

Diversified Pediatric Salivary Gland Pathologies: A Review

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Abstract: Paediatric diseases or pathologies are not autonomous and diversified. They are actually categorized into the similar group of the diseases occurring in the adults salivary glands, falling in the paediatric age range but differs in their incidence and symptoms. These pathologies in children are uncommon and rare, requires early initial diagnosis with proper treatment. A systematic approach and a high suspicion index is required for its early recognition. Also, to characterize particular salivary gland pathology, physical findings, history and diagnostic test should carefully be monitored. Treatment approach should include a greater surgical experience especially in tumors of salivary gland. The current paper provides an general idea of all the benign and malignant salivary gland neoplasms, non-neoplastic salivary gland pathologies and salivary gland cysts occurring in children and adolescence.

Key words: Tumor, Salivary gland, capsule, encapsulated

INTRODUCTION

Paediatric salivary gland pathologies fall into the same spectrum of lesions as adult salivary glands but with less frequency and rare occurrence.¹ Some viral induced salivary gland diseases are more predominant in children and adolescents and are frequently pragmatic. Among all the paediatric pathologies as whole, autoimmune disorders, etiologies concerned with viruses and bacteria's and tumors of salivary glands were the most common findings besides congenital diseases.² Malignant salivary gland lesions are rare and are approximately half the total number of entities after excluding lesions of haematogenous or vascular origin.³ These lesions have good prognosis with prevalence in older children and similar survival rate as that of adults (over 90%).⁴ Parotid gland is the mainstream and the widely held major salivary gland for malignancy to occur, in which mucoepidermoid carcinoma which is also radiation induced is on the whole and the most frequent lesion, and in contrast to adults, mostly tumors of minor salivary glands and submandibular Gland belongs to the benign category.³ Adenocarcinoma, adenoid cystic and acinic cell carcinoma are some of the malignant lesions described in this review.

For any salivary gland disease recurrence case, re-excision is preferred and radiotherapy should be the treatment of choice barely in suspiciously particular cases.⁴

BENIGN TUMOR

PLEOMORPHIC ADENOMA

Synonyms: *Mixed tumor, enclavoma, branchioma, endothelioma, enchondroma*⁵

Pleomorphic adenoma is one of the most prevalent salivary-gland tumor in children, representing 66-90% of all the salivary-gland tumors. Between 70% and 85% of pleomorphic adenoma occur in the major salivary gland commonly parotid; while 5% occur in minor salivary glands.⁶ Incidence of pleomorphic adenoma during childhood is usually known to occur between 7 years and 16 years with an average age of 10.5 years⁷

Definition -

Pleomorphic adenoma of salivary gland tissue also known as a mixed tumor has its origin from epithelial as well as mesodermal elements. The epithelial part is known to originate from the duct-lining epithelium, while myoepithelial cells (contractile cells surrounding the tubules draining individual acini) give rise to the mesodermal part.

Clinical features

- Slow growing, masses of the parotid.
- Painless.
- Untreated, pleomorphic adenomas have a 2–25% risk of malignant degeneration.⁸
- Some cases exhibiting rapid growth have been reported especially in the palate.⁷

Histology

Macroscopic features

Pleomorphic Adenoma macroscopically appears as shiny to translucent well circumscribed mass with multifocality.² The mixed tumors generally appear as an irregular to ovoid mass with well-defined borders. The tumors which occur in the major glands have either a fibrous capsule which is incomplete or are unencapsulated whereas in the minor glands they are unencapsulated. The cut surface may be rubbery, mucoid, fleshy with a homogeneous tan or white color. Areas presenting haemorrhage and infarction may be noted occasionally.⁵

Histologically, it is formed of acini, cords and thin strands of epithelial cells which appear to be suspended within the stroma, which often has a myxomatous appearance. Pleomorphic adenoma being a tumour of high implantability have lateral growth extensions as infiltrations in the capsule and may possibly come into view as non-malignant encapsulated tumor.⁶ Myxoid Stroma (80%) with a tendency to reoccur, Cellular (80%) and mixed (Classic) are the three histological structural variants of pleomorphic adenoma exposing epithelial ductal structures^{9,10}

