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The primary aim of *World Journal of Gastrointestinal Endoscopy* (*WJGE*, *World J Gastrointest Endosc*) is to provide scholars and readers from various fields of gastrointestinal endoscopy with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGE mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal endoscopy and covering a wide range of topics including capsule endoscopy, colonoscopy, double-balloon enteroscopy, duodenoscopy, endoscopic retrograde cholangiopancreatography, endosonography, esophagoscopy, gastrointestinal endoscopy, gastroscopy, laparoscopy, natural orifice endoscopic surgery, proctoscopy, and sigmoidoscopy.

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MINIREVIEWS

Strategies to manage the difficult colonoscopy

Mike T Wei, Shai Friedland

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Abstract

During endoscopy, an endoscopist is inevitably faced with the occasional "difficult colonoscopy," in which the endoscopist finds it challenging to advance the endoscope to the cecum. Beyond optimization of technique, with minimized looping, minimal insufflation, sufficient sedation, and abdominal splinting when needed, sometimes additional tools may be needed. In this review, we cover available techniques and technologies to help navigate the difficult colonoscopy, including the ultrathin colonoscope, rigidizing overtube, balloon-assisted colonoscopy and the abdominal compression device.

Key Words: Difficult colonoscopy; Incomplete colonoscopy; Overtube; Water immersion; Colonoscopy; Balloon enteroscopy

Core Tip: In all colonoscopies, we recommend optimizing technique, with minimal insufflation, sufficient sedation, minimal looping, water immersion, and having staff apply abdominal pressure when needed. When the cecum cannot be reached despite this, we consider utilization of additional tools, including overtube or specialized endoscope (*e.g.,* ultrathin colonoscope).

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INTRODUCTION

The American Society for Gastrointestinal Endoscopy and American College of

Gastroenterology recommends cecal intubation of 90% in all colonoscopies and 95% for screening colonoscopies[1]. During endoscopy, an endoscopist is inevitably faced with the occasional "difficult colonoscopy," in which the endoscopist finds it challenging to advance the endoscope to the cecum. At times, the cecum is not reached, leading to an incomplete colonoscopy. In this review, we cover available techniques and technologies to help navigate the difficult colonoscopy. We will not be focusing on specific techniques in managing issues such as looping, as this has been extensively covered in articles and books such as by Haycock *et al*[2] and Rodrigues-Pinto[3].

FACTORS FOR DIFFICULT COLONOSCOPY

Several factors for increased cecal intubation time have included female sex[4,5], inadequate bowel preparation[4-7], older age[5-7] constipation[6], lower body mass index[5,8], patient pain[5], previous hysterectomy[4,8], diverticular disease in women[9,10]. Unfortunately, the data available for incomplete colonoscopy is significantly more sparse. This may likely be related to difficulties of evaluating this, given overall lower frequency of incomplete colonoscopy, with most endoscopists only encountering a few a year. In a study by Koido *et al*[11], evaluating 11812 patients that underwent colonoscopy at Juntendo Hospital (Tokyo, Japan), cecal intubation was 95.0%. Risk factors for incomplete colonoscopy included female sex, history of prior abdominal or pelvic surgery, increased age (≥ 60), inflammatory bowel disease, and poor bowel preparation. In a similar study by Shah *et al*[12], utilizing the Ontario Health Insurance Plan reviewing 311608 colonoscopies, of which 13.1% were incomplete. Factors identified were similar to the Koido *et al*[11] study (older age, female sex, prior abdominal or pelvic surgery). In addition, Shah *et al*[12] found colonoscopies performed in a private center had increased odds of incomplete colonoscopy compared to at an academic hospital (OR: 3.57, 95%CI: 2.55-4.98)[12].

OPTIMAL TECHNIQUE

While tools are available to help with difficult colonoscopy, it is important to try to always utilize optimal technique during colonoscopy, with minimized looping, minimal insufflation, sufficient sedation, and abdominal splinting when needed[2,3]. In the case of a difficult colonoscopy, prior to considering utilizing different or additional devices, we recommend trying to classify the issue and tackle it appropriately. Difficulty reaching the cecum during colonoscopy may be due to inadequate sedation, a redundant/looped colon, tortuous anatomy, or a hernia. Patients who vigorously contract their abdominal musculature when experiencing pain during colonoscopy may hinder advancement of the scope. In this situation providing adequate sedation and analgesia, sometimes with the assistance of an anesthesiologist, may facilitate completion of the procedure. The redundant/looped colon may be best managed with adult colonoscope (in comparison to a pediatric colonoscope), with water immersion or water exchange technique during insertion, and with early and effective abdominal splinting. An angulated/tortuous colon is usually easier to navigate with a pediatric colonoscope, or at times an ultrathin colonoscope or enteroscope, which can allow for improved navigation around tight turns. In this case, underwater immersion may also help straighten the colon. Abdominal wall hernias are best managed with adequate counter pressure to prevent the hernia from billowing out. Underwater immersion can also be effective in assisting with this[13]. Finally, large inguinal hernias containing colon should be reduced if possible prior to colonoscopy and constant pressure can be applied to prevent the colon from re-entering the hernia during the procedure. In cases of difficult colonoscopy despite optimized technique, alternative/additional tools may be required.

DEVICES TO MANAGE DIFFICULT COLONOSCOPY

Ultrathin colonoscope

Ultrathin colonoscopes [*e.g.*, EC-530XP (7.0 mm diameter); Fujifilm Corp, Tokyo, Japan] have been found in a randomized controlled trial (RCT) evaluating its use compared to pediatric colonoscope to achieve lower pain as well as trend towards higher cecal intubation rate (97.4% *vs* 92.1%, P = 0.36) in female patients ≥ 70 years of age[14]. Ultrathin colonoscope can also be useful in navigating stenotic colons. In one study by Ito *et al*[15], in 100 patients with stenotic colorectal cancer (CRC) in which a standard pediatric colonoscope could not traverse the CRC stenosis, cecal intubation was achieved for 58% of patients utilizing the ultrathin colonoscope. This has similar been demonstrated in Crohn's strictures[16].

Rigidizing overtube

In August 2019, the Pathfinder Endoscope Overtube (Neptune Medical, Burlingame, Calif, United States) was approved by the United States Food and Drug Administration (Figure 1)[17]. With the use of an overtube that can be flexible or rigid depending on application of a vacuum, the overtube has been found to assist in difficult colonoscopies[18]. In a retrospective case series, in 12 patients in which the overtube to assist with incomplete colonoscopy, the cecum was reached in all cases, with median cecal time of 6 minutes (IQR 4-7.25 min)[19].

Figure 1 Rigidizing overtube. Citation: Available from: https://gipathfinder.com/technology/. Copyright © Neptune Medical Inc. The authors have obtained the permission for figure using from the Neptune Medical Inc (Supplementary material).

G-EYE colonoscope and NaviAid AB

In April 2020, G-EYE® colonoscope (SMART Medical, Ra'anana, Israel) achieved FDA approval. The G-EYE® colonoscope involves the remanufacturing of a reusable balloon at the bending section of the colonoscope. The balloon can be inflated and deflated using the NaviAid™ SPARKC inflation system, allowing for more controlled maneuvering around folds. In addition, the NaviAid AB device is a through-the-scope inflatable balloon which can be inserted through a standard adult colonoscope (requires working channel minimum 3.7 mm). In 2015, Ali *et al*[20] performed a retrospective multicenter study evaluating utility of the NaviAid AB device in enteroscopy (either anterograde or retrograde). While the indications of these endoscopic procedures did not include difficult or incomplete colonoscopy, it is interesting to note that of the 33 retrograde cases, average depth of insertion was 89 cm (range 20-150 cm) proximal to the ileocecal valve utilizing a push-pull technique[20]. In a smaller study involving 9 patients, NaviAid AB device was found to be safe and successfully lead to completion of all colonoscopies[21].

Abdominal compression device

Given the importance of abdominal splinting during endoscopy but its burden on staff[2], the abdominal compression device (ColoWrap, LLC, Durham, NC) has been found to assist with decreasing cecal intubation time and improvement in need of additional manual compression[22,23]. While an abdominal compression device may assist in difficult colonoscopy, it has not been specifically studied in incomplete colonoscopy.

Stiffening wire

In 1994, Kasmin *et al*[24] described a technique of colonoscopy "over the forceps." In this technique, the forceps is advanced 10 cm beyond the colonoscope, and the colonoscope jiggled forward over the forceps with tension on the forceps. In an RCT evaluating the utility of a standard as well as firm stiffening wire (Zutron Medical™, Lenexa, KS, United States), there was no difference in cecal intubation rate of unaided colonoscope (81.1%), standard wire (71.1%), and firm wire (74.3%) However, use of the wire for endoscopies with the unaided colonoscope that were unable to reach cecum led to improvement in cecal intubation from 81.1% to 97.3% (P = 0.0313)[25].

Balloon-assisted colonoscopy

While developed primarily for evaluation of small bowel, single-balloon and double-balloon enteroscopy has been utilized to help manage incomplete colonoscopy. Balloon-enteroscope technology utilizes the balloon to help pleat and stabilize the colon, allowing the colon to be shortened and thereby allowing further endoscope advancement[26]. In a randomized controlled trial by Despott *et al*[10] in 2017, patients defined as technically difficult (based on a scoring system utilizing factors for difficult colonoscopy) were randomized to double-balloon colonoscopy or conventional colonoscopy (22 patients in each arm). Double-balloon colonoscopy was able to achieve similar cecal intubation time (17.5 *vs* 14 min, P = 0.18) but had improved patient discomfort and pain scores[10]. In a meta-analysis by Tan *et al*[27], evaluating single and double-balloon enteroscopy in the context of previous incomplete colonoscopy, cecal intubation rate was 97%. There was little difference between SBE and DBE in cecal intubation rate (98% *vs* 97%, P = 0.63) and time to cecum (22 *vs* 19 min, P = 0.40).

WHAT IF THE CECUM CAN STILL NOT BE REACHED?

