MANAGEMENT OF RANULA

3rd Literature review

Submitted by:
Puji Sulastri
09/303021/PKU/11459

OTORHINOLARINGOLOGY HEAD AND NECK SURGERY DEPARTEMENT
FACULTY OF MEDICINE GADJAH MADA UNIVERSITY
YOGYAKARTA

2014
APPROVAL SHEET

3\textsuperscript{rd} Literature review

MANAGEMENT OF RANULA

Submitted by:
Puji Sulastri
09/308818/PKU/11975

Approved by:
Supervisor:

dr. Camelia Herdini, M.Kes, Sp.THT-KL
Head of Study Programme
Otorhinolaryngology Head and Neck Surgery Department
Faculty of Medicine Gadjah Mada University

dr. Sagung Rai Indrasari, M.Kes, Sp. THT-KL (K)
TABLE OF CONTENT

Table of content ........................................................................................................... 1
Chapter I. Introduction .................................................................................................. 1
  A. Background ........................................................................................................... 1
  B. Problem statement ............................................................................................... 3
  C. Purpose of literature review ................................................................................ 3
Chapter II. Literature Review ...................................................................................... 4
  A. Anatomy Submandibular Glands and Sublingual glands .................................... 4
    1. Submandibular Glands ......................................................................................... 4
    2. Sublingual glands ............................................................................................... 6
  B. Physiology of Salivary Glands .............................................................................. 7
  C. Ranula .................................................................................................................. 8
    1. Definition ........................................................................................................... 8
    2. Etiology ............................................................................................................. 9
    3. Epidemiology .................................................................................................... 9
    4. Pathogenesis ..................................................................................................... 10
    5. Classification ................................................................................................... 12
    6. Diagnosis ........................................................................................................ 13
    7. Additional examination .................................................................................... 15
    8. Differential Diagnosis ..................................................................................... 17
    9. Treatment ........................................................................................................ 18
      a. Marsupialization .............................................................................................. 18
      b. Excision of the sublingual gland .................................................................. 20
      c. Excision of plunging ranula ......................................................................... 22
      d. Intralvesional Injection of OK-432 .............................................................. 24
      e. Hydrodissection ......................................................................................... 28
Chapter III. Summary .................................................................................................. 30
Alghoritm Management of Ranula ............................................................................. 32
References ................................................................................................................... 33
CHAPTER I
INTRODUCTION

A. Background

Ranula is reported by Hippocrates and celcius. Theoretically, the ranula formation is excretory duct rupture followed by extravasation and accumulation of saliva into the surrounding tissue. The accumulation of mucous into the surrounding connective tissue forms a pseudocyst that lacks an epithelial lining. The analysis of the saliva reveals a high protein and amylase concentration consistent with secretions from the mucinous acini in the sublingual gland. The high protein content may produce a very intense inflammatory reaction and mediate pseudocyst formation (Jaishankar et al., 2010).

The classic ranula presents as a blue-domed, translucent swelling in the floor of the mouth. The term ranula is derived from the Latin word rana, meaning frog, and describes a blue translucent swelling in the floor of the mouth reminiscent of the underbelly of a frog (Al-Sadhan R, 2009). Ranula may be seen at birth or in later life. It is commonly seen in young adult. Ranula commonly occurs unilaterally, and bilateral ranulas are extremely rare (Yaman et al., 2006).

Ranula develops from extravasation of mucus after trauma to the sublingual gland or obstruction of the ducts. Ranula can present at any age. It has been reported from 2 to 61 years of age with a slight female preponderance. Regarding the Patel et al. study a total of 26 ranulas were identified at their institution over an 18-year
period. There were 54% male and 46% female patients with an average age of 25.6 and a median age of 26. Of the 26 ranulas identified, 16 were oral (62%) and 10 were plunging (38%) (Sheikhi et al, 2011). The prevalence of ranula is about 0.2 cases per 1000 persons and accounts for 6% of all oral sialocysts. Only 1% to 10% of the ranulas are true retention cysts. Ranula usually occurs in children and young adults. The peak frequency of ranula occurs in the second decade of life (Zhao et al, 2004).

A Study of 83 cases of ranula in Zimbabwe revealed high prevalence of ranula in HIV positive subjects, suggesting HIV salivary gland disease could be an etiologic factor is possibly a result of obstruction for the following reasons: there is an increase of inflammation and fibrosis in minor salivary glands of patients with untreated HIV (this would also involve the biologically similar sublingual glands), inflammation and fibrosis cause obstruction of salivary glands, and obstruction of the sublingual glands leads to extravasation and possibly the development of ranulas in patients with untreated HIV infection (Chidzonga et al, 2007).

Sublingual glands are the smallest of the paired major salivary glands, weighing about 2 g, and shaped like a flattened almond measuring about 2.5 cm anteroposteriorly, each gland has a row of about 12–20 short ducts that open independently along the summit of the sublingual fold in the floor of the mouth, obstruction of one of these ducts results in formation of a mucous retention cyst in the sublingual space, termed simple ranula, further accumulation of secretions with time results in extension along sublingual space anteriorly and posteriorly, if posterior
extension extends or extravasates beyond the free edge of, or through the mylohyoid muscle (Sheikhi et al, 2011).

