

UNIVERSITY OF MEDICINE AND PHARMACY CRAIOVA

DOCTORAL SCHOOL

PHD THESIS

– ABSTRACT –

ROLE OF RADIO-IMAGING EXAMINATION IN DIAGNOSIS OF PHARYNGOLARYNGEAL NEOPLASIA

PHD ADVISOR:

PROF. UNIV. DR. BONDARI ANDREI

PHD STUDENT:

RAICA VICTOR PAUL

CRAIOVA

2019

TABLE OF CONTENTS

| | | |
|-------------|---|----------|
| I. | INTRODUCTION | 3 |
| II. | LEVEL OF KNOWLEDGE | 4 |
| III. | PERSONAL CONTRIBUTIONS | 5 |
| | 1. Objectives of personal study | |
| | 2. Materials and methods | |
| | 3. Radio-imaging examination techniques used for diagnosis and assessment of pharyngolaryngeal neoplasia | |
| | 4. Analysis of radio-imagistic changes | |
| | 5. Discussion | |
| IV. | FINAL CONCLUSIONS | 8 |

Keywords:

Pharyngolaryngeal neoplasia, radioimaging characteristics and modifications, diagnosis and staging, histopathology, squamous carcinomas.

I. INTRODUCTION

Pharyngo-laryngeal cancer is one of the neoplastic pathologies commonly encountered in the ENT departments.

More than 300,000 patients with pharyngeal and laryngeal cancer are diagnosed annually in the world, and more than 185,000 people die from these cancers. Of these neoplasms, approximately 165,000 cases are pharyngeal cancers and over 136,000 patients are affected by laryngeal cancers.

The rates of incidence of pharyngeal and laryngeal neoplasia worldwide, standardized in age groups, are 12.7 / 100,000 for men and 3.7 / 100,000 for women.

Most of the pharyngeal and laryngeal neoplasias are squamous cell carcinomas according to histological results. The main risk factors for the appearance of these squamous cell carcinomas are smoking and alcohol consumption.

The prevalence of smoking among the population is very high in recent years, reaching up to 48.7% according to data from 2015, being statistically more frequent among men.

Alcohol consumption is also incriminated in the occurrence of pharyngeal or laryngeal cancers.

Associated, tobacco and alcohol, represent the risk factors responsible for approximately 51% of the pharyngeal and laryngeal neoplasms in the United States, 84% of these diseases in Europe, and 83% in Latin America. The combined impact of tobacco and alcohol consumption is greater than the sum of individual harmful effects of each, resulting in a multiplier increase in the risk of pharyngeal and laryngeal cancers.

Besides the two above-mentioned risk factors, infection with HPV is a significant risk in the development of malignancies in pharynx and larynx, most commonly affecting the oropharynx.

The diagnosis and the evaluation of pharyngo-laryngeal neoplasia are essential for optimal treatment. The purpose of radio-imaging exploration in pharyngo-laryngeal neoplasia is to identify the tumor masses as soon as possible, properly staging the disease, highlighting the presence of complications, and monitoring response to treatment.

Radio-imaging exploration plays an important role in the staging of malignant pharyngo-laryngeal tumors, in monitoring response to treatment, in detecting relapses, and in evaluating complications. Radio-imaging investigations for the evaluation of pharyngo-laryngeal neoplasms include computed tomography and magnetic resonance imaging. In addition, nuclear imaging methods - PET-CT- can be used.

The advantage of computed tomography (CT) is its good anatomical resolution, soft tissue contrast and detailed morphology. CT is a routine method to study pharyngo-laryngeal neoplasia, becoming indispensable when cartilage or bone segments are involved.

II. LEVEL OF KNOWLEDGE

The pharynx is a connective segment in the form of a semi-cylindrical tube that makes the connection between the nasal fossa and the larynx, and the mouth and esophagus, respectively, thus providing the passage for both food and air flow, the digestive tract intersecting at this level with the respiratory one. The functions that the pharynx performs are: swallowing, breathing, phonation, hearing and protection.

The larynx is a segment of the respiratory system with dual-function: it guide the air to and from the lungs, and at the same time constitutes the main organ of the phonation. The functions of the larynx are as follows: respiration, phonation, and also protection.

The lateral deep cervical spaces are located on both sides of the pharyngeal visceral axis. They are divided into pre and retrostiloïd spaces. Retropharyngeal space is a virtual median space, located behind the posterior pharyngeal wall and anterior to the vertebral column, continuing to inferior with the posterior mediastinum, which implies a thoracic tomographic examination if the pathological process affects this space.

