Digestive submucosal masses : endoscopic evaluation

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The term *"submucosal lesion or tumor"* is often used generically to refer to any bulging lesion covered by normal- or nearly normal-appearing mucosa and having a smoothly elevated contour that makes its margins less sharply demarcated than lesions that arise from the mucosa (1,2). Usually these lesions are detected incidentally as smooth masses on endoscopy or barium studies and fortuitously discovered during the exploration of another pathology. These lesions are rare and their incidence at autopsy is only about 0.2 to 0.5% (3,4,5). They are most often small, asymptomatic lesions without degenerative potential. However, lesions that are large or ulcerated may cause symptoms.

Endoscopy shows only the mucosal aspect of the lesion and can evaluate neither the depth nor the extend of the lesion (6,7). In addition, endoscopy often cannot differentiate between true lesions involving the submucosa, lesions involving the other layers of the gastrointestinal tract wall, and adjacent extrinsic lesions. This endocopic appearance can be associated with a wide variety of lesions such as lipomas, lymphomas, carcinoïd tumors, granular cell tumors, duplication cysts, heterotopic pancreas, varices, gastrointestinal stromal tumors, extrinsic compressions…) These lesions arise within or outside the wall of the gastrointestinal tract as well as normal structures adjacent to the gut. Endoscopic biopsies are rarely diagnostic because they sample small pieces limited to the superficial layers of the gastrointestinal tract wall (8). SMT's endoscopic diagnosis can be therefore difficult to achieve.

In such cases, *Endoscopic Ultrasonography* (EUS) frequently provides more detailed and useful information (9,10). The placement of high-frequency transducers immediately adjacent to the gastrointestinal tract wall affords high-resolution imaging of the wall configuration itself and that of adjacent extraluminal structures as well (11, 12).

Before the development of endoscopic ultrasound, submucosal masses were generally assumed to be benign, and often were assumed to be either lipomas or leiomyomas. The accuracy of these assumptions can now be tested with EUS because the actual wall layer from which these lesions originate can now be defined. EUS is then a uniquely useful adjunct in the diagnosis of subepithelial lesions.

The rational management of benign and malignant SMT is critically dependent on endoscopic ultrasonography. Diagnostic EUS has three objectives with regard to accessible GI lesions :

– to examine the gross pathologic characteristics of the lesion, according to the occupied layer by the lesion, according to the echo-graphic feature (hypo-, hyperechoic, homogenous, heterogeneous),
– to obtain tissue samples,
– and to estimate the extent of the disease.

The latter is necessary for planning treatment and to assess prognosis.

Before undertaking endoscopic excision of a submucosal tumor, for example, it is extremely helpful to know the exact location of the lesion within the wall and whether a plane exists between the lesion and the normal structures of the gastric wall (13).

Because the true nature of a submucosal lesion cannot be determined by endoscopic observation, it is advisable to visualize such lesions by EUS and/or Doppler color EUS before undertaking aggressive endoscopic biopsy or excisional procedures in order to exclude intrinsic or extrinsic vascular structure, hypervasculatity, presence of large vessels….

Characterization of the lesion, second diagnostic step, is necessary for the management and the decision-making : surveillance, surgical or even endoscopic resection. Depending on their histologic features, some benign tumors are also important because of an associated risk of malignant degeneration. For instance, it is important to distinguish between esophageal leiomyomas and gastric GISTs because the latter group have a high risk (10%) of malignant behaviour (14). Although these lesions demonstrate different histologic findings, the overlap of radiologic, endoscopic, endosonographic or CT findings makes differentiation difficult.

As eso-gastro-duodenal lesions are readily accessible to the ultrasound endoscope, EUS findings are now routinely utilized in planning therapy. Another problem is to differentiate benign and malignant submucosal tumors. The most common subepithelial lesion in the upper gastrointestinal tract, the leiomyoma, exhibits characteristic features at endosonography. The EUS appearance of

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stromal cell tumors is usually a hypoechoic mass originating from the muscularis propria. However, studies confirm that endosonographic appearance of these benign lesions overlaps with that of malignant leiomyosarcoma or leiomyoblastoma. Malignant smooth muscle tumors involving the gastrointestinal wall tend to be larger lesions, having inhomogenous internal echoes and an irregular outer border. But unless the mass is clearly seen to disrupt the outer margin of the muscularis propria layer, thus indicating invasion, the differentiation between benignity and malignancy cannot be made with certainty. However, because small smooth muscle tumors are very rarely malignant, a policy of close follow-up using endoscopic ultrasound, especially for patients with an elevated risk of surgery, may be justified. Growth of the lesion, a change in the echogenic pattern, or necrosis would allow the clinician to refer a small subgroup of patients for excisional surgery.

