

# Review of clinical and endoscopic features of metastatic tumors of the gastrointestinal tract

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## Abstract

Metastatic tumors may occur at any site within the digestive tract. Most of these metastasis are observed in the stomach, small bowel, duodenum, and rarely in the esophagus and colon. The progress in cancer treatment, improved survival of cancer patients combined with increased use of endoscopy is likely going to increase the findings of secondary tumors of the gastrointestinal tract. As such the endoscopist has to be aware about the clinical and endoscopic features of these lesions, maintain high index of suspicion in proper clinical settings and alert the pathologist about the possibility of metastatic tumor.

## Key words

Endoscopic, gastrointestinal, metastasis

## Introduction

The three cancers commonly reported to be associated with metastasis to the gastrointestinal tract include melanoma, lung cancer, and breast cancer. However, a retrospective review of 42 patients in Taiwan with metastasis to the gastrointestinal tract showed that hepatocellular carcinoma was the leading primary lesion for such metastasis.<sup>[1]</sup> This led them to speculate that for different countries, differences exist as regards cancer epidemiology, and that the primary cancer most commonly metastasizing to the digestive tract may differ from country to country or ethnicity to ethnicity.

The incidence of gastrointestinal tract metastasis is rare. The reported incidence has been found to be about 1/3847 in upper endoscopic procedures and 1/1871 colonoscopies in one retrospective review of endoscopy database.<sup>[1]</sup> The other study, based on a questionnaire survey of the staff of 34 medical clinics, demonstrated that the metastasis to the gastrointestinal tract were verified among 3477 upper gastrointestinal endoscopic procedures while no lower gastrointestinal tract

metastasis appeared to have been detected from among 1634 colonoscopies.<sup>[2]</sup> Based on the multiple autopsy studies the incidence of metastatic lesions in the esophagus has been reported to range from 0.3 to 6.1%<sup>[3-6]</sup> and in the stomach the incidence ranged from 0.2 to 5.4%.<sup>[7,8]</sup>

In patients with melanoma, the incidence of the metastasis to the gastrointestinal tract was 43.5% in one autopsy series.<sup>[9]</sup> Another large review of autopsies from Memorial Sloan Kettering Cancer Center found the metastasis from melanoma in liver around 68%, colon 22%, stomach 20%, duodenum 12%, rectum 5%, esophagus 4%, and anus 1%.<sup>[10]</sup> Most patients who have been reported to have metastatic lesions in the gastrointestinal tract have also had a number of other sites of metastasis.<sup>[6]</sup>

The autopsy series record an incidence as high as 8–16% of breast cancer metastasis to the gastrointestinal tract.<sup>[8,11]</sup> The median latency time interval between the diagnosis of breast cancer primary and the gastrointestinal metastasis may vary from few months to years.<sup>[12-14]</sup> Lobular carcinoma of the breast represents a minor group of the histological subtype in breast cancer (10–15%), but it is the most common metastatic histological type from breast cancer to the gastrointestinal tract.<sup>[15,16]</sup>

The autopsy data on the gastrointestinal tract metastases from primary carcinoma of the lung suggest about 14% incidence with esophagus being the most common site of metastasis followed by small bowel and colon.<sup>[17]</sup>

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## Clinical Features

The clinical features of patients with metastatic tumors of the gastrointestinal tract can be quite variable. As such it is very important to maintain a high index of suspicion even with nonspecific symptoms in patients who have current, recent or remote history of above-mentioned tumors.

The presenting symptoms may be nonspecific, although, the symptoms of gastrointestinal bleeding and abdominal pain seem to be the two most common symptoms in most studies.<sup>[1,18,19]</sup> Occasionally, symptoms of weight loss, dysphagia,<sup>[3]</sup> dyspepsia, and bowel obstruction<sup>[20]</sup> may be the presenting complaints. In Taiwanese review of 42 patients, gastrointestinal bleeding was the presenting symptom for about 60% patients while abdominal pain was present in about 19%.<sup>[1]</sup> The gastrointestinal bleeding can be gross, occult, acute or chronic. Small bowel palpable mass from metastatic melanoma<sup>[20]</sup> and obstructive jaundice from metastasis to the ampulla has been reported.<sup>[21]</sup> The metastasis to the esophagus can result in dysphagia<sup>[3]</sup> and metastasis to the stomach can produce dyspepsia. Rarely malabsorption has been reported due to metastasis to the small bowel from melanoma.<sup>[22]</sup> At the same time, some patient's may exhibit no symptoms as happens about 3–22% in patients of melanoma with metastasis to the small bowel.<sup>[23,24]</sup>

Lung cancer metastases to the gastrointestinal tract involve usually the small bowel and appear clinically more frequently as intestinal perforation. Such presentation is believed to be due to the tendency of these tumors to necrosis.<sup>[17,25]</sup>

## Endoscopic Features

The endoscopic patterns of metastatic tumors to the gastrointestinal tract can be variable as well. Such tumors on endoscopy can present as solitary [Figure 1] or multiple nodular lesions [Figure 2]. The appearance of these tumors as subtle mucosal changes, multiple nodules, bull's eye lesions [Figures 3-5], extrinsic mass lesions, ulcerations,

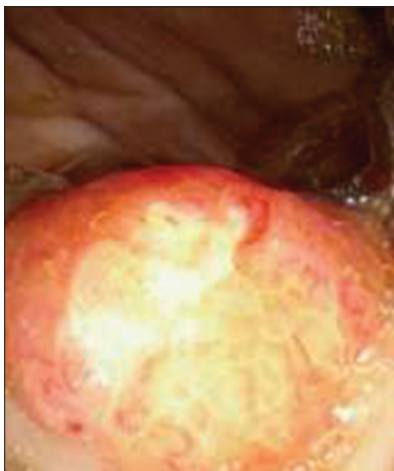
subepithelial growths or polypoid tumor masses [Figure 6] has been reported.