The radio-imaging techniques of pharyngo-laryngeal cancer are: CT, MRI and PET-CT.

Radio-imaging exploration plays an important role in the staging of pharyngo-laryngeal neoplasms, in monitoring treatment response, in detecting relapse, and in evaluating complications.

The objectives of radio-imaging explorations in pharyngo-laryngeal neoplasia are: detection of tumor lesions, loco-regional or distant extension; the existence of loco-regional adenopathies; imaging staging of pharyngo-laryngeal neoplasias for treatment.

The pharyngeal and laryngeal neoplasms are usually studied together as a result of their anatomical proximity, the invasion of the two regions being frequently encountered at the time of diagnosis, usually delayed. There are large differences in the geographical distribution of pharyngo-laryngeal cancer, with increased incidence in India, Brazil, Central and Western Europe. The maximal incidence is seen in the age group 50-59 years, but frequent cases have been reported in patients aged 45 to 60 years. There is also a marked predominance of male cases.

From the point of view of the anatomo-pathological diagnosis, 95% of the pharynx and larynx neoplasia are squamous carcinomas.

The appearance of pharyngeal and laryngeal neoplasia is frequently associated with exposure to a number of risk factors. As with the majority of head and neck-afflicting neoplasms, the following factors are incriminated in the occurrence of pharyngo-laryngeal malignancies: tobacco and alcohol consumption, genetic factors, occupational and food factors, and pre-existing pathological lesions in these regions. Recent research has added HPV infection, Epstein-Barr virus, and other viruses to the list of risk factors in the development of pharyngo-laryngeal neoplasms.

The overall trend is to increase the incidence of pharynx and larynx cancer, both in women and men, through the continuous increase of tobacco and alcohol consumption.

Positive and staging diagnosis is based on anamnesis, ENT clinical examination with endoscopy, radiographic and imaging examination, ultrasound examination, scintigraphic examination, usual laboratory exams, tumor biopsy, biopsy/dissection of lymph node, histopathological examination.

Therapeutic options, depending on the location, stage and histology type, are surgical resection, chemotherapy and radiotherapy.

III. PERSONAL CONTRIBUTIONS

1. The objectives of the personal study

The purpose of this paper is to assess the role of radio-imagistic exploration techniques in the diagnosis and assesment of pharyngo-laryngeal neoplasia. This objective required the study of elementary radio-imagistic modifications, both general and applied to each type of localization.

2. Materials and methods

The paper comprises a retrospective and prospective study, which includes a number of patients admitted and treated between 2014-2018. Cases have been selected from Colțea Clinical Hospital, Bucharest. The prospective study required the elaboration of an examination protocol, depending on the clinical suspicion of the type and localization of pharyngo-laryngeal neoplasia.

The retrospective study concerns the radio-imagistic assessment of malignant pharyngo-laryngeal diseases in their diagnosis and after appropriate treatment of each type of neoplasia. To achieve the retrospective study the images and the results of the examinations performed in the Colțea Bucharest Clinical Hospital during 2014-2016 were analyzed for the patients with pharyngo-laryngeal neoplasms.

In the 209 cases of pharyngo-laryngeal neoplasms studied in this paper, gender distribution revealed a major predominance of male to female sex, with 93.30 percent of male patients.

Distribution by age group in the analyzed group showed that the highest incidence of pharyngo-laryngeal neoplasia is in the decades of age 50-59 years and 60-69 years. Thus, 33.97% of the patients were aged 50-59 years, and 44.02% of the studied cases were in the 60-69 age group.

3. Radio-imaging examination techniques used for diagnosis and assesment of pharyngo-laryngeal neoplasia

Radio-imaging investigation is required in any suspicion of malignant pharyngo-laryngeal tumors. Computed tomography exam is the first choice, due to the accuracy of identifying changes in the pharynx and larynx.

Computed tomography was used in all 209 cases studied, being necessary both for the diagnosis of pharyngeal and laryngeal malignancies and for the staging of these conditions.

The characteristics of the equipment, the contrast media used and the technique of its administration were as follows:

- CT – Siemens Duo Emotion, multislice of 2mm, contiguous, FOV 200, KV 130, mA 100, mAs 58.
- Water-soluble iodinated contrast agent, concentration of 350mg / ml, intravenously with injector system, the minimum flow rate of 2.5 ml / sec, with a delay of 25 seconds at the first acquisition postcontrast.

