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HISTORY OF ONCOLOGY

Hallmarks in history of esophageal carcinoma

Marianna Karamanou[1], Kostas Markatos[2], Theodoros G. Papaioannou[3], George Zografos[4], George Androutsos[5]

[1]University Institute of History of Medicine, Faculty of Medicine, Claude Bernard Lyon 1 University, Lyon, France; [2]Henry Dunant Hospital, Athens, Greece; [3]Biomedical Engineering Unit, 1st Department of Cardiology, Hippokration Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece; [4]1st Propaedeutic Surgical Dept, Hippocrateio Hospital, Medical School, University of Athens, Athens, Greece; [5]Biomedical Research Foundation, Academy of Athens, Athens, Greece

Summary

Esophageal cancer is one of the deadliest cancers due to its aggressive behavior and poor survival. It was mentioned in the works of ancient Chinese and Arabo-islamic physicians, centuries before the recognition of high incidence in the Asian esophageal cancer belt. Till the 19th century the disease was considered incurable and the main goal of the proposed treatments was to alleviate dysphagia and pain. The introduction of esophagoscope in 1868 by Adolf Kussmaul (1822-1902) contributed to the observation of the living esophagus and to the diagnosis of esophageal pathologies, paving the way for new therapeutic approaches. In 1877, Vincenz Czerny (1842-1916) performed the first successful resection of the cervical esophagus for carcinoma, followed by Franz Torek (1861-1938) who carried out in 1913 the first successful subtotal thoracic esophagectomy and Tohru Ohsawa (1882-1984) who performed the world's first esophagectomy with an intrathoracic esophagogastric anastomosis. Nowadays, despite the advent of biomedical technology and the development of operation techniques, the surgical treatment of esophagus still remains a challenge.

Key words: *gastrointestinal cancer, history of oncology, Vincenz Czerny, Tohru Ohsawa*

Across the globe, esophageal cancer is considered the eight most common cancer and the sixth most common cause of cancer-related death. Gastro-esophageal reflux disease, cigarette smoking, alcohol consumption and obesity are implicated as causal factors. The majority of esophageal tumours are squamous carcinomas and adenocarcinomas arising in areas of squamous metaplasia (Barrett's oesophagus). Regardless of the cell type, esophageal cancer has an aggressive biologic behavior. Tumours rapidly infiltrate the two-layer esophageal wall while the rich vascular and lymphatic supply facilitates the spread to regional lymph nodes. Advanced disease, appearing mainly with dysphagia and weight loss, is common at the time of presentation and contributes to high mortality rates. The geographic variation in the incidence of esophageal cancer still remains noteworthy. The Asian oesophageal cancer belt which spans from North-Central China to Iran and the eastern to southern Africa belt, records high incidents of the disease since antiquity [1].

Evidence for esophageal cancer in China and Iran arises from the writings of ancient Chinese and Arabo-islamic physicians. Ancient Chinese medical literature, going back more than 2000 years ago, seems to recognize esophageal cancer as a distinct disease entity commonly seen in the

Correspondence to: Marianna Karamanou MD, PhD. 4, Themidos str, Kifissia, 14564, Athens, Greece. Tel: +30 6973606804, E-mail: mariannakaramanou@yahoo.com

elderly, presenting with dysphagia and having a poor prognosis : "those discovered to suffer in the autumn...will not live through the next summer" [2]. Centuries later, the eminent Greek physician Galen (130-201), mentioned fleshy growths partially or entirely obstructing the esophagus associated with cachexia and a fatal outcome [3]. In the 11th century, the distinguished Arab physician Avicenna (980-1037) included tumours of the esophagus among the causes of dysphagia [4]. In Arab population a mixture of dietary and social customs seem to have been the main causative factor: drinking very hot beverages like tea, eating the residue from opium pipes, consuming goat and sheep meat and having a dietary lack in fruits and vegetables. In his turn, Avenzoar (1091-1162), a leading authority of Arabo-islamic medicine, known for his work on cancer, in his book *al-Taysir* (Book of Facilitation), described the symptoms of esophageal cancer as "beginning with mild pain and difficulty in swallowing" and suggested the insertion of a long silver cannula into the esophagus for pouring liquids [5]. Furthermore Avenzoar believed that stomach had an attractive power which drew-upwards any nourishment present in any part of the bowel. For this reason, he was also proposing rectal feeding in the form of nutrient enema containing milk, eggs and gruel in patients presenting with cancer of the esophagus [6].

Renaissance physicians documented several cases of esophageal cancer in an attempt to collect and systematize medical knowledge. Jean Fernel (1497-1558), one of the most outstanding medical figures of renaissance, in his *De Morbis Universalibus et Particularibus*, described the case of a woman who died in consequence of a large hard mass located in the esophagus [7] (Figure 1) and few years later, the Dutch anatomist Volcher Coiter (1534-1576) mentioned the case of a woman who was suffering for eight years of dysphagia and died. In autopsy, he noticed the presence of an enlarged tumour obstructing the lower end of the esophagus [8]. During that period, the last entry in the diary of the British physician John Casaubon (1637-1693) is deplorable. He described the first signs of his own fatal illness, cancer of the esophagus: "At dinner I was almost choaked by swallowing a bit of a roasted sirloin mutton which as I thought stuck in the passage about the mouth of the stomach. But it suffered noething to goe downe and the stomach threw all up, though never so small in quantitie... an unusuall afflixion which my melancholie suggested it an extraordinarie judgment...I grew as lean as a skeleton and at some tymes very faint and feeble, although I

Figure 1. The physician and humanist Jean Fernel (1497-1558).

recovered in some measure and had stomach to eate, my meate doeth noe great good and I am in a kind of atrophie" [9]. In the following centuries, the invention of microscopy and the advent of pathology contributed further to the study of esophageal cancer. The precursor of pathology Théophile Bonet (1620-1689) recorded several cases of esophageal growths which provoked obstruction, leading to death [10]. In 19th century, the British surgeon Sir Everard Home (1756-1832) was the first to link the esophageal strictures to cancer [11].

