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Occurrence of a Signet Ring Cell Carcinoma in the Gastrium and Rectum at the Same Time: A Case Presentation

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Abstract: **Gastric cancer (GC) and Colonic Rectal Cancers, (CRC are among the frequent cancers today, most of them are adenocarcinomas. The occurrence of the GC metastasizing to the CRC is rare and the metastasizing of CRC to GC is even worse in being rare. The other issue about these cancers is the occurrence of Synchronous or Metachronous development in the GC or in the CRC. It is always a challenge to know what really is happening in the patient. We present MS a Male 43 years who developed a GC and a CRC at the same time. Our challenge was to arrive at a diagnosis at what really happened to him.**

Keywords: **CRC, GC, Metachronous, Metastasizing, Synchronous, SRA.**

1. BACKGROUND

Gastric cancer (GC) is among the frequent cancers today, most of which are adenocarcinomas. From the Colonic Rectal Cancers,(CRC) the metastases are observed in the liver, lungs, lymph nodes, and peritoneum. Hepatic metastases of gastric adenocarcinomas are frequently observed due to the drainage into portal vein. Intestinal metastases disseminate from gastrocolic and mesenteric ligaments but they are seen very rarely and in most cases detected in postmortem studies [2]. It is also known that the most common pattern of recurrence of gastric cancer (GC) is peritoneal dissemination known as the Krukenberg's tumor or Plummer's rectal shelf. However, GC metastasis via hematogenous or lymphatic spread does occur but it is exceedingly rare. Norio Uemura, et al presented a case of a 65-year-old man with an intramucosal GC who developed a rectal recurrence, possibly via a hematogenous route[3].

The prognosis of GC is generally poor, especially in Western countries where the overall survival rate at 5 years has not changed, oscillating between 8 and 26%, even though the resectability rate has increased (currently 60–80%) [6].

Most malignant rectal tumors are histopathologically characterized as adenocarcinoma and generally metastasize to distant organs such as the lungs or the liver. Metastasis of rectal carcinomas to the GC or skull is extremely rare [7].

It is well known that patients with primary colorectal carcinomas or Gastric carcinomas may have more than one malignant lesion within the Colon and rectum or Gastrium at the time of initial presentation. It is called the synchronous carcinoma. Synchronous colorectal or Gastric neoplasias are defined as or more primary tumors identified in the same patient and at the same time. The most voluminous synchronous cancer is called "first primitive" or "index" cancer[10]. Synchronous colorectal or Gastric carcinoma denotes more than one primary colorectal carcinoma detected in a single patient. On the other had the Metachronous colorectal or Gastric carcinoma is the presence of more than one primary colorectal carcinoma detected consecutively in a single person after a set time interval. In the literature, many studies have mixed these two entities together in their analysis [11].The reported incidence of synchronous colorectal carcinoma ranged between 2.3% and 12.4%[8].Some workers say that the synchronous and consecutive (metachronous) development of two or more primary adenocarcinomas accounts for 3 to 5 % of cases of colorectal cancer cases[9]. Most

studies of multiple malignancies have found colorectal cancer (CRC) as the second tumor of GC in patients .But the occurance of CRCs spreading to the Gastrium are rare. The other sites of second CRCs tumors include breast, lung, prostate, uterus, small intestine, liver, esophagus, and kidney [12]

Stomach cancer (GC) can occur during chronic inflammation from *Helicobacter pylori* (*HP*) infection. In fact, patients with gastric cancer who, have undergone *HP* eradication after treatment of early gastric cancer with endoscopy, they may develop metachronous cancer recurrences over a period of 5 to 13 years .So eradication of *HP* does not completely suppress the occurrence of metachronous gastric cancer, and some cases of recurrence after eradication have been reported[16].

2. CASE PRESENTATION

We present the case history of a male CT who was 43 years old. He was healthy until 2000 when he started having occasional constipation. At that time he would pass hard stools with occasional bleeding after passing hard stool. This was probably a fissure in ano. This was on and off, the hard stool passage went on up to 2010. In 2010 he had a road accident and ended up with many fractures. He was in hospital for almost a year needing major operations. It is believed that his immune status brought a set of malignant occurrences. As for the presence of HIV, he was negative.

