Review Article

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Ranula: a narrative review

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ABSTRACT

A ranula is a pseudocystic lesion of the sublingual salivary gland, found in the floor of the mouth. Ranula is classified into types such as simple and plunging type. Plunging ranula arises when a simple ranula extends beyond the floor of the mouth into the neck. A simple ranula is seen above the level of the mylohyoid muscle and is often the result of sublingual gland duct obstruction. A plunging ranula refers to a pseudocyst that develops with salivary duct rupture and is seen below the level of the mylohyoid muscle. Diagnosis of the ranula is difficult even with modern imaging techniques as this mimic to other neck lesions. The correct diagnosis of the ranula is essential for the most effective treatment. The treatment modalities of the ranula currently include marsupialization, excision of the ranula with or without excision of the sublingual gland, cryosurgery, laser excision, sclerotherapy, fenestrations, and continuous pressure. The treatment of the ranula includes complete excision and marsupialization is not a sufficient treatment. Misdiagnosis of a plunging ranula leads to unnecessary and extensive surgery. This review article discussed the epidemiology, etiopathogenesis, clinical features, diagnosis, and current treatment of ranula.

Keywords: Ranula, Sublingual salivary gland, Plunging ranula, Oral cavity

INTRODUCTION

A ranula is a cystic lesion that originates from the sublingual salivary glands and it is considered as the most common intraoral salivary gland mass.¹ The term ranula was derived from the Latin word 'rana', meaning frog, and the ranula describes a little frog, because of its similarity to a bulging frog's underbelly.² Ranulas are uncommon mucoceles found in the floor of the mouth.

Ranulas may be simple or plunging on the basis of the location of the ranula relative to the mylohyoid muscle, with simple ranula being confined above the mylohyoid muscle and plunging ranula extending inferior to the mylohyoid muscle.² A simple ranula can be either a mucus retention cyst or more commonly a mucus extravasation pseudocyst, which is confined to the floor of the mouth.³ A plunging ranula or cervical ranula is a mucus

extravasation pseudocyst originating from the sublingual gland and presents as a swelling in the neck.³ Ranulas have been treated by marsupialization, excision of the mucocele, excision of the sublingual gland, or combined excision of both the ranula and the sublingual gland.⁴ Due to the rarity of the ranula in clinical practice, there is a dearth of literature on this subject. The purpose of this review article is to discuss the epidemiology, etiopathology, clinical presentations, investigations, and treatment of ranula.

METHODS

Multiple systematic methods were used to find current research publications on the ranula. We started by searching the Scopus, PubMed, Medline, and Google Scholar databases online. A search strategy using PRISMA (Preferred reporting items for systematic reviews and meta-analysis) guidelines was developed. This search strategy recognized the abstracts of published articles, while other research articles were discovered manually from the citations. Randomized controlled studies, observational studies, comparative studies, case series, and case reports were evaluated for eligibility. There were a total number of articles 68 (22 case reports; 18 cases series; 28 original articles) (Figure 1). This paper focuses only on the details of the evaluation of the ranula. This review article describes the surgical anatomy, etiopathology, clinical manifestations, diagnosis, and treatment of the ranula. This analysis provides a better understanding of the ranula and its etiopathology, clinical profile along with its management. It will also catalyse further study of the evaluation of the ranula and the development of newer methods for the ranula.

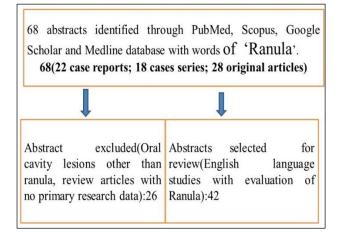


Figure 1: Methods of literature search.

EPIDEMIOLOGY

The prevalence of ranula is 0.4% of institutional operative cases and 1.2% of ENT surgeries.⁵ In an 18-year retrospective study conducted at the North Carolina University in the USA, only 26 cases of ranulas were documented.⁶ Due to the rarity of the ranulas in clinical practice, there is a dearth of literature on this subject and many are reported as case reports rather than studies.⁷ The prevalence of ranula is 0.2% per 1000 patients.⁸ Ranulas account for approximately 6% of all salivary gland cysts.⁸ Ranulas are commonly found in children and young adults. However, the plunging type of ranulas is seen in the later third decade.⁸