A variety of surgical procedures have been quoted in the literature ranging from marsupialization, excision of the ranula, sclerotherapy, and excision of the sublingual gland. The recurrence rate varies according to the procedure performed (Sheikhi et al, 2011).

B. Problem statement

The ranula is a form of mucocele which specially occurs in the floor of the mouth. Several surgical techniques had been introduced to treat intraoral ranula. Marsupialization, excision of the sublingual gland or combined excision of both the ranula and the sublingual gland have been used with variable success rates. The optimal treatment option is still very controversial.

Ranula diseases we encounter in everyday practice ENT specialist so we need a broad knowledge of management. Discussed in the literature about the management of ranula wide range of both surgical and non-surgical. because it was expected we could provide therapeutic ranula well.

C. Purpose of literature review

This literature review provides a knowledge about management of ranula.
CHAPTER II

LITERATURE REVIEW

A. Anatomy Submandibular Glands and Sublingual glands

1. Submandibular Glands

The second largest major salivary gland is the submandibular (submaxillary) gland. It comprises both mucous and serous cells. The gland lies in the submandibular triangle, which is formed by the anterior and posterior bellies of the digastric muscle and the inferior margin of the mandible (Fig. 1). The gland lies medial and inferior to the mandibular ramus and wraps around the mylohyoid muscle in a C-shaped fashion to produce a superficial and deep lobe (Fig.2).

Figure 1: The submandibular triangle. Note the relationship of the marginal mandibular nerve to the mandible and facial vessels. (Bailey, 2006)

The superficial lobe of the submandibular gland lies in the lateral sublingual space. The deep lobe of the gland (actually first encountered during a routine submandibular gland excision) lies inferior to the mylohyoid muscle and constitutes the bulk of the gland. The superficial layer of deep cervical fascia splits to envelop the gland. Wharton duct exits from the medial surface of the gland and travels
between the mylohyoid and hyoglossus muscles onto the genioglossus muscle. It then opens intraorally lateral to the lingual frenulum at the floor of the mouth. The duct is approximately 5 cm in length. As the duct exits the gland, the hypoglossal nerve lies inferiorly and the lingual nerve superiorly (Bailey, 2006).

**Figure 2**: The superficial and deep lobes of submandibular gland are separated by the mylohyoid muscle. The sublingual gland has multiple ducts that open along the plica of the floor of the mouth (Bailey, 2006). The submandibular gland is innervated by the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS), which stimulate the gland to produce mucoid and watery saliva, respectively. The PNS supply is from the chorda tympani nerve, which is a branch of the facial nerve. The chorda carries preganglionic parasympathetic fibers to the submandibular ganglion by means of the lingual nerve. At the submandibular ganglion, the fibers synapse onto postganglionic parasympathetic fibers that stimulate the gland to produce saliva. The sympathetic fibers originate in the superior cervical ganglion and travel with the lingual artery to the gland (Bailey, 2006).

The facial artery provides the major blood supply to the gland. The artery, which is a major branch of the external carotid artery, grooves the deep portion of the
submandibular gland as it courses superiorly and anteriorly. At the superior aspect of the gland, it passes laterally and curves around a notch in the mandible to supply the face. The anterior facial vein drains the gland. The marginal mandibular branch of the facial nerve lies superficial to the anterior facial vein. One maneuver to preserve the nerve during dissection is ligation and elevation of the vein superiorly off the gland, thereby protecting it in the elevated fascia. Lymph nodes are present between the gland and the capsular fascia but not deep in glandular tissue. The nodes drain into the deep cervical and jugular chains (Bailey, 2006).

2. **Sublingual glands**

The sublingual gland is the smallest of the major salivary glands and lies just below the floor of mouth mucosa. It contains primarily mucus-secreting acinar cells. The gland is bordered by the mandible and genioglossus muscle laterally and the mylohyoid muscle inferiorly. The submandibular duct and lingual nerve travel between the sublingual gland and the genioglossus muscle. In contrast to the parotid and submandibular glands, no true fascial capsule surrounds the sublingual gland.

Approximately 10 small ducts (ducts of Rivinus) exit the superior aspect of the gland and open intraorally along the sublingual fold or plica of the floor of the mouth. Occasionally, several of the ducts may join to form a major sublingual (Bartholin) duct, which then empties into Wharton duct. Like the other major salivary glands, the sublingual gland is innervated by both the SNS and PNS. The lingual nerve carries postganglionic parasympathetic fibers to the gland from the
submandibular ganglion. The facial artery carries the sympathetic fibers from the cervical ganglion. The sublingual branch of the lingual artery and the submental branch of the facial artery provide the blood supply to the sublingual gland. The venous drainage is by the corresponding veins. The major lymphatic drainage is to the submandibular nodes (Bailey, 2006).

B. Physiology of Salivary Glands

The salivary gland's major function is the production of saliva. There are five major functions of saliva: (a) lubricating the food bolus and lavaging the oral cavity surfaces with a biofilm barrier, (b) providing buffering capacity, (c) maintaining tooth integrity, (d) performing antibacterial functions, and (e) aiding taste and digestion. The buffering system in saliva consists of bicarbonate, phosphate, urea, and amphoteric proteins that neutralize acid. These substances act in concert to buffer ingested chemicals and maintain a resting oral cavity pH of 6 to 7. Tooth integrity is maintained by continual demineralization and remineralization. Demineralization occurs chiefly by diffusion of acid through plaques to the tooth structure, and remineralization occurs via super saturation of calcium and phosphate, which promotes hydroxylapatite deposition in the substance of the tooth. Fluoride augments the remineralization process forming a dental caries resistant matrix.

Antimicrobial activity conferred by saliva is a complex interaction of immunologic components, including secretory IgA, IgG, and IgM and nonimmunologic components, including proteins, mucins, peptides, and enzymes (3). Secretory IgA provides the largest immunologic function of saliva, acting to
neutralize viruses, deactivate bacterial antigens, and aggregate bacteria. Lactoferrin binds ferric iron, a food source for microbes, effectively starving bacteria and providing nutritional immunity. Lysozymes aid in breaking down cell walls leading to bacterial cell lysis. Peroxidase catalyzes bacterial metabolic byproducts with thiocyanate and oxidizes hydrogen peroxide protecting the mucosa. Mucins play a multifunctional role in saliva. When complexed with IgA they have a greater bacterial binding affinity than either alone. Mucins are closely involved in regulating bacterial and fungal colonization and adhesion of organisms to the oral tissue surfaces. In addition, mucins are the best lubricating substance in saliva, forming a biofilm that protects the mucosa and dentition from chemical irritants, carcinogens, and desiccation. Salivary proteins such as glycoproteins, statherins, agglutins, and histadine- and proline-rich proteins work to aggregate bacteria reducing their ability to adhere to surfaces. Protein content increases proportionally with salivary flow rate. Paradoxically, the immunologic function of saliva selectively supports a healthy oral flora that assists in maintaining a healthy oral cavity.

C. Ranula

1. Definition

A ranula is an extravasation pseudocyst arising from the sublingual salivary gland. The classic ranula presents as a blue-domed, translucent swelling in the floor of the mouth. The term ranula is derived from the Latin word *rana*, meaning frog, and describes a blue translucent swelling in the floor of the mouth reminiscent of the underbelly of a frog (Al-Sadhan R, 2009). They are cystic and are frequently blue
owing to the Tyndall effect, whereby blue light is reflected more than red light at the interface of soft tissue and cyst (McGurk et al, 2008).

Figure 3: A ranula of the right floor of the mouth. Classic signs of elevation and the blue discoloration are present. (Carlson, 2008)

2. Etiology

The etiology is unknown, but it has been described in association with congenital anomalies, trauma, and disease of the sublingual gland (Sheikhi et al, 2011). The causes of ranula formation were thought to be trauma or surgery to the floor of the mouth, neck region which may rupture the sub lingual gland acini or cause obstruction of the sublingual gland ducts which results in mucous extravasation (Jaishankar et al, 2010).

3. Epidemiology

Zhao et al, in a review of 580 cases, reported that ranulas are most prevalent in the second decade of life and are slightly more common in females (male to female ratio of 1:1.2), but a distinct male predilection was noted for the plunging ranula (male to female ratio of 1:0.74). Oral ranulas most commonly involved the left side (left to right ratio of 1:0.62), while the plunging and mixed ranula commonly involved the right side.
Patients with a plunging ranula tend to report the presence of a mass in the neck for greater than 6 months, indicating that with time a simple ranula may eventually dissect by hydrostatic pressure into the neck and become a plunging ranula. Chidzonga and Rusakaniko, in a review of 83 cases of ranulas in Zimbabwe, reported a concomitant positive serology for human immunodeficiency virus (HIV) in 88%, with most of the patients in the 0–10 year age group. They suggested that sublingual ranulas in Zimbabwe be considered another HIV/AIDS-associated lesion, especially when found in children.

4. Pathogenesis

Ranula is a clinical term generally used for cystic lesions in the floor of the mouth. There are two different concepts for the pathogenesis of ranula. One is a true cyst due to ductal obstruction with an epithelial lining, and the other is a pseudocyst due to ductal injury and extravasation of mucus without an epithelial lining. Recently, typical ranulas have been considered exclusively as an extravasation phenomenon of the sublingual gland.

The pathophysiology involved in extravasation is hypertension in the duct due to obstruction leading to acinar rupture in the salivary gland and then extravasation of the mucus. The initial stage is a traumatic rupture of the excretory duct and the second stage is the extravasation and subsequent accumulation of saliva within the tissue (Sheikhi et al, 2011).

Plunging and sublingual-plunging ranulas cause swelling in the neck by one of the following four mechanisms. Firstly, sublingual gland may project through the
mylohyoid muscle, or alternatively an ectopic salivary gland may present on the cervical side of the mylohyoid. This mechanism can explain the development of plunging ranulas without intraoral components (Verma, 2013).

Figure 4: Muscles encountered and area of dehiscence in mylohyoid through which plunging ranula typically passes into the neck. Visscher et al 1989, have the opinion that mucus secretion from these ectopic glands may drain saliva directly into neck mass. Secondly, a hiatus or dehiscence in the mylohyoid muscle may occur (Figure 4). Several anatomical studies showed the presence of an opening in the mylohyoid muscle through which submental artery, lymph vessels, and branches of the sublingual artery and vein passes. This defect is observed along the lateral aspect of the anterior two-third of the muscle. Mucus from sublingual gland may pass through this defect and reach the submandibular space.