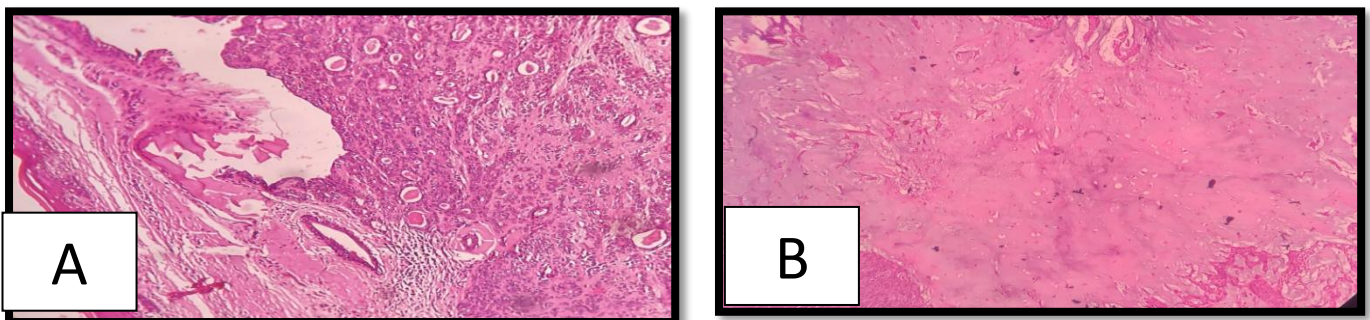
Differential Diagnosis -

1. Myoepithelioma
2. Mucoepidermoid Carcinoma
3. Basal Cell Adenoma^{1,2}

Treatment

In children, fine needle aspiration often requires sedation, and has the risk of insufficient cells for diagnosis and therefore is not as much of advantageous in children. As an alternative for this, assistance with preoperative imaging along with surgical excision are indicative of its diagnosis, usually with the aid of preoperative imaging. For the assessment of masses of parotid gland in paediatric patients, ultrasonography came out to be a highly compatible method.⁸

Pleomorphic adenomas are best treated by surgical excision. Superficial parotidectomy with detection and perpetuation of the seventh cranial nerve is suggested. Seeding of the tumor bed can occur because of the violation of the capsule and therefore the risk of non-removal of the entire tumor can persist. So, local enucleation should not be made as a treatment of choice. With adequate surgery the prognosis



PLEOMORPHIC ADENOMA: Fig 1 A & B shows well-circumscribed tumor with epithelial and myoepithelial cells in ductal and trabecular pattern myxoid stroma

MALIGNANT MUCOEPIDERMOID CARCINOMA

Introduction

Originating from epithelial (parenchymal) cells, this malignant neoplasm of salivary glands is for the most part familiar in paediatric patients and adolescents.¹²

It was first studied and described as a take apart thing by Stewart, Foote and Becker in 1945.⁵ These salivary glands malignancies from parenchymal origin have prevalence after 10 years of age i.e. after late adolescence. Mehta and Willing, stated this carcinoma as emission-induced in children.¹²

Definition

Mucoepidermoid carcinoma is a malignancy of parenchymal origin and is composed of both mucus-secreting cells and epidermoid-type cells in varying proportions.⁵

Clinical features

- The mucoepidermoid carcinoma is for the most part frequent in the large salivary gland i.e. parotid
- Usually appears as an asymptomatic swelling.¹³
- Pain or facial nerve palsy may develop usually in association with high-grade tumors.¹¹

Histology⁵

- It is poised of mucous secreting cells, epidermoid type (squamous) cells and intermediate cells
- The mucous cells are of various shapes and have abundant, pale, foamy cytoplasm that stains positively for mucin stains.
- The epidermoid cells have squamoid features, demonstrate rare keratinization, intercellular bridges and have polygonal shape
- A group of highly proliferative, basaloid cells referred to as the intermediate cells. These cells are generously proportioned as compared to basal cells and smaller than the squamous cells and are believed to be the progenitor of epidermoid and mucous cells. Occasionally clusters of clear cells can be present. These clear cells are generally mucin and glycogen free.
- Epidermoid and mucous cells may be precisely ordered in a glandular pattern.