Under circumstances in which the cecum cannot be reached despite techniques described above, non-invasive options can be considered, including computed tomography (CT) colonography or colon capsule endoscopy. Particularly in elderly patients or those with significant comorbidities, after discussion with the patient a decision not to pursue additional testing may also be appropriate. In a meta-analysis by Deding *et al*[28], while completion rate of CT colonography was higher than colon capsule endoscopy (98 *vs* 76%), colon capsule endoscopy had increased detection of polyps of any size (37 *vs* 10%). Of note, colon capsule in the studies referenced were all utilizing PillCam (1st or 2nd Generation). In a randomized controlled trial by Sali *et al*[29] comparing CT colonography with three rounds of FIT (every 2 years), there was low participation overall for both CT colonography (26.7%) and all three rounds of FIT (33.4%) (though 64.9% participated in at least one FIT)[29]. In reviewing patients who completed screening, advanced neoplasia was detected at a higher rate with CT colonography compared to FIT (5.2 *vs* 3.1%, $P = 0.0002$).

Our experience

In our experience, when we encounter a referral for incomplete colonoscopy, we try to first understand the issue leading to incomplete colonoscopy. In general, our referring endoscopists are extremely experienced, and oftentimes will document the issue leading to difficult colonoscopy. If patient intolerance was an issue, then we will have the procedure performed under monitored anesthesia care instead of moderate or conscious sedation. If the procedure was notable for tortuous colon with significant diverticulosis, we may start with a pediatric colonoscope and if needed switch to an ultrathin colonoscope or upper endoscope, with the upper endoscope being less preferred given its shorter length. If the procedure was notable for significant looping, we will request the help of our more experienced staff to help with abdominal splinting and may be more inclined to utilize overtube technology, including the single or double-balloon enteroscope, or the rigidizing overtube. In our experience, a "long" colon usually occurs in combination with tortuosity or looping, or both. As such, utilization of the techniques above would be helpful in managing the long colon. However, in the absence of tortuosity or looping, one could consider utilization of the enteroscope (without the overtubes for the additional length), or utilization of single or double-balloon enteroscope. In all these cases, we tend to perform the majority of the colonoscopy with water immersion.

CONCLUSION

In all colonoscopies, we recommend optimizing technique, with minimal insufflation, sufficient sedation, minimal looping, water immersion, and having staff apply abdominal pressure when needed. When the cecum cannot be reached despite this, we consider utilization of additional tools, including overtube or specialized endoscope (*e.g.*, ultrathin colonoscope). In the rare instance in which the cecum cannot be reached despite best effort including referral to specialized center, consideration can be made for non-invasive imaging (CT colonography or colon capsule endoscopy).

FOOTNOTES

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Review of oral and pharyngolaryngeal benign lesions detected during esophagogastroduodenoscopy

Masaya Iwamuro, Kenta Hamada, Seiji Kawano, Yoshiro Kawahara, Motoyuki Otsuka

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Abstract

Recent advancements in endoscopy equipment have facilitated endoscopists' detection of neoplasms in the oral cavity and pharyngolaryngeal regions. In particular, image-enhanced endoscopy using narrow band imaging or blue laser imaging play an integral role in the endoscopic diagnosis of oral and pharyngolaryngeal cancers. Despite these advancements, limited studies have focused on benign lesions that can be observed during esophagogastroduodenoscopy in the oral and pharyngolaryngeal regions. Therefore, this mini-review aimed to provide essential information on such benign lesions, along with representative endoscopic images of dental caries, cleft palate, palatal torus, bifid uvula, compression by cervical osteophytes, tonsil hyperplasia, black hairy tongue, oral candidiasis, oral and pharyngolaryngeal ulcers, pharyngeal melanosis, oral tattoos associated with dental alloys, retention cysts, papilloma, radiation-induced changes, skin flaps, vocal cord paresis, and vocal fold leukoplakia. Whilst it is imperative to seek consultation from otolaryngologists or dentists in instances where the diagnosis cannot be definitively ascertained by endoscopists, the merits of attaining foundational expertise pertaining to oral and pharyngolaryngeal lesions are unequivocal. This article will be a valuable resource for endoscopists seeking to enhance their understanding of oral and pharyngolaryngeal lesions.

Key Words: Benign diseases; Diagnosis; Esophagogastroduodenoscopy; Non-neoplastic lesions; Oral lesions; Pharyngolaryngeal lesions

Core Tip: During esophagogastroduodenoscopy, various lesions other than squamous cell carcinoma can be detected in the oral cavity and pharyngolaryngeal regions. These include dental caries, cleft palate, palatal torus, bifid uvula, compression by cervical osteophytes, tonsil hyperplasia, black hairy tongue, oral candidiasis, oral and pharyngolaryngeal ulcers, pharyngeal melanosis, oral tattoos associated with dental alloys, retention cysts, papilloma, radiation-induced changes, skin flaps, vocal cord paresis, and vocal fold leukoplakia. Endoscopists must possess adequate knowledge about these lesions and promptly identify and diagnose them during an endoscopic examination.

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INTRODUCTION

Recent advances in endoscopy equipment have enabled endoscopists to detect neoplasms in the oral cavity and pharyngolaryngeal region. In particular, image-enhanced endoscopy using narrow band imaging (NBI) or blue laser imaging (BLI) play an integral role in the endoscopic diagnosis of oral and pharyngolaryngeal cancers[1-4]. For instance, early-stage squamous cell carcinoma in the oral and pharyngolaryngeal regions typically exhibits a well-demarcated brownish area with irregular microvasculature on NBI or BLI, which resembles the features of early-stage esophageal cancer. A prospective, controlled cohort study on structured screening of the oropharynx, hypopharynx, and larynx using esophagogastroduodenoscopy revealed significantly increased detection rates of precancerous and early cancerous lesions compared with those without structured examination of the pharyngolaryngeal area[5]. A retrospective observational study revealed that the prevalence of pharyngeal cancer, which was detected during esophagogastroduodenoscopy using NBI, was 0.26% (29/11050)[6]. These results reinforce the growing importance of screening examinations of the laryngopharyngeal area. However, despite the increasing number of articles on the endoscopic features and treatment of squamous cell carcinoma, few articles have focused on benign lesions occurring in the oral and pharyngolaryngeal regions. Herein, we present the endoscopic images of 17 types of lesions detected in the oral and pharyngolaryngeal areas, and review articles associated with these lesions.

DENTAL CARIES

Dental caries, also known as dental cavities or tooth decay, are areas of the teeth that have been damaged and weakened by acid-producing bacteria. This damage results in a hole or pit in the tooth, which can cause pain, sensitivity, and other oral health problems[7]. Progressive damage results in significant destruction of the teeth. If the infection is left untreated or becomes severe, the bacteria causing dental caries spread to other parts of the body *via* the bloodstream, *i.e.*, sepsis, which is a life-threatening condition. Thus, it is important to diagnose dental caries promptly, and maintain good oral hygiene from the standpoint of internists. Furthermore, diabetes is significantly correlates with dental caries[8]. High blood glucose levels make the teeth and gums more susceptible to decay and periodontal diseases. Additionally, patients with diabetes may produce less saliva, leading to dry mouth, another factor that contributes to tooth decay. While visual dental examinations by dental professionals such as hygienists and dentists are crucial, esophagogastroduodenoscopy screening of teeth may be advantageous, particularly in individuals with diabetes. Unfavorable dental health and untreated cavities also lead to periodontal diseases, which are reportedly associated with an increased risk of certain digestive conditions, such as gastroesophageal reflux disease and peptic ulcers[9,10].

Dental caries are visible as discolored or darkened spots, rough or uneven surfaces, visible cavities or holes, or even grossly destroyed areas on teeth. Figure 1 shows representative images of grossly decayed teeth. A 28-year-old man (Case 1) underwent craniotomy for craniopharyngioma, and was treated for panhypopituitarism, diabetes insipidus, and diabetes mellitus. The intraoral view revealed multiple residual roots with carious lesions (Figure 1A). In another 69-year-old man with diabetes mellitus (Case 2), esophagogastroduodenoscopy revealed a severely damaged tooth (Figure 1B).

CLEFT PALATE

Cleft palate is a congenital anomaly characterized by a split or opening in the palate, which serves as a demarcation between the oral and nasal cavities. This condition arises from inadequate fusion of the tissues that form the palate during fetal development, and may manifest in varying degrees of severity, size, and location, affecting the soft palate (posterior part of the mouth), hard palate (anterior part of the mouth), or both[11-13]. In severe cases, fissures may extend into the nasal cavity. The global incidence of cleft lip and/or palate is approximately 1 in 700 live births, signifying its substantial occurrence as a congenital anomaly[14]. Surgical intervention is the primary treatment modality for cleft palate, although additional therapeutic measures, such as speech therapy and dental management, may be warranted.

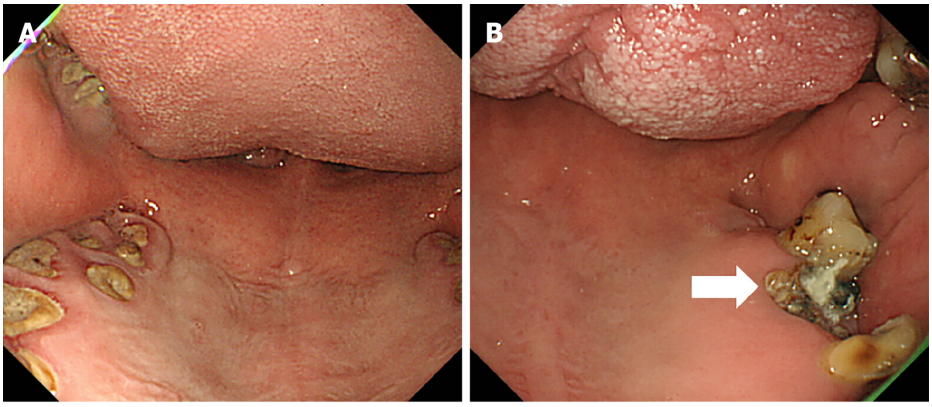

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Figure 1 Endoscopic images of dental caries. A: Case 1. A 28-year-old man with panhypopituitarism, diabetes insipidus, and diabetes mellitus had multiple residual roots and carious lesions; B: Case 2. A 69-year-old man with diabetes mellitus also had a severely damaged tooth (arrow).

A hole on the palate was observed in a 67-year-old man (Case 3) during esophagogastroduodenoscopy (Figure 2). The patient had been previously diagnosed with cleft palate and mild dysarthria.

PALATAL TORUS

Palatal torus, or torus palatinus, is a bony lump that develops in the hard palate. Protrusions are benign, non-neoplastic lesions caused by overgrowth of osseous tissue[15-17]. The palatal torus is typically round or lobed and varies in size. Treatment is not required because it is generally asymptomatic.