In the stomach, solitary metastasis appears more common than multiple. In one endoscopy series by Wei *et al.* 42 patients with metastasis to the gastrointestinal tract presented more frequently as solitary (61.9%) rather than multiple (38.1%) lesions.<sup>[1]</sup> The results in this series also indicated that most tumors were primary (mucosa-origin) carcinoma-like lesions (90.5%). This result was quite different to that of a previous report, for which Oda *et al.* reported a submucosal tumor-like appearance of metastases (51%) being more common than primary (mucosa-origin) carcinoma-like lesions (39%).<sup>[7]</sup>

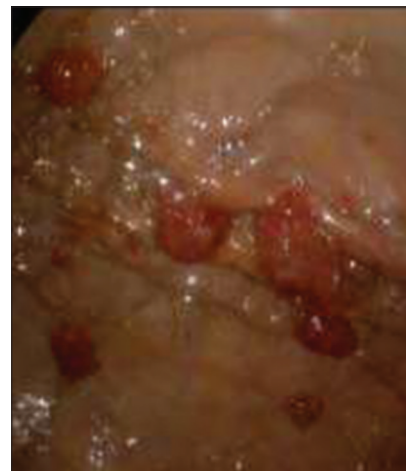
This discrepancy appeared to be due to the fact that Oda *et al.*, included metastatic tumors involving the stomach alone while the Wei *et al.* included patients with metastatic tumors to the entire digestive tract.

In cases of melanoma, although all histologic subtypes of cutaneous melanoma may metastasize to the gastrointestinal tract, the superficial spreading melanoma is the most common subtype which exhibits such spread.<sup>[26]</sup> Metastatic gastric and duodenal melanomas classically appear as small submucosal nodules that may have central ulceration producing a well-known “target or bull’s-eye lesions” on endoscopy.<sup>[27]</sup> These lesions may be either pigmented or amelanotic. The small bowel involvement with metastatic tumors is more common in melanoma than upper or lower gastrointestinal tract which is believed to be due to its rich blood supply. These lesions in the small bowel can appear as intraluminal masses or serosal implants and usually diagnosed on imaging studies.<sup>[24]</sup>

Metastatic breast cancer with gastrointestinal tract involvement represents evidence of a systemic disease.<sup>[14]</sup> The endoscopic findings display great variability, including lesions with a benign appearance but also diffusely infiltrative lesions, and localized tumor formation with nodules



**Figure 1:** Nodular metastatic deposit in stomach from melanoma



**Figure 2:** Multiple Nodules in stomach from metastatic melanoma



**Figure 3:** Metastatic "bull's eye lesion" in stomach from melanoma



**Figure 4:** Metastatic lesion in stomach from clear cell renal carcinoma



**Figure 5:** Metastatic deposit from renal cell carcinoma in colon



**Figure 6:** Submucosal lobulated nodules noted on EGD and EUS in stomach from metastatic melanoma

and/or ulceration. Diagnosis can be difficult due to an often prolonged tumor-free interval and a benign appearance of the lesions.<sup>[28]</sup> On the other hand, gastric metastasis may occasionally mimic a gastric primary.<sup>[29]</sup> Stomach is the most frequent gastrointestinal site for metastatic breast cancer. The most characteristic endoscopic finding of metastatic lobular breast carcinoma is a linitis-plastica-like appearance, showing tumor infiltration along the stomach wall with mural thickening of the involved segment shown in the series of Winston *et al.* with submucosal infiltration.<sup>[30]</sup> This intramural and submucosal pattern of infiltration of the gastrointestinal tract makes the diagnosis difficult on endoscopic and imaging examinations.<sup>[31,32]</sup>

Advances in imaging techniques like CT scan and endoscopic ultrasound with guided biopsy have aided confirmation of the diagnosis.<sup>[30,31]</sup> The hepatocellular carcinoma with gastrointestinal tract metastasis is a rare condition, being found only in 4–12% of cases in autopsy series.<sup>[33,34]</sup> These patients usually present with gastrointestinal bleeding. In one series of 11 patients with proven gastrointestinal metastasis from hepatocellular carcinoma the endoscopic

features included ulcerative tumors mimicking advanced gastric carcinoma (43%) and submucosal tumors (29%). The sites of organ involvement in this series were stomach (five), duodenum (two), colon (three) and both duodenum and colon (one).<sup>[35]</sup> The prognosis in these patients is extremely poor.

The gastrointestinal metastasis in renal cell carcinoma is very rare. A review of 17 cases consisted of 5 cases with duodenal metastasis and 12 cases of gastric metastasis with endoscopic appearance of solitary or multiple nodules.<sup>[36]</sup> The other tumors reported to develop metastasis to the gastrointestinal tract include malignant pleural mesothelioma,<sup>[37]</sup> hepatic angiosarcoma,<sup>[38]</sup> primary leiomyosarcoma,<sup>[39]</sup> testicular seminoma<sup>[40]</sup> and head and neck tumors.<sup>[41]</sup>

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