SYNCHRONOUS GASTRO-INTESTINAL MALIGNANCIES - A CASE SERIES

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Abstract:
The occurrence of multiple gastrointestinal cancers in the same patient was previously thought to be extremely rare. But with advancements in investigative modalities and with greater implementation of screening programs, the occurrence of synchronous Gastro-intestinal cancers is being increasingly recognised. Apart from it being a diagnostic oddity, the importance of a synchronous primary is that the diagnosis alters the prognosis and management of the patient considerably. In this case series, we report three cases of synchronous cancers, where both the first and the second primary cancers were found in the gastrointestinal tract. Case 1 65 year old Male presented to us with history of recurrent stale food vomiting and dysphagia. He was diagnosed to have synchronous oesophageal and gastric cancers. The oesophageal cancer was poorly differentiated squamous cell carcinoma and the gastric malignancy was a moderately differentiated adenocarcinoma. Case 2 70 year old lady presented with symptoms of gastric-outlet obstruction and dyschezia. She was found to have synchronous gastric and rectal cancer. The gastric cancer was a poorly differentiated adenocarcinoma and the rectal malignancy was a well differentiated adeno-carcinoma. Patient had omental deposits at presentation. Case 3 59 year old male presenting with dysphagia, was found to have dual oesophageal cancers. One lesion was well differentiated while the other was a poorly differentiated squamous cell carcinoma. Each of the cancers was symptomatic and in all three patients curative management was not possible, since the cancers were advanced. We suggest screening upper GI endoscopy in those with colorectal cancers and vice-versa, so that synchronous GI cancers can be diagnosed at an early stage, thereby making curative treatment options feasible.

Keyword: synchronous, malignancy, gastro-intestinal, carcinoma, dual

INTRODUCTION:
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Advancements in investigative modalities and with greater implementation of screening programs, the occurrence of synchronous Gastro-intestinal cancers is being increasingly recognised. Apart from it being a diagnostic oddity, the importance of a synchronous primary is that the diagnosis alters the prognosis and management of the patient considerably. In this case series, we report three cases of synchronous cancers, where both the first and the second primary cancers were found in the gastrointestinal tract.

CASE1:
65 year old male patient, presented to us with a 4 month history of recurrent vomiting. The vomiting occurred around 3 to 4 hours after meals and contained non-bilious, undigested, stale food. He also gave history of dysphagia, predominantly for solids, over the preceding 2 months. These symptoms were associated with a significant loss of weight and appetite. He was a chronic smoker. There was no history of cancer in his family. On examination, the patient was emaciated and pale. Per abdomen findings included visible gastric peristalsis, demonstrable succussion splash and a hard and nodular hepatomegaly. Ultrasound of the abdomen revealed multiple hypoechoic lesions in both the lobes of the liver, suggestive of secondaries. At Upper GI endoscopy, the patient had a circumferential ulceroproliferative lesion between 18 and 20 cm [Fig. 1]. The Oesophago-gastric junction was at 40 cm. Stomach showed an extensive ulceroproliferative lesion along the greater curvature, starting from the body and extending onto the antrum and pylorus [Fig 2], with luminal obstruction at pylorus. Biopsies were taken from both the lesions.

Figure 1: Growth oesophagus 18-20

Figure 2: Growth Stomach causing GOO

HISTOPATHOLOGY
The biopsy from the oesophageal lesion showed features suggestive of poorly differentiated non-keratinising squamous cell carcinoma [Fig. 3], and biopsy from the stomach showed features suggestive of moderately differentiated, infiltrating adenocarcinoma of the intestinal type [Fig. 4].
Figure 3: Growth Oesophagus: poorly differentiated, non-keratinising squamous cell carcinoma

Figure 4: Growth Stomach: moderately differentiated, infiltrating adeno-carcinoma – intestinal type

Since the patient had metastatic disease, curative treatment was not possible. Patient underwent a naso-jejunal tube placement [Fig 5] for nutrition, and was started on palliative chemotherapy and radiotherapy.

Figure 5: Patient with Naso-jejunal tube

CASE 2:
70 year old lady presented with the complaints of post-prandial abdominal discomfort and early satiety, over the preceding 3 months. Patient had complaints of dyschezia with passage of frequent small volume stools mixed with blood, over the preceding one month. It was also associated with a sensation of incomplete evacuation. There was weight loss of around 7 kgs, since the onset of symptoms. She had no history of cancers in the family. Examination revealed a firm epigastric fixed mass of about 6 x 7 cms. Per rectal examination revealed a nodular growth along the antero-lateral wall extending from 4 cm from the anal verge. Per vaginal examination was not contributory. Upper GI endoscopy revealed a fleshy proliferative growth involving the antrum and pylorus with luminal narrowing [Fig. 6]. Colonoscopy showed a semi-circumferential ulceroproliferative friable growth extending from 4 to 10 cms [Fig 7]. The rest of the colon was normal. Multiple biopsies were taken from the lesions.

Figure 6: Growth stomach – involving antrum & pylorus

Figure 7: Growth Rectum Semi-circumferential ulceroproliferative growth

Figure 8: CT showing thickening of antrum
Figure 9: CT showing rectal wall thickening

**HISTOPATHOLOGY:**
Biopsy from the gastric growth showed features suggestive of *Infiltrating poorly differentiated adenocarcinoma* [Fig. 10] and biopsy from ano-rectal growth showed features of *Infiltrating well differentiated adenocarcinoma* [Fig. 11]

The patient was inoperable due to the presence of omental metastases. Patient underwent a palliative antro-pyloro-duodenal stenting [Fig. 12] for the gastric growth, and a sigmoid colostomy [Fig. 13] for the ano-rectal growth.