Projection of the sublingual gland through the hiatus between anterior and posterior part of the mylohyoid muscle were reported in 45% of the cadaver specimens and it clearly shows involvement of this herniation in cervical extensions of the ranulas. Thirdly, approximately 45% of plunging ranulas occur iatrogenically as a result of surgery to remove oral ranulas. It has been reported that plunging ranulas may develop secondarily after surgical procedures such as implant placement, removal of sialolith and duct transposition (Loney et al, 2006).
Additionally, Bridger et al. after reviewing plunging ranulas, found that 44% of them developed iatrogenically after single or multiple attempts at eliminating oral ranulas by either marsupialization or simple drainage. They stated that surface fibrosis after repeated failed procedures could be responsible for diversion of the saliva inferiorly leading to plunging ranula (Verma, 2013).

Lastly, a duct from the sublingual gland may join the submandibular gland or its duct, allowing the ranula to form in continuity with the submandibular gland. Therefore, ranula may reach the neck from behind the mylohyoid muscle. Patton postulated that an aberrant duct from the deep lobe of the sublingual gland may open into the submandibular duct. This abnormal communication may cause stasis of salivary flow in the duct leading to extravasation of the saliva into the neck in the submandibular region (Visscher et al, 1989).

The cause of ranula in neonates is however not known. In older children it is associated with trauma to the salivary duct. When the duct orifice is not patent this may end up with congenital sialocele which is a true cyst with epithelial lining. This is thought to result from a congenital failure of canalization of the terminal end of the duct (Simba et al, 2011).

5. Classification

According to the variations of its extension, ranula has been classified into three clinical types; sublingual type, sublingual-submandibular type, submandibular type. The sublingual type is a simple ranula, while the sublingual-submandibular type and submandibular type are plunging ranula.
Ranula can be classified into two groups, simple (intraoral)) and the plunging (cervical) type. Simple ranula is much more common than plunging type. A simple ranula represents a localized collection of mucus within the floor of the mouth. In plunging ranula, the mucus collection is in the submandibular and submental space of the neck with or without an associated intraoral collection. The formation of the plunging ranula may originate from sublingual gland mucus leakage in the deeper areas of the gland, and the fluid drainage inferior into the submandibular space as a result of gravity (Zhi et al, 2008).

6. Diagnosis

Intraoral lesions were blue and fluctuant whereas plunging lesions were the color of normal mucosa or skin. The plunging ranula typically manifests as a soft, painless, and nonmobile swelling in the neck. The mixed ranula had both intraoral and extraoral swellings, usually intraoral swelling was found earlier than cervical lesion.
Clinically, the oral ranula, though they are generally small to medium in size, displaces the tongue, and interferes with oral function. Very large oral ranulas or ranulas located in the area of the caruncula sublingualis may lead to partial obstruction of the Wharton duct resulting in submandibular swelling during eating. In this study, obstructive symptoms were observed preoperatively in 16 patients, in whom 13 postoperative specimens showed chronic inflammation in the submandibular gland parenchyma. The formation of the plunging ranula may originate from sublingual gland mucus leakage in the deeper areas of the gland, and the fluid drainage inferior into the submandibular space as a result of gravity. Therefore, the lesion less interferes with function, and patients with the plunging ranula may seek treatment later than the patients with oral ranula (Zhao et al, 2004).

A ranula does not cause serious symptoms of pain except some discomfort, and it hardly gives rise to any severe clinical manifestation. According to Baurmash, clinical findings such as discomfort in speech, mastication, and swallowing and external swelling differ depending on the size and location of the ranula. In the case of a very large mucocele in the sublingual gland, the tongue may compress the ranula during eating and swallowing such that there is interference with the salivary flow of the submandibular gland. When a plunging ranula increases in size, it may cause dyspnea and dysphagia and may expand as far as the mediastinum. While a plunging ranula is a mucus extravasation pseudocyst arising from the sublingual gland located below the myelohyoid muscle and present as a swelling in the upper part of the neck (Rho et al, 2006).
7. Additional examination

a. Computerized Tomography

On computed tomography, the simple ranula present as a rough ovoid-shaped cystic lesion with a homogenous central attenuation of 10 to 20 HU. The wall of the ranula is either very thin or not seen at all. The sublingual ranula is positioned above the mylohyoid muscle and lateral to genioglossus muscle. It can extend anteriorly behind the symphysis of the mandible, above the genioglossus and geniohyoid muscles. In case of plunging ranula there is infiltration of the lesion into the adjacent tissue planes, extending dorsally and inferiorly to the submandibular region. Although a plunging or sublingual-plunging ranula may extend into the submandibular triangle and displace the submandibular gland, it does not lead to any intrinsic changes within the gland (Verma, 2013).

b. Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is the most sensitive method to examination the sublingual glands. On MRI, the ranula's characteristic appearance is dominated by its high water content. Therefore, it has low T1-weighted intermediate proton density and high T2-weighted signal intensity. This appearance, especially in case of plunging ranula, may be similar to that of a lateral thyroglossal duct cyst, a lymphangioma and an inflamed lymph node. However, the signal intensity may vary if the protein concentration of the ranula's cystic content is high. In such instances the MRI differential diagnosis should includes pathologies like lipomas, dermoid and epidermoid cysts (Verma, 2013).
c. Needle aspiration

Analysis of fluid from ranulas demonstrates mucus with prominent histiocytes. The biochemistry of this fluid shows high amylase and protein content. A fine-needle aspiration biopsy may be helpful in demonstrating the mucus with inflammatory cells (Yaman et al., 2006).

