INCIDENTAL DISCOVERY OF ORO-PHARYNGEAL CANCER DURING ROUTINE UPPER GASTROINTESTINAL TRACT ENDOSCOPY. IS IT THAT OBVIOUS?

Gheorghe G. BĂLAN1, Vasile SANDRU2, Ana PETCU3, Gabriel CONSTANTINESCU4

1 M.D., PhD student, „Gr. T. Popa” University of Medicine and Pharmacy of Iaşi, Romania
2 M.D., PhD student, Research Assistant, Clinical Emergency Hospital of Bucharest, Romania
3 D.M.D., PhD, „Gr. T. Popa” University of Medicine and Pharmacy of Iaşi, Romania
4 M.D., PhD, „Carol Davila” University of Medicine and Pharmacy of Bucharest, Romania
Corresponding author: Ana Petcu; e-mail: a_ciulei@yahoo.co.uk

Abstract

Background: Hundreds of thousands of routine diagnostic upper digestive tract procedures are performed yearly worldwide either with a screening purpose or to investigate various digestive symptoms in selected groups of patients. Traditionally, digestive endoscopists used to endoscopically explore the digestive tract starting below the upper esophageal sphincter, leaving the oral cavity, hypopharynx and larynx for either oral examination or ear nose and throat (ENT) clinical and endoscopic investigations. As the imagery and technical features of digestive endoscopes progressed, nowadays oropharyngeal lesions may be diagnosed endoscopically, as well.

Case series: Our study aims at presenting a small series of cases receiving routine upper digestive tract endoscopy, permitting the detection of asymptomatic oropharyngeal lesions and further proper surgical and oncological management.

Discussion: Despite the up-to-date quality indicators of upper digestive tract endoscopy referring to a proper and strict examination of the digestive tract below the upper esophageal sphincter, the new trends in digestive endoscopy lay stress on the fact that the endoscopist should begin endoscopic examination with the oral cavity, uvula, glottis and glottis orifice, hypopharynx and only then to proceed with the examination of the digestive tract. In this way, digestive endoscopy procedures may help detection of incipient pre-malignant or malignant lesions, thus allowing a proper timely therapy. Conclusions: Digestive endoscopists should be trained to properly assess oropharyngeal spaces. Such endoscopic examination requires patience and good technique and skills, patient sedation being mandatory in most of the cases.

Keywords: squamous cell carcinoma, narrow-band imaging, oral surgery, digestive endoscopy.

1. INTRODUCTION

Diagnostic upper digestive tract endoscopy (frequently referred to as gastroscopy) is performed yearly with an annual estimated ratio of 3,000 procedures per 250,000 population, [1] because of the various indications of cases requiring either exclusion of malignant lesions in patients with recurrent, refractory or ‘red flag’ (also known as alarm) gastrointestinal signs and symptoms, or for screening purposes in selected populations of patients [2]. Nevertheless, diagnostic upper digestive tract endoscopy is an integrating part of the workup of many disorders, requiring complex multidisciplinary management and interventions. As to what current quality standards in upper digestive tract endoscopy state, digestive endoscopists should assess the endoscopic aspect of the digestive mucosa below the upper esophageal sphincter, evaluating successively the upper esophagus, the gastro-esophageal junction, the fundus of the stomach in retroflexion, the body of the stomach, the incisura in retroflexion, the antpyloric region, the duodenal bulb and the distal duodenum [3].

Passage of the endoscope through the oral cavity and hypopharynx to the upper esophagus is performed in different ways, depending on the skill and technique of each endoscopist, in most of the cases not allowing a proper exploration of such regions. Moreover, the new generation of digestive endoscopes allows high definition inspection of the mucosae, while also associating close focus and magnification features that further help in refining optical diagnosis in various types of lesions. Producers have also developed virtual chromoendoscopy features, of which narrowband imaging (NBI) developed by Olympus, Japan is widely known and intensely used. NBI is an optic technique using various optical filters that narrow the light bandwidth,
in order to enhance visualization of the mucosa surface and microvasculature [4,5]. When used concomitantly with the magnification features, NBI allows the endoscopist to establish an accurate diagnosis of early cancers, due to the contrast observation of vascular architecture, the pathognomonic features being the intrapapillary capillary loops (IPCL) [6,7].

During diagnostic endoscopic examinations of the digestive tract, continuous search and mucosal assessment for malignant or premalignant lesions is the gold standard and aim of the procedure. Although rarer than the adenocarcinomas, squamous-cell carcinoma (SSC) of both upper respiratory and upper digestive tracts is epidemiologically linked to excessive use of tobacco and alcohol, as well as to chewing of betel nuts in some populations of patients, especially in the developing countries [8,9]. Currently, although a multidisciplinary workup and management including endoscopy, pathology followed by surgery, radiotherapy, and chemotherapy is mandatory, the overall survival rates of such patients are still poor [10,11]. On the other hand, oral cancers are worldwide detected mainly by visual inspection of the lesions on the surface of the mucosa, clearly an early detection of cancer being the best possible alternative, as most advanced lesions require extensive surgical resection. Even if, in most cases, clinical examination is revelatory for further workup, precise observation of the color field and assessment of the fine structural pattern of the mucosa are often required to diagnose possible malignancy [12,13], thus targeting the site for biopsy and enhancing the accuracy for histopathologic evaluation.

