Head & neck cancer. Its impact on the history of mankind

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Abstract

Squamous cell carcinoma is the most common head & neck malignancy, and its first descriptions date from the pharaonic era. It has impacted humanity by affecting labor, scientific and cultural productivity and, sometimes, it has influenced the course of history. Head & neck cancer is more common in economically impoverished countries and individuals; however, it can affect any socioeconomic stratum; it has been suffered by known, famous, economically powerful celebrities, intellectuals and artists. Head & neck cancer treatment has been controversial since its initial description up to the present day. Therapeutic decisions have been influenced not only by the stage but by the patient's environment and, sometimes, in an effort to reduce the morbidity resulting from the various oncological treatments, erroneous decisions have been made that have implied the loss of the patient's life. Unfortunately, currently we continue to see these behaviors. A synthesis of cases of renowned celebrities that suffered from this cancer is presented, and the impact this implied in the society of their times is described.

KEY WORDS: Squamous cell carcinoma. Head. Neck. History of medicine.

Cáncer de cabeza y cuello. Su impacto en la historia de la humanidad

Resumen

El cáncer epidermoide es el más frecuente en cabeza y cuello y sus primeras descripciones datan de la época faraónica. Ha impactado en la humanidad al afectar la productividad laboral, científica y cultural y, en ocasiones, ha influido en el derrotero de la historia. El cáncer de cabeza y cuello es más frecuente en países e individuos depauperados económicamente, sin embargo, puede afectar cualquier estrato socioeconómico; lo han padecido personajes conocidos, famosos, económicamente poderosos, intelectuales y artistas. El tratamiento del cáncer de cabeza y cuello ha sido motivo de controversia desde su descripción inicial hasta la actualidad. En la decisión terapéutica ha influido no solo el estadio del cáncer sino el entorno del paciente; en ocasiones, en un afán de disminuir la morbilidad derivada de los diversos tratamientos oncológicos, se han tomado decisiones erróneas que han implicado la pérdida de la vida del enfermo. Infortunadamente, en la actualidad seguimos viendo estas conductas. Se presenta una síntesis de casos de connotados personajes que presentaron este cáncer y se describe el impacto que ello implicó en la sociedad de ese momento.

PALABRAS CLAVE: Epidermoide. Carcinoma. Cabeza. Cuello. Historia de la medicina.

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Introduction

Squamous cell carcinoma originating in the mucous membranes of the head and neck is the most common malignant tumor in that area. It is considered a health problem, given that it affects working-age people. Sometimes, the sequelae of treatment or of the neoplasm itself are devastating for the individual and can make it difficult, and even impossible reintegrating the patient to his/her socio-economic environment.¹

Despite progresses in the knowledge of the biology and prognostic factors of this neoplasm and advances in diagnostic and therapeutic methods, mortality continues to be high due to a delay in its identification: 500,000 new cases are estimated to be diagnosed annually in the world, 60 % at locoregionally advanced stages, which implies an approximate 5-year survival of 50 %.²⁻⁴

Squamous cell carcinoma of the head and neck has been known since time immemorial, and although there is evidence of this condition since the pharaonic era, it was not paid attention to until five celebrities suffered from it at different times in history: Emperor Frederick III of Germany, US presidents Ulysses Simpson Grant and Grover Cleveland, Sigmund Freud and the famous musician and operatic composer Giacomo Puccini, who due to this condition left the *Turandot* opera unfinished. This is how efforts for early recognition of this cancer and the search for the best therapeutic alternative began.

Historical background

The earliest traces of head and neck carcinoma were found in Egyptian mummies dating back 5000 years B.C.; at least three cases of nasopharyngeal cancer (endemic in the area to date) and three cases of maxillary osteosarcoma have been identified in them.

In the Ebers Papyrus, written in the time of Amenophis I, early in the 16th century B.C., the case of a cancer in the mucosa of the lower gum that was treated with tumor ablation using a red hot metallic instrument is described. Numerous tracheotomies are also described for the management of tumors that blocked the airway. In the 1st and 2nd centuries, the Greeks Celso and Galen reported various carcinomas on the lip and tongue. In addition, skulls with lesions in the paranasal sinuses have been found in excavations

from the time of imperial Rome dating from the 1st to 3rd centuries of our era.