In 2011 he started having epigastric pain, it was associated with early satiety. He had no distended abdomen, vomiting and no nausea. In 2015 he stated having vomiting especially after meals. The vomit was the colour of food mixed with blood – It was coffee grounds. After three weeks he developed easy fatigability and had an awareness of palpitations of his heart.This mean that the patient was anaemic. The abdominal ultrasound scan did not reveal any abnormality.

Investigations and Treatments done:

A Barium meal for GI and endoscopy were done. He was told he had a gastric tumour in his stomach. Partial Gastrectomy (Billroth type II) was done.

This biopsy sample from the stomach was collected on the 20th of December 2015. These were sent to a Private laboratory. The Histopathology results were concluded that the patient had Undifferentiated Signet Ring Cell Adenocarcinoma (SRA). The histopathology report came back to the patient within a week and chemotherapy was started. The patient felt better until end of 2016.

From December of 2016 he started having severe constipation, it went on until March 2017. He redeveloped early satiety again and restarted to vomit after meals. He started vomiting after meals. He vomited only foods there was no bleeding. His abdomen was getting distended. He became pale again. At this stage he was having difficulty in passing stool and the stool was mixed with blood. A barium meal was done in February 2017. The man could not pass the barium through the stool. The Ultra sound scan showed an irregular stomach.

At this stage in the March of 2017 he underwent a DRE. There was a big mass in the rectum which at this stage revealed a rectal malignancy (CRC).

A Laparotomy was done on 10th of March 2017. The finding were that he had a large Rectal mass which at this stage prevented passing of stool. There was also a large gastric tumour as well. The Liver was free of tumours but there were tumours spread all over the abdomen.

On the transverse colon a colostomy was done to help the patient to pass stool and lessen the abdominal distension. The biopsy was taken from the tumour in the colon and the Ndola Teaching Hospital laboratory reported an invasive Signet Ring Cell Carcinoma, in the colon biopsy sample!

The latest development was that he became jaundiced. Subsguently, the man died after three weeks

3. DISCUSSION

There are several issues on this patient.

1. It could be that he developed a Gastric malignancy which started as an epigastric pain, associated with early satiety. Later it metastized to a rectal malignancy.
2. This patient could have developed a rectal tumour which started in 2000 as a fissure in ano. In 2016 it developed more seriously when he stated having severe constipation and DRE was missed all these years only done in March 2017 when a large rectal tumour was diagnosed. Probably this tumour must have metastasize to the Gastric tumour.

3. There is a possibility that the tumours started differently or similarly at the two sites ie the Gastric area and at the rectum. The terms system could have been either Synchronous or metachronous malignancies. The two tumours grew up separately at the same period from 200 to 2017.

Intestinal metastasis from gastric cancer is rare, although the most common cause of secondary neoplastic infiltration of the colon is gastric cancer[1]. We present the work of Takehiro Noji et al presented the following case**:** To the best of their knowledge, they found only two reports in the English literature which described lower intestinal metastasis from gastric cancer to the colon occurring more than 5 years after primary surgery. From January 1999 to July 2012, they performed 1020 gastric cancer surgeries and encountered 3 cases with late-onset lower, that is colon, intestinal recurrence of gastric cancer occurring in 9 to 11 years. In fact in their latest report they had 2 cases of late-onset colon metastasis from gastric cancer. Histologically it was poorly differentiated adenocarcinoma involving the signet-ring cell carcinoma. Deniz Tura et all reported a case report of a 74-year-old female who presented with no known history of disease. Her complaints were epigastric pain, burning sensation, and constipation. Her Gastroscopy showed a submucosal mass in the greater curvature of fundus and in the colonoscopy, a mass with polypoid appearance that narrows the lumen at the rectum was detected. In our case the Gastrectom was very similar to their patient's picture[2]. We did not do a colonoscopy but the rectal examination showed that narrowing of the lumen at the rectum. This was their first in literature reporting a rectum metastasis without any other organ metastasis[2]. It is a fact that the most common pattern of recurrence of gastric cancer (GC) is peritoneal dissemination known as Krukenberg's tumor or Plummer's rectal shelf. However, rectal metastasis via hematogenous or lymphatic spread is exceedingly rare. Norio Uemura, et al present a case of a 65-year-old man with an intramucosal GC who developed a rectal recurrence, possibly via a hematogenous route[3]. They concluded that although rectal metastasis from GC, particularly when attributable to hematologic or lymphatic metastasis, is very rare, metastatic gastric adenocarcinoma should be considered as a differential diagnosis for patients who present with a rectal tumor and a past history of GC, even if it is an early GC. It is possible that our patient could have developed this problem.