Pathogenically, esophageal cancer was described as synchronous or metachronous tumors in approximately 14% of the patients with head and neck cancers [14,15], a process referred to as the concept of field carcinogenesis [16]. Such oncological situation may explain the poor prognosis, despite adequate control of the primary tumor, suggesting that a proper and timely diagnosis could allow a better control. Therefore, advanced endoscopic techniques have been developed to allow better evaluation of mucosal surface, which would itself improve the detection rate of small premalignant lesions. Either real or virtual chromoendoscopy, together with high-resolution and magnifying endoscopy, have enabled an early detection of esophageal and digestive cancers [17,18].

On the other hand, in what oropharyngeal malignant lesions are concerned, most of them are represented by SCC, so that a proper management of such conditions should always be conducted by accurate evaluation, physical examination followed by biopsy remaining the gold standard. However, such asymptomatic lesions are rarely discovered by dental, oral or ENT practitioners, as routine screening programs are scarce in most of patients’ population.

Therefore, more and more experts tend to recognize the role of digestive endoscopists in the early diagnosis of such lesions, mainly due to the frequency of procedures and to the quality of the high resolution and virtual chromoendoscopic examination features of the scopes [19].

2. CASE SERIES

In order to support such a hypothesis, we present a small series of cases including patients referred to the gastroenterology department for routine upper digestive tract evaluation secondary to refractory gastrointestinal symptoms. All patients were evaluated in the Institute of Gastroenterology and Hepatology of the “St. Spiridon” Emergency Hospital of Iasi, between January and May 2018. Beside proper endoscopy indication and incidental findings, inclusion criteria for both groups were: age over 18 years, clinically normal cognitive status and possible pathology and oncology follow-up. All patients signed an informed consent for inclusion in this case series presentation.

Case 1 is represented by a 55 year-old female referred by the general practitioner for upper digestive tract endoscopy because of a recurrent epigastric pain associated with nausea and vomiting episodes refractory to proton pump inhibitor (PPI) and antiemetic therapy. She was admitted as a day patient, physical examination revealing only some skin atrophy and hair loss. History talking was suggestive for some degree of weight loss, but with no objective proof. She experienced 4 weeks of Esomeprazol 40mg qD
and Domperidone 10mg q8H oral therapy with no change in the intensity and frequency of symptoms. Upper digestive tract endoscopy was performed under mild sedation with Midazolam i.v. 2mg. Assessment of the digestive tract revealed gastric distention with no mucosal injury. Upon scope retraction, inspection of the oral cavity showed in the right floor of the mouth an elevated lesion, 1cm in size, with central micro-ulcers covered by fibrin and hyperemic mucosa with an abnormal surface pattern. Assessment of IPCL was done with close focus NBI evaluation that revealed large vessels with no loops in the terminal branches and diffuse destruction of loops, a suggestive aspect for type IV IPCL and carcinogenesis. The endoscopic aspect in white light imaging and NBI is showed in Figure 1. The patient was referred to oral surgery evaluation. Biopsy of the lesion confirmed the diagnosis of oral SCC. Further biological examination was suggestive for unstable type 2 diabetes mellitus and therefore differential diagnosis of diabetic gastroparesis was discussed in what the digestive symptoms were concerned.

Case 2 is that of a 40 year-old female referred for upper digestive tract endoscopy from the psychiatric clinic for intermittent globus attacks, firstly interpreted as a anxiety disorder stigmata refractory to anxiolytic therapy. Clinical examination and history talking revealed no red flag sign or symptom. On the other hand, the biological panel was consistent for microcytic anemia, with a hemoglobin value of 10.5 g/dL and a mean corpuscular value of 70 fl. Upper digestive tract endoscopy was performed without sedation. Upon insertion of the scope below the piriform sinuses, traces of blood were observed. Despite patient’s discomfort, slow instrumentation was performed on retraction above the upper esophageal sphincter. Endoscopic appearance is

Fig. 1. White light imaging (lower left, upper right) and Narrowband imaging (upper left, lower right) assessment of an elevated lesion of the right floor of the oral cavity Close focus (left images) shows micro-ulcers, fibrin and altered IPCL pattern with no loops and distortion of branches in NBI
that of a 0.8 cm pedunculated lesion with a frail pattern associated by active oozing bleeding. The base of the stalk appears to be in the hypopharynx, while the surface pattern of the pedicle is a squamous one. Active bleeding did not allow NBI evaluation because of the artifacts produced by the presence of blood on the mucosal surface. The endoscopic aspect of the lesion and upper esophagus is illustrated in Figure 2. Biopsy of the lesion, performed in the ENT sector, was consistent with a metaplastic inflammatory squamous lesion with intraepithelial low grade dysplasia. Resection of the lesion was scheduled to be performed endoscopically.

Case 3 is represented by a 65 year-old male with a history of heavy tobacco smoking (40 pack/year) and chronic alcohol abuse (4-5 units per day). He was referred for diagnostic upper gastrointestinal endoscopy by his pneumologist during the follow-up of chronic bronchitis, as the patient complained of weight loss and intermittent difficulty in swallowing, with associated dysgeusia (described by the patient as a metallic taste). Physical examination revealed a poor hygiene, halitosis and severe ronchi. Detailed history talking was suggestive for intermitent episodes of impaired swallowing with no limitation for food or liquid intake. Non-sedation endoscopy of the upper gastrointestinal tract did not reveal mucosal lesions. On retraction of the scope above the glotic orifice, examination of the base of the tongue revealed a depressed lesion with an irregular surface pattern, approximately 1cm in size. NBI evaluation was highly suggestive for type IV IPCL, probably in the context of invasive SCC. The patient was referred to the oral surgery department for diagnosis and management. Histopathology was conclusive for
INCIDENTAL DISCOVERY OF ORO-PHARYNGEAL CANCER DURING ROUTINE UPPER GASTROINTESTINAL TRACT ENDOSCOPY. IS IT THAT OBVIOUS?

3. DISCUSSION AND ASSESSMENT OF LITERATURE

There is no thorough epidemiologic evaluation of the incidence and prevalence of neoplastic lesions of the oro-pharynx in patients with nonspecific digestive symptoms in need for upper digestive tract endoscopy. Nevertheless, in cases of high risk stigmata for malignancy, despite the absence of abnormal mucosal findings in the upper gastrointestinal tract, endoscopists should also check and assess the base of the tongue, the hypopharynx, the glottis and the glotic orifice and, when possible, the piriform sinuses. Such anatomic segments could, even though not in all cases, be relatively well visualised by a trained endoscopist.

Given the fact that digestive scopes became equipped with new generation optical enhancement features like close focus, magnification or virtual chromoendoscopy, abnormal mucosal patterns of the oropharyngeal lesions could be evaluated and the risk for malignancy can, as stated by Takano et al., be stratified by IPCL classification. Figure 4 shows the different patterns of IPCL, each one associated with a different risk for malignancy. Types III and IV IPCL are frequently encountered in SCC of the oral cavity [20].

Fig. 4. IPCL classification and progression from normal pattern to carcinoma (according to Tanako et al.)
Normal IPCL (type I) appears with waved arms and non-dilated capillaries. Type II IPCL has an increased diameter but with preserved anatomy of branches similar in shape to type I. Type III IPCL is characterized by elongation of the capillaries, dilation and tangling of branches. Type IV is characterized by large vessels, amorphous pattern with no loops [20]
However, a clear delineation for the NBI aspect of the head and neck cancers evaluated by endoscopy and NBI is difficult, because of the epidermal variations and interference of lymphoid tissue in the identification of subepithelial microvascular architecture [21]. Subsequently, various studies describe that the floor of the mouth, the ventral tongue, soft palate, epiglottis, vocal cords, hypopharynx and esophagus are covered by nonkeratinized thin stratified squamous epithelium and therefore present an altered NBI appearance that does not allow proper vascular patter analysis [22,25]. Moreover, having in mind such anatomical variations, differential diagnosis of multiple oral lesions secondary to diseases of the gastrointestinal tract may be established [24-27].

Similar incidental findings were reported by Muto et al., who described numerous SCC cases of the oral cavity, hypopharynx and glottis prior to the common NBI use on the market [7]. Similar lesions of the floor of the mouth were described by Lin et al., who outlined the importance of brown spot detection during NBI analysis of lesions as a marker for increased risk of malignancy [21]. Endoscopic incidental detection of SCC of the vocal cords was described by Ni et al., [28], nevertheless such detection requires patience and cooperation from the part of the patient. In the same manner, evaluation of the glottic web and detection of SCC at this site were described by McMullen et al. [29-31]. Despite the multitude of sites where such lesions may occur, it is our belief that the endoscopist should be trained to assess at least the glottis and glotic orifice and not to rush in scope retraction, allowing as much time as possible for the visualization of the tongue and hypopharynx.

4. CONCLUSIONS

Upper digestive tract endoscopy procedures may clearly facilitate diagnosis of asymptomatic neoplastic lesions of the head and neck. Primarily, the diagnosis of such lesions is performed clinically during oral examination and by nasolaryngeal flexible endoscopy during ENT examination. Nevertheless, feasibility of endoscopic detection is clear, yet it requires training and skills from the part of the endoscopist.

References

INCIDENTAL DISCOVERY OF ORO-PHARYNGEAL CANCER DURING ROUTINE UPPER GASTROINTESTINAL TRACT ENDOSCOPY. IS IT THAT OBVIOUS?