d. Sialographic examination

Takimoto suggested a simple radiographic technique for preoperative diagnosis of plunging ranula. This technique involves administration of a contrast medium in the sublingual space. Sialographic examination of the patient with a sialocyst presents smooth displacement of the glandular ducts around the mass. Sialographic examination failed to demonstrate direct communication of the lesion with the ductal system of the gland.

e. Ultrasonographic

Ultrasonography: Sublingual glands and their pathologic states are difficult to visualize on ultrasonography because of their location (Shelley et al., 2002).

f. Pathological examination

The pathological examination revealed that the cyst wall consisted of fibroconnective or granulation tissue, usually with a scanty or minimal degree of chronic inflammatory infiltration. The cyst-like space contained mucus, histocytes, polymorphs, and lymphocytes. The cystic cavity was occasionally lined with a small area of ductal epithelium (Fig 7A). The adjacent salivary gland acini showed some chronic inflammatory changes and part of their ducts were dilated. In a few cases, the
surrounding loose edematous stroma showed numerous dilated, blood-filled vascular channels (Fig 7B). The histologic findings were not significantly different between the oral and plunging or mixed ranula.

**Figur 7.** The part of the cyst lining was formed by a single or double layer of ductal epithelial cells (A). A mucus-containing space lined fibrous connective tissue or granulation tissue with various sizes of vascular lumen (B).

**8. Differential Diagnosis**

The diagnosis of a plunging ranula is of clinical significance for there are many benign as well as malignant lesions that have the same appearance during physical examination. In particular, neoplastic and inflammatory lesions of the submandibular and sublingual glands, of the lymphnodes, granulomatous, vascular, nerve or adipose tissue diseases, branchial or thyroglossal duct cysts, dermoid and epidermoid cysts, cystic hygroma and laryngocele could appear as a soft palpable mass of the submandibular region, complicating the diagnosis. There are no specific tests for the diagnosis of cervical ranulas. Differential diagnosis should be based on the history of the lesion that shows up as a cystic fluctuating lesion, gradually increasing in size. Additionally, the fluid of ranulas consists of a higher salivary amylase and protein content compared to serum (Sheikhi *et al*, 2011).
9. Treatment

Ranulas have been managed by various surgical methods: marsupialization, excision of the sublingual gland or combined excision of both the ranula and the sublingual gland. Other treatment modalities include intra-cystic injection with OK-432, hydrodissection, cryosurgery. The treatment of choice is still very debatable and controversial.

a. Marsupialization

Simple marsupialization, the oldest and most widely reported method to surgically manage oral ranula, has fallen into disfavor primarily because of the excessive number of failures following this procedure. The failure rate, as reported in the literature, has been anywhere from 6 1% to 89%, with clinical evidence of recurrence appearing between 6 weeks to 12 months.

Figure 9: Clinical aspect of the injury in the buccal wooden floor (1), Draining of the mucous during the surgical procedure (2), Dissection of the injury with shears rhomb (3), Immediate postoperative aspect with the injury completely marsupialized (4), Fourteen days postoperative with the wire of suture in position (5)(Gaertner et al, 2005).
The proposed treatment was the marsupialization of the injury under local anesthesia. During the surgical procedure, the membrane that coats the injury was breached and all mucous contained in its interior was extravasated. With the aid of a shears rhomb the injury was dissected, its sutured evertides edges and then in the buccal wooden floor with the use of the wire of Poliglactina 910, scales 4-0 (Vycril, Johnson & Johnson). The suture points had been kept until its complete resorption. The patient after meets in ambulatorial accompaniment without signals of return of the injury one year of the surgical procedure (Gaertner et al., 2005). When conventional marsupialization is undertaken, the wound margins tend to be in contact with each other because of the narrow space and the movement of the tongue and the floor of the mouth. As a result, the lesion tends to reform. The failure rate of marsupialization, as reported in the literature has been anywhere from 61% to 89%, with clinical evidence of recurrence appearing between 6 weeks to 12 months. In addition, Bridger et al. in reviewing cervical or plunging ranula, found that 44% were iatrogenic, occurring after single or multiple attempts at eliminating oral ranulas via marsupialization or simple drainage. They suggested that repeated failed procedures could lead to surface fibrosis and divert the salivary leakage inferiorly, and then a plunging ranula might result. Therefore, Crysdale et al. recommended that oral ranula larger than 1 cm should be treated by removal of the offending sublingual gland; other authors have proposed that this treatment be used regardless of the size of the lesion. We found that recurrence rate was 66.67% after marsupilaization. Therefore, in our department, this procedure has only been used an
initial treatment of the lesion is superficial and the patient has a poor general condition.