Sang Woo Lim et all reported that Gastric cancer is one of the most common malignancies in the world and is the second most common cause of cancer-related death in Korea[4]. In Zambia we do not have that record so far. They also agree that Colonic metastases from gastric adenocarcinoma are known to be very rare. They presented a case like ours but their patient was a female we had a male: She was a 43-year-old woman who first presented with epigastric pain was diagnosed with gastric cancer. She had undergone radical total gastrectomy with D2 lymph node dissection, and splenectomy. At thirty-four months after surgery, during a routine review the patient complained of difficulty with defecation and constipation since the last time. On digital rectal examination and colonoscopy, hard induration and stenosis of the rectum. This was very similar to our DRE findings in our patient March 2017. In their patient they postulated that the rectal tumor was a metastatic tumor from gastric malignancy[4].Even in Asia background Gastric cancer is one of the most common malignancies in the world and is the second most common cause of cancer-related death but Colorectal metastases from gastric adenocarcinoma are known to be very rare there also. Emad Dawoud et all report a 43-year-old female patient who was exactly like the Korean patient also similar to our male patient. Their patient at Endoscopic biopsy confirmed the presence of Signet Ring Adenocarcinoma(SRA), in the same time she developed Synchronous Solitary Colon Metastasis from Gastric Signet Ring Adenocarcinoma[5]. Also very similar to what we found in our patient.

There is another problem in our patient;did he get the gastric malignancy from the colon? The incidence of CRC in Iran is lower than that in Western countries, being the fifth and third most common cancer in men and women. , Its incidence in Iran is rising. This is very similar to the Zambian situation. The Iranian writers could not say specifically that they actually noticed a CRC spread to GC[6]. Metastatic gastric cancer is uncommon, and metastasis of colorectal cancer to the stomach is extremely rare[7]. Nushijima Y et al carried out a case of a 52-year-old woman who underwent a left hemicolectomy and D3 lymph node dissection based on a diagnosis of transverse colon cancer. The pathology results were as follows: They found a mucinous adenocarcinoma. This histology showed that this tumor was a mucinous adenocarcinoma similar to the primary transverse colon cancer, which led to a diagnosis of metastatic gastric cancer originating from transverse colon cancer.

In our patient he had the invasive Signet Ring Cell Carcinoma. In our patient's CRC it is hard to assume that his invasive Signet Ring Cell Carcinoma metastasized to the GC.

In fact our reading reveals that Metastasis of CRC to GC is very uncommon, compared with the GC matastization to CRC[6][7]. Most malignant rectal tumors are histopathologically characterized as adenocarcinoma and generally metastasize to distant organs such as the lungs or the liver. Metastasis of rectal carcinomas to the skull, skin,the hard pallet, and Pancreas does occur, may be un common but it occurs yet the Metastasis of CRC to GC is very rare[18][19][20].