A 62-year-old man with maxillary cancer (Case 4) underwent esophagogastroduodenoscopy for cancer screening. A protruding lesion was identified in the roof of the mouth (Figure 3A and B). Computed tomography (CT) images showed a bony structure in the hard palate (Figure 3C), confirming the diagnosis of palatal torus. In this patient, although the CT scan was performed for maxillary cancer, the diagnosis of palatal torus was easily and definitively established through palpation of the protrusion with the index finger, thereby confirming its bony solidity.

BIFID UVULA

Bifid uvula is a congenital anomaly in which the uvula is split into two lobes or appears notched[18,19]. The bifurcation of the uvula is considered a minor variation in the normal anatomy, and is usually not associated with any health problems. The prevalence of bifid uvula is estimated to be 0.4%–3.3% among the general population[20].

A uvula with a bisecting tip was unexpectedly identified in a 75-year-old woman (Case 5) (Figure 4). As the patient did not present with either cleft palate or any discernible subjective symptoms, no intervention was deemed necessary for the bifid uvula.

COMPRESSION BY CERVICAL OSTEOPHYTE

Compression by cervical osteophytes, which are bony outgrowths on the cervical vertebrae, can cause deformities in the oropharynx, hypopharynx, and larynx due to their proximity and pressure on these structures. As osteophytes grow and compress, they can lead to narrowing or obstruction of adjacent tissues[21-23]. The presence of a deformity in the pharyngolaryngeal region, specifically in proximity to the pyriform sinus, may pose a challenge during endoscope insertion. The diagnosis of cervical osteophytes is made based on CT imaging. Previous reports have suggested that a similar deformity may manifest with medialization of the common carotid artery[5].

Esophagogastroduodenoscopy revealed a submucosal bulge on the dorsal side of the oropharynx in an 87-year-old man (Case 6) (Figure 5A). CT images showed a bone protrusion on the anterior side of the cervical vertebra (Figure 5B). Another patient (69-year-old man, Case 7) exhibited deformation of the right dorsal side of the hypopharynx (Figure 5C). CT images revealed bone outgrowth on the right anterior side of the cervical vertebra (Figure 5D).

TONSIL HYPERTROPHY

Tonsil hypertrophy can be caused by diverse etiological factors such as recurrent infections, allergies, and genetic factors.

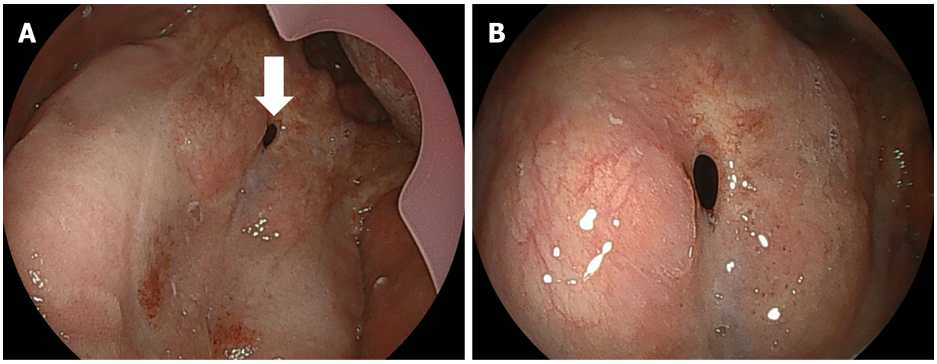

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Figure 2 Endoscopic images of cleft palate. A and B: Case 3. A 67-year-old man had a hole in the palate (arrow). The patient was previously diagnosed with cleft palate and mild dysarthria.

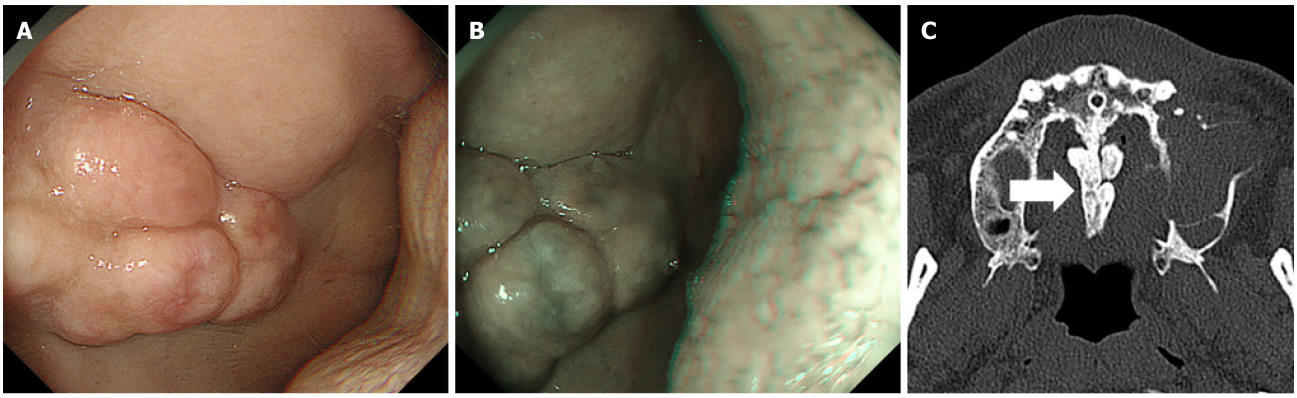

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Figure 3 Endoscopic and computed tomography images of palatal torus. A–C: Case 4. A protruding lesion was identified in the roof of the mouth of a 62-year-old man; A: White light; B: Narrow band imaging; C: Computed tomography image showing a bony structure in the hard palate (arrow).

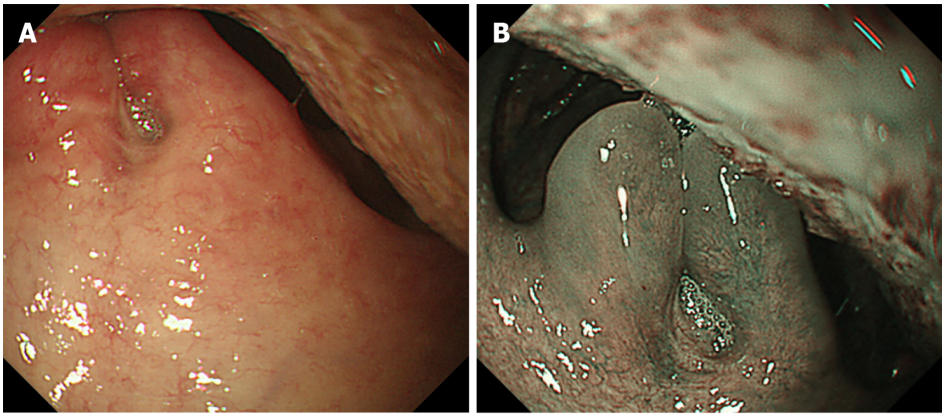

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Figure 4 Endoscopic images of bifid uvula. A and B: Case 5. A 75-year-old woman had a uvula with a bisecting tip; A: White light; B: Narrow band imaging.

Tonsil hypertrophy can lead to several related issues depending on the severity and extent of enlargement[24]. The associated symptoms include difficulty in swallowing, breathing difficulties such as snoring or sleep apnea[25], chronic infections, speech problems, and changes in facial structure called "adenoid face". Evaluation of the tonsils is generally important before endoscopic examination using sedatives because significant tonsil hypertrophy potentially causes breathing difficulties. If a patient has enlarged tonsils, a healthcare provider may choose to take additional precautions, such as adjusting the dosage of sedative medication, or monitoring the patient's breathing more closely during the sedation procedure. In addition, hypertrophic tonsils prevent endotracheal intubation[26].

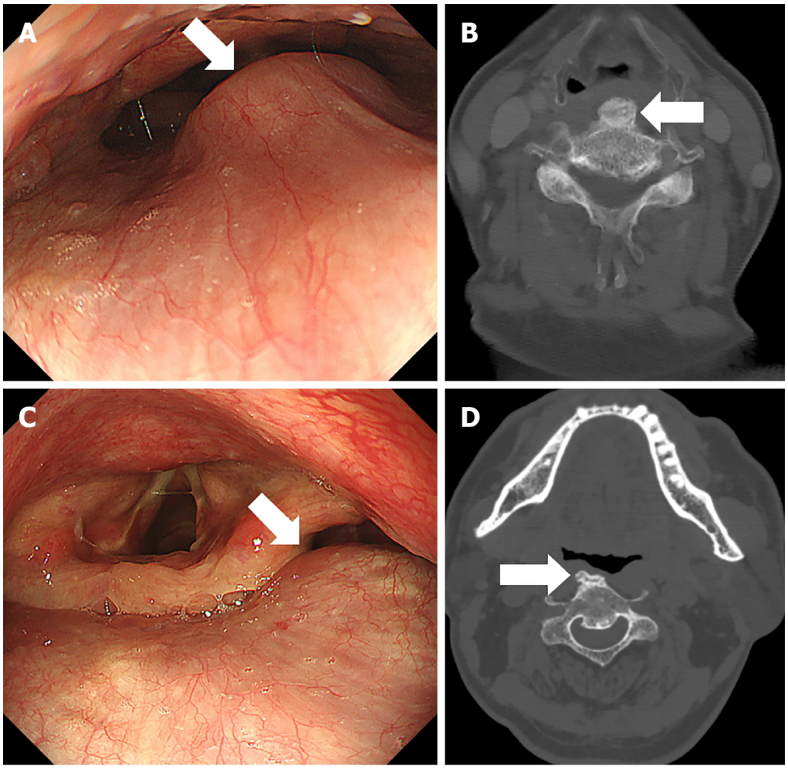

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Figure 5 Endoscopic and computed tomography images of compression by cervical osteophyte. A: Case 6. An 87-year-old man had a submucosal bulge on the dorsal side of the oropharynx (arrow); B: Case 6. Computed tomography (CT) imaging showed a bone protrusion on the anterior side of the cervical vertebra (arrow); C: Case 7. Deformation was observed on the right dorsal side of the hypopharynx in a 69-year-old man (arrow); D: Case 7. CT image showing outgrowth of the bone of the cervical vertebra (arrow).

A 23-year-old woman (Case 8) underwent screening *via* esophagogastroduodenoscopy, and hypertrophic tonsils were unexpectedly identified (Figure 6). The patient was asymptomatic, therefore no therapeutic intervention was required for the tonsil hypertrophy.