4. The analysis of radio-imagistic changes

This paper attempts an evaluation of radio-imaging techniques in the diagnosis and evaluation of pharyngo-laryngeal neoplasia. For this purpose, I analyzed the following radio-imaging changes within the study group: radio-imaging aspect (protruding mass, parietal thickening, nodule, mucosal asymmetry), localization (rhinopharynx, oropharynx, hypopharynx, larynx or extensive), contours and dimensions of tumor mass, their behavior in contrast media administration, neoplasia extension in adjacent tissues, cervical vascular structures impairment, presence of associated cervical adenopathies, presence of distant secondary determinations and histological type of pharyngo-laryngeal neoplasia.

5. Discussions

The total number of 209 cases includes 201 cases of squamous cell carcinoma, representing 96.17%, 5 patients with lymphoma, corresponding to 2.39%, 2 cases of adenocarcinoma, representing 0.96%, and one patient with verrucous carcinomas, corresponding to 0.48% of the total study group.

Concerning the form encountered in the pharyngeal and laryngeal neoplasia, the most frequently highlighted was the protruding mass present in 181 subjects, representing 86.6%, followed by the parietal thickening that was highlighted in 19 patients, representing 9.09%, then the nodular form in 6 patients (2.87%) and the mucosal asymmetry in only in 3 patients, representing 1.44%.

From localization point of view, I found that the most affected segment is the pharynx, regardless of the form or type of neoplasia (42.58%), followed by extensive localization affecting both pharynx and larynx (35.89%) and then of laryngeal localization (21.53%).

Regarding the dimensions of the pharyngeal and / or laryngeal malignant tumors, the patient grouping was performed according to the 2 and 4 cm threshold values according to the most recent TNM staging criteria. One hundred and seven of the patients in the study group had maximum diameters of over 4 cm, thus being classified

as T3, representing 51.2% of the total patients. A total of 59 patients presented tumor sizes ranging from 2 to 4 cm, belonging to the T2 stage, representing 28.23%. The remaining 21 subjects, representing 10.05%, showed dimensions below 2cm, being in the T1 stage.

With regard to the contours of pharyngeal and / or laryngeal neoplasia, 193 out of 209 patients, representing 92.34%, the margins of malignant tumor mass was ill-defined and irregular, and in 16 cases constituting 7.66%, the contours of the tumor was described imagistically as being net, regular or well defined.

The intratumoral necrosis areas were present in 142 subjects, representing 67.94%, being absent in the remaining 67 patients representing 32.06% of the study group.

Concerning the behavior of the contrast media, in all 209 cases, the contrast enhancement has been noted. In this study, 71 of the subjects, representing 33.97%, showed intense enhancement of the contrast substance; in 132 patients, constituting 63.16% of the study group, contrast enhancement was moderate, and the remaining 6 (2.87%) the enhancement was poor.

As for the extension of malignant tumor masses in adjacent tissues, it was present in a number of 185 subjects, representing 88.52%, in the remaining 24 cases, constituting 11.48%, the invasion of the adjacent structures was not highlighted.

The impairment of the cervical vascular structures was highlighted in 73 patients, representing 34.93%. Of these, 31 subjects, representing 42.47%, had vascular damage by direct invasion of the major vessels of the cervical region by the tumor mass, leading in all cases to compression, caliber narrowing, and flow disturbances. In the remaining 42 patients, representing 57.53%, vascular damage was due to the presence of cervical adenopathies, which by compression also caused changes in caliber and vascular flow. Intravascular thrombosis was reported in 19 patients, representing 9.09%

The presence of adenopathy was highlighted in 182 patients, representing 87.08%. Grouping of patients with cervical adenopathies was performed at 3 and 6 cm, according to the most recent TNM staging criteria. Of the 182 cases with cervical adenopathy at 155, representing 85.16%, the diameter of the adenopathies was less than 3 cm, in 19 patients (10.44%) the adenopathic diameters ranged from 3 to 6 cm , and in 8 cases (4.40%) the adenopathic diameter exceeded 6cm. Of the 182 patients with cervical adenopathy, 86 of them, representing 47.25%, I encountered ipsilateral adenopathies to the tumor mass, and in 96 of the patients, representing 52.75%, adenopaths located both ipsilateral and contralateral with the tumor. In 42 of the 182 patients with present cervical adenopathy, representing 23.08%, they were grouped into adenopathic blocks. A total of 65 patients, representing 35.71%, presented necrosis.