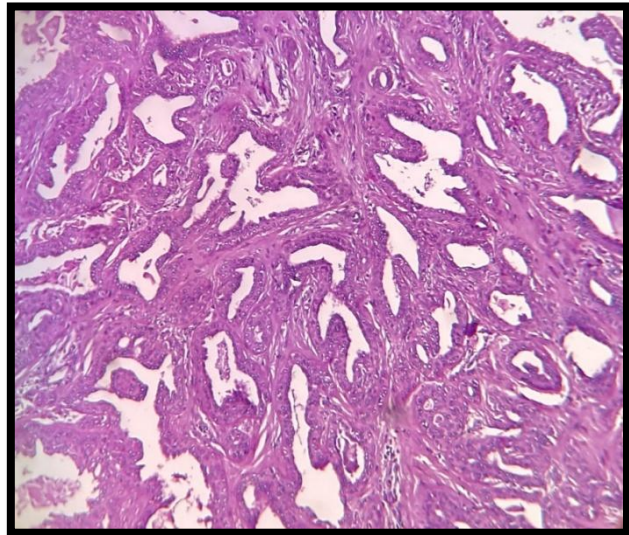
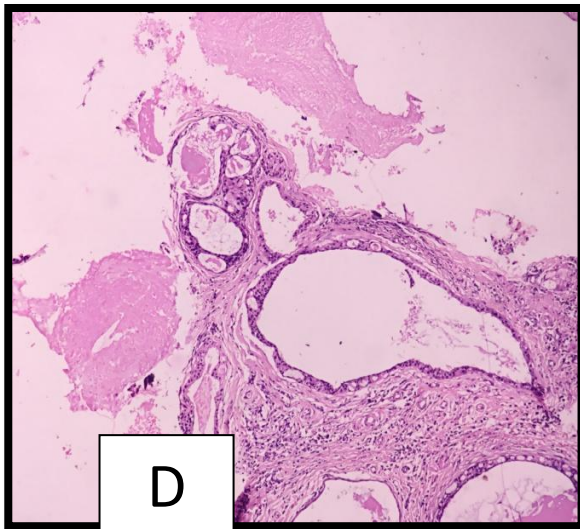
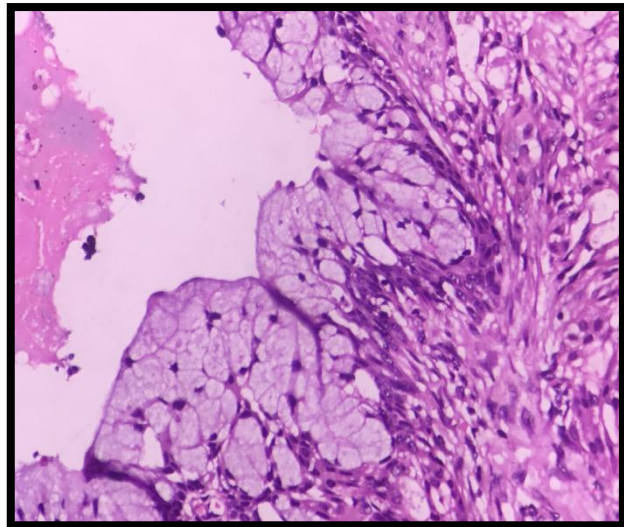
Histological Grading –

Mucoepidermoid Carcinoma was sub classified¹⁴ as follows-

1. Low grade Mucoepidermoid Carcinoma –
 - Single layered mucous secreting cells which are columnar in shape
 - Intermediate and epidermoid cells are rarely present
 - Foreign body giant cells are also seen
2. Intermediate grade Mucoepidermoid Carcinoma-
 - Predominant intermediate cells of basaloid variety
 - Epidermoid cells in abundance and are squamoid in shape
 - Mucous secreting cells are not evident
3. High Grade Mucoepidermoid Carcinoma-
 - Solid cords of epidermoid, intermediate and basal cells
 - Active mitosis and anisonucleosis are evident and the neoplastic cells are poorly differentiated¹

Treatment¹²

Mucoepidermoid carcinomas originating from intraorally in children and adolescents can be effectively managed by wide local surgical excision that ensures tumor-free surgical margins. Wide surgical excision in combination with bone removal is preferred only when there is gross periosteal involvement or bone erosion by the mucoepidermoid carcinoma.



