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ESOPHAGEAL MALIGNANCIES AND PREMALIGNANT CONDITIONS: A REMARKABLE EVOLUTION – PART II

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Growth Rate of Esophageal Cancer

The acquisition of information regarding the growth rate of esophageal cancer is available only from high-incidence areas. The best data thus far have been obtained by follow-up studies on patients with early esophageal squamous cell cancer who either have refused therapy or have been lost to follow-up. There appears to be a significant window for curative treatment when screening programs are able to detect lesions still localized to the mucosa (top cell layer) and prior to esophageal wall invasion and regional lymph node metastasis.

Esophageal carcinoma has been classified as a rapidly growing cancer. The relationship between factors such as age, cancer location, sex and degree of differentiation, and growth rate of esophageal carcinoma were analyzed and there was no correlation found. Data from Chinese studies of early squamous cancer suggest that a period of several years may be needed for development into an advanced stage. In 1976, it was reported in a study of 19 cases, that the average period of early squamous cancer to progress to an advanced stage was 32.5 months, with a further 10.5 months for the advanced stage to progress to death. It appears that a natural history of 4-5 years is more likely for a carcinoma in-situ (superficial, non-invasive) to progress to symptomatic, advanced cancer.

Anatomy of the Esophagus and the Spread of Cancer

From an anatomic viewpoint, the esophagus is an ideal location for the silent development and spread of intrinsic cancer and at the same time its anatomy poses a serious and sometimes insurmountable obstacle for adequate surgical management. The esophagus is unique in the digestive tract in that it does not have a serosa or thin, outer covering layer as do stomach and

intestines. The serosa offers a measure of protection against spreading of the cancer. The wall of the esophagus is richly supplied by lymphatics in the submucosal and muscular layers that provide a ready pathway for dissemination of cancer.

It is now widely accepted that the esophageal cancer that invades through the surface layer or epithelium spreads early and distant due to the anatomical structure of the esophagus mentioned above. The esophagus is surrounded throughout its length by important and vital organs, which may be invaded relatively early in the course of this cancer. The lymphatic vessels in the esophageal wall distribute cancer cells in a longitudinal direction often to a considerable distance above and below the visible or palpable limits of the primary cancer. The disease spreads by direct extension, lymphatic permeation and through the blood stream.

New surgical techniques with lower operative risks with or without combined radiation and chemotherapy offer a better chance for longer survival and even cure. However, the key to successful, curative therapy continues to be identification in higher risk patients of the pre-cancerous and early cancer stages that are amenable to cure by modern surgical and non-surgical techniques.

Diagnosis of Esophageal Cancer

The historical presentation of esophageal cancer has changed little, if at all, during the past century. Still, most patients and some physicians remain unaware of the significance of the cardinal symptoms that time has not altered. A history of dysphagia (difficulty with swallowing), weight loss, ill-defined mid-chest discomfort, odynophagia (painful swallowing), and unexplained hiccups, alone or in combination, should suggest the possibility of esophageal cancer. Solid-food dysphagia occurs relatively late but is typically progressive for three to six months before a patient first seeks medical

ESOPHAGEAL MALIGNANCIES AND PREMALIGNANT CONDITIONS: (continued)

attention. Some patients report the earliest symptom to be a vague sensation or discomfort noted when swallowing a solid food bolus. These warning symptoms must be investigated completely by barium radiography and endoscopy with biopsy for confirmation.

Screening for Esophageal Cancer

Squamous-Cell Cancer

Accurate screening for esophageal squamous-cell cancer is most likely to be achieved by endoscopy and accessory procedures, although proper time intervals for surveillance have not been established. However, it is logical to recommend that patients at highest risk (i.e., with prior upper aerodigestive tract [mouth, throat, larynx] cancer, tylosis [a rare inherited disorder], longstanding caustic injury) have an endoscopic surveillance at 1 to 2-year intervals. In such patients, the likelihood of finding early cancer is greatly enhanced by using chromoendoscopy techniques using iodine and/or toluidine blue to stain the mucosa.

Adenocarcinoma

Patients with columnar-lined esophagus are known to develop a premalignant dysplasia in the metaplastic intestinalized (Barrett) epithelium, which is characteristic of this condition. A precise surveillance interval has not been established, but most authorities recommend surveillance endoscopy at 1 to 2-year intervals with four quadrant biopsies at 2 cm intervals throughout the Barrett segment. Severe or high-grade dysplasia documented by an expert pathologist formerly was considered an indication for esophagectomy. Frank early carcinoma is found in about 30% of such cases. Photodynamic Therapy (PDT) is proving to be an effective alternative to surgery in selected cases of high-grade dysplasia.

