

# Treatment of Laryngeal Cancer in 33-Year-Old Female - A Case Report

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## Summary

Laryngeal cancer is a rare cancer whose diagnosis and treatment is a challenge for both oncologists and ENT specialists. The risk of developing laryngeal cancer is 8 times higher in men than in women. The highest incidence rate is observed in the population older than 50 years of age. Environmental factors and substance use are most important in the aetiology of laryngeal cancer, and exposure to tobacco smoke and high-proof alcohol has the highest carcinogenic potential.

Laryngeal cancer in young non-smoking women is a very rare condition. In this article, the authors have presented a case of a 33-year-old woman with squamous cell laryngeal carcinoma, with negative environmental risk factors. 41 months have passed from the first symptoms noticed by the patient to the diagnosis, despite regular ENT examinations and numerous specialist consultations.

The patient underwent surgical treatment followed by adjuvant radiochemotherapy. Despite a very long time period between the onset of the first symptoms and the start of the treatment, good local control and overall survival were achieved.

## Introduction

Laryngeal cancer is a rare cancer whose diagnosis and treatment is a challenge for both oncologists and ENT specialists. According to the report of the Polish National Cancer Register, 1933 new cases of laryngeal cancer were noted in men and 291 - in women in 2017 in Poland, representing 2.3% and 0.4% of all cancers cases among men and women, respectively.

The risk of developing laryngeal cancer is 8 times higher in men than in women. The highest incidence rate is observed in the population older than 50 years of age. In women, it reaches peak values at the turn of the fifth and sixth decades of life and in men - in the seventh decade of life. In Poland, the incidence

of laryngeal cancer in men was growing up to the 1990s and since the mid-1990s it is decreasing. Among women, the incidence of this condition remains at a stable level. This reflects the trend toward a declining number of smoking men and constant levels of smoking-dependent women. Less than 4% of patients with this diagnosis are younger than 45 years of age [1,5,8].

Laryngeal cancer aetiology is strongly related to environmental factors and substance use. Tobacco smoke and high-proof alcohol are the most carcinogenic factors in this setting. The habit of concomitant tobacco smoking and alcohol drinking increases the risk of laryngeal cancer development by a factor of about 330. Additional risk is related to the exposure to the wood dust, charcoal dust and asbestos. Additionally, alimentary deficits play an important role in the development of laryngeal cancer: a diet deficient in A and C vitamins and polyunsaturated fatty acids, and consumption of highly processed food, especially canned food. The role of immunological and genetic factors in the development of laryngeal cancer is currently under extensive investigation [5].

The effect of gastroesophageal reflux disease (GERD) on the incidence of laryngeal cancers in non-smokers is also of note. In a study by Bacciu et al., 36 non-smoker and alcohol-abstinent patients with laryngeal cancer were compared with 125 non-smoker and alcohol-abstinent patients without any neoplastic disease. In patients with laryngeal cancer, they have found a higher incidence of gastroesophageal reflux disease than in the control group. In this study, attention was drawn to the effect of continuous irritation of the larynx by gastric acid as a factor favouring the development of laryngeal cancer. These results confirm the fact, that gastroesophageal reflux disease may be associated with an increased risk of laryngeal cancer development [7].

Among young non-smoking women, laryngeal cancer is an extremely rare disease. A case of a 33-year-old patient diagnosed with squamous cell carcinoma of the larynx is presented below.

### Description

KS, a 33-year-old woman, diagnosed with squamous cell carcinoma of the larynx, reported to the Centre of Oncology in Krakow in November 2016 for adjuvant radiotherapy. The first symptoms of the neoplastic process appeared in 2013, which indicates that they preceded the final diagnosis by three years. During this time, the patient was repeatedly consulted by laryngologists and remained under constant ENT care.

The first symptom experienced by KS was hoarseness that appeared in May 2013. Laryngological examination carried out at that time showed the presence of a polyp on the right vocal cord but this diagnosis was not confirmed during further observation. Persistent hoarseness was the reason for a phoniatic consultation, and fiberoptic examination performed during this consultation showed impaired mobility of the right vocal fold. It was suggested that pressure of an intrathoracic tumour might be the cause of this impairment, however no tumour was found on chest CT. At the same time new symptoms appeared: chronic fatigue and weakening of the voice force. Fiberoptic examination was repeated in January 2014, and a diagnosis of chorditis was made. This condition was treated with glucocorticosteroids and phonophoresis. After three-month therapy the symptoms were still present. During this time, the patient was regularly, monthly, examined by a phoniatic with use of a videostroboscope.

In December 2014, due to persistent hoarseness (present for more than a year), the patient was reconsulted by a laryngologist who found palsy and monochorditis of the right vocal fold. In 2015, numerous consultations were performed (by specialists in endocrine medicine, gastroenterology, rheumatology, neurology and hemodynamics) that excluded extralaryngeal causes of the persistent hoarseness. A follow-up CT scan of the larynx showed asymmetry of the laryngeal structures at the level of the vocal folds. This was suggestive of paralysis of the right vocal fold and a diagnosis of idiopathic vocal cord paralysis was established.

At the end of 2016 (41 months after the first symptoms), dyspnoea, weakness and progressive swallowing difficulties appeared. The patient was consulted by a cardiologist and a pneumonologist and these consultations showed no abnormalities. The above symptoms aggravated during the subsequent weeks. Due to dyspnoea and stridor the patient was transported to an emergency department. Bilateral immobility of vocal folds was found on laryngological examination. Imaging studies showed the presence of a tumour. It involved all levels of the larynx, the main mass was centralised within the glottis and had necrotic areas. It penetrated towards the neighbouring structures: laryngeal adipose body, subhyoid muscles, the left vocal fold and the right aryepiglottic fold.