Synchronous or metachronous colorectal/gastric neoplasias, are defined as two or more primary tumors identified in the same patient and at the same time, are caused by common genetic and environmental factors. The Question is what is the most likely event? It is well known that patients with primary colorectal carcinomas may have more than one malignant lesion within the colon and rectum at the time of initial presentation (synchronous carcinoma). Masatoshi Oya et al reported the incidence of synchronous colorectal carcinoma ranged between 2.3 and 12.4%[8]. Tziris N et all add up to Masatoshi Oya e tal that the synchronous and consecutive (metachronous) development of two or more primary adenocarcinomas accounts for 3 to 5 % of cases of colorectal cancer [9].In their view Patients with colorectal cancer must be followed up regularly after surgery,the aim is aimed at an early diagnosis and treatment of metachronous lesions that can appear many years after diagnosis of the primary lesion. Alessandro Spizzirri etal carried a study on Synchronous colorectal neoplasias. From January 2001 till December 2009, 557 patients underwent colectomy for colorectal cancer. On the observation period the only had 6 patients, 4 males and 2 females, were diagnosed with synchronous colorectal neoplasias; 3 of them had no comorbility while the others were affected by hypertension (2 males and 1 female) [10]. Alfred King-Yin Lam et al did their study and came up with the following: Differences in the range of prevalence of synchronous colorectal carcinoma were obtained from studies in Europe, Asia and America and their findings were Europe 1.1% to 8.1%, Asia 1.1% to 8.1%, and America 1.2% to7.0%.[11]. Most studies of multiple malignancies have found colorectal cancer as the second tumor in GC patients so although rare CRCs can occure in the GC. The other sites of second tumors include breast, lung, prostate, uterus, small intestine, liver, esophagus, and kidney.Many studies of multiple malignancies have been conducted in Asia; only a few have been conducted in Europe. We do not know the situation in Africa[12].

Ja Seong Bae et al investigated the characteristics of synchronous cancers in gastric cancer patients and came up with the following terms; the differentiation of gastric cancers was the only risk factor for synchronous cancers on the multivariate analysis and the serious thing is that gastric cancer cells may be a risk factor for synchronous cancers in gastric cancer patients[13]. The Koreans said something very significant that as follows "In recent advances of diagnostic methods and precise histopathologic examination, the incidence of synchronous multiple gastric cancer has increased" The purpose of their study was to evaluate the clinicopathologic features of patients with synchronous multiple gastric cancer. Their overall incidence of multiple synchronous gastric cancer was 2.33%.very similar their coleauges work. Their mean age was 57.2 years old (27-84), our patient was only 43 years old. Their peak incidence was sixth decade. The male was predominant like ours, and the sex ratio was 3.9: 1. [14]. Naturally it makes us think that our patient's problem was synchronous GC occurring in the CRC. Nozaki I et all did a study to clarify the risk factors for metachronous gastric cancer after partial gastrectomy for early gastric cancer. With regard to metachronous lesions; if the gastric cancer partially remains after the surgery, the risk of metachronous gastric cancer rises in patients[15].

We also have to remember that eradication of (*HP)* does not completely suppress the occurrence of metachronous gastric cancer (MGC), and some cases of recurrence after eradication have been reported[16].Some workers have said MGC can occur even if was defined as a gastric cancer newly detected at least 1 year after successful H. pylori eradication[17]. In our patient there was no evidence of HP treatment.

4. CONCLUSION

The fact that hematogenous or lymphatic metastasis between the stomach and the colorectum does occur, it is very rare. In our patient, the occurrence of a Gastric cancer(GC) metastizing to the rectum most likely occurred because the spread of the cancer from the colorectal cancer (CRC) to the gastrium is far less common. We Know that CRCs can occur in the Stomach and we know that most studies of multiple malignancies have found that colorectal cancer is the second tumor in GC patients although rare.

We also believe that Synchronous and metachronous primary tumours are a likely reality in an oncological patient like ours. Males have been shown to be at higher risk of developing synchronous or metachronous tumours than females. The overall incidence of this phenomenon in the populations studied so far is 2.3-12.4%. There are no studies that have been done to demonstrate the extent of this phenomenon in Zambia Africa, thus far. The incidence of synchronous or metachronous tumours is expected to increase and occur as our cancer patients get to live longer with therapy, even in Zambia Africa.

Apart from GC or CRC synchronous or metachronous tumours, like our patient, the other sites of second tumors include breast, lung, prostate, uterus, small intestine, liver, esophagus, and kidney.

Even if these patients went into complete clinical remission, it is imperative to remember the dreadful reality which warrants thorough and regular follow up of most cancer patients. Our patient was clinically diagnosed as a gastric SRA and started on Chemotherapy, one year later we found him with a CRC , SRA tumour. Most likely it was a consecutively occurrence. So it was most likely a metachronous tumour. Even if we consider the fact that he had Rectal difficulties at first and later was diagnosed as a Gastric Malignancy and assume that he initially had a rectal malignancy it still comes to a metachronous malignancy.

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