BLACK HAIRY TONGUE

Black hairy tongue manifests as a superficial, dark, and furry carpet-like growth on the tongue. The precise etiology of this lesion remains uncertain, although it is deemed to be a transient and benign condition that is linked to inadequate oral hygiene, tobacco use, and specific medications such as antibiotics[27-29]. Medical intervention is typically not necessary for black hairy tongue, despite its unattractive appearance. It can be resolved by maintaining better oral hygiene and eliminating causative agents, such as abstaining from smoking and refraining from the use of specific medications.

A 65-year-old man (Case 9) diagnosed with schizophrenia and advanced colon cancer, who had become incapacitated due to mental impairments, was admitted to our hospital. Esophagogastroduodenoscopy revealed a black hairy tongue (Figure 7A). A black hairy tongue was also observed in an 86-year-old woman (Case 10) diagnosed with polymyalgia rheumatica after administration of steroids (10 mg prednisolone) (Figure 7B).

ORAL CANDIDIASIS

Candida sp. are commensal fungi that reside in the oral mucosa. However, in individuals with compromised immune systems, they can become pathogenic and instigate opportunistic infections. Oral candidiasis can be caused by different species of *Candida*, among which *Candida albicans* is the most common pathogen. Other species that can cause oral candidiasis include *C. glabrata*, *C. tropicalis*, *C. parapsilosis*, and *C. krusei*. Oral candidiasis, also known as oral thrush, is characterized by white or creamy plaques within the mouth[30-32]. Antifungal medication and proper oral hygiene practices are effective for the treatment of oral candidiasis.

Physical examination revealed white adhesions in the mouth of a 63-year-old woman with hypertension and chronic thyroiditis (Case 11). Esophagogastroduodenoscopy revealed multiple white plaques in the oral cavity, pharynx, larynx, and esophagus (Figure 8). A biopsy of the white lesions showed fungi, confirming the diagnosis of oral, pharyngolaryngeal, and esophageal candidiasis.

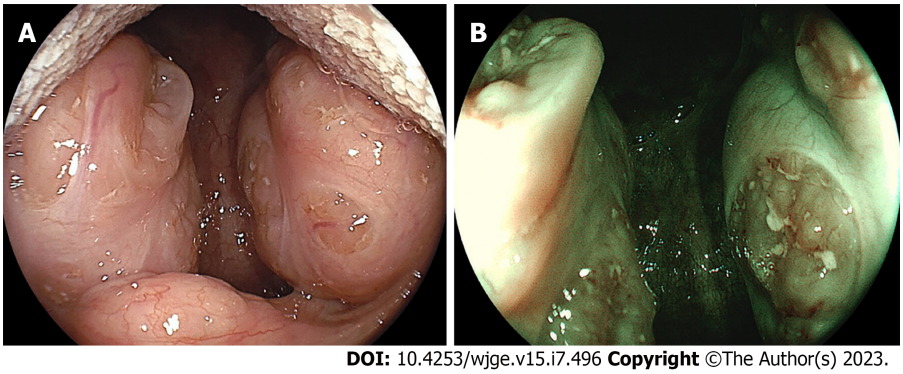

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Figure 6 Endoscopic images of tonsil hyperplasia. A and B: Case 8. Hypertrophic tonsils were unexpectedly identified in a 23-year-old woman who underwent screening esophagogastroduodenoscopy; A: White light; B: Blue laser imaging.

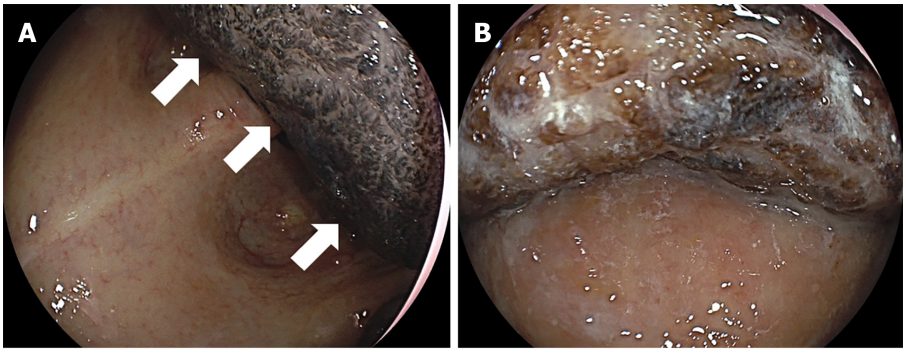

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Figure 7 Endoscopic images of black hairy tongue. A: Case 9. A 65-year-old man with schizophrenia and advanced colon cancer presented with black hairy tongue (arrows); B: Case 10. A black hairy tongue was observed in an 86-year-old woman with polymyalgia rheumatica.

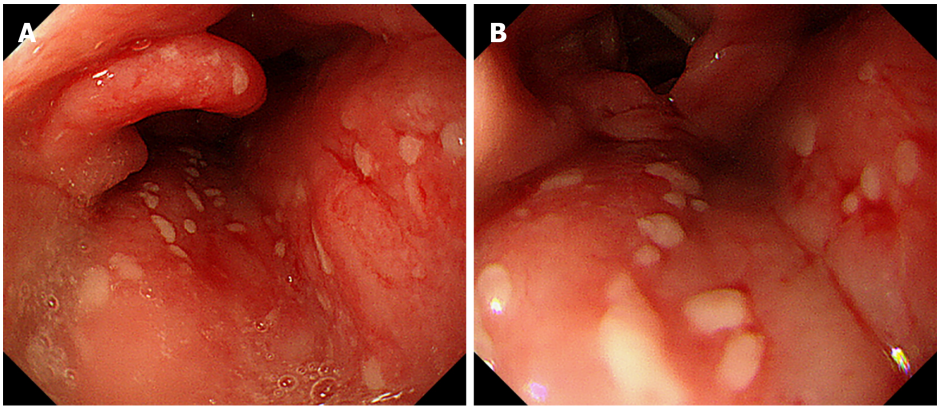

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Figure 8 Endoscopic images of oral candidiasis. A and B: Case 11. A 63-year-old woman had multiple white plaques in the oral cavity, pharynx, larynx, and esophagus. Endoscopic biopsy revealed fungal infection, confirming the diagnosis of candidiasis.

CORROSIVE INJURY

Corrosive injury in the oral and pharyngolaryngeal regions occurs following exposure to corrosive agents, including acids, alkalis (bases), or other potent chemicals[33]. The ingestion of corrosive substances primarily occurs as acts of deliberate self-harm in adults and accidentally in children. Corrosive substances can induce profound harm upon contact with the mouth, throat, and larynx. According to a study investigating individuals who ingested ammonia, 69.8% of patients (30 out of 43) displayed oropharyngeal lesions[34]. The severity of the injury is contingent upon multiple factors, including the concentration, volume, and duration of exposure to the corrosive substance, as well as the nature of the chemical involved. Reports indicate that early endoscopy within 12–24 h after ingestion enables careful assessment of anatomical disruptions in the oropharyngolaryngeal areas[35] and the esophagus, stomach, and duodenum.

ORAL AND PHARYNGOLARYNGEAL ULCERS

The manifestation of oral and pharyngolaryngeal ulcers stems from their diverse etiologies. Differential diagnosis depends on the patient's history, physical examination findings, and any accompanying symptoms. Common differential diagnoses include bacterial (*e.g.*, *Streptococcus* sp.) and viral infections (*e.g.*, herpes simplex virus, Epstein-Barr virus, cytomegalovirus, and Coxsackie virus), autoimmune disorders (*e.g.*, Behcet's disease, systemic lupus erythematosus, and Crohn's disease), skin diseases (*e.g.*, pemphigus vulgaris and mucous membrane pemphigoid), trauma (*e.g.*, biting and scratching), allergic reactions, chemical irritation, and neoplasms[36,37]. Thus, physicians must uncover the underlying cause of the disease in patients with chronic relapsing or intractable ulcers in the oral and pharyngolaryngeal regions.

A 64-year-old woman (Case 12) was referred to our hospital for evaluation of oral ulceration and fever. During her hospitalization, the patient developed macrocytic anemia and neutropenia. Subsequent bone marrow examination led to a diagnosis of myelodysplastic syndrome with trisomy 8. Colonoscopy revealed multiple ulcers involving Bauhin's valve, and esophagogastroduodenoscopy revealed ulcers in the oral cavity (Figure 9). Behçet's disease-like symptoms have been reported to arise in conjunction with myelodysplastic syndrome involving trisomy 8[38].

MELANOSIS

Melanosis is characterized by the presence of dark pigmentation in the epithelium. Melanosis in the oral and pharyngolaryngeal regions is also known as smoker's melanosis, as it typically manifests in up to 30% of chronic smokers and gradually regresses following smoking cessation[39]. One study demonstrated a robust correlation between the presence of melanosis and elevated susceptibility to squamous cell carcinoma in the oral cavity, pharynx, larynx, or esophagus[40]. These results suggest that screening for squamous cell carcinoma is important in patients with melanosis.

In a 58-year-old man (Case 13) with advanced esophageal cancer (Figure 10A), melanosis was identified in the pharynx (Figure 10B). The patient had a history of smoking 20 cigarettes daily for 39 years.

ORAL TATTOOS ASSOCIATED WITH DENTAL ALLOYS

Oral tattoos, also known as amalgam tattoos or intraoral tattoos, are characterized by pigmentation or staining of oral tissues, most commonly affecting the gingiva and mucosa of the oral cavity[41-43]. Discoloration arises from exposure to dental restorative materials containing metals including amalgam, gold, and various alloys. Although oral tattoos are generally considered benign and do not cause any symptoms, they can be a source of cosmetic concerns. Additionally, in some instances, they can be misdiagnosed as oral melanoma or other pigmented lesions, warranting an appropriate diagnosis and follow-up by a dental professional or otolaryngologist.

Multiple points of black pigmentation were identified bilaterally on the buccal mucosa of a 68-year-old man (Case 14) (Figure 11)[42]. We performed an endoscopic biopsy of the lesion to exclude melanoma, which revealed no neoplastic cells. Since the pigmented lesions were adjacent to the metal crowns of gold-silver-palladium alloys, we diagnosed oral tattoos associated with dental restorative materials.

RETENTION CYSTS

Retention cysts are the most prevalent benign lesions of the pharyngeal and laryngeal mucosa. These cysts are lined with epithelial tissue and are characterized by the presence of serous or mucous fluid[44,45]. The pathogenesis of these cysts is believed to involve dilation and obstruction of the mucous gland ducts within the lamina propria or deeper layers of the pharyngolaryngeal region due to the retention of secretions and/or chronic inflammatory processes. Most small and asymptomatic cysts do not require treatment. However, larger cysts or those causing significant symptoms, such as dysphagia, dysphonia, or respiratory distress, may require intervention.