Baurmash modified marsupialization by identifying the full dept of the pseudocystic cavity after the unroofing procedure and firmly packing this cavity with gauze rather than merely leaving it open. The packing is left in place for 7 to 10 days, allowing it to naturally exfoliate. Baurmash performed the marsupialization for 12 cases, with only 1 failure requiring subsequent sublingual gland removal. Therefore he recomended that oral ranulas be treated initially by marsupialization with packing and, if recurrence occurs, the offending sublingual gland should be excised. However, some surgeons still prefer initially treat ranulas by marsupialization, perhaps because of the potensial surgical complications when removing the sublingual gland, most notably injury to the lingual nerve, injury of Wharton’s duct with the possibility of stenosis leading to obstructive sialadenitis, and ductal laseration causing salivary leakage. Authors reporting results using marsupialization as the primary treatment for oral ranulas experienced a lower incidence of tongue hypesthesia and bleeding/hematoma when compared to sublingual gland plus ranula excision.

b. **Excision of the sublingual gland**

Surgery was performed under general anesthesia. The lesion was approached intraorally through a mucosal incision placed over the lesion. Careful dissection in the sub-mucosal plane revealed a well encapsulated soft swelling which was friable but could be separated from the sur-rounding connective tissue and muscle plane. The swelling on the deeper aspect was extending towards the sublingual gland. The
submandibular and sublingual ducts were separated from the dissection plane. Sublingual gland was then dissected out along with the duct and then completely excised. Complete hemostasis was achieved and primary closure performed. The excised specimen was sent for histological examination which confirmed the diagnosis of ranula (Gaertner et al, 2005).

Unfortunately we were unable to find a case series in which oral ranulas were treated with sublingual gland excision alone. However we were able to ascertain that complication rates (including recurrence rate) were lower for sublingual gland plus ranula excision compared to less invasive techniques such as OK-432 sclerotherapy and aspiration. Likewise, recurrence rates were lower in sublingual gland excision combined with ranula excision when compared to marsupialization or ranula excision only. There appeared to be a strong association between leaving the sublingual gland in place and a higher recurrence rate.

Excision of the sublingual gland or ranula may carry the potential risk of severe hemorrhage from the lingual and sublingual vasculature, lingual nerve
damage, and duct severance. Anatomically, the submandibular duct, as it traverses in anterior and superior direction from the gland to its orifice, is in immediate contact with the medial surface of the sublingual gland. As such, the submandibular duct may damage during ranula surgery or more likely during removal of the sublingual gland. To avoid severing the Wharton duct, we advise that a large lacrimal probe indwelling catheter be inserted into the duct to facilitate identification of the structure during surgical exposure and removal of the sublingual gland. Another structure to be concerned with when considering excision of the sublingual gland and ranula is the lingual nerve, which in close relation to the posterior part of the gland before it crosses beneath the submandibular duct to enter the substance of the tongue.

Our finding show that numbness of the tongue resulting from lingual nerve damage was more common after excision of both the sublingual gland and ranula than after excision of the gland alone. Fortunately, this postoperative numbness of the tongue is transient and usually resolved within 6 months postoperatively. In addition, postoperative infection and dehiscence of wound and hematoma occurred (Zhao et al., 2004).

c. Excision of plunging ranula

A horizontal incision, placed in a skin crease and at least 3cms below the mandible or at the level of the hyoid bone, and extending anteriorly from the anterior border of the sternocleidomastoid muscle, is made through skin, subcutaneous tissue and platysma. The common facial and anterior facial veins are identified posteriorly, and divided and ligated if required for access. The ranula is identified in the anterior
part of the submandibular triangle. The anterior belly of digastric is identified and retracted anteriorly. The mylohyoid muscle is identified deep to and behind the anterior belly of digastric. The surgeon may have to mobilise and resect the SMG (submandibular gland) for better access. The ranula is mobilized with sharp and blunt dissection from the surrounding muscles and the SMG posteriorly. It is traced to where it generally passes through a dehiscence in the mylohyoid muscle, or less commonly behind the mylohyoid, into the floor of the mouth. The surgeon then completes the resection transorally, including resection of the sublingual salivary gland. Should the SMG have been preserved, then the status of the submandibular duct is checked to determine whether it needs to be translocated. The mucosal defect in the floor of mouth is then closed with absorbable sutures, and the neck is closed in layers over a suction drain.

**Figure 11:** Plunging ranula in right neck (A), SMG mobilised to better expose plunging ranula (B).

Ichimura *et al* 1996, treated 7 patients with a plunging ranula. All patients underwent surgery via a cervical approach. Although total sublingual gland excision was not performed in 2 patients, no recurrence was observed in any patient. They suggest that a cervical approach may still be the method of choice for the first operation or for salvage surgery after recurrence subsequent to intraoral procedure if
there is no swelling of the oral floor. Mizuno and Yamaguchi at 1993 suggest since a plunging ranula is due to extravasation from the sublingual gland herniating through the mylohyoid muscle, excision of the sublingual gland followed by transoral drainage of the plunging ranula is regarded as the best treatment. Our results show that the intraoral excision of the offending sublingual gland is a simple and curable procedure with minimal potential complications for all plunging ranulas, where as the extraoral approach is a relatively destructive procedure, which may result in skin scarring, and is unacceptable.

c. **Intralesional Injection of OK-432**

There are variable conservative and surgical treatments for ranula, including simple aspiration, incision and drainage, excision and surgical excision of ranula along with sublingual gland. Surgical complications, including nerve injury, recurrence, and cosmetic problems, need to be considered. It has been reported that OK-432 therapy may become a first line treatment for lymphangioma. OK-432 is a lyophilized streptococcal preparation made from the Su-strain of group-A Streptococcus pyogenes. It was originally developed as an immunotherapeutic agent for cancer. It was reported that OK-432 therapy is effective in the treatment of lymphatic malformation, thyroglossal duct cyst, auricular hematoma, bronchial cleft cyst, auricular hematoma and salivary mucocele. OK-432 seems to be more safe and effective than other sclerosing agents such as boiling water, hypertonic saline, ethanol, tetracycline, cyclophosphamide, sodium morrhuate, and bleomycin. Although the complication rates of treatment with these sclerosing agents are
minimal, limited success and unpredictable local scarring, as well as systemic side effects caused by spread of the agents beyond the epithelial lining of the lesion, have been observed. Bleomycin, in particular, can have serious side effects, including fibrosis of the lung, independent of the total dosage (Ohta et al, 2013).