MUCOEPIDERMOID CARCINOMA

FIGURE 2A: Shows clinical presentation of swelling in palate

Figure: B, C & D shows tumor composed of mucous, epidermoid, and intermediate cells arranged in solid and cystic areas

ACINIC CELL CARCINOMA

Synonyms: Acinar cell or serous cell adenoma, adenocarcinoma⁵

Introduction

This carcinoma in children is very rare, since it represents about the 3% of all malignant parotid neoplasms.¹⁶ Acinic cell carcinoma was referred to as an entity for the first time more than 50 years ago by Godwin et al.¹⁷ It is a neoplasm of low grade that occurs most often in the large salivary gland with a predilection for females and prevalence at a younger age than other salivary gland tumors. Despite of low malignant behaviour, acinic cell carcinoma has reoccurent predisposition, which bring into being metastases of lungs and cervical lymph nodes and have a belligerent progression with death rates ranging from 1.3% to 26%.¹⁸ This epithelial malignancy is second most common in children subsequent to Mucoepidermoid carcinoma.¹⁷

Definition

According to the world health organization, this salivary gland malignant epithelial neoplasm has serous acini differentiating into neoplastic cells and has characteristic presence of zymogen granules in the

cytoplasm which are secretory in nature. This low grade salivary gland neoplasm can also have ductal cells and is most commonly seen parotid gland with prevalence in adolescents.¹⁷

Clinical features¹⁹

- In children, there is complicated irrefutable appraisal of parotid masses.
- The lesions are slow growing, enlarging and painless clinically i.e. possesses no symptoms
- A sign of malignancy in this tumor is the involvement of the seventh cranial nerve but this is not always present and is bizarre.

Histologic features²⁰

The tumor is encapsulated with varying compositions of differentiated cells. Normal acini are well-differentiated whereas immature acini are less differentiated cells. Embryonic ducts are also categorized into poorly differentiated variety.

Four Growth patterns described by Abram are as follows -

- (1) Solid
- (2) Papillary-cystic
- (3) Follicular
- (4) Microcystic.

The cell that largely constitutes this tumor has the characteristic of serous acini, with copious cytoplasm which is granular and basophilic and a nucleus which is eccentrically placed and stained darkly. Small intercalated duct cells and vacuolated cells are also seen in this neoplasm. Connective tissue is precisely fibro vascular collagenous tissue. Lymphoid elements are commonly found in parotid acinic cell carcinomas, a feature which is helpful in the diagnosis.

Treatment-

In general, supervision of this tumor consists of its removal completely by surgical excision i.e. parathyroidectomy (Total or subtotal). Postoperative radiotherapy may be useful for recurrent, undifferentiated cases of this carcinoma, positive margins, and advanced tumors with cervical lymph node spread.¹⁷

In cases of solemn complications including trismus, facial hypoplasia, facial bones growth retardation, osteoradionecrosis and pituitary deficiency radiotherapy is suggested and well thought-out as a conduct of preference

DEVELOPMENTAL-

1. ATRESIA

Atresia is defined as a developmental non- neoplastic congenital lesion characterized by salivary duct absence or occlusion leading to xerostomia or mucous retention phenomenon.²¹

2. AGENESIS

This exceptionally infrequent hereditary incongruity causes insightful xerostomia in children.²² It may possibly transpire in segregation or be associated with other malformations of the first branchial arch. These include Hemifacialmicrosomy, Treacher Collins syndrome and other congenital malformations of the face. Matsuda et al. in their study reported a total number of 43 cases of aplasia emerging in the literature. Also, Gruber in 1885 reported first case of aplasia.²³

Etiology

The foremost etiological factor proposed is metamorphosis in fibroblast growth factor 10 (fgf10) affecting the Fibroblast Growth factor receptor signalling²³