Figure 12A and B show a retention cyst incidentally observed on the ventral side of the epiglottis in a 60-year-old man (Case 15) during esophagogastroduodenoscopy (Figure 12A and B). In an 80-year-old woman (Case 16), a retention cyst was identified on the left side of the epiglottis (Figure 12C). Neither of the patients exhibited any symptoms associated with the presence of epiglottic cysts.

PAPILLOMA

Papillomas in the oral and pharyngolaryngeal regions are benign tumors that generally present exophytic growth with wart-like projections[46,47]. The microscopic features of pharyngeal papillomas typically include papillary architecture, hyperkeratosis, koilocytosis, and fibrovascular cores. Considering the benign nature of papillomas, treatment is reserved only for symptomatic cases.

Reddish wart-like projections were observed on the uvula of a 67-year-old man (Case 17) during esophagogastroduodenoscopy (Figure 13A). Magnifying NBI revealed dilated microvasculature, arranged in an orderly manner, and

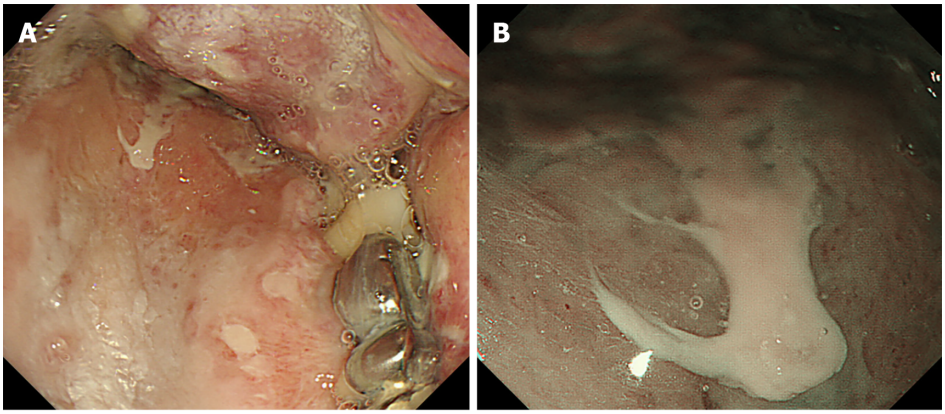

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Figure 9 Endoscopic images of oral and pharyngolaryngeal ulcers. A and B: Case 12. A 64-year-old female patient was diagnosed with myelodysplastic syndrome with trisomy 8. The patient had multiple ulcers in the oral cavity. A: White light; B: Narrow band imaging.

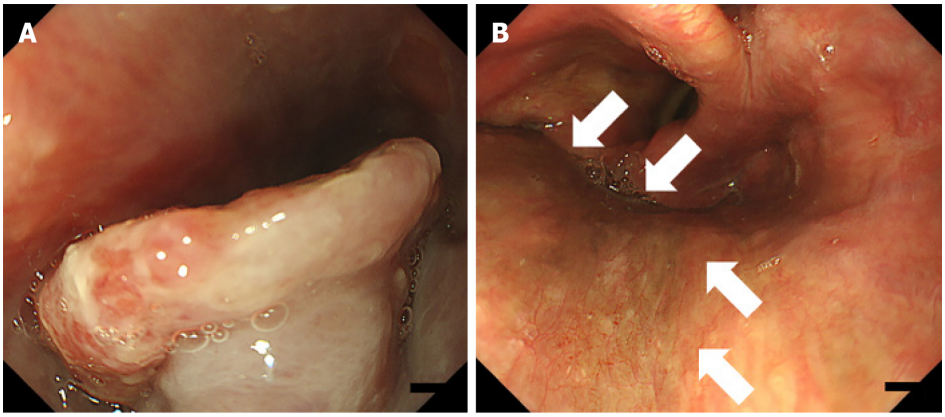

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Figure 10 Endoscopic images of pharyngeal melanosis. A: Case 13. A 58-year-old man presented with advanced esophageal cancer; B: Case 13. The patient had melanosis in the pharynx (arrows).

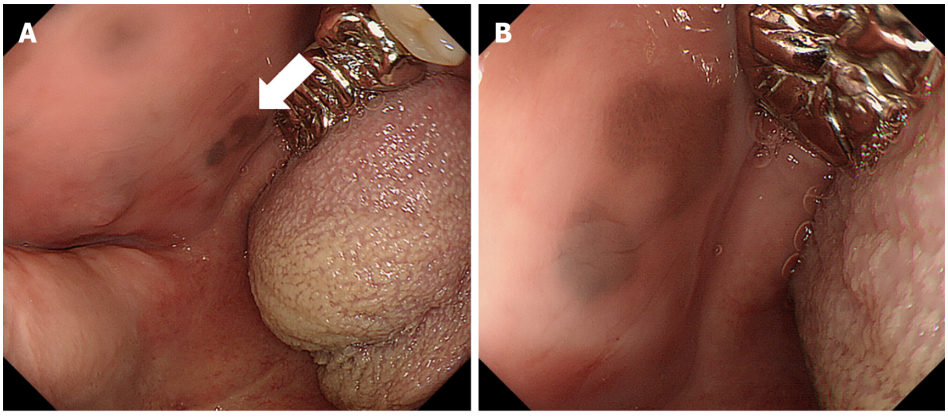

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Figure 11 Endoscopic images of oral tattoos associated with dental alloys. A and B: Case 14. Multiple points of black pigmentation were identified on the bilateral buccal mucosa of a 68-year-old man (arrow). The pigmented lesions were adjacent to the metal crowns of the gold-silver-palladium alloys.

demarcated into clusters (Figure 13B). Histopathological examination of the endoscopic biopsy specimen confirmed a diagnosis of papilloma.

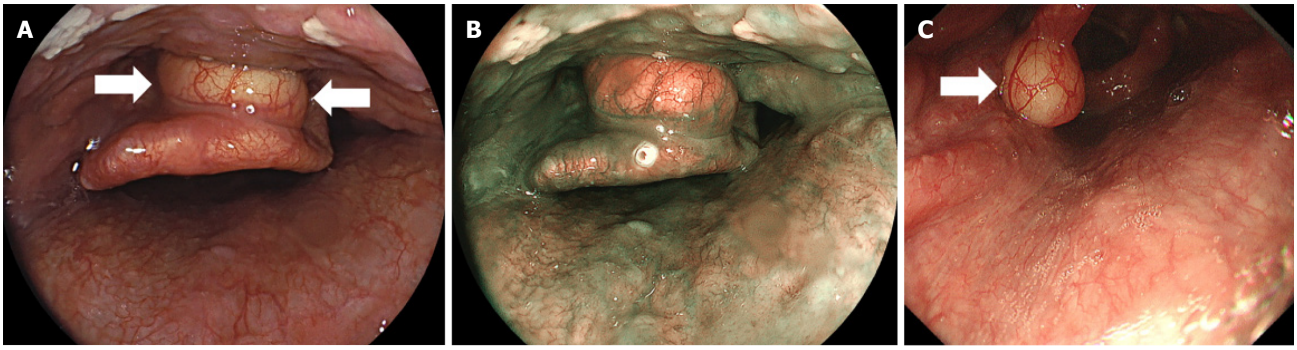

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Figure 12 Endoscopic images of retention cysts. A and B: Case 15. A 60-year-old man had a retention cyst on the ventral side of the epiglottis (arrows); A: White light; B: Blue laser imaging; C: Case 16. An 80-year-old woman also presented with a retention cyst on the left side of the epiglottis (arrow).

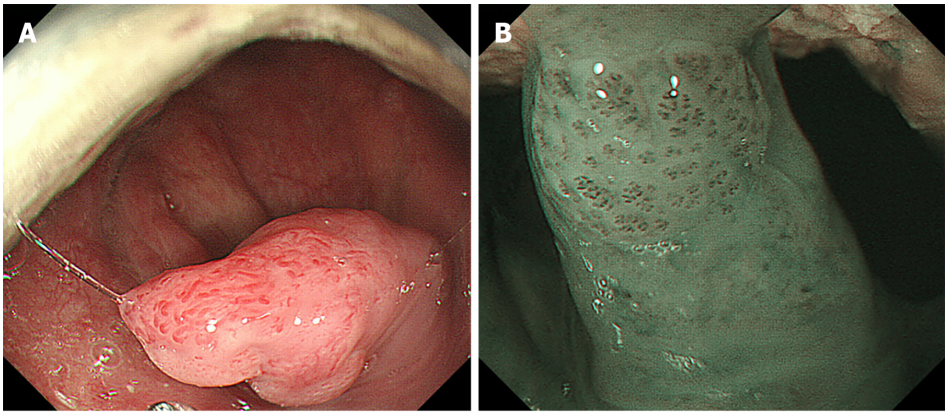

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Figure 13 Endoscopic images of papilloma. A and B: Case 17. A 67-year-old man had reddish wart-like projections on the uvula; A: White light; B: Magnified observation with narrow band imaging. Papilloma was diagnosed based on the pathological analysis of the biopsied specimen.

RADIATION-INDUCED CHANGES

Radiation therapy is used to treat malignant lesions in the oral cavity, pharynx, and larynx[48,49]. This therapeutic modality induces several mucosal alterations, including mucosal erythema, friability, erosion, and angiectasia. Caution is required during endoscopic observation of irradiated regions, as differentiating between neoplastic lesions (*i.e.*, recurrence of cancer) and radiation-induced mucosal alterations may be challenging.

A 58-year-old man who had undergone radiotherapy for laryngeal cancer (Case 18) showed patchy redness in the pharyngolaryngeal region (Figure 14A). Another 70-year-old man with a history of laryngeal cancer treated with radiotherapy (Case 19) showed vascular dilatation in the larynx (Figure 14B), which was observed more strongly on BLI (Figure 14C).

SKIN FLAP

In reconstructive surgery for oral and pharyngeal defects, skin flaps or skin grafts are sometimes used for both functional and cosmetic restoration. Differentiation between these techniques is defined by vascularization, as a skin graft relies on the vascular bed of the recipient site for blood supply, whereas a skin flap retains its intrinsic blood supply from the donor site[50,51].