On the other hand, the complication rate of OK-432 is minimal, and use of this agent does not require local anesthesia or patient hospitalization and leaves no scar on the skin at the injection site. Benefits of OK-432 therapy over other surgical procedures are summarized as follows. 1) No local anesthesia was required during procedure. 2) The treatment was painless and time for procedure was brief, therefore children and anxious patients can be well tolerated. 3) The nerve injury and cosmetic problems could be avoided. 4) Secondary infection and hemorrhage are rare. 5) Recurrences are less frequent. 6) From the point of cost-performance, no hospitalization and no special equipment and medication was required. OK-432 therapy is economically and cosmetically more advantageous than surgery and could be considered as possible alternative therapy.

The mechanism underlying the effectiveness of OK-432 therapy is very strong production of IFN-γ, TNF-α, IL-6, IL-8 and VEGF, as found in fluids aspirated after OK-432 therapy. When OK-432 is administered locally, inflammatory cells such as neutrophils and monocytes infiltrate the cyst and various cytokines, including IFN-γ, TNF-α, IL-6, IL-8 are secreted. These cytokines induce strong local inflammatory reactions in the cyst wall, resulting in fluid drainage, shrinkage, and fibrotic adhesion of the cyst.
In plunging ranula, we aspirated as much of the fluid content of each lesion as possible. To aspirate the contents sufficiently, compression of the ranula was sometimes needed. After determining the capacity of the lesion, we prepared a sufficient quantity of OK-432 (Picibanil, Chugai Pharmaceutical Co., Tokyo, Japan) diluted with saline solution [0.5 to 5 Klinische Einheit (KE) per milliliter; 0.05 to 0.5 mg/mL]. With the same needle as that used for aspiration, we injected OK-432 solution (at a volume equal to about half that of the fluid removed) into the cyst by changing the syringe (Ohta et al, 2013).

In ranula occurring in the oral cavity, we prepared 0.5 KE; 0.05mg of OK-432 diluted with 0.2 ml saline solution and injected the solution into the lesion with a 27-gauge needle to prevent leakage of the agent out of the lesion. There was no resistance in cases of successful injection into the cystic lesion.

Aspiration on 2nd day after the injection, the swollen ranula was punctured by a syringe with a 20-gauge needle, and the intralesional fluid was aspirated as much as possible. The intralesional fluid was relatively viscous, so it was necessary to use a larger needle for aspiration at this time. Follow-Up all patients were regularly observed for a mean of 14.1 months (range 9-49 months) after the final injection. To treat potential fever, we gave analgesics for 3 to 5 days to all patients. Analgesic suppositories were also used as needed. The skin at injection site became red and indurated on next day, we punctured the skin over ranula and aspirated the fluid on 2nd day after injection. We examined all patients on days 2, 7, 14 and 28 after OK-432 infection and judged the response between 4 and 6 weeks. In case, the response was
insufficient, we repeated the same therapy with a 100% increase of OK-432. The “cure” and “marked reduction” of ranula were defined as a negative palpation and a decrease of more than one half compared with pretreatment size respectively (Ohta et al, 2013).

![Figure 12:](image)

**Figure 12:** There was total shrinkage after a single OK-432 treatment at a dose of 2 KE in this 8-year-old woman with right submandibular swelling. (A, B, C); Local findings before OK-432 therapy, showing a plunging ranula in the left submandibular and oral floor regions (about 7.3 x 6.6 cm). (D) Initial T1-weighted magnetic resonance image before treatment, showing a plunging ranula in the left submandibular space; (E, F, G) Local finding after OK-432 therapy, showing absence of marked swelling in the right submandibular and oral floor regions (6 weeks after treatment). (Ohta et al, 2013)

A study comparing the outcomes of OK-432 sclerotherapy in adults with simple and plunging ranulas found that many of the simple ranulas had to be treated surgically anyway because they ruptured during sclerotherapy or because the treatment did not resolve the ranula or reduce its size. It also seems that sclerotherapy is less effective with simple ranulas than with plunging ranulas because the cysts in simple ranulas are smaller, which makes the procedure more difficult and increases the rate of rupturing. It also means that the OK-432 drug tends to leak in the injection area more often. Moreover, because of the rupturing of the ranula, OK-432 must be injected more frequently, which in turn elevates the time and cost of the procedure.
Thus, sclerotherapy may not be as suitable for > 2-cm diameter simple ranulas in children as surgical resection of the ranula and the sublingual gland (Roh, 2006).

e. Hydrodissection

Ranulas typically arise superior to the mylohyoid muscle. They are caused by obstruction of the sublingual ducts, which can result within the substance of the sublingual gland. The diagnosis can be easily made because the lesion is readily apparent on physical examination. A suprahyoid or plunging ranula is large and can manifest as a neck mass that extends through the mylohyoid (Choi, 2003).