Oral manifestations-

- The oral sequele includes dental caries, candidiasis, and ascending sialadenitis.²²
- Hereditary anaplasia, hypoplasia, far-reaching occlusal teeth wear are also some of the conditions associated with salivary agenesis.²¹

- Patients face dyspepsia and drinking fluid, have dental caries associated with xerostomia.²³

Treatment

The treatment is supportive²¹, in the early hours analysis (on quantifiable assessment, Magnetic resonance imaging, ultrasound and scintigraphy) results in suitable and untimely prophylaxis against sequelae and substantial respite of the symptoms²³

FUNCTIONAL- JUVENILE SJÖGREN'S SYNDROME

Synonyms: *Sicca syndrome, gougerot-sjögren syndrome*⁵

Introduction-

The disease was described by Henric Sjogren in 1933.²¹ It is rare or underdiagnosed condition seen in children and adolescents. Throughout the syndrome route and furthermore at its commencement, patient presents parotid gland swelling which is prime and recurring. The disease also in a smaller amount frequently presents oral and ocular symptoms. A total of 81 patients aged between four and 16 (mean 10 years of age) were reported in the literature from 2000 to 2010.²³

Definition²⁴

This systemic syndrome is autoimmune and chronic which predominantly necessitates lacrimal and salivary consequentially resulting in dry eyes i.e. xerophthalmia and dry mouth i.e. Xerostomia

Etiology

It is an autoimmune disorder associated with hla-dr3 and hla-b8.²¹

Clinical features²³

- Hepatitis, Lymphoma which is B cell derived, Vasculitis and neuropathy are some of the extra glandular systemic manifestations. These are in a lesser amount and are unusually seen throughout the syndrome itinerary.
- Sjögren's syndrome may occasionally give rise to life-threatening situations, such as hypocalcaemic paralysis due to renal tubular acidosis.
- In addition, it may involve brain and liver.
- In children no pertinent oral and ocular symptoms are widespread excluding recurrent parotid gland swelling merely.

Treatment

The treatment of juvenile Sjögren's syndrome is largely symptomatic. The symptoms of the syndrome can be guarded by immunosuppressant's which lessens fibrosis and infiltration of lymphocytes. When systemically concerned, Rituximab is the existing endorsed drug of choice.²³

SALIVARY GLAND CYSTS

1. MUCOCELE

Synonym: *Mucous extravasation phenomenon*²⁵, *mucous retention cyst*⁵, *mucus escape reaction*²⁴

Introduction

Mucocele is pigeonholed by minor salivary gland obstruction and is categorised as a frequent pronouncement in those individuals mostly in young age group who devastate their oral mucosa with a reported predominance involving 0.04% and 1.00% of children.^{25,26}

Definition

Mucous extravasation phenomenon is an outcome following rip apart of minor salivary gland duct and is characterized by extravasation of mucous into the oral mucosa connective tissue stroma.²⁵

The major etiological factor included is mucous pooling in an obstructive excretory duct which is dilated due to trauma driven mechanically to a minor salivary gland²⁷

Clinical presentation^{28,27}

- With a history of fluctuating sizes, these lesions are smaller than 1.5 cm in size most frequently. Clinically they are nodular with bluish color vaguely and are firm or fluctuant when palpated.

- The color of the lesion varies depending upon the location of mucous extravasation and its extent to connective tissue stroma. If Mucocele is located deep to the connective stroma, the nodules appear pink.
- Labial mucosa of the lower side which repeatedly gets distressed on biting is the on the whole a pervasive site. Also, buccal mucosa, tongue and floor of the mouth are several erstwhile frequent locations.
- With size ranging less than 1 cm in diameter, mucoceles have smooth surface with bluish hue or can be translucent and presents no pain.

Histopathologic features^{11,5}

- Mucin is spilled surrounded by new blood vessels and collagen fiber bundles i.e. neovascularisation and angiogenesis. Also, deep into the connective tissue copious macrophages i.e. histiocytes are apparent.
- Chronic inflammation and ductal dilation are also seen in the adjoining minor salivary glands. In the area of Mucocele, ruptured duct of salivary glands are also marked
- Occasional mucoceles demonstrate an intact, flattened epithelial lining.