We performed a screening esophagogastroduodenoscopy in a 68-year-old man (Case 20). The patient underwent surgery for laryngeal cancer and reconstruction with a pectoralis major myocutaneous flap. Esophagogastroduodenoscopy revealed a clearly demarcated, yellowish-white skin flap through the pharynx, larynx, and esophagus (Figure 15A and B). In a 71-year-old man who underwent reconstructive surgery for laryngeal cancer (Case 21), a pectoralis major myocutaneous flap was observed during esophagogastroduodenoscopy (Figure 15C).

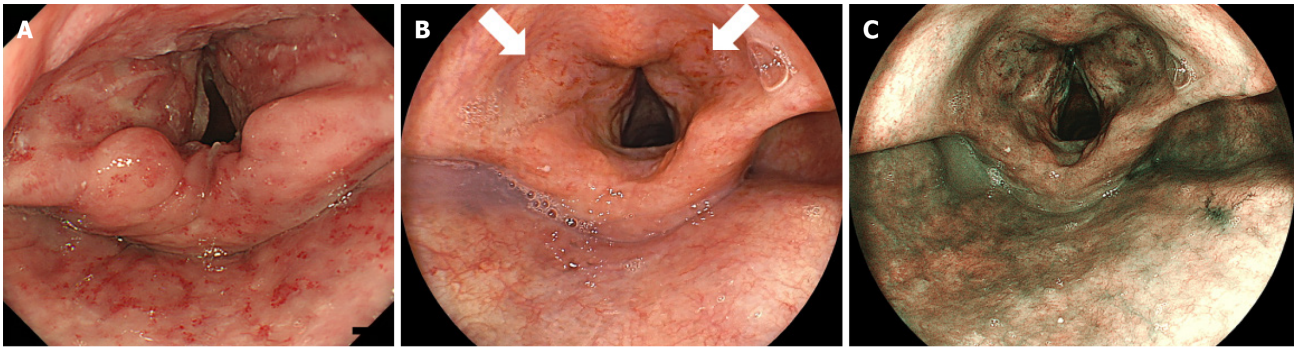

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Figure 14 Endoscopic images of radiation-induced changes. A: Case 18. A 58-year-old man who had undergone radiotherapy for laryngeal cancer developed patchy redness, White light; B and C: Case 19. A 70-year-old man with a history of laryngeal cancer treated with radiotherapy shows vascular dilatation of the larynx (arrows); B: Blue laser imaging.

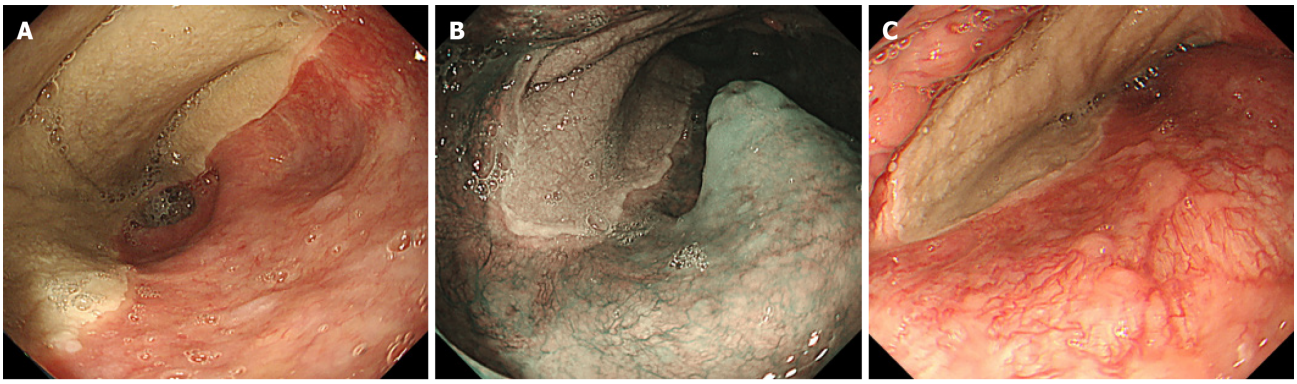

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Figure 15 Endoscopic images of skin flap. A and B: Case 20. In a 68-year-old man who underwent surgery for laryngeal cancer and reconstruction with a pectoralis major myocutaneous flap, esophagogastroduodenoscopy revealed a clearly demarcated yellowish white skin flap; A: White light; B: Narrow band imaging; C: Case 21. A pectoralis major myocutaneous flap was observed in a 71-year-old man who underwent reconstructive surgery for laryngeal cancer.

VOCAL CORD PARESIS

Paresis of the vocal cords denotes a condition in which one or both the vocal cords suffer an impairment in their motility or function[52,53]. The possible etiologies of vocal cord paresis include congenital factors, infectious agents, neoplasms, traumatic incidents, endocrine diseases (*e.g.*, thyroid disorders), and systemic neurological disorders. Hoarseness, breathiness, dysphonia, dysphagia, and/or dyspnea may occur because of vocal cord paresis.

A 65-year-old man (Case 22) underwent surgery for advanced esophageal cancer. His right recurrent laryngeal nerve was injured during surgery, resulting in unilateral vocal cord paresis. Subsequent esophagogastroduodenoscopy revealed that the right vocal cord displayed no movement during respiration (Figure 16A) and phonation (Figure 16B) owing to paresis.

VOCAL FOLD LEUKOPLAKIA

Vocal fold leukoplakia, also known as laryngeal leukoplakia, refers to the manifestation of white patches or plaques on the mucosa of the vocal cords[54,55]. Smoking or chewing tobacco is a primary risk factor for the development of vocal fold leukoplakia. In addition, this condition is commonly linked to excessive alcohol consumption, viral infections such as human papillomavirus, chronic laryngopharyngeal reflux, and voice misuse[56]. It is important to note that the term "leukoplakia" does not indicate a specific histological diagnosis, as it encompasses several histological features, including benign, premalignant, and malignant lesions[57]. Although excisional surgery is the primary modality for treating vocal fold leukoplakia, a definitive threshold for surgical intervention remains elusive owing to the need for judicious therapeutic decision-making that optimizes both vocal function and oncologic safety[58]. Consequently, referral to an otolaryngologist is a crucial step when vocal fold leukoplakia is identified during esophagogastroduodenoscopy.

Figure 17 shows vocal fold leukoplakia observed in a 68-year-old man (Case 23). A whitish nodular lesion was observed mainly on the right side of the vocal fold (Figure 17A), which was emphasized on NBI (Figure 17B). The patient had undergone a biopsy of the leukoplakia lesion at 64 years of age. A pathological diagnosis of dysplasia was made, and

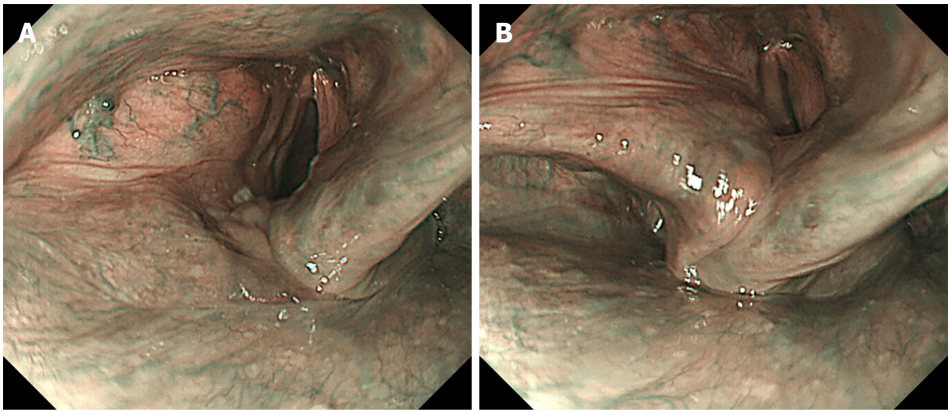

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Figure 16 Endoscopic images of vocal cord paresis. A and B: Case 22. Esophagogastroduodenoscopy of a 65-year-old man with right vocal cord paresis revealed that the right vocal cord displayed no movement during respiration and phonation; A: Respiration; B: Phonation.

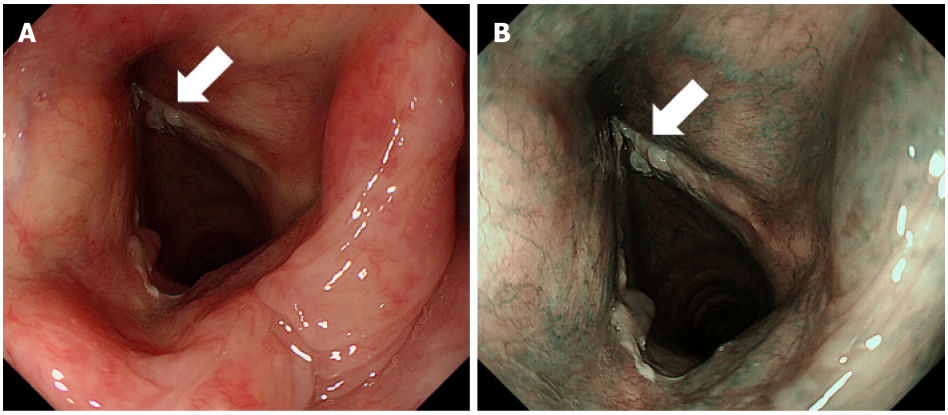

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Figure 17 Endoscopic images of vocal fold leukoplakia. A and B: Case 23. A 68-year-old man presented with leukoplakia of the vocal fold (arrow). A pathological diagnosis of dysplasia was made; A: White light; B: Narrow band imaging.

the vocal fold lesion was under active surveillance by otolaryngologists.

CONCLUSION

We presented representative endoscopic images of dental caries, cleft palate, palatal torus, bifid uvula, compression by cervical osteophytes, tonsil hyperplasia, black hairy tongue, oral candidiasis, oral and pharyngolaryngeal ulcers, pharyngeal melanosis, oral tattoos associated with dental alloys, epiglottic cysts, papilloma, radiation-induced changes, skin flap, vocal cord paresis, and vocal fold leukoplakia. The images show various lesions observed in the oral and pharyngolaryngeal regions during esophagogastroduodenoscopy. While it is essential to consult otolaryngologists or dentists when the diagnosis cannot be established by endoscopists, the benefits of acquiring foundational knowledge concerning oral and pharyngolaryngeal lesions and identifying them for the welfare of patients cannot be denied. We believe that this mini-review will be valuable to endoscopists seeking to enhance their understanding of oral and pharyngolaryngeal lesions.