Despite these descriptions and findings, head & neck cancers went unnoticed and were little mentioned in history, until the personalities that motivated our paper were diagnosed with this disease.^{5,6}

Prince Frederick larynx cancer

Frederick III of Hohenzollern, last Emperor of Prussia, a heavy pipe smoker, heir to the throne for 27 years, finally succeeded his father as King of Prussia and German Emperor in March 1888. In 1871, supported by Chancellor Otto von Bismark, he created the Second Reich and favored the German unification and the adhesion of the Imperial Territory of Alsace and Lorraine in a lavish ceremony held in the gallery of mirrors of the Palace of Versailles.

In January of 1887, being the first in the line of succession to the throne and with 56 years of age, he suffered a cold that caused dysphonia, which was looked after until March of that year. Professor Gerhardt, who performed the clinical examination, identified a "polypoid lesion in the left vocal cord", for which he prescribed symptom treatment, without improvement. Two months later, doctors van Bergman and Todd suggested a laryngofissure (medial thyrotomy) to perform a biopsy on suspicion of laryngeal cancer. The prince's physician, Dr. Wegner, Princess Victoria and Queen Victoria, (Prince Frederick's wife and mother-in-law) leaned towards the opinion of Dr. Morell Mackenzie, a famous English laryngologist,⁷ who ruled out the existence of cancer and diagnosed "laryngeal syphilis". A biopsy of the lesion was taken by direct laryngoscopy and was evaluated by the famous histopathologist Rudolf Virchow,⁸ who reported pachydermia; treatment continued to be symptomatic.

Due to the worsening of the condition, another biopsy was performed, which was again negative for cancer. Dr. Mackenzie instituted treatment with iron chloride baths; however, the dysphonia was increasing and data consistent with respiratory distress appeared. In June, the doctors palpated a cervical adenopathy; despite the evidence, Mackenzie still denied that it was laryngeal cancer, and the condition was left to evolve freely. In February 1888, 13 months after the onset of dysphonia, the prince had to undergo emergency tracheotomy. The procedure was bloody; the doctors had to insert their fingers across the tumor to open the trachea; there was transoperative bleeding and Prince

Frederick almost died. As a sequel of the surgery, a cervical and peristomal abscess was formed, which persisted until the ruler's death.

On March 9, 1888, Emperor William I of Germany died and Frederick III ascended to the throne. People on the streets chanted "the emperor is dead, long live the dying emperor". In the days following his coronation, the new emperor expelled tumor fragments through the tracheostomy stoma, which were analyzed by Waldeyer and only thus the histological result, squamous cell carcinoma of the larynx, was obtained. Despite the evidence, Mackenzie continued to support his laryngitis diagnosis. Progression of the condition was accelerated and the tracheostomy cannula was repeatedly blocked by tumor fragments, which caused severe respiratory distress. Finally, in June 1888, 17 months after the onset of dysphonia, the emperor died due to massive hemorrhage caused by the tracheostomy. Frederick III is known as "the 99-day emperor".

The death of the emperor implied a disaster for Germany and for the world. Frederick III was a liberal; however, his successor, his son William II, who was authoritarian and impulsive, blocked the pacifist policy of Chancellor Otto von Bismarck and encouraged the conflict that led to World War I, which cost 2 million deaths to Germany and 10 million to the world, and where 70 million human beings were mobilized to the front lines.

The first total laryngectomy had been described in 1874 by Billroth. In France, the first series of laryngectomized patients was detailed by Labbé in 1885. The technique had been described by both these authors and by Gluck in Germany, by Périer in France and by Tapia in Spain, and thus the way to proceed in laryngeal cancer was known. Management was probably conservative, since mortality within the first week after total laryngectomy was 40 %, with a survival of only 8.5 %, as reported in a series of 103 laryngectomies published by Wolfender in 1887. The case of the emperor focused the attention on timely diagnosis, initial symptoms, the causes of the neoplasm and the mistakes made in diagnosis and treatment.^{9,10} Paradoxically, these errors regarding laryngeal cancer are still observed to date.