SURGICAL ANATOMY

Ranula occurs specifically in the floor of the oral cavity due to sublingual salivary gland duct obstruction or disruption.⁹ Each sublingual salivary gland is drained by 5 to 15 minor excretory ducts (Rivinus ducts) that carry saliva into the oral cavity through mucosal folds in the floor of the mouth (Plica sublingualis).⁹ The sublingual salivary gland produces a constant flow of saliva that is highly proteinaceous in consistency and they yield 10% of the oral cavity; total saliva output.¹⁰ The sublingual salivary gland is bounded by the floor of the mouth mucosa superiorly, mylohyoid muscle inferiorly, mandible laterally, genioglossus muscle medially, and submandibular gland posteriorly.¹⁰

Ranulas are extravasation mucoceles that originated from the sublingual gland owing to a ruptured main duct or ruptured acini after obstruction.¹¹ The sublingual salivary gland is the smallest and the only unencapsulated major salivary gland.¹¹ There are no limits to the sublingual glands posteriorly; thus, lesions that originate from the gland can exit and spread to the submandibular and parapharyngeal spaces.¹¹ The plunging ranula is a mucous extravasation cyst of the sublingual gland.⁹ The plunging ranula develops when mucus herniates through or behind the mylohyoid muscle along the fascial planes into cervical, submandibular, or submental space. Mucous is the exclusive secretion of the accessory (minor) salivary glands and a more prominent product of the sublingual (major) salivary glands.¹¹ The extravasation of the mucus is the primary cause for mucocele formation with physical trauma as the initiating factor.

ETIOPATHOLOGY

Based on the location, the ranula can be classified into three groups such as sublingual, sublingual-submandibular and submandibular.¹² Sublingual group of ranula are pseudocysts that occurs due to extravasation or retention of mucus in the floor of the oral cavity.¹² The sublingualsubmandibular and submandibular ranula group represents the plunging ranula. This happens due to herniation of the mucus content via the mylohyoid muscle.¹²

The prevalence of congenital ranula is 0.74%.¹³ The present scientific knowledge shows that ranula originates mainly from the sublingual salivary gland which is a spontaneous secretor of saliva. The sublingual salivary gland produces saliva without parasympathetic stimulation that happens during feeding, which is drained by 6 to 20 ducts scattered in the floor of the oral cavity known as ducts of Rivinus.¹⁴ They are seen mainly at the posterior and superior aspects, while at the anterior part, they unite into a single duct called the Bartholin's duct which empties into the Wharton's duct of the submandibular salivary gland.¹⁵ The sublingual salivary gland is almond-shaped, weighs 2 to 4 grams, and produces mainly mucus secretions.¹⁶ The sublingual salivary gland has no true capsule but a rather mucosal fold of the floor of the oral cavity which covers it.¹⁵ The sublingual salivary gland is resistant to blockage because of this unique anatomical arrangement.

Congenitally, the ranula may occur following imperforate sublingual salivary gland duct and ostial stenosis resulting in cyst formation. Injury to the sublingual salivary gland duct leads to mucus extravasation into the submucosa via hydrostatic pressure and the development of pseudocyst from mucus escape reaction.¹⁷ Direct trauma can damage

the acini with consequent ductal blockage, and backpressure secretion builds up with subsequent acini rupture. Subsequently, there is raised hydrostatic pressure, extravasation of mucus, and then the formation of the pseudocyst. Congenital narrowing of the sublingual salivary gland duct, dehiscence of the mylohyoid muscle, and sialolithiasis have also been implicated in the formation of the ranula. This was confirmed in a study where experimental ligation of the sublingual gland duct resulted in ranula formation, while ligation of the submandibular gland duct did not and that of the parotid gland led to atrophy.¹⁸

For the development of superficial mucoceles, trauma does not always play an important role in pathogenesis. In many cases, inflammation of the mucosa that involves a minor salivary gland duct results in obstruction, dilation, and rupture of the duct with sub-epithelial spillage of the fluid.¹⁹ Alteration in minor salivary gland function and composition of the saliva may result in the development of the ranula. In a few cases, an immunological reaction may be the etiology. One study revealed increased levels of matrix metalloproteinase, tumor necrosis factor-a, type IV collagenase, and plasminogen activators in mucoceles in comparison to that of the whole saliva. These factors are further thought to enhance the accumulation of proteolytic enzymes that are responsible for the invasive character of extravasated mucus.²⁰