Tumor Markers

The use of tumor markers from tissue or blood may be useful in the near future, not only for early detection of esophageal carcinomas, but also for monitoring and follow-up of various therapeutic procedures.

Staging of Esophageal Cancer

Computed Tomography

Computed tomography (CT) initially was considered highly accurate for staging esophageal cancer. However, with further experience and comparison with surgical pathology, it was recognized that intramural and transmural invasion (T stage) often is not accurately detected, leading to under staging in up to 40% of cases. The overall accuracy of CT in evaluating mediastinal lymph nodes is only about 50%. The major advantage of CT for esophageal cancer staging is the detection of gross invasion of adjacent organs and

distant metastases.

Endoscopic Ultrasonography

The latest diagnostic technique involved with staging evaluation of esophageal cancer is endoscopic ultrasonography (EUS), introduced in the 1980s. It is capable of determining the longitudinal, circumferential and transmural extent of esophageal malignancy. EUS has proven to be excellent and superior to CT for determining the T stage (depth of wall penetration) and the N stage (regional lymph node metastasis) with about 85% and 75% accuracy, respectively. In most cases, it is not capable of evaluating distant metastasis (M stage), which is best done by CT, conventional ultrasound, and other methods.

Conclusions

The history of progress and acquisition of knowledge about esophageal malignancies and premalignant conditions has been hindered mostly by our inability to understand the biologic nature of these disorders. Squamous-cell cancer and adenocarcinoma of the esophagus begin insidiously, grow steadily, and metastasize transmurally and to regional nodes readily – all before the patient becomes aware of any disturbing symptoms. Diagnosis also is delayed because the patient, even with significant dysphagia, often fails to seek medical help for three to six months. Further delay in diagnosis occurs when the physician fails to recognize the significance of dysphagia and other symptoms with or without weight loss. However, in the vast majority of patients, the diagnosis is promptly suspected on the basis of the medical history, precisely localized by barium esophagram, and accurately confirmed by endoscopy with guided biopsy. Diagnosis is not usually the problem. Therapy is the major challenge and has been the focus of effort during the past century by surgeons, radiotherapists, chemotherapists and gastroenterologists.

Future research and clinical efforts must be directed toward screening and earlier cancer diagnosis before invasion and distant metastasis occurs if cure rates are to improve. Surgical resection with radiation and/or chemotherapy offer the only current hope for curing symptomatic malignancies in a few highly selected patients who can only be identified properly with the most modern staging methods. Knowledge most needed for the future includes development of sensitive and specific screening methods; identification of the populations at highest risk; specific, safe and effective radiation and chemotherapy regimens; and most importantly, methods to reduce risk and to prevent malignant transformation of esophageal epithelial cells.

AVOIDING DANGEROUS ERRORS WHEN TAKING MEDICATION

Medication errors – such as forgetting to take medicines at the proper times or taking more or less than the prescribed amounts account for 10% of hospital admissions.

The most common errors and how to prevent them are listed below:

Error #1: Ignoring Label Directions

Check the label for the right dosage. Taking the wrong dose of a medication can be dangerous.

Example: Taking too much of a blood thinner can cause internal bleeding. Labels also state other directions. For example, you may need to take painkillers with food to prevent stomach upset.

What to do: Every time you get a new drug or a refill, review the label and the pharmacy drug summary. To keep the label clean and legible, cover it with clear tape.

Error #2: Missing Doses

It is easy to forget to take medications at the proper times.

What to do: Keep bottles where you will see them, such as on your desk or next to your toothbrush. If you take multiple medicines, use a pillbox that has a compartment for each day.

Important: If you forget to take a dose, read the package insert for directions or ask your doctor or pharmacist. For some drugs, such as antibiotics, you can usually take a double dose at the next scheduled time. For others, such as blood pressure drugs, it is safer to skip the missed dose and take your usual amount at the next scheduled time.

Error #3: Not Knowing Which Drugs You Take

If you don't know the names of all the drugs you are taking – and you aren't sure why you are taking them – there is no way to know if your doctor or pharmacist accidentally gives you the wrong ones.

Different drugs may have similar names. For example, the cough medicine Benlyn is easily confused with the antihistamine Benadryl.

If you don't know what drugs you are taking, you also won't be able to alert doctors in an emergency. You could be given the wrong treatment in a hospital emergency room.

Example: Beta-blockers, which are often used to control high blood pressure, can cause severe asthma-like symptoms.