Treatment²⁵

Occasionally, mucoceles ruptures spontaneously. Surgical excision is the cure of preference for the persisting mucoceles so that recurrence is prohibited. Cryosurgery, electrosurgery, co2 laser removal, or laser vaporization are several erstwhile healing choices. Ranulas i.e. Mucocele on the floor of the mouth are treated by marsupialization or removal of the lesion and the associated salivary gland.

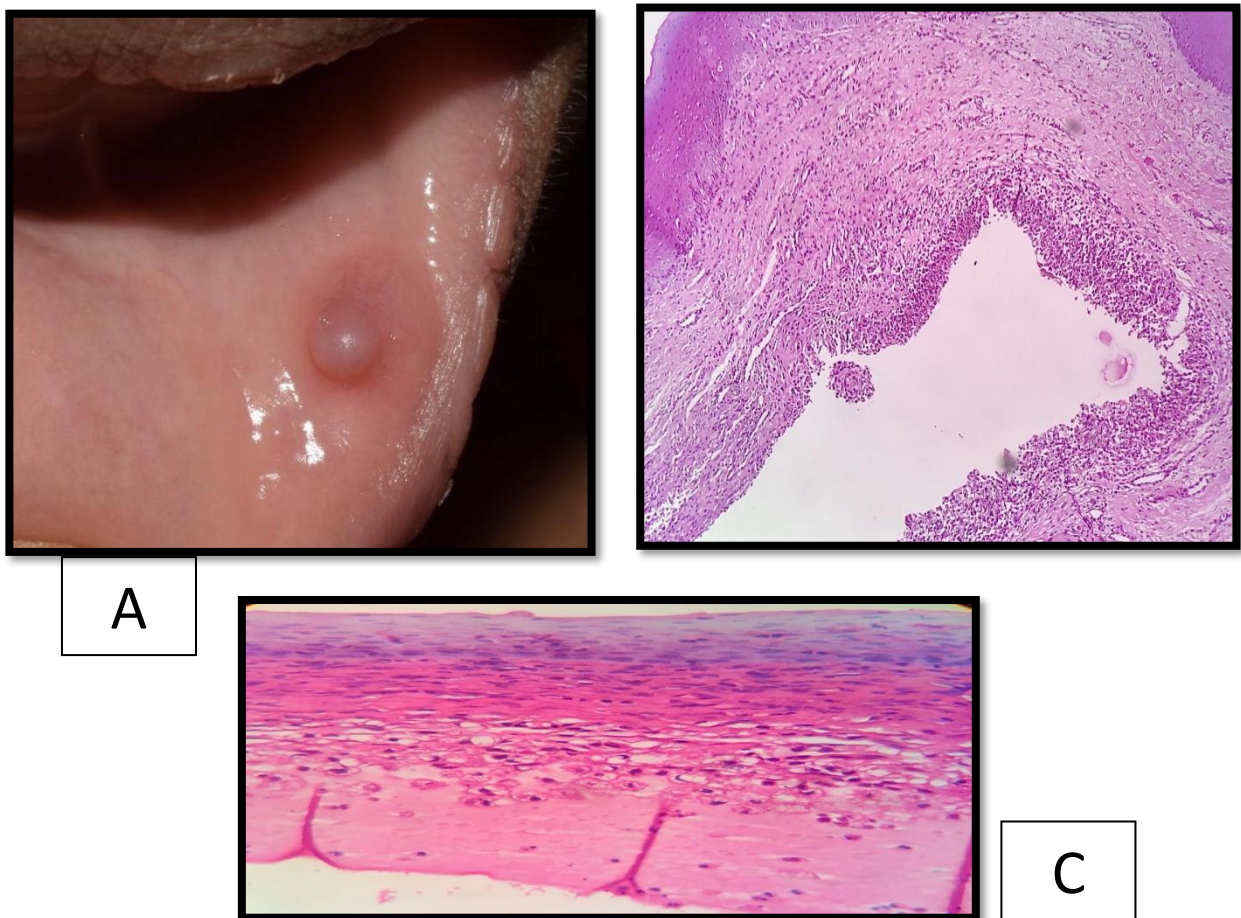


Fig 3 A shows clinical presentation of swelling in the lower lip, B & C shows mucin-filled cavity without epithelial lining, surrounded by granulation tissue and foamy macrophages; consistent with extravasation type.