FOOTNOTES

Author contributions: Iwamuro M designed the research study and wrote the paper; Iwamuro M, Hamada K, Kawano S, and Kawahara Y collected the data; Hamada K critically reviewed the manuscript for important intellectual content; and Otsuka M approved the manuscript.

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SYSTEMATIC REVIEWS

Candy cane syndrome: A systematic review

Ricardo Rio-Tinto, Jorge Canena, Jacques Devière

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Abstract

BACKGROUND

Candy cane syndrome (CCS) is a condition that occurs following gastrectomy or gastric bypass. CCS remains underrecognized, yet its prevalence is likely to rise due to the obesity epidemic and increased use of bariatric surgery. No previous literature review on this subject has been published.

AIM

To collate the current knowledge on CCS.

METHODS

A literature search was conducted with PubMed and Google Scholar for studies from May 2007, until March 2023. The bibliographies of the retrieved articles were manually searched for additional relevant articles.

RESULTS

Twenty-one articles were identified (135 patients). Abdominal pain, nausea/vomiting, and reflux were the most reported symptoms. Upper gastrointestinal (GI) series and endoscopy were performed for diagnosis. Surgical resection of the blind limb was performed in 13 studies with resolution of symptoms in 73%-

100%. In surgical series, 9 complications were reported with no mortality. One study reported the surgical construction of a jejunal pouch with clinical success. Six studies described endoscopic approaches with 100% clinical success and no complications. In one case report, endoscopic dilation did not improve the patient's symptoms.

CONCLUSION

CCS remains underrecognized due to lack of knowledge about this condition. The growth of the obesity epidemic worldwide and the increase in bariatric surgery are likely to increase its prevalence. CCS can be prevented if an elongated blind loop is avoided or if a jejunal pouch is constructed after total gastrectomy. Diagnosis should be based on symptoms, endoscopy, and upper GI series. Blind loop resection is curative but complex and associated with significant complications. Endoscopic management using different approaches to divert flow is effective and should be further explored.

Key Words: Candy cane syndrome; Blind pouch syndrome; Post-gastrectomy syndromes; Side-to-side enteral anastomosis; End-to-side enteral anastomosis

Core Tip: Enteral resections with side-to-side or end-to-end anastomosis, if a long blind end is left in place and dilates, can cause symptoms that may appear many years later. The classic designation for this clinical condition is blind pouch syndrome, although it is possible to find references under other designations, causing confusion. Candy cane syndrome (CCS) is a particular case of the blind pouch syndrome following gastrectomy or gastric bypass. CCS was first reported in a 2007 paper describing a series of patients with gastrointestinal symptoms associated with a long blind loop proximal to the gastro-jejunostomy after gastric bypass and creation of an end-to-side anastomosis to a jejunal loop. With unknown prevalence, few reports and case series have described the condition. Yet, with the increasing prevalence of obesity and number of operations being performed worldwide, surgical complications such as CCS are expected to become more frequent. Knowledge of candy cane syndrome is important to avoid delays in diagnosis and inadequate treatments. Thus, the goal of this study was to collate evidence on CCS symptoms, diagnosis, treatments, and outcomes. To the best of our knowledge, no previous literature review on this topic has been published.

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INTRODUCTION

It has long been recognized that when long, blind enteral loops are left in place after a side-to-side or end-to-side anastomosis, they can dilate and be the cause of symptoms that may appear many years later[1]. The classic term for this clinical condition is "blind pouch syndrome", although it is possible to find references under other designations, causing confusion[2,3]. A particular case of blind pouch syndrome following gastrectomy or gastric bypass is called candy cane syndrome (CCS). CCS was first reported in a 2007 paper describing a series of patients with gastrointestinal (GI) symptoms associated with a long blind loop proximal to the gastro-jejunostomy after gastric bypass and creation of an end-to-side anastomosis to a jejunal loop[4]. Few case reports and retrospective studies have described this condition. However, with the increasing prevalence of obesity and number of obesity-related surgeries being performed worldwide, CCS is expected to become more frequent[5].

Probably, the pathophysiology of CCS is exclusively mechanical: A long, mispositioned blind loop preferentially directs luminal contents, increasing pressure and causing dilatation, pain, regurgitation, postprandial vomiting, and weight loss (Figure 1)[4-7]. Cachexia and spontaneous rupture of the blind loop are described[8,9]. Given its nonspecific presentation, the diagnosis of CCS is often subjective and based on clinical symptoms in conjunction with the endoscopic and/or radiographic appearance of a long and dilated blind jejunal limb proximal to the anastomosis, a finding which is known as the candy cane sign (Figure 2)[6,7,9,10].

CCS can be prevented by the avoidance of an unnecessary elongated jejunal (blind) loop proximal to the anastomosis during the initial surgery[2-4]. A blind loop of less than 3 to 4 cm is usually not associated with obstruction and therefore does not cause CCS. In addition, construction of a jejunal pouch after total gastrectomy prevents CCS and improves feeding, weight recovery, and quality of life[11-14].

For treatment, surgical resection of the dilated loop is curative but technically complex, due to previous surgeries and adhesions, and is associated with non-negligible morbidity[15,16]. Endoscopic management of CCS using various approaches to divert the flow from the blind loop is possible, safe, and effective[6,7,17-19].

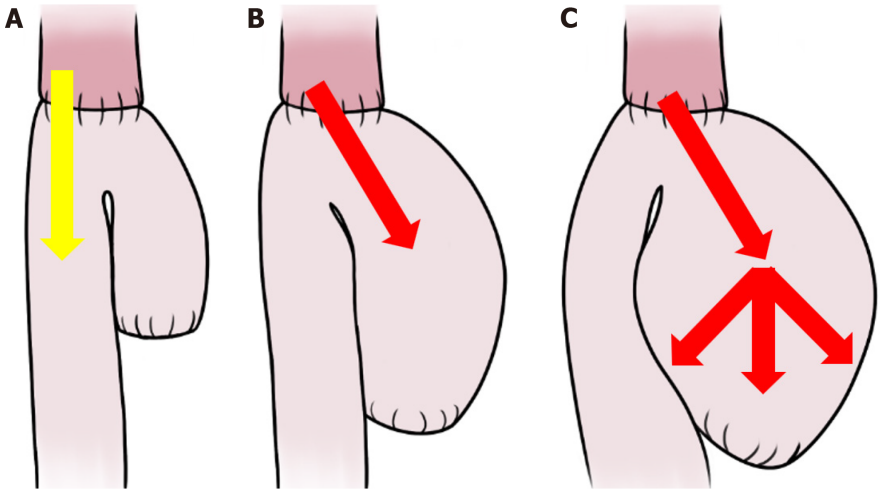

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Figure 1 An esophago-jejunal anastomosis. A: The optimal morphology of an esophago-jejunal anastomosis, where the blind loop is short, and the efferent loop is properly aligned (yellow arrow); B: A long blind loop preferentially aligned with the axis of the esophagus (red arrow) favoring the passage of food towards it; C: A blind loop filled with food compresses the efferent loop and progressively dilates (red arrows), which over time worsens patient's food intolerance.

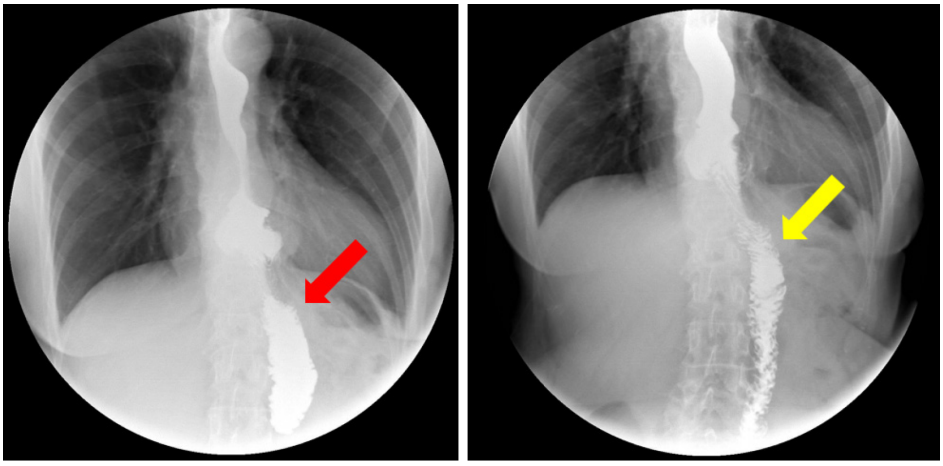

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Figure 2 An upper gastrointestinal series in a patient with candy cane syndrome demonstrates. Left, the preferential filling of the blind limb (red arrow). Right, a delayed "spill" of contrast to the efferent limb (yellow arrow).

Knowledge of CCS is important to avoid delays in diagnosis and inadequate treatments. Thus, the goal of this study was to collate evidence on CCS symptoms, diagnosis, treatments, and outcomes.

To the best of our knowledge, no previous literature review on this topic has been published.

MATERIALS AND METHODS

A literature search was conducted using the PubMed database and Google Scholar, and by searching the electronic links to related articles, from May 1, 2007 through March 31, 2023.

Search terms included candy cane syndrome, blind pouch syndrome, blind loop syndrome, afferent loop syndrome, Roux limb syndrome, post-gastrectomy syndromes, complications of gastrectomy, side-to-side intestinal anastomosis, end-to-side intestinal anastomosis, and symptoms (pain, reflux, regurgitation, vomiting, and/or weight loss) after gastrectomy. The latter terms were used in various combinations for the search. Language restrictions were not applied.

The bibliographies of the retrieved articles were manually searched for additional relevant articles. The articles were carefully read to identify only those exclusively focusing on candy cane syndrome.

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Figure 3 A keep-in-mind image: This condition was first called candy cane syndrome in 2007 in reference to the so-called cane-shaped candy.

RESULTS

In accordance with the search criteria, we identified a total of 21 articles (135 patients), including 13 case reports, 3 case series, 4 retrospective studies, and 1 prospective study. Among these studies, the most reported symptoms were abdominal pain, nausea/vomiting, and reflux. In addition, almost all studies performed upper GI series and endoscopy for diagnosis.

Fourteen studies reported surgical resection of the excessive and/or dilated blind limb (13 studies, 111 patients) or construction of an enteral pouch (1 study, 1 patient) with resolution of symptoms in 73%–100% of patients[4,15,16,20-24]. In one case, the surgical procedure was performed through thoracoscopy[25]. These studies reported a total of 9 complications (1 biliary leak, 3 infections, 1 anastomosis ulcer, 1 enterotomy, 1 hematoma, 1 pneumonia\hepatic infarction, 1 leak) with no mortality[16,20,22].