CLINICAL MANIFESTATIONS

There is no age is spared from the ranulas.²¹ One study showed the variance of age recorded between 3 to 61 years for ranula.²¹ Ranulas slowly develop and are typically found in the second and third decades of life or even later in life with a male-to-female ratio of 2:1.²² It occurs in the floor of the mouth associated with the sublingual or submandibular salivary glands as a fluctuant, unilateral, bluish soft tissue mass.²² Large ranula tend to cause medial and superior deviation of the tongue. The plunging ranula was reported to have a predilection for the right side.²³

Depending on the type of the ranula, the patient may present with a painless, fluctuant sublingual, or submental or submandibular neck swelling. Simple types of ranulas in the floor of the oral cavity often reflect a mucus escape reaction that occurs after disruption of sublingual gland enlargement. So, these lesions comprise an accumulation of mucus within connective tissue with a lack of epithelial lining. The duration of clinical symptoms tends to be shorter in children and young patients in comparison to adults. The oral cavity subserves important functions such as deglutition and respiration which can be easily compromised by a space-occupying lesion like a ranula in a small space with rigid boundaries.²⁴ Patients with a large ranula may manifest with snoring.²³ In adults, the duration of the symptoms tends to be longer, as the oral cavity is wider as ranulas tend to expand slowly and herniate through the myeloid dehiscence and extend into deep neck

spaces.²⁵ When the ranula extends into the neck and distant locations, the ranula is called a plunging ranula.²⁵

DIAGNOSIS

Ranula is a clinical diagnosis and the correct diagnosis is essential for the most effective treatment, which is the excision of the sublingual gland.²⁶ The diagnosis of the ranula is done by fine need aspiration cytology (FNAC), ultrasound, magnetic resonance imaging (MRI), or computed tomography (CT) scan.²⁷ In FNAC, the aspirated liquid appears to be highly viscous in nature, with salivary content.²⁸ If the size of the ranula is greater than 2cm in diameter, or of plunging type, investigation such as CT, MRI or ultrasound is suggested. If the ranula size is less than 2 cm, FNAC is employed to aid in the diagnosis of this condition.²⁸ Imaging is advised mainly to know the extension of swelling before surgery or when the diagnosis is unclear.²⁹

Ultrasound is recommended for ranula as a preferred diagnostic tool. Ultrasound provides additional information about the relationship between the pseudocyst on the floor of the oral cavity and the sublingual gland and mylohyoid muscle. It helps to provide a differential diagnosis in patients with plunging ranula. Ultrasound is an inexpensive and repeatable examination method that is helpful during follow-up.²⁹ Ultrasound is a safe and reliable method in ranula, especially in patients with plunging ranula, and can help with differential diagnoses like other types of cystic lesions and benign tumors and with monitoring the patients during follow-up.³⁰ Highresolution ultrasound determines the extent of the plunging ranula and confirms the cystic nature of the lesion and assesses the status of the mylohyoid muscle and evaluates the sublingual gland for rupture or herniation.³¹ CT scan and specifically the presence of 'tail sign' is pathognomonic for plunging ranula.³² MRI and CT scan have been used for differential diagnosis in some patients with plunging ranula. Aspiration of mucus from the lesion and laboratory testing for amylase content is helpful to make a diagnosis of ranula.33 These findings may be useful, but these do not appear to modify the indication for surgery.

HISTOPATHOLOGY

Histopathologic examination of the ranula demonstrates a mucin-containing pseudocyst surrounded by a wall made up of vascularized fibroconnective tissue, mimicking granulation tissue with a predominance of histiocytes (macrophages).³⁴ There is a lack of epithelial tissue in the wall of the ranula. A biopsy of the cystic wall at the time of sublingual gland excision confirms the diagnosis.³⁵

TREATMENT

There is no consensus opinion regarding the definitive treatment of the ranula, and there is often great variation in clinical practice.³⁶ Treatment of ranula is a polarizing

topic, with conflict of evidence as to which modality is the ideal to the existing gap in knowledge on the present concept of its etiopathogenesis. There are several surgical techniques have been described for the treatment of oral and plunging ranulas, and the results have found that sublingual gland excision is associated with the lowest recurrence. There is a variety of surgical procedures have been mentioned in the medical literature from simple aspiration to complete or partial excision of the ranula (Figure 2) and/or sublingual salivary gland. These include marsupialization, dissection, sclerotherapy, cryotherapy, hydro-dissection, and light amplification by stimulated emission of radiation (LASER) ablation.³⁷ The sclerotherapy uses bleomycin, an antineoplastic antibiotic Streptomyces verticillus-OK-432 (Picibanil), a of lyophilized mixture of a low virulent strain of Streptococcus pyogenes incubated with benzyl penicillin, that has been seen to produce a good effect.³⁸ Incision of the ipsilateral sublingual gland 'marsupialization' or simple excision of the cystic mass of the ranula is recommended for the treatment of simple ranulas. Alternatively, the ranula can be treated with the placement of a silk suture or seton into the dome of the cyst.³⁹



Figure 2: Intra-operative picture showing complete excision of the ranula.

