The Use of Methylene Blue in Early Detection of the Vocal Fold Cancer

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Laryngeal cancer represents an important problem in the public health department, mainly due to the fact that the lack of early symptoms leads to most cases being diagnosed in advanced stages, when surgical procedures must be extensive and will affect the quality of life of the patient. Nowadays, the problem of early diagnosis of laryngeal cancer and procedures that may facilitate it is of great importance, with contact endoscopy following in vivo methilene blue coloration being one of the most promising options.

Keywords: methilene blue, vocal fold, cancer

Laryngeal cancer represents a major health concern [1], accounting for approximately 3% from the total cancers in males and approximately 40% from the head and neck cancers. The clinical diagnosis of this pathological entity is based on the following procedures: visualizing the lesion thru indirect laryngoscopy, endoscopic examination (flexible nasendoscopy, rigid endoscopy) or direct examination thru laryngoscopy (a metallic laryngoscope is introduced thru the mouth of the patient down to the level of the vocal folds). However, in the light of the recent technological breakthroughs, modern methods of assessing the lesion are gaining importance, such as the acid-induced fluorescence [2,3], the narrow band imaging [4] or the comtact endoscopy [5].

Romania is on the third place in the chart of European countries concerning the incidence, prevalence and mortality thru laryngeal cancer, after Hungary and the Republic of Moldavia. Laryngeal cancer is the second most frequent neoplastic process of the airways in both international and national statistics, after lung cancer. Due to the large number of subjects that present habitual risk factors (tobacco, alcohol consumption), it represents a major problem of public health.

The endoscopic approach aiming for total resection addresses lesions that classified T1 to T3 according to the TNM international classification. These type of techniques, that are suitable only for certain carefully selected cases, are performed under microscopic control, while visualizing the lesion in white light.

In order for the patient to benefit from microscopically assisted LASER CO2 techniques, the cancer must be detected early.

One of the techniques used for early diagnosis of cancers of the vocal folds is contact endoscopy using methylene blue in vivo coloration [6,7].

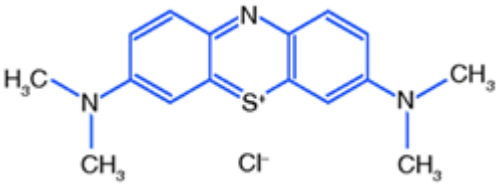

Fig. 1. Chemical formula of methilene blue

The purpose of this paper is to critically evaluate the method of contact endosocpy using methylene blue in vivo coloration and to establish it's capacity in detecting an early cancer.

Experimental part

In patients that presented lesions suspected of malignant degeneration we performed a direct laryngoscpy under general anesthesia with tracheal intubation. Before performing the biopsy, we used the method contact endoscopy with methilene blue in vivo coloration to evaluate the lesion.

After introducing the metallic laryngoscope, one can expose the level of the vocal folds.

Both vocal folds are colored by a moist gauze soaked in 1% methylene blue solution that is introduced in the larynx with an endoscopy forceps. Each vocal fold is colored by moving it repeatedly along it's free edge. One must wait for approximately 3 min in order for the methylene blue to be absorbed by the superficial layer of the vocal fold. Afterward, the vocal fold is washed with acetic acid.

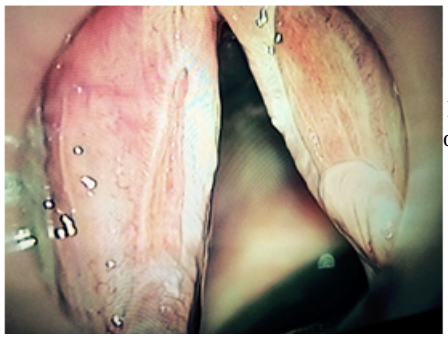

Fig. 2. Inspection of the glottis level thru direct laryngoscopy

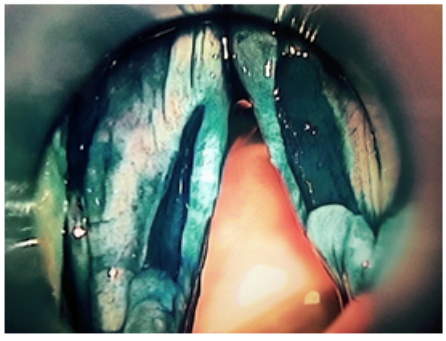

Fig. 3. Clear limits of the lesion suspected of malignant degeneration, after methylene blue in vivo coloration