Seven studies, including 5 case reports, 1 case series, and the only prospective study available, described various endoscopic approaches: In two studies, a lumen-apposing metal stent was used to divert the luminal content into the efferent loop[18,26]; in another two cases, a suture device was used to prevent the passage of food content into the blind loop[17-19]. These approaches are technically complex and have low reproducibility; A case report and a prospective study used a magnetic device to cut the tissue between the blind loop and the efferent loop, creating a pouch and allowing the free passage of the food contents[6,7]. In this case, the food is not retained in the blind loop and progresses unhindered to the efferent loop. All these endoscopic approaches led to resolution of symptoms in 100% of patients with no reported complications. One case report described CCS treatment by endoscopic dilation, which does not divert the blind loop, without success[9] (Table 1).

DISCUSSION

CCS remains underrecognized and misdiagnosed due to a lack of knowledge about the condition. However, its manifestations have been described as common after gastrectomy[27]. In this review, we collected the current evidence on CCS symptoms, diagnosis, and treatment.

When the luminal contents preferentially pass into an overly long blind loop that retains food and distends, the characteristic symptoms of CCS appear, most commonly postprandial abdominal pain associated with nausea and vomiting. These symptoms can appear several years after surgery. Although CCS is a particular case of blind pouch syndrome, it has characteristics that justify being considered an independent clinical entity. As the obesity epidemic persists worldwide and the use of bariatric surgery increases, the prevalence of CCS will likely rise. Thus, CCS should be included in the group of post-gastrectomy syndromes and should be more readily recognized to avoid misdiagnosis, delayed treatment, and inappropriate interventions (Figure 3).

The differential diagnosis of CCS should include other surgical complications such as anastomotic stenosis, dysmotility syndromes secondary to surgery, and recurrence in cases of an oncologic indication for gastrectomy.

Collective evidence indicates that the diagnosis of CCS can be suggested based on clinical history and symptoms and should be confirmed by endoscopy and dynamic fluoroscopy.

The characteristic finding in upper GI series is a preferential filling of the blind loop followed by delayed passage of contrast into the efferent loop, the so-called "candy cane sign"[10].

Table 1 Studies reporting candy cane syndrome from May 2007 to January 2023

Ref.	Type of study	*n* of patients	Symptoms	Timing of symptoms	Specific test	Management	Improvement rate	Complications
Dallal *et al*[4], 2007	Case series	3	AP, N/V, GERD	3 wk, 1 year, 3 years	UGS, endoscopy	Surgical resection	1	None
Romero-Mejía *et al*[28], 2010	Case report	1	AP	2 years	UGS, endoscopy	Surgical resection	1	None
Biju *et al*[29], 2012	Case report	1	AP, N/V, GERD	9 years	Endoscopy, UGS	Surgical resection	1	None
Razjouyan *et al* [9], 2015	Case report	1	Dysphagia	2 mo	UGS, endoscopy	Endoscopic dilation	0	None
Aryaie *et al*[20], 2017	Retrospective	19	AP, N/V	3-11 years	UGS, endoscopy	Surgical resection	0.94	1 biliary leak
Marti Fernandez *et al* [30], 2017	Case report	1	AP	Not mentioned	UGS, endoscopy	Surgical resection	1	None
Granata *et al* [17], 2019	Case report	1	N/V, AP	1 year	UGS, endoscopy	Endoscopic suture	1	None
Khan *et al*[15], 2018	Case series	3	AP, N/V	1 year	UGS, endoscopy, CT	Surgical resection	1	None
Kommunuri *et al*[21], 2018	Case report	1	N/V, AP	6 years	UGS, endoscopy	Surgical pouch	1	None
Frieder *et al* [23], 2019	Retrospective	26	AP, N/V, GERD	10 years	Not mentioned	Surgical resection	0.92	1 leak
Cartillone *et al* [31], 2020	Case report	1	AP, D, Vasomotor	5 years	CT	Surgical resection	1	None
Kamocka *et al* [16], 2020	Retrospective	28	AP, N/V, GERD	Not mentioned	CT, endoscopy, UGS	Surgical resection	0.73	3 Infections, 1 anastomosis ulcer, 1 enterotomy, 1 hematoma
Cobb and Banki [25], 2020	Case report	1	Dysphagia, regurgitation	1 year	UGS, CT, endoscopy	Surgical resection[1]	1	None
Wundsam *et al* [18], 2020	Case series	4	Not mentioned	Not mentioned	Not mentioned	Endoscopic LAMS	1	None
Acín-Gándara and Ruiz-Úcar [22], 2021	Case report	1	Dysphagia, GERD, AP	Not mentioned	Endoscopy, UGS	Surgical resection	1	Pneumonia, hepatic infarction
Greenberg *et al* [19], 2021	Case report	1	AP, N/V, GERD	8 years	Endoscopy, UGS	Endoscopic suture	1	None
Rio-Tinto *et al* [6], 2022	Prospective	14	AP, N/V	Not mentioned	Endoscopy, UGS	Endoscopic marsupialization	1	None
Rio-Tinto *et al* [7], 2022	Case report	1	AP, N/V	24 mo	Endoscopy, UGS	Endoscopic marsupialization	1	None
Shamia *et al* [32], 2022	Retrospective	25	AP, N/V, GERD	Not mentioned	Endoscopy	Surgical resection	0.84	Not mentioned
Ouazzani *et al* [26], 2023	Case report	1	N/V, GERD	40 years	Endoscopy, UGS	Endoscopic LAMS	1	None
Prakash *et al* [24], 2023	Case report	1	GERD	15 years	Endoscopy, UGS	Surgical resection	1	None

[1]Thoracoscopy.

AP: Abdominal pain; N/V: Nausea/vomiting; GERD: Gastroesophageal reflux disease; UGS: Upper gastrointestinal series; CT: Computed tomography.

Endoscopy in patients submitted to gastrectomy or gastric bypass should include the careful exploration of the blind loop and of the passage to the efferent loop. In these patients, access to the blind loop is usually easy and direct, and access to the efferent loop is difficult and done after passing through an angulation[21].

When CCS does arise, effective treatment options are available. Surgical resection of the excessively long and/or dilated loop is curative. However, this method is technically complex, due to previous surgeries and adhesions, and is associated with serious complications in a significant number of patients. By contrast, endoscopic management of CCS using various approaches to divert the flow from the blind loop is safe and effective and should be further explored.

CONCLUSION

CCS is still an unknown diagnosis for most physicians, including gastroenterologists who are often the first clinicians to deal with these patients.

Although it is underreported, the prevalence of CCS is probably higher than is commonly thought. Its diagnosis is based on clinical, endoscopic, and imaging findings. Symptoms such as dysphagia, pain, regurgitation, or reflux after food intake are relatively frequent in patients after gastrectomy or gastric bypass and should lead to a detailed clinical investigation. Although surgical revision of the blind loop is an effective treatment, it is associated with complications in frail patients with comorbidities. Sectioning of the septum and marsupialization is the current standard mini-invasive treatment for esophageal diverticula. The development of a simple and safe endoscopic technique, such as the blind loop marsupialization described in the only existing prospective study, will in our opinion be the preferred treatment for CCS in the future.

ARTICLE HIGHLIGHTS

Research background

Candy cane syndrome (CCS) is a particular case of the blind pouch syndrome after gastrectomy or gastric bypass, so named in a 2007 paper describing a small series of patients with gastrointestinal symptoms associated with a long blind loop proximal to the gastro-jejunostomy after gastric bypass and creation of an end-to-side anastomosis to a jejunal loop. The pathophysiology of CCS appears to be predominantly mechanical, as an excessive long or mispositioned blind loop proximal to the anastomosis may preferably direct food and increase luminal pressure, causing dilatation, early satiety, fullness, pain, reflux, regurgitation, post-prandial vomiting, weight loss, and, ultimately, inability to eat and cachexia.

Research motivation

CCS remains underrecognized and misdiagnosed due to the lack of knowledge about this condition, however, its manifestations have been described as common after gastrectomy. Since gastroenterologists are often the first clinicians to come into contact with patients with CCS, it is important that this clinical condition be part of the list of differential diagnoses for patients with digestive symptoms after gastrectomy or gastric bypass. To our knowledge, there is no published review on this subject.

Research objectives

The objective of this work was to systematically gather all the published evidence on CCS, in order to make this clinical condition known and to systematize the diagnostic and therapeutic approach.

Research methods

A literature search was conducted using PubMed and Google Scholar, and by searching in addition to electronic links to related articles, from May 1, 2007, through March 31, 2023. Search terms included candy cane syndrome, blind pouch syndrome, blind loop syndrome, afferent loop syndrome, Roux limb syndrome, post-gastrectomy syndromes, complications of gastrectomy, side-to-side intestinal anastomosis, end-to-side intestinal anastomosis, and symptoms (pain, reflux, regurgitation, vomiting, and/or weight loss) after gastrectomy. The bibliographies of the retrieved articles were manually searched for additional relevant articles.

Research results

We found 20 articles on CCS, most case reports or case series in which the treatment was surgical, usually resection of the blind loop. In seven articles the treatment was endoscopic, using lumen-apposing metal stents to divert the passage of the luminal contents (two case reports), suture devices to close the blind loop (two case reports), or by cutting the septum between the blind loop and the efferent loop, promoting the marsupialization of the blind loop (one clinical case and the only prospective study available). In one case, balloon dilatation was performed, without clinical success. In general, treatment results are good, but the surgical approach is associated with complications in a significant number of patients.

Research conclusions

CCS remains an under-recognized clinical condition and since gastroenterologists are usually the first clinicians to come into contact with these patients it is important to make it more familiar. As the number of bariatric surgeries increases, it is likely that the number of patients with CCS will increase as well. CCS patients are usually frail, with comorbidities, and it is important to establish the best diagnostic and therapeutic approach. Surgical treatment is effective but is associated with complications and there is still no optimal and reproducible endoscopic treatment.

Research perspectives

We believe that, in the same way that the treatment of Zenker's diverticulum has changed from surgery to the endoscopic section of the diverticular septum, in a simple, fast, effective and reproducible procedure, marsupialization of the septum between the blind loop and the efferent loop can become the ideal treatment for CCS.

FOOTNOTES

Author contributions: Rio-Tinto R reviewed the literature and wrote the manuscript; All authors critically reviewed the manuscript.

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