General Grant and oropharyngeal cancer

Ulysses Simpson Grant is a very popular general in the United States because he was chief of staff of the Union troops in the Civil War, and because his victory

over General Lee brought peace to that nation. A heavy cigar and cigarette smoker since the age of 23, he was elected 18th president of his country in 1869.

In June 1884, seven years after having completed his term as president, he complained of odynophagia and in October of that year, doctors de Acosta and Douglas issued the diagnosis of cancer of the oropharynx. The tumor invaded the tonsil, the palatine veil and the base of the tongue, onto which it was fixed; it was accompanied by bilateral lymphadenopathy in the neck. Transmandibular oropharyngectomy was proposed; however, after reassessment, the procedure was discarded. The general retired to write his memoirs and nine months later died, amidst economic ruin, neuropathic pain, periods of asphyxia and constant hemorrhages from the oral cavity.

Transmandibular oropharyngectomy was described by General Grant's treating physicians: Sands, Douglas and Shadry; however, due to hemorrhage, surgical wound infections and to the advanced stage, the procedure was not performed. In France, transmandibular oropharyngectomy was reported in 1906 by Vallas and Latarjet, but it was Dargent, in 1952, who obtained better results with a careful patient selection. Finally, the procedure was popularized in the 1950s by Hayes Martin in New York, who called it a COM-MAND operation, due to the type of combined access (oral and cervical), which reminded the Canadian commands in the battle of Dieppe in then recently concluded World War II.¹⁰⁻¹²

President Grover Cleveland and cancer of the oral cavity, hard palate subsite

Grover Cleveland –a lawyer, member of the Democratic Party and considered the father of financial orthodoxy– was elected as the 22nd President of the United States in 1884. At the beginning of his second presidential term, he noticed a lump on the hard palate, which prompted him to seek medical help. His case exemplifies the importance of timely diagnosis, adequate treatment and the importance of oral cavity tumors resection.

When Dr. O'Reilly, the White House doctor, saw the lesion, he took a biopsy that was secretly submitted for analysis; the report indicated invasive squamous cell carcinoma. The president feared that making the diagnosis public would unleash financial panic on Wall Street; therefore he decided to be treated in secret. The large hall of a private yacht anchored in New York was adapted as an operating room. Due to the president's

corpulence and short neck, anesthesia had to be combined with nitrous oxide and local cocaine injections. The resection encompassed from the first premolar to the intermaxillary region, lasting one hour and 45 minutes; the postsurgical cavity was plugged with a iodine wick. The surgery was carried out by Dr. Joseph Bryan, who had published a review of 250 maxillectomies (out of which only two had been performed by him). Evolution was adequate and a rubber prosthesis perfectly sealed the site where the surgery was performed, which allowed adequate swallowing and language articulation. The president died 15 years later from other causes, without ever having experienced a relapse.

President Grover Cleveland's disease was made public in 1917, and thanks to its good evolution, the treatment, follow-up and rehabilitation of patients undergoing this type of interventions were given importance.¹⁰⁻¹⁴ In 1980, the case was reevaluated and it was concluded that it had been a verrucous carcinoma of the hard palate, which explains the good prognosis with a single therapeutic variety.¹⁵

Giacomo Puccini

Giacomo Antonio Domenico Michele Secondo Maria Puccini, the famous Italian composer, was born in 1858 in Luca, in Tuscany, Italy. He has been considered the greatest opera composer of the late 19th and early 20th centuries. His famous works include *Manon Lescaut*, *La Bohème*, *Tosca*, *Madame Butterfly* and *Turandot*, with the latter being left unfinished due to the progression of the author's laryngeal cancer.¹⁶

Puccini, an intense cigarette and cigar smoker, consulted with different otolaryngologists in February 1924 for dysphonia, otalgia, dysphagia and odynophagia. The diagnosis was "rheumatic inflammation of the throat", for which he received symptomatic treatment. In November of that year, he noticed weight loss, increased otalgia and that he was unable to close the shirt collar due to cervical lymph nodes growth. In Florence, Torregiani diagnosed him with "supraglottic extrinsic cancer of the size of a nut". In those days, laryngeal carcinomas were classified as intrinsic (with slow evolution and good prognosis) and extrinsic (with palpable lymph nodes in the neck, aggressive and of poor prognosis, with the recommendation therefore being to leave patients to evolve freely). A biopsy confirmed squamous cell carcinoma.^{10,16}