2. RANULA

Introduction

Mucocele happening in the floor of the mouth are termed as ranula. Since this swelling has similitude with frog's translucent underbelly, it has its cradle from the Latin word *rana*, depicting frog.²³

Definition²⁴

It is an outline of mucous extravasation or retention occurrence positioned laterally to the midline in the mouth floor.

Etiology

It is caused by outflow of mucin as the result of trauma to a salivary gland,²⁶ although some workers believe that it may arise through duct blockage or through the development of a ductal aneurysm.²⁰

The sublingual gland is commonly affected, followed by the submandibular and minor salivary glands.²⁶

Clinically-

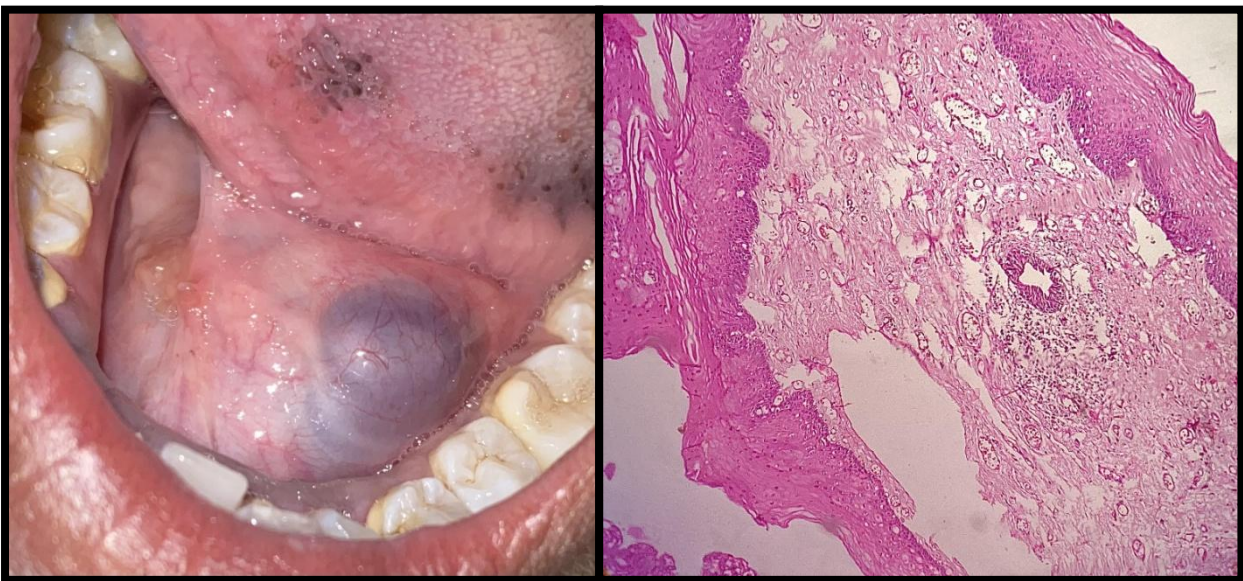
- With varying sizes from 1 to several centimetres, ranulas are bluish to pinkish and have distinguishing dome like swellings.
- Infrequently, ranula can happen to be contaminated by oral flora.²⁶
- The tongue may be elevated.⁵

Histopathologic features²⁵

- Have analogous facade microscopically to Mucocele
- Neovascularisation and angiogenesis occurs in rejoinder to spilling of mucin. In addition, a small number of macrophages are also seen.

Treatment

Treatmnt for ranula is surgical excision.²⁶



RANULA

Fig 4 A shows clinical presentation of swelling in the floor of the mouth, B shows large mucin collection in the floor of the mouth with chronic inflammatory cells and mucinophages

CONCLUSION: Paediatric salivary gland diseases and its differential diagnosis should be properly monitored for a proper and promising therapeutic approach. However, new technological advances in diagnostics, imaging and treatment therapy for different salivary gland disorders are still in progress for better results.

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