Regarding the presence of distant metastases, incidental pulmonary determinations were found in 4 out of 209 patients, representing 1.91%.

IV. FINAL CONCLUSIONS

1. The pharyngo-laryngeal region is an anatomical structure with polymorphic composition, perfectly adaptable to CT and MRI imaging. Given the majority of tissue structures, MRI exploration brings more detail than CT.
2. Radio-imaging examinations by computed tomography is the primary diagnostic stage in the investigation algorithm of a suspicion of pharyngo-laryngeal neoplasia.
3. The absence of specific clinical manifestations can not exclude the diagnosis of pharyngo-laryngeal malignancy, so imaging exploration is an absolutely necessary investigation.
4. Under the conditions of a correct and, above all, complete investigation technique, and the observation of specific radio-imaging changes, the CT scan can confirm the diagnosis of pharyngo-laryngeal neoplasia.
5. Computed tomography may be the first-line method in the diagnosis of pharyngo-laryngeal malignant tumors, but with a lower accuracy than MRI exploration for the soft tissue.
6. Computed tomography is the most effective radio-imaging method for an accurate diagnosis of skull-base and laryngeal cartilage damage in pharyngo-laryngeal neoplasia.
7. T1 weighted MRI sequences are useful in identifying adjacent fat infiltration by the tumor mass.
8. T2 weighted MRI sequences are useful in detecting the lesion and the surrounding surrounding edema.
9. T1 weighting postcontrast images identifies the structure of the tumor mass and the infiltration of the adjacent tissues.
10. In Romania, pharyngo-laryngeal neoplasias are more common in the male population aged 50-70 years.
11. Exophytic, protruding forms were the most common types of tumor lesions encountered as radio-imaging aspects of pharyngo-laryngeal neoplasia in the studied group.
12. Topographic, the most frequent localization of pharyngo-laryngeal neoplasia encountered in the studied group was oropharyngeal. Due to the aggressiveness of these types of neoplasia, the second largest is the extensive pharyngo-laryngeal tumors.
13. Taking into account the anatomical structures that form the oropharynx, in the study group I concluded that the palatine tonsil and the tongue base represent the most frequent places of origin of these malignant tumors.
14. At the level of the hypopharynx, in the presented study group, the neoplasms are located predominantly in the pyriform sinus.
15. Among the neoplasms that affected the larynx, most had the starting point in the vocal cords.
16. The dimensional criterion is a diagnostic element of great importance for tumor staging, but also for clinicians in the evaluation of possible surgery.

17. From a dimensional point of view, in more than half of the cases, the maximum tumor diameter encountered at the time of imaging diagnosis included patients in stages T3 and T4. Of the total of pharyngo-laryngeal malignancies, the largest number of cases diagnosed in stage T2 had the oropharynx and the hypopharynx as origin.
18. Contour analysis provides information on the degree of tumor infiltration of its own or neighborhood structures. The ill defined contour, characteristic of malignant mass, was found in 92.34% of patients. The larynx, given its anatomical structure, is less infiltrated than pharynx, which is why most of the neoplasms that showed a clear contour had this localization.
19. Tumor necrosis was present in over two thirds of cases, directly proportional to tumor volume.
20. The contrast enhancement was present in all patients, and the intensity was most frequently moderate.
21. Vascular involvement in malignant tumors may be direct or indirect by compression. In the case of pharyngo-laryngeal neoplasia, approximately one-third of patients experienced vascular damage through adenopathic compression.
22. Cervical adenopathies have been encountered in the vast majority of patients. Most adenopathies from rhinopharyngeal, hypopharyngeal and extensive tumors were in N3 stage. The most common cervical adenopathies in cases of oropharyngeal and laryngeal neoplasia have been classified in stage N2.
23. Since most of the cases studied were T2 stage neoplasms, I could not draw a pertinent conclusion regarding distant metastases.
24. Histopathologically, the most commonly encountered pharyngo-laryngeal neoplasia in the study group was squamous cell carcinoma.
25. Considering the objectives of analyzing imaging exams, the exploration protocol was adapted to clinical suspicion, clinical data and anatomical region.
26. Radio-imaging examinations have an important role in the pre-therapeutic evaluation, but also in post-operative monitoring of patients.
27. For the evaluating phases and, in particular, postoperative follow-up, MRI examination is much more reliable than CT exam.