

# Signet-ring Gastric Carcinoma, at Bahrain

Amal Almahroos<sup>1</sup>, Khalid A. Al-Sindi<sup>2</sup>, Mandeep Bedi<sup>3</sup>, Maitham Alsadadi<sup>4</sup>, Mohamed A. Alhamar<sup>5</sup>,  
Mulazim Hussain Bukhari<sup>6</sup>

<sup>1</sup>SHO, University Medical Center, King Abdulla Medical City, Kingdom of Bahrain, <sup>2</sup>Prof of Pathology, King Hamad University Hospital, Bahrain, <sup>3</sup>Pathologist, Kolkata Police Hospitals, Kolkata, India, <sup>4</sup>Consultant gastroenterologist, University Medical Center, King Abdulla Medical City, Kingdom of Bahrain, <sup>5</sup>Senior House officer, Histopathology, King Hamad University Hospital, Building 2345, Road 2835, Block 228, Busaiteen, Kingdom of Bahrain, <sup>6</sup>Prof of Pathology, Punjab Medical University, Faisal Abad, Pakistan

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Amal Almahroos

## ABSTRACT

Signet ring carcinoma (SRC), a variant of gastric adenocarcinoma, is known to have a poor prognosis, especially when arising in the young population. In this report, two cases of gastric SRC carcinomas with different outcomes are described. The first case is a 49 years old Bahraini lady who presented with abdominal pain and was found to have a gastric ulcer over the lesser curvature on endoscopy and her biopsy showed features of a poorly differentiated signet ring adenocarcinoma. This patient was managed by a timely subtotal gastrectomy with adjuvant chemoