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EVOLUTION OF ESOPHAGEAL STRICTURE TREATMENT BY USE OF STENTS IN BENIGN AND MALIGNANT CONDITIONS

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ABSTRACT

The esophagus is a muscular membranous organ that participates in the swallowing process by passing solid and liquid substrates from the pharynx into the stomach. The embryonic endoderm, mesoderm, and neural crest cells participate in the development of the esophagus. The pathology of the esophagus is very varied and surgical correction techniques require numerous improvements and refinements. The most common condition is Barret's esophagus due to gastroesophageal reflux, but strictures can also occur either from neoplastic causes or from chemical burns. Studying the anatomy and physiology of the esophagus is essential for both internal medicine and surgical approaches. The treatment of esophageal strictures in recent times is done with esophageal stents. These are made of a variety of materials including metal, polymer, or biodegradable. Clinical results are very good but complications are quite common. The first attempt at stenting was made in the mid-19th century using an ivory tube. In the case of ingestion of caustic substances dilation and stenting have very good results. Immediate and late complications are multiple and can range from pain to failure of the stent to expand completely.

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Introduction

Embryology of the Esophagus

The esophagus is a tube with striated and smooth musculature that conducts the food bowl from the laryngopharynx to the stomach. Embryologically the esophagus develops from the foregut. The development of the digestive system is achieved by growth factors in four axes. Antero-posteriorly under the influence of the growth factors Wnt5a, Six2/Sox2, and Hoxa-2,3,4 proteins. These factors contribute to the migration of neural crest cells. In weeks 7 and 8 the foregut lumen proliferates and almost completely occludes the epithelium [1].

In week 10 a vacuolization process begins in the lumen creating the foregut lumen covered by a ciliated epithelium. During the 4th developmental moon, the ciliated epithelium is replaced by a squamous epithelium layered with small islands of ciliated epithelium that will give rise to the oesophageal glands. Thus the endoderm is the source for the mucosa and submucosal glands. During the 6th week of gestation, the musculature and myenteric plexus are formed. During week 7 the blood vessels are formed. The smooth muscle of the lower pate of the mesogastrium derives from the somite mesenchyme surrounding the foregut.

The striated muscle in the upper part of the esophagus derives from the mesenchymal arches 4, 5, and 6. The middle part of the esophagus containing both striated and smooth fibers is not known. In week 9 the circular and longitudinal smooth muscles along the rostro-caudal axis are differentiated. In week 4 the neural crests migrate rostro-caudally to form the myenteric plexus

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so that in week 7 they reach the hindgut. In week 6 the neural crests also start migrating through the circular layer to form the submucosal plexus. In week 9 the interstitial cells of Cajal form. Cajal cells form after smooth muscle cell differentiation and do not require the presence of neural crests [2, 3].

Normal Anatomy

The esophagus is the structure of the digestive tract with a length between 18 and 26 cm. The distance of the esophagus during the passage of food is 2 cm anteroposteriorly and 3 cm laterally [4]. Bartholian esophagus is a fairly common pathology of the esophagus and is attributed to gastroesophageal reflux [5].

Topography of the Esophagus

The topography of the esophagus can be divided into two regions. Thus we have the cervical region from the hypopharynx to the thoracic inlet. The upper thoracic esophagus is bounded superiorly by the thoracic inlet and inferiorly by the lower border of the azygos vein. The middle thoracic esophagus is bounded superiorly by the inferior border of the azygos vein and inferiorly by the inferior pulmonary vein. The lower thoracic esophagus is bordered superiorly by the inferior pulmonary vein and inferiorly by the stomach [6].

Pathology

Esophagitis is considered the most common inflammatory esophageal disease. Esophagitis can be manifested by the thickening of the longitudinal folds due to edema and inflammation. In some cases of chronic reflux oesophagitis, an oesophageal inflammatory polyp may occur, which is in the form of a single transverse polyp at the cardiac orifice. Scarring due to gastro-oesophageal reflux disease can be explored using barium passage examination is represented as longitudinal folds converging towards the scarred site. The continuation of the inflammatory phenomenon eventually leads to a circular stricture located above a hiatal hernia.

Sometimes it can appear as a ring formation which must be differentiated from the Schatzki ring in people with diphagia. Scarring of the esophagus can also lead to a shortening of the esophagus in the longitudinal axis giving the appearance of a step ladder. These must be distinguished from the fine longitudinal striations known as feline esophagus, which occurs as a reaction to reflux [7].

Barret's esophagus is caused by metaplasia of the oesophageal mucosa into the gastric or intestinal mucosa and occurs in approximately 10% of patients with gastro-oesophageal reflux. The main function of the oesophageal mucosa is to protect the underlying tissue from ingested food and fluid. The lining of the oesophageal mucosa contains minor salivary glands that secrete bicarbonate to neutralize acid reflux from the stomach. The oesophageal mucosa also has muscularis mucosae which can be used as a demarcation criterion from other overlying and underlying structures [8, 9].

Optical Microscopy and Immunohistochemistry

In ultrastructural and immunohistochemical studies the presence of numerous cell types was observed, including melanocytes, Langerhans cells, Merkel cells, and inflammatory cells such as lymphocytes. All these cells lack desmosomes, the only exception being Merkel cells. Melanocytes produce melanin in melanocytes and are secreted among keratinocytes. These cells lack both tonofilaments and desmosomes. Another type of cell present is Langerhans cells which can migrate from the epithelium into regional lymph nodes and can present antigen to T helper lymphocytes. Merkel cells present tonofilaments and desmosomes and are thus attached to surrounding cells. They play a role in touch detection. As for inflammatory cells, polymorphonuclear lymphocytes and mast cells can be found [10].

Physiological Studies of the Esophagus

The upper esophageal sphincter is an area where increased pressure is exerted and is positioned at the border between the larynx and the upper part of the esophagus. This area has elastic and tonic properties that allow it to expand sufficiently to allow the food bowl to pass. From a functional point of view, the upper oesophageal sphincter is considered to prevent the food bolus from returning into the airways and preventing a large amount of air from entering the digestive tract [11-13].

The anterior part is formed by the cricoid arytenoid cartilage and the internal arytenoid muscle. In the posterior part, the sphincter structure is formed by the cricopharyngeus and thyropharyngeus muscles. As the food bolus passes the upper oesophageal sphincter, signals are sent to the Instituut center in the brainstem which sends signals to contract the sphincter. Also stimulated in this process is the cessation of breathing during the passage of the food bolus. The structure of the esophagus is made up of four layers, the deepest being the mucosa, followed by the submucosa, the muscularis with a longitudinal and a circular layer, and finally the outermost serosa. The interaction between the circular and longitudinal layers is manifested by the reduction of tension in the circular musculature, with the help of the longitudinal layer.

The swallowing process is different in the striated muscles compared to the striated muscles. Thus the striated muscle is controlled by the ambiguous nucleus in the bulb which sends excitatory signals for contraction while the smooth muscle is controlled by the dorsal nucleus of the vagus which sends relaxation signals simultaneously to the entire smooth muscle of the esophagus. The difference is made by the fact that the distal muscle relaxes for a longer time.

The lower sphincter is a high-pressure area located at the entrance to the stomach that possesses no dilation mechanism. The only factor that allows food to enter the stomach is the relaxation of the smooth muscles [14].

Adenocarcinoma of the esophagus may appear in patients with a barred esophagus if an additional risk factor such as obesity is present.

Esophageal Stricture

Malignant and benign esophageal strictures can be treated endoscopically by a procedure called stenting. There are several types of stents including fully coated removable selfexpandable plastic stents (SEPSs), self-expandable metallic stents (SEMSs), and biodegradable stents. A SEMS stent is composed of a mesh of a tough, non-woven material such as stainless steel nitinol, or polymers coated with a silicone shell. The main drawback of this type of stent is migration due to persistence. The frequency of this phenomenon has been reported in 30-50% of cases. In choosing the type of stent to be implanted the guidelines recommend 6 steps;

Compression force testing, Expansion force testing, Corrosion testing, Tensile strength tests, Deployment testing, and Dimensional testing. Among the latest technologies for the study of oesophageal stenosis is the bio-mimicking robotic soft esophagus (RoSE). The implantation of oesophageal stents is a useful method for the treatment of malignant and benign stenosis, providing immediate relief of symptoms. However, this procedure is followed by adverse events such as stent migration [15].

Symptoms of esophageal stenosis include dysphagia, odynophagia, aspiration, or chest pain. Long-term stenosis can lead to weight loss and malnutrition. As for benign esophageal stenosis, the most common causes include peptic reflux, radiation, caustic substances, Schatzki ring, and post-surgery strictures.

First-line therapy in the treatment of strictures is endoscopic dilation. The main contraindication is incomplete healing of the perforation, with other contraindications being an inability to sedate the patient, hemodynamic instability, or coagulopathy. Fluoroscopic guidance is used for stenting or when the superior approach is not possible, the retrograde approach through the stomach can be used.

Either balloon or spark plug dilation can be used, with studies showing no significant difference between the effectiveness of the two methods. Complications of dilation may include perforation, bacteremia, or hemorrhage. The risk of perforation is between 0.1% and 0.6%, that of hemorrhage less than 0.5%, and that of bacteremia is higher, ranging from 2-23%. However, guidelines do not routinely recommend antibiotic prophylaxis. About 80-90% of strictures can be treated with dilatation. However, about 30% of patients experience a recurrence of stenosis [16].

Anatomically simple strictures are short, focal, and straight. Complex strictures are longer than 2 cm, irregularly shaped, angulated, or with a stenotic lumen.

Pharmacological methods of treatment include steroid injections which are supposed to reduce the inflammatory reaction and collagen production. Another substance used is Mitomycin C, which like steroids has the effect of reducing scar formation after surgery. Other methods include surgical incisions applied to Schatzki rings and anastomotic strictures.

The use of temporary stents is considered an effective method of preserving the patent lumen during scar formation in the healing process. Biodegradable stents that do not require endoscopic removal have also been developed [17].

Another technique for repairing esophageal injuries is tissue engineering, which was first introduced in the 1990s. This technique involves the collaboration of several fields including medicine, molecular biology, physics, and biochemistry. This technique involves the reconstruction of tissue ex vivo and subsequent implantation in vivo for the reappearance of lesions.

Strictures are the main complication after surgery on the oesophageal mucosa in the case of neoplasm. One of the drugs used to prevent strictures is Tranilast which is from the anti-allergic class, it prevents the formation of collagen and IL-6. It has been shown to be more effective in reducing stricture formation than endoscopic dilation.

There are currently two tissue engineering techniques. One cost is the application of an extracellular matrix together with a stent. The second technique involves the use of a thermo-responsive polymer on which cell cultures are grown at 37 degrees C and when the temperature is lowered the cells detach, with the advantage that they retain their matrix, unlike enzymatic detachment [18].

In surgical practice, due to limited resources, some improvisations such as orotracheal tubes have been used as a palliative treatment with acceptable results [19].

Biodegradable stents are capable of maintaining radial tension for approximately 8 weeks, and their degradation eliminates the need for endoscopy, thus eliminating patient disc discomfort and surgery costs [20].

The first attempt to treat malignant strictures dates back to 1845 when stenting with a tube made of ivory was tried. The first clinical trial dates back to the 1960s also on patients with malignant strictures. Another indication for stenting is esophageal leakage which can contaminate the mediastinum and consequently lead to septic shock. The etiology of oesophageal leakage can be benign or malignant. The malignant one includes tracheal esophageal fistulas and the benign one can be spontaneous as in Boerhaave's syndrome, iatrogenic during endoscopy or after esophageal reconstruction [21].

In the case of iatrogenic esophageal perforation, which is a life-threatening condition, the standard clinical practice in the past was surgery and drainage, but in recent years the introduction of esophageal stents offers a viable alternative for these conditions. Thus the use of a temporal stent can treat oesophageal leakage but the time required to hold the stent in place must be individualized for each patient [22].

A rarer pathology that may require esophageal endoprosthesis for palliative purposes is breast cancer metastasis. In this case, the procedure faces the same risk of prosthesis migration as in other diseases.

Esophageal perforation is a rare but potentially life-threatening condition. It was first reported by Hermann Boerhaave in 1724 after repeated episodes of vomiting. In cases of perforation, the prosthesis acts to limit bacterial penetration, occludes underlying perforations, and postpones surgery if the patient is hemodynamically unstable [23].

In the case of caustic ingestion studies have shown that strictures occur between 3-57% and respond to medical and dilatory treatment between 64-100%. Those that do not respond require complex surgery. In these cases stenting should be maintained for several weeks with periodic endoscopic monitoring to monitor for displacement [24-26].

Esophagus duplication is a rare condition more commonly seen in children than in adults. This condition has two forms, cystic in 80% of cases or tubular in 20% of cases. If it is decided not to resect the cyst surgically to remove the obstruction, the use of endoprosthesis is an extremely useful method [27, 28].

For advanced esophageal cancers, elective treatments are considered to be radiotherapy and esophageal stenting. In terms of complications, no deaths were reported during the procedures and complications occurred in about 28% of cases. Chest pain was the first complication as frequency of 18.7%. The second was stent occlusion 13.1%. Tumor growth in 9.7% of patients. Food blockage was recorded in 3.4% of the patients studied. Reflux symptoms had 9.4% of patients. Cough was observed in 5.7% of patients. Nausea or vomiting was also reported. Bleeding occurred in only 3.1% of patients and was of mild intensity. Aspiration pneumonia was also reported. In 2.9% of patients, the stent was mispositioned. The stent did not expand in 2.6% of patients [29-31].

Conclusion

Malignant and benign esophageal strictures can be treated by an endoscopic procedure called stenting. Stents can be made of metal, polymer, or biodegradable. The most common problem with esophageal stenting is stent migration. The first attempt at stenting was made in the mid-19th century using an ivory tube. In the case of ingestion of caustic substances dilation and stenting have very good results. Immediate and late complications are multiple and can range from pain to failure of the stent to expand completely.

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