**CASE 3:** 59 year old male presented with a two month history of dysphagia. The dysphagia was progressive and was more for solids than liquids. He was a chronic smoker and had a history of coronary heart disease. There was no history of any cancers in the family. On examination
, hewas and a hard palpable liver, emaciated and pale, with cervical lymphadenopathy. Upper GI endoscopy revealed an eccentric fleshy lesion [Fig 14] from 17 to 20 cm. There was a second oesophageal lesion [Fig 15] which was ulceroproliferative and circumferential, extending from 32 to 37 cm. The intervening oesophageal mucosa between the two lesions was normal. The oesophago gastric junction was at 37 cm and the gastric cardia was not involved by the growth. Multiple biopsies were taken from both the lesions.

HISTOPATHOLOGY:
The proximal lesion revealed features suggestive of moderately differentiated squamous cell carcinoma [Fig: 16], whereas the biopsy from the distal lesion [Fig: 17] revealed feature suggestive of poorly differentiated squamous cell carcinoma.
The patient was inoperable, owing the presence multiple liver secondaries. The patient underwent palliative Percutaneous Endoscopic Gastrostomy [PEG] [Fig. 18] for feeding and was started on palliative Chemo-RT.

**DISCUSSION:**

*Synchronous cancers are those which are detected during or within 6 months of diagnosis of the primary cancer.* Billroth, in 1869 was the first to report the simultaneous occurrence of two independent cancers at two different sites in the same individual. He laid down the following criteria for the diagnosis of synchronous cancers.

1. The two lesions must differ histologically so as to exclude the possibility that they are of the same origin.
2. Each lesion must develop from its parent epithelium.
3. Each lesion must produce its own separate group of metastases.

It was believed that these postulates and criteria were too strict and impossible to fulfill if the two malignancies occurred in the same organ. Hence in 1932, Warren and Gates broadened the criteria as follows. [14]

1. All cancers must be malignant as determined by histological evaluation.
2. Each cancer must be geographically separate and distinct, and the lesions should be separated by normal-appearing mucosa.
3. Metastatic cancer must be differentiated from multiple primary cancers and ruled out.

The incidence of synchronous cancers in the gastrointestinal tract has been reported to vary from 0.7% to 3.5% [1-5] in various studies. This variation in the incidence, probably relates to the heterogeneity of the studies, with respect to study population and methods. As would be expected, population based studies show a lesser incidence when compared to hospital based studies. Over the years, the incidence of synchronous cancer has been on the rise – possibly related to the availability of better screening tools and increasing longevity of the population.

The risk factors determining the development of synchronous cancers are not clearly known. Advanced age is probably the single most important risk factor. Almost all cases of multiple synchronous malignancies reported in literature have occurred in the elderly. The occurrence of synchronous cancers also tends to be higher in males [9]. Patients with multiple cancer-related risk factors, like smoking and alcohol are also more prone to harbour synchronous malignancies [9]. However, the exact mechanism...
b\basis for the development of synchronous cancers is largely unknown. [7, 8] Apart from common environmental cancer-related risk factors, an underlying genetic predisposition for these cancers has also been hypothesized. These include HNPCC syndrome, microsatellite instability and mutations in DNA repair genes. [8] Nevertheless, most reported cases to date have not shown any particular genetic aberration to account for this phenomenon.

In our case series, two patients had gastric cancers with synchronous oesophageal and rectal cancers. In the study by Jun Ho et al [9], the incidence of gastric cancer having another synchronous primary cancer was 3.4%. The most common synchronous malignancy associated with gastric cancer was colo-rectal cancer [37.2%], followed by lung cancer [18.6%] and thirdly by oesophageal cancer [16.8%]. The risk factors in this study was advanced age. Both our patients were in the seventh decade. Both patients had symptoms related to each of the primary cancer. The cancers were also inoperable since both cases had evidence of metastatic disease at diagnosis. The origin or the primary of these metastases was not investigated since it was likely to be inconsequential to the management. In view of the metastatic status of the cancers, only palliative management was possible in both these cases. One patient underwent a naso-jejunal tube placement for feeding, while the patient with synchronous gastric and rectal cancer underwent antro-duodenal stenting and a sigmoid colostomy. The incidence of synchronous cancers along with oesophageal cancers is well documented in literature. The incidence of synchronous cancer associated with oesophageal cancer varies from 2.9% to 3.6%. The most common second primary is head and neck tumours. The third patient in our case series had two distinct oesophageal primary cancers. The incidence of two synchronous oesophageal cancers is exceeding rare. In a study by Rui Wang et al [12], which was a retrospective analysis of 45,302 cases undergoing UGI scopy, two synchronous oesophageal cancers were present in only seven cases [0.01%]. Our patient had both the conventional risk factors for squamous cell carcinoma, namely smoking and alcohol. The patient was inoperable due to the presence of liver metastasis. Palliative stenting was not feasible owing to the proximity of the proximal lesion to the crico-pharynx. Patient underwent a Percutaneous Endoscopic Gastrostomy for feeding and palliative Chemo-RT.

To conclude, we suggest that synchronous malignancies should be actively looked for in gastro-intestinal cancers. The common dietary, environmental and genetic factors that underlie various gastro-intestinal cancers, argues for the same. The detection of synchronous cancers early, would give us the opportunity to treat both cancers simultaneously, using less invasive techniques and thereby influence the prognosis and quality of life positively. In our case series all cancers were symptomatic, advanced, and inoperable at diagnosis. In a few centres around the world, Upper GI endoscopic screening is being practiced for colorectal cancers and a screening Lower GI endoscopy for Upper gastro-intestinal cancers [9]. Implementation of the same is likely to detect more synchronous cancers at the pre-symptomatic stage and would possibly contribute to a curative management. Underlying genetic predisposition in these cases should also be analysed to improve our understanding of these tumours.
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