What to do: Before leaving your doctor's office with a prescription, ask him/her to write down the drug's name and why you are taking it. Review this information with the pharmacist.

Error #4: Failure to Take Medication Properly/Safely

There are over 70 drugs reported to cause significant injury if they remain in

the esophagus. If you have a condition that causes dysphagia or hang-up of food in the esophagus you should consider converting to a liquid form or crushing pills and opening capsules (with your doctor's approval) to reduce the risk of delayed passage and esophageal injury.

What to do: Whether or not you have an esophageal disorder you should never take medication and lie down without drinking several ounces of fluid and remaining upright for at least five to ten minutes.

Error #5: Failing to Recognize Side Effects

Patients do not always make the connection between a drug and symptoms that are actually side effects.

Example: Blood pressure drugs called ACE inhibitors can cause a dry cough that may be dismissed as a sign of a cold or allergy. Other drugs may cause nausea, dry mouth, blurred vision, or problems with urination.

What to do: Tell your doctor about any symptom that begins after starting a new drug, even if it seems unrelated. Most side effects can be reduced or eliminated by switching drugs or adjusting the dose, with medical supervision.

Error #6: Failing to Take Medication at the Proper Time

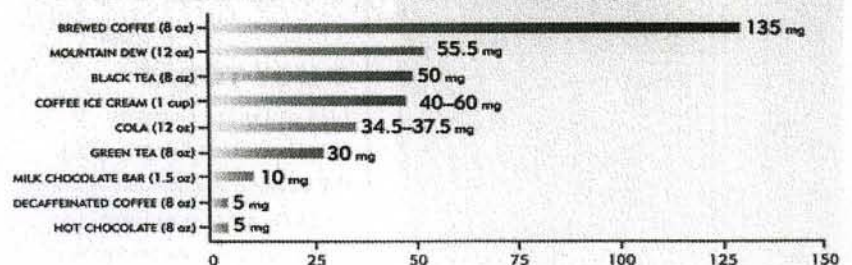
For optimum effect some drugs require taking the medication at the proper time in relation to meals.

Example: Proton pump inhibitors (Aciphex, Nexium, Prevacid, Prilosec, Protonix) used for reduction of stomach acid all work best if they are absorbed into the blood before meals at which time the acid production is greatest.

What to do: Take these medications at the daily frequency your physician recommends but remember the effectiveness of each dose depends on how long before a meal they are taken. The best effect is achieved by taking the medication 30 minutes or longer before a meal so that it has time to be absorbed into the blood before you start eating. Failure to do so may reduce the acid suppression effectiveness by as much as 50%.

buzz on caffeine

Caffeine, popular worldwide, has been linked to osteoporosis, decreased fertility, and sleeplessness. But benefits include increased alertness, improved stamina, and possible improvements in short- and long-term memory. Experts, including the American Heart Association, okay moderate consumption (1–2 cups of coffee a day).



THINGS TO REMEMBER

1. **OFFICE HOURS:** 8:00 a.m. 'til 5:00 p.m. Monday through Friday. Telephone hours: 8:00 a.m. 'til 5:00 p.m. Also, our emergency telephone number for after hours is (813) 974-2201

2. **BILLING:** Payment for services rendered is due at the time of your visit. Please be prepared to pay any co-payments due at the time of your visit to the Center.

Patients who have problems with their physician or facility fee bills should contact Gayle Stephens, Financial Specialist, at the University of South Florida Medical Clinics at (813) 974-3575 between the hours of 9:00 a.m. and 4:00 p.m. Monday through Thursday.

For those patients who are from out-of-town, a new toll-free number has been added for you to call with billing questions. The number is 1-888-873-3627. This number is for calls originating in Florida and is only for billing questions and help with insurance authorizations.

3. **HAS YOUR INSURANCE COMPANY OR PRIMARY CARE PHYSICIAN CHANGED?** With an ever changing medical insurance market (shopping for the best contract, companies merging, others closing their doors, etc), you may have changed insurance company. If you changed your insurance company you may have a new primary care physician. Maybe you have moved and had to choose a new doctor closer to your home. Regardless of the circumstances we would very much appreciate your contacting our office to let us know, (813) 974-3374. This will not only insure we can obtain the necessary authorizations/pre-certifications and that your medical bills go to the right insurance company but it will help us make sure your medical records are forwarded to the right doctor. Thank you for helping us keep the records straight.

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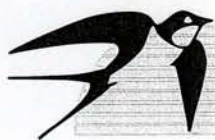
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