Lugol Iodine Staining Test in Early Detection of Head and Neck Cancer

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Head and neck cancer represents 3% of malignancies, and it is associated with high mortality due to advanced stage diagnosis. In early stages, the symptomatology can either be absent or be very common, misleading the patient who often ignores it. Early diagnosis of head and neck neoplasia is essential for a favorable long-term outcome. Lately new in vivo examination techniques were developed, and older ones have been improved. Today, in vivo staining techniques are an important tool in the diagnostic of head and neck cancer. Lugol iodine staining method provides valuable information concerning the tumor, allowing the surgeon to differentiate premalignant and malignant lesions.

Key words: lugol iodine, head and neck cancer, early diagnosis

Head and neck cancer represents 3% of malignancies, and it is associated with high mortality due to advanced stage diagnosis. The most frequent histologic type of tumor in this area is the squamous cell carcinoma [1]. Often, in early stages, the symptomatology can either be absent or be very common, and the patients ignore it. Due to late presentation to the ENT specialist, when the tumor is in advanced stages (it has large dimensions, it is invasive affecting the surrounding structures, often with lymph node metastasis and complications – infection, bleeding), the therapeutic resources are limited, and the long-term prognosis is poor. Advanced stage malignancies require extensive surgical procedures with higher risk and greater impact on the patients' quality of life. Also, complete resection of the tumor with disease-free margins and organ function preservation is more difficult. For these reasons, the medical community is focusing on early diagnostic methods to improve the results of oncologic treatment (surgery, radiotherapy, chemotherapy), survival rate and the quality of life for patients with head and neck cancer.

As mentioned before, in early stages a patient with head and neck cancer may present nonspecific symptoms of the organ involved. For example, for nasal carcinoma the most common symptoms are a unilateral nasal obstruction and purulent nasal discharge that can easily be considered rhinosinusitis. Patients with pharyngeal carcinoma can present a persistent sore throat and foreign body sensation, and patients with laryngeal cancer can report hoarseness and breathing difficulties [2].

When discussing head and neck cancer one has to take into account the risk factors: smoking and alcohol abuse are the most important, but occupational exposure to pollutants (asbestos, nickel or wood dust), history of infection with cancer-inducing types of human papilloma virus or Epstein-Barr virus can also play an important part in carcinogenesis [3]. Teething problems can also be a risk factor in the onset of head and neck cancers. Proper dental treatment using composite resins and new dentistry techniques may be seen as protective factors in these cases [4].

Early diagnosis of head and neck carcinoma is mandatory for favorable long-term results. Today, the key for early diagnosis is in vivo examination of the lesion with refined optical technologies and staining techniques. In the past years, important progress was made concerning optical examination methods – NBI (narrow band imaging) and SPIES (Storz Professional Image Enhancement System) are optical analysis technologies that allow better inspection and evaluation of the lesion and are making possible for the ENT surgeon to distinguish between non-malignant and malignant tumors [5,6]. Staining techniques are quick and easy methods to use when the surgeon needs further information about the tumor and its' extension. The most used staining agents in ENT are methylene blue, lugol iodine and toluidine blue. They are used for early detection of pharyngeal (especially oropharynx and tongue) and laryngeal carcinoma, and for intraoperative examination of the resection margins [7-9].

To improve the assessment of the tumor, the ENT specialist can associate a staining method with an optical technology- e.g. lugol iodine staining and NBI, methylene blue staining and NBI [10, 11].

Imagistic investigations (CT, MRI) are mandatory for a complete examination of the tumor. These investigations must be performed before surgery and can also be used during follow-up.

It is important to have in mind that neither optical examination methods nor imagistic investigation can replace biopsy sampling and histologic examination of the tissue specimen. Cutting-edge technologies like ELISA and flow cytometry are of great value for cellular and molecular analysis of the tumor cells [12].