There are several situations that influenced the treatment decision that was made with Puccini: his quality as a noted musician, the morbidity total

laryngectomy entailed in those days, the uncertainty that he would benefit from conservative laryngeal surgery and the advent of a novel treatment, radiation, which was chosen in order to avoid mutilation. Puccini went to Brussels, where the only European center that offered radiation was located.¹⁷ Ledoux started treatment with a "necklace that contained radius", about which Puccini complained: "they are crucifying me like Christ. I have a necklace around the throat with radiation in it; it is torture".

A few days later, under local anesthesia, Ledoux inserted seven needles with radiation in the composer's neck, performed a tracheostomy and placed a nasogastric tube; the procedure took three hours. Regarding his condition, Puccini wrote: "I feel like I have bayonets in my throat. This is horrible!" Four days later, Puccini had a terminal hemorrhage from the mouth and tracheostomy, and died on November 29, 1924, at dawn, which reminds of the finale of his aria *Nessun Dorma*, when Prince Calaf sings *All'alba, vincerò!*

Puccini died without concluding the opera *Turandot*, thus depriving humanity of a surely extraordinary "finale". *Turandot* last two scenes were finished by Franco Alfano under the supervision of Arturo Toscanini. The night of the premiere at *La Scala*, Toscanini himself, who directed the orchestra, interrupted the performance where the *maestro* had left the composition, turned to the audience and said: "This is where the opera concludes, because here is where the *maestro* died".

The composer popularity and the therapeutic novelty of the moment, radiation, influenced on total laryngectomy and neck dissection not being performed as it was indicated, even though the technique had been described more than three decades earlier and there was enough experience.^{10,16,18} The wrong therapeutic decision was probably based on various factors other than the extent of the neoplasm. Even today, in locoregionally advanced neoplasms, preserving the larynx is not the best decision, despite the therapeutic novelty of treating with chemotherapy and radiotherapy. With this treatment at its peak, mortality of patients with laryngeal cancer due to non-cancer-related causes has been reported to have increased, perhaps due to treatment-associated complications.¹⁹

Sigmund Freud and cancer of the oral cavity and central facial skeletal structures

Of Austrian nationality, born in Moravia, father of psychoanalysis and a heavy, regular consumer of cigars, Freud had a tumor on the hard palate discovered

at 67 years of age. He was evaluated by Dr. Majek, who tried to resect the tumor,²⁰ but the procedure had to be interrupted due to major bleeding. Only a biopsy was obtained, which revealed a squamous cell carcinoma. Radiation therapy was advised, given the “non-resectable” nature of the tumor, which persisted despite radiation. Dr. Pischler initially performed an external carotid ligation, lymph node resection and large resection of the oral cavity in the area of the intermaxillary region and the palatine veil; the defect was occluded with a forearm graft.²¹

In addition to complementary radiotherapy, Freud was advised to have vasectomy performed in order to “slow down aging”. After radiotherapy, a palatal rubber obturator was placed, which was repeatedly adjusted to the surgical cleft. Over the ensuing 13 years, Freud underwent 32 operations with the purpose to resect carcinoma foci on the palate and maxillary remnant; he suffered a destruction of the central facial skull, both by the tumor and due to cocaine habitual consumption.²² Finally, he had massive tumor progression to the central facial skull and oropharynx, which caused his death in 1939.

Although a 13-year survival was achieved in Freud, the neoplasm never disappeared. Again, we are faced with different non-cancer-related factors that influence on therapeutic decisions. With radical maxillectomy, which was described by Genzoul in France since 1827, radical excision of the tumor would probably have been achieved, along with adequate control. Ferguson had even already replaced the original transoral with the transfacial route (still in use today). This approach was never tried in Sigmund Freud, without the reason for that decision being known.¹⁰

The impact of head & neck cancer on other celebrities in history

The celebrities mentioned below had head & neck cancer; some of them were subjected to medical malpractice. Many other celebrities have died due to this neoplasm, although the impact of this fact on the development of humanity has not been as transcendent as in the referred cases. Some of the most renowned include the following:

- John Steele, paratrooper of the 82nd Airborne Division, who, when being dropped during Operation Overlord in 1944 (the Normandy landings), had his parachute caught in one of the pinnacles of the Saint Mère Eglise church tower, leaving him hanging. He saved his life by not being able to

participate in the battle, where most of his comrades died. Years later, in 1969, he died of laryngeal cancer.