In some cases, only the ranula itself is removed, in other cases, both the lesion and the sublingual gland are removed via an intraoral approach. The most common complication of surgery in completely, which result in the presence of residual gland tissue in increases the risk of the recurrence. Revision surgery is significantly more difficult than primary surgery, and it is associated with a higher risk of complications. Meticulous dissection and complete removal of the lesion during the first surgery are therefore important. Hydrodissection has been used to facilitate dissection of difficult cases in various surgical fields (Choi, 2003).

All procedures were performed in the operating room. Patients ages 16 years and older were administered local anesthesia with sedation, and younger patients were administered general anesthesia. After adequate infiltration of the submucosal area of the ranula with normal saline and lidocain with 1:100,000 epinephine, we extirpated the ranula carefully. The hemostatic effect of the epinephrine minimized bleeding, which helped achieve a precise and rapid resection and minimized the risk
of the recurrence and neural and soft tissue injury. Injection technique involves beveling the needle toward the ranula and meticulously injecting the solution under pressure into the plane. A small amount (<10 ml) of solution can be injected with a dental syringe and a 30 gauge (25 mm) needle along the margin of the ranula. A multiple injection technique can be used around the mass, but is important to limit the depth of the needle to avoid inadvertently rupturing it the ranula capsule. Once injected, the fluid dissects along the ranula and creates a bloodless and safe dissection plane within a few minutes (Choi, 2003).

We dissected along the infiltration plane to the ranula while managing to avoid rupturing it and preventing the loss of too much soft tissue. Surgical dissection can be performed with either a scalpel, Metzenbaum scissors, or electrical needle device. Care must be taken to avoid injury to the lingual nerve and submandibular duct. Rarely is bleeding encountered, but when it is, it can be controlled by meticulous bipolar cautery. Following removal of the cyst, we performed a primary closure with Vicryl 4-0 suture. A Penrose drain was not placed in the operating wound, and stitches were not removed.

Removal of a ranula via hydrodissection preserves the surrounding normal tissue and the dissection plane. During the past 7 years, we have found that this technique is a safe and simple means a removing a ranula. Compared with the other technique, hydrodissection is associated with less bleeding, fewer incidents of neural and soft tissue damage, and a much shorter operating time (Choi, 2003).
CHAPTER III
SUMMARY

Most ranulas are large extravasation mucoceles that arise from the sublingual gland and are sufficiently extensive to form a swelling that resembles the belly or vocal air sac of frog. They are cystic and are frequently blue owing to the Tyndall effect, whereby blue light is reflected more than red light at the interface of soft tissue and cyst. Most extravasation mucoceles occur in the lower lip and are treated successfully by removal of the mucocele with the feeding minor salivary gland. Although the floor of the mouth is the second most common site for extravasation mucoceles, the treatment of the ranula is varied and not always successful. Treatment by incision, simple marsupialization, and excision of the ranula alone have a high recurrence rate, whereas excision of the sublingual gland with or without the ranula is almost always successful. Although the removal of the sublingual gland as the source of the extravasated mucus may be appealing, it is technically demanding and associated with notable morbidity that can include damage to the lingual nerve, Wharton’s duct, submandibular gland, and blood vessels. This has encouraged a search for a satisfactory conservative approach to treatment. Marsupialization with packing of the ranula is successful in about 90% of cases and intracystic injection of the sclerosing preparation OK-432 has given variable results.

However surgical excision of ranula along with sublingual gland has been the first line treatment, surgical complications, including nerve injury, recurrence, and
cosmetic problems, need to be considered. These complications could be avoided by the use of nonsurgical procedures. Although simple aspiration of ranula is a satisfactory nonsurgical treatment, recurrence is commonly observed despite repeated aspiration. Thus, we have developed a new simple and safe method that can be used easily in private clinics and hospitals at an outpatient basis without hospitalization. This method is intralesional injection therapy with OK-432. OK-432 (Picibanil) was originally developed as an immunotherapy agent for cancer. It is thought that its immunopotentiating actions are caused by strong local inflammation that promotes the release of various cytokines (Ohta et al., 2013).

Regardless of the procedure that is used, the surgeon should endeavor to avoid injury to the lingual nerve and wharton’s duct and should take steps to minimize the risk of recurrence. Moreover, when excision is performed with a cold knife or laser, the surgeon must take great care to avoid rupturing the ranula because the cystic wall is thin and friable. Excision of the both the ranula and the sublingual gland via an intraoral approach has been recommended, but we believe that complete extirpation of the sublingual gland is a unnecessary. The most common pitfall during excision is a failure increases the risk of recurrence (Choi, 2003).
Translucent swelling in the floor of the mouth

Anamnesa
Physical examination

RANULA

SURGERY

Incision & Drainage
Marsupialization
Excision of the sublingual gland
Hydrodissection

NON-SURGERY

Intralesional Injection of OK-432

- Computerized Tomography
- Magnetic Resonance Imaging
- Needle aspiration
- Ultrasonographic
- Sialographic examination
- Pathological examination
REFERENCES


Gaertner DL, Clóvis M, Lopes J, Rodrigues M, Pastori L Ranula Surgical Treatment By The Marsupialization Technique, Professor of Oral and Maxillofacial Surgery and Traumatmatology Specialization course and adviser of this report, 2005