The early diagnosis of head and neck cancers diminishes the locally-advanced or metastatic cancer rate. Survival rate in these types of cancers is lower and therapies are accompanied by a number of adverse drug reactions with a negative impact on the patient's quality of life, such as the papulopustular rash [13]. There are some local therapies attempting to place natural or synthetic cytotoxic agents in collagen [14-16]. Their administration reduces systemic adverse effects.

There is a number of serum markers showing predictive value for the prognostic of head and neck cancers. The latest research studies demonstrate the value of the serum matrix metalloproteinase-2 as a histopathologic prognostic factor in head and neck squamous cell carcinomas [17].

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Experimental part

The aim of this paper is to evaluate and present the advantages of the lugol iodine staining test in early detection of head and neck cancers. The technique is used for assessment of cancers in the nasal cavity, oral cavity, pharynx, and larynx and it can be associated with other in vivo enhancing examination techniques like NBI, SPIES, or with video contact endoscopy.

For a diagnostic purpose, before the surgery, an endoscopic examination is performed, either with a rigid optic, or with a flexible one, and imagistic investigations are done to obtain a complete assessment of the tumor.

The test with lugol iodine is performed at the beginning of the surgery, with the patient under general anesthesia. After the lugol staining test surgical resection of the tumor is carried out. Complete resection of the tumor with disease-free margins is the goal for every patient, but sometimes this is not possible to achieve.

The staining technique with lugol is quick and easy to perform: the examined area is cleaned with saline solution, after that 3% lugol iodine solution is applied to the tumor, and the surrounding tissue and the stained area is rewashed with saline solution. After using lugol, the normal tissue becomes dark brown due to the glycogen contained in the healthy cells, and the dysplastic or cancer area remains uncolored because cancer cells are glycogen free. Once the lugol is washed, the tumor and the adjacent structures are thoroughly examined. One has to pay attention to the following characteristic after staining: size and shape of the tumor, the pattern of staining (uniformity of the dye retention, differences of color intensity within the lesion and between the tumor and the surrounding areas), and aspect of the peripheral field of the lesion.

Results and discussions

Lugol iodine staining test is currently used for intraoperative assessment of head and neck cancer in the attempt to diagnose the disease as early as possible, and provide the best therapeutic option for every patient [18, 19].

This technique has many advantages, allowing the surgeon to evaluate both the lesion and the resection margins, making possible a complete ablation of the tumor with preservation of healthy tissue. Disease-free resection margins are mandatory for good surgical outcome and better long-term survival rates.

Another important aspect of this test is guiding the surgeon in performing targeted biopsies, enhancing the effectiveness of histologic diagnosis. Also, the lugol staining test can be used for assessing premalignant lesions and differentiating non-cancerous tumors from cancerous ones. Nevertheless, the lugol iodine staining test does not replace biopsy sampling and histologic examination of the tissue specimen. It helps the surgeon to choose the best approach for the lesion, combining aggressive tumor resection techniques with healthy tissue preservation methods.

The lugol staining test is easy to use, reproducible, safe, and economic, but the technique is not standardized. Every clinic has its protocol, and there is no common ground when it comes to concentration.

There are studies showing that associating lugol iodine test with other optical enhancement examination methods like NBI, SPIES, methylene blue or toluidine blue staining test provide better results concerning macroscopic examination of the head and neck tumor [20, 21].

Conclusions

Lugol iodine staining method provides valuable information concerning the tumor, allowing the surgeon to differentiate between premalignant and malignant lesions, to perform targeted biopsies and to achieve disease-free resection margins. It contributes to early detection of head and neck malignancies, improving the results of the surgery.

This test can be used as screening test for ENT tumors due to its effectiveness in early diagnosis of malignant lesions, and its low cost. It can be applied for patients with tumors in the nose, pharynx, and larynx.

We consider further studies are necessary for creating an accepted protocol in the ENT departments about the usage of lugol iodine staining test in early detection of head and neck cancer.

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