cytopathological diagnosis of ameloblastoma can be used for surgical planning and early diagnosis of recurrence

Conclusion

The fine needle aspiration biopsy cytology is a reliable procedure for the pre-operative diagnosis of ameloblastoma. Pre-operative diagnosis of ameloblastoma can be for the pre-operative diagnosis of ameloblastoma. It can reduce the limited incisional biopsy.

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radiological findings can assist in evaluating cases. Early diagnosis of ameloblastoma cases can improve patient survival rates ([Chae et al., 2015](#)).

used for planning therapy and early diagnosis of recurrence cases that can improve patient survival. The fine needle aspiration biopsy procedure is a simple, safe, inexpensive, and minimally invasive procedure

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