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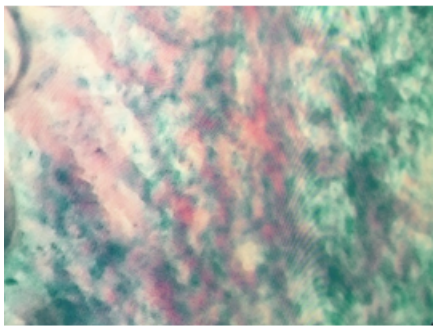

Fig. 4 In vivo microscopic-like image obtained by methilene blue contact endoscopy (60X magnification). The superficial vascular network and modified cell parameters are evaluated

The contact endoscopy rod is applied on the colored surface of the vocal fold and the obtained microscopic image can be studied. In our study, we used 8715 A Karl Storz contact endoscopy rod with an angle of 0^0 and a high resolution camera, necessary for assessing the finest details [8].

By means of contact endoscopy we can obtain an in vivo histological image. The parameters that must be studied are the uniformity of the cellular field, the nucleus/cytoplasm ratio of the cell and the size and shape of the cells.

Another parameter that must be studied is the distribution of the vascular network of the vocal fold. In a healthy individual, the vascular network is parallel with the free edge of the vocal fold.

A neoplastic process as little as 1 millimeter at the level of the vocal fold will secrete endothelial growth factor. This will lead to an increase in the number of blood vessels at this level, and the vascular network will become disorganized, chaotic.

We used the method of contact endoscopy in a number of 29 patients with lesions suspected of malignant degeneration at the level of the vocal folds. 8 women and 21 men were evaluated. The age of the patients ranged from 42 to 64 years. In all patients we used the methylene blue in vivo coloration of the vocal fold prior to contact endoscopy examination.

After carefully evaluating the cellular field and the superficial vascular network, we performed multiple targeted biopsies from the areas suspected of malignant degeneration. The results obtained thru the contact endoscopy technique were compared to the histo-pathological result of the biopsy pieces.

Results and discussions

The results obtained after comparison of the contact endoscopy technique and the histopathological result are as follows:

-the sensitivity of the contact endoscopy technique was 79.21%;

-the degree of specificity was 79.62%

-the accuracy of the technique was 91.2%

These results allowed us to conclude that the method is of practical importance, allowing the surgeon to perform targeted biopsies from areas highly suspicious of malignant degeneration. This in turn will translate into an early diagnosis and a conservative procedure, meaning a lower morbidity for the patient.

However, the surgeon must always bare in mind the fact that in cases of high clinical suspicion, even if the result of the contact endoscopy is negative, only a histopathological result can confirm for certainly the absence of a malignant process.

Conclusions

The advantages of using in vivo methilene blue coloration of the superficial layer of the vocal fold consist in the facts that it is a cheap and easy to obtain substance. Furthermore, the local effects of methylene blue are bacteriostatic, antioxidant and a stimulus for cicatrization.

The methilene blue coloration with contact endoscopy at the level of the vocal fold is a minimally invasive endoscopic technique the can detect early malignant lesions with an important rate of success. However, the endoscopic exam with a 0^0 rigid rod after methylene blue coloration does not replace the histopathological result.

Also, there is a learning curve for the ENT surgeon, that must learn to interpret alone the aspect of the cellular field.

The instruments necessary for contact endoscopy have a high price (rigid contact endoscopes, high resolution video camera).

One of the disadvantages of contact endoscopy is that it requires for the patient to undergo general anesthesia with tracheal intubation.

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