However, the disease was considered incurable and the main goal of the proposed treatments was to alleviate dysphagia and pain. If the cancerous lesion was situated at the orifice of esophagus, physicians were using cautery or cutting forceps. Also an astringent mixture was prescribed containing persulfate iron and starch to reduce the size of the tumour. The patient was receiving a specific diet based on nutritive and non irritating foods such as milk, eggs, broth and soft farinaceous substances. In cases of esophageal strictures and severe obstruction physicians were passing once or twice a week a bougie through the stricture to achieve dilatation and to facilitate food ingestion [12]. Moreover, during that period, several studies started to link esophageal cancer to alcoholic and absinth consumption, one of the most popular alcoholic beverages of late 19th century containing wormwood (Artemisia absinthium L) [13].

In 1868, Adolf Kussmaul (1822-1902) performed the first esophagoscopy using a modification of the cystoscope invented in 1853 by the French urologist Antonin Jean Desormeaux (1815-1894). Kussmaul attached a 47mm long and 13 mm wide tube which included a speculum and he passed the scope down to stomach (Figure 2). He tested with success his device initially to a professional sword-eater. It was a major contribution in the observation of the living esophagus and in diagnostics of esophageal pathologies, paving the way for new therapeutic approaches [14,15]. Few years later, in 1877 Kussmaul's son-in-law and one of the brightest assistants of Theodor Billroth (1829-1894), Vincenz Czerny (1842-1916), resected a carcinoma of the cervical esophagus without restoring the continuity of the esophagus [16,17] (Figure 3). The patient was a 51-year-old woman who was suffering from dysphagia for months. Czerny made an incision from the level of the hyoid bone down to the sternum along the anterior edge of the sterno-mastoid on the left side; the omo-hyoid muscle was divided, the thyroid body was pushed upward and inward, and the esophageal tumor, which could then be felt with the finger, was carefully dissected out. A segment of the gullet, involving the upper 6 cm of the canal, was removed, and the upper orifice of the lower section of the divided tube was stitched to the edges of the skin-wound. A catheter, through which the patient could be fed, was then passed into the esophagus through the wound, and the lips of the superficial incision were brought together. By the fourth day the sutures were removed, and the catheter was replaced by a large hollow bougie, which initially was left permanently in situ, but shortly afterwards it was taken out and it was introduced when nourishment had to be given. The patient learned to feed herself by using the sound. However, a year after the operation recurrence of the disease appeared to an extent that Czerny had to perform tracheostomy. She died some weeks after the operation. Despite the fatal outcome of the case, Czerny performed a challenging operation as preo-operative imaging, blood transfusion, advanced anesthesia and antibiotics were missing [12]. In 1913, the versatile surgeon Franz Torek (1861-1938) performed, in the German Hospital of New York, the first successful subtotal thoracic esophagectomy. The histology confirmed a squamous cell carcinoma of the esophagus and an anthracotic lymph node. The patient, a 67-year-old woman who presented with progressive dysphagia and weight loss, lived free of disease for twelve years and she died of pneumonia [18,19].

However, almost twenty years passed between the first and second successful esophagectomy proving the challenge of a safe esophagectomy posed to surgeons at that time, as the postoperative mortality rate was reported to be 91%. In 1929, the Japanese surgeon Tohru Ohsawa (1882-

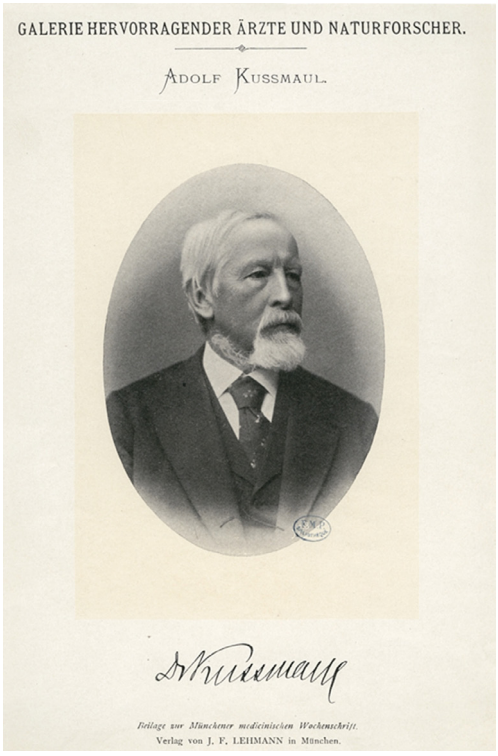

Figure 2. The German physician Adolf Kussmaul (1822-1902) who performed the first esophagoscopy.

Figure 3. The surgeon Vincenz Czerny (1842-1916) who resected the upper esophagus for cancer in 1877.

1984) reported the first use of stomach for reconstruction of resected esophagus and carried out the world's first successful esophagectomy with an intrathoracic esophagogastric anastomosis. Furthermore, he performed in eight patients suffering with carcinoma of the lower esophagus and cardia, a simultaneous esophagectomy and esophagogastrostomy [20].

Nowadays, 90 years after Ohsawa's operation and despite the advent of technology and the development of surgical techniques, the surgical treatment of esophagus still remains a challenge. Minimal invasive esophagectomy brought down the operative mortality and morbidity while the integration of chemotherapy and radiation helped to improve survival outcomes [21].

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