- Lana Turner, American actress, famous for countless films, especially *The Postman Always Rings Twice*, died in 1992 from cancer of the hypopharynx and cervical esophagus.
- Sylvia Kristel, an actress who was native to Utrecht, the Netherlands, icon of erotic cinema of the 1970s and 1980s for the movie *Emmanuelle*, died in 2012 due to oropharyngeal cancer related to heavy smoking.
- Jack Klugman, recognized for playing the leading character of the TV series *Dr. Quincy*, died of laryngeal cancer in 2012.
- Russell Means, known for his role in the movie *The Last Mohican*, perished in 2012 due to oral cancer (tongue).
- René Houseman, who was soccer world champion with the Argentina national team in 1978, died of tongue cancer in 2018.
- Juan de Borbón, father of the emeritus king of Spain, Juan Carlos de Borbón, died of laryngeal cancer.
- Prince Tomohito, in the line of succession of the Japanese Empire, died of supraglottic laryngeal cancer associated with alcoholism.
- Aldous Huxley, British writer, famous for his novel *A Brave New World*, died of laryngeal cancer.
- William Hanna, producer of *The Flintstones* among other cartoon series, died of laryngeal cancer.
- Jack Hawkins, a British actor famous for his performance in *Land of the Pharaohs* and *Lawrence of Arabia* and remembered as Quintus Arrius in the 1959 *Ben-Hur* movie, died of laryngeal cancer.
- Katharine Hepburn, actress, died of oropharyngeal cancer.
- Ed Sullivan, famous for conducting the television show that had his name and where he presented the Beatles for the first time in America, died of oropharyngeal cancer.
- George Harrison, member of the Beatles and heavy smoker, developed two primary tumors, bronchogenic and larynx; complications of the latter ended his life.
- Sammy Davis Jr., actor, died of laryngeal cancer.
- Babe Ruth, a regular cigar smoker, died of oropharyngeal cancer. He set a record for home runs in the major baseball leagues in 1935, a record that was broken until 1974 by Hank Aaron.

- Henry of Prussia, son of Frederick III, just like his father died of laryngeal cancer associated with the intense habit of smoking tobacco.
- Tito Vilanova, coach of the Barcelona Soccer Football Club, died of parotid cancer.

In recent years numerous public figures have been diagnosed with squamous cell head and neck cancers, although they have survived them:

- Michel Douglas, who, after to the proper management of his oropharyngeal cancer, controlled with chemotherapy and radiotherapy, has become an activist for the timely detection of this neoplasm.
- Edie van Halen, rock performer, had tongue cancer.
- Bruce Dickinson, vocalist of the Iron Maiden rock group, had tongue cancer.
- Charlie Watts, drummer for The Rolling Stones, had laryngeal cancer.
- Val Kilmer, who played the protagonist of one of the Batman movies, had laryngeal cancer.

Conclusion

Currently, head & neck cancer ranks sixth among all neoplasms. In Mexico, 60 to 70 % of patients are diagnosed at advanced stages, in which 5-year survival hardly exceeds 50 %, even with all therapeutic resources available. The causes of this include patients' lack of knowledge about their risk factors, underestimation by patients themselves of incipient symptoms and signs such as dysphonia, mouth ulcers or oral bleeding and lack of knowledge of primary care doctors about the warning signs that are indicative of immediate referral to the specialist.

Survival improvement is achieved, as in other neoplasms, not with more radical or expensive treatments, but with diagnosis at early stages and implementation of a therapeutic approach (even non-radical), which offers better oncological control and survival.

Despite being widely known, as I have described, mistakes are still being made in this neoplasm in terms of diagnosis and treatment, as it occurred to Emperor Frederick III of Prussia and Giacomo Puccini.

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