Which lesions need sampling ?

It is important to be aware of the limitations of endoscopy in diagnosing the nature of SMT because they are often covered with normal mucosa. As a rule, biopsy is not advisable if the mucosa overlying a SMT is normal in appearance. Mucosal biopsies will not usually reveal the nature of the lesion, except in some cases when they are taken from an ulcerated area. Biopsy is justified only if roughening, irregularity, or peculiar ulceration of the mucosa overlying the tumor suggests malignancy.

The EUS features associated with malignant stromal tumors include tumor size greater than 4 cm, irregular extraluminal border, echogenic foci, and cystic spaces (15). If two or more of these criteria are present, the lesion is likely of high malignant potential, and if none of the criteria are present, then it is probably benign.

Despite its advantages, endoscopic ultrasound does not provide an histologic diagnosis of subepithelial lesions. At present, EUS cannot accurately differentiate benign from malignant GIST, and EUS criteria should not be the only basis for classification of malignant potential.

EUS results can help determine when it is safe and useful to obtain tissue sampling. Various techniques can obtain tissue for cytologic or histopathologic findings but we have to keep in mind that they should be used selectively in only those cases in which the information will change management. A hypoechoic lesion in the muscularis propria is almost certainly a stromal cell tumor, and FNA cytology or even large- particle biopsies will not yield enough tissue for the pathologist to determine the malignant potential of the lesion. FNA and snare resection are potentially very useful when the diagnosis is in doubt, such as a heterogeneous lesion in the submucosal layer, which could be lymphoma, carcinoid tumor, granular cell tumor, pancreatic rest or other lesion. Contraindications to tissue sampling are EUS findings of a vascular lesion such as varices, or an extrinsic mass causing the observed abnormality such as compression by vascular structure, liver or spleen. Submucosal masses that are not typical lipomas or stromal cell tumors should have tissue sampling performed.

The optimal management of submucosal masses that are suspected to be stromal tumors by EUS is unknown. Surgical or endoscopic resection should be performed for all lesions causing symptoms, lesions greater than 3 cm in diameter, lesions with suspicious EUS findings, and lesions that increase in size on serial EUS exams. Small (less than 3 cm in diameter), asymptomatic, incidentally discovered lesions that are suspected to be benign stromal cell tumors may be observed with repeat EUS every 6 to 12 months. If the lesions increase in size, develop suspicious-appearing EUS features, or become symptomatic, they should be resected.

When the diagnosis of malignancy has been established, proper staging of the tumor is needed to determine the appropriate treatment and assess prognosis. In addition to the histopathological grade of malignancy, the prognosis is indeed predominantly determined by the intramural penetration depth of the tumour and presence or absence of peri-gastric lymph-node involvement. With EUS, staging can be carried out much more accurately.

After endoscopic or surgical removal of a submucosal tumor, attention should be given to complete removal of the tissue. If residual tumor tissue is suspected, periodic EUS surveillance should be performed.

Conclusion

Subepithelial tumors of the GI tract arise from one of the five layers of the digestive wall. These tumors can be benign or malignant and result from a self or more or less limited proliferation of cells which are usually present or not inside one of the constituent of the digestive tract. Most benign submucosal tumors are discovered as incidental findings on barium studies or on endoscopy. They are most often small, asymptomatic lesions without degenerative potential. However, lesions that are large or ulcerated may cause symptoms and have degenerative potential. The rational management of benign and malignant submucosal tumors is critically dependent on Endoscopic Ultrasonography. EUS is the most accurate imaging modality for lesions located within or compressing the gastrointestinal wall. EUS findings can be diagnostic based on ultrasound characteristic alone and can identify lesions that require tissue sampling. Sometimes, definitive treatment can be guided by EUS and can be rendered endoscopically for many lesions particularly those that are benign. Proper EUS staging is also important, so that rational decision can be made about treatment options, such as endoscopic or laparoscopic removal.

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