The sublingual salivary gland is always removed via an intraoral approach. Primary attention must be given to avoid injury to the lingual nerve or Wharton's duct that might result in perforation or stenosis. Treatment that does not include excision of the involved sublingual gland, such as incision and drainage, excision of the ranula, and marsupialization, have a high chance of recurrence.⁴⁰ The traditional surgical treatment of the plunging ranula required a two-pronged approach, one via the mouth and the other via the neck. The former approach removes the sublingual gland, the latter one removes the ranula sac in conjunction with the submandibular gland.⁴¹ Despite the aggressive treatment, the recurrence rate is high, especially if the sublingual gland is not removed completely. Carbon dioxide laser is an effective treatment option for ranula with limited side effects but many randomized trials are needed. In case of recurrence of ranula, a surgical approach

with removal of the associated salivary gland is the best treatment option. $^{\rm 41}$

COMPLICATIONS

Complications associated with a surgical procedure for ranula include injury to the Wharton duct, bleeding or hematoma, wound dehiscence, and sensory deficits in the tongue.⁴² Excision of the sublingual gland is associated with a major risk of injury to the lingual nerve and injury to the Wharton duct.⁴³ One study showed complications following sublingual gland excision include a sensory deficit in the tongue, consisting of paresthesia or numbness at the tip of the tongue, episodes of recurrent obstructive sialadenitis, possibly due to stenosis of Wharton duct injury. Probability of injury to the marginal mandibular, lingual and hypoglossal nerves is common in the transcervical approach for ranula. There is also a risk for orocervical fistula formation and cervical scar in the cervical approach. The choice of the incision should be based on the extension of the ranula for avoiding unwanted complications.44

RECURRENCE

There are different outcomes have been reported in each treatment or surgical approach with varying complications. There is always controversy about whether the recurrence of the rupture of the ranula occurs or not intraoperatively.⁴⁵ One study showed no relation between the rupture and recurrence of the ranula.⁴⁶ In this study, 68.75% of the cases had ruptured during surgery whereas only one case recurred, which was a plunging ranula case.⁴⁶

Simple marsupialization and excision of the ranula alone are associated with higher recurrence rates.¹¹ However, another study showed marsupialization as a favorable outcome with a recurrence rate of 13.6%.⁴⁶ Recurrence has been documented in the approach of excision either ranula alone, ranula with the sublingual gland, or ranula with the submandibular gland. This demonstrates that the etiopathogenesis of ranula was yet to be completely understood. In one study, 65 patients reported a recurrence of 3.6% following complete excision of the sublingual gland compared with 36.7% prevalence with ranula excision alone.⁴⁷

In one series, recurrence of the following aspiration was 100%, while intra-/extraoral ranula excision alone was 50%.⁴⁸ However, combined ranula with sublingual gland excision resulted in zero recurrences where the surgeon utilized the transcervical approach with blunt dissection for approaching ranula and removal of the sublingual salivary gland in case of plunging ranulas rather than combined transcervical with transoral approaches.⁴⁸ One study showed that neither marsupialization nor excision showed any difference in terms of the success of surgery in the oral cavity ranulas. Marsupialization should be performed in case it repeats and Marsupialization is

considered a conservative treatment.⁴⁹ With the simple addition of packing the entire pseudocystic cavity with gauze after its unroofing (marsupialization), the rate of recurrence is reduced.⁴⁹

CONCLUSION

Ranulas are uncommon surgically amenable disease of the salivary glands. The ranula is a mucous extravasation cyst that is seen in the floor of the mouth. Ranula is easily diagnosed clinically from its appearance and location. Plunging ranula is a rare clinical entity that should be considered in the differential diagnosis of a neck mass. Removal of the ranula with the sublingual gland is the most reliable treatment. Removal of the submandibular gland is recommended in plunging the ranula, extending into the parapharyngeal space. The surgical excision in the ranula can be carried out through a transcervical or transoral approach.

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