The patient underwent tracheotomy and tumour specimens were collected. Histopathological examination revealed squamous cell carcinoma. The patient was referred for surgery. The surgery, performed in the Greater Poland Cancer Centre, included complete laryngectomy with partial right pharyngectomy, removal of the right thyroid lobe and selective right cervical lymphadenectomy (RND, IIA, IIB, III, IV).

### Adjuvant Treatment

The patient was then referred to the Centre of Oncology in Cracow (Poland), where adjuvant combined radiochemotherapy was performed, due to clinical stage T4N0 of the disease. In radiotherapy, the technique of simultaneous integrated boost was used (SIB-IMRT). The target volume was based on a fusion of MRI and CT scans performed prior to the total laryngectomy and MRI and PET scan performed post surgery. A total dose of 60 Gy, at 2.0 Gy fractions, was administered to the CTV - the area of an increased risk of microscopic residual disease. The elective area (ETV) received a total dose of 54 Gy, at 1.8 Gy fractions. As the pre-radiotherapy PET scan did not reveal any foci of pathologically elevated glucose metabolism suggestive of an active neoplastic process, no GTV was defined. The patient was irradiated once daily, five days per week.

Radiotherapy was administered concomitantly with chemotherapy. The patient received cisplatin at a dose of 100mg/m<sup>2</sup>. After the first cycle, the patient developed G2 leukopenia, G3 neutropenia and ototoxic symptoms. Symptomatic treatment was used – steroid therapy, intravenous electrolyte infusions and antifungal prophylaxis. Patient's condition improved and the symptoms resolved. During the subsequent chemotherapy courses the treatment regimen has been modified; a dose of 35 mg/m<sup>2</sup> was administered at 7-day intervals. The patient received 3 cycles of the treatment according to the above regimen in total, with good immediate tolerance.

Radiation-induced reaction on the mucous membranes and on the skin was monitored during the treatment. The patient was seen three times per week and the CTCAE V criteria were used. Early radiotherapy toxicity included G2 skin and mucous membrane reaction within the irradiated area. This reaction improved after symptomatic treatment was started.

The patient remains under regular outpatient follow-up. The last follow-up visit took place in January 2020. Both on clinical examination and on imaging (CT), no signs of cancer recurrence were found.

### Discussion

The average time for diagnosis of the laryngeal cancer in Poland (from the onset of clinical symptoms to the histopathological diagnosis) varies from 60 to 365 days (190 days on average). This period is significantly affected by the onset of patient's symptoms, the time after which the patient visits the physician, and the time when the necessary examinations are performed to make the appropriate diagnosis. Reduction of this time

directly affects treatment results, which in the case of laryngeal cancer is associated with organ sparing, which in turn has a significant impact on patient's quality of life. Laryngectomy, to the contrary, is often associated with social exclusion of the patient, because of the loss of speech function and breathing or swallowing difficulties.

In the presented case, the patient reported to the doctor 2 weeks after the onset of the first symptom, i.e. hoarseness. Laryngitis was diagnosed initially, which however did not resolve after the treatment used. Hoarseness was a sole symptom in this patient for a long time. Only shortly before cancer diagnosis, dysphagia and dyspnoea appeared. Young age of the patient and a negative history of typical risk factors, such as smoking and frequent consumption of alcohol, caused that cancer was not taken into consideration in the first place. In a young woman, it can be assumed that hoarseness has other causes, more commonly seen in medical practice than cancer. These can be the following: laryngitis, a polyp of the vocal fold, singer's nodules, allergic oedema, gastroesophageal reflux disease, thyroid function disorders, systemic lupus erythematosus, rheumatoid arthritis, injury of laryngeal muscles or nerves. The patient underwent numerous consultations (by gastroenterology, endocrine medicine, rheumatology, neurology, hemodynamics specialists), which have not identified the cause of persistent hoarseness, present since more than ten months at that time.

The factor that makes the patient seek medical assistance early is appearance of symptoms suggesting a pathological condition. The first symptoms are often underestimated by the patient, as they imitate common inflammatory conditions. Over the time, along with the development of the neoplastic disease, the symptoms depend on cancer stage, tumour location in the larynx, directions of cancer spread and infiltration of the neighbouring areas [6].

Carcinoma of the laryngeal aspect of the epiglottis is initially asymptomatic, and in later stages the patient experiences pain on swallowing and a sensation of obstructed throat; these symptoms are sometimes accompanied by haemoptysis. Cancer of the vestibular fold manifests initially as periodic hoarseness that evolves into chronic hoarseness over time. Lowered pitch of patient's voice may be another symptom of this cancer. Cancer of the laryngeal ventricle develops asymptotically for a long time and the nature of clinical symptoms depends on the direction of cancer spread and involvement of specific laryngeal structures. In the course vocal fold cancers, chronic hoarseness occurs very early. In contrast to the above, very long asymptomatic periods are typical for cancers of the subglottic area. This depends on the nature of its growth. This cancer forms a sort of "wallpaper" layer over the laryngeal walls, which only at an advanced stage causes a reduction of the laryngeal lumen resulting in severe dyspnoea [4,5,6].

Prognosis in laryngeal cancer depends on clinical stage and location of the disease. The best treatment results are achieved for cancers of the glottic area, where the 5-year survival rate is about 90% with mobile vocal folds. Epiglottic cancer has a 5-year survival rate of 80% in patients with negative lymph

nodes and 40% - in patients with positive lymph nodes. Pharyngeal cancer of the subglottic area has a poorer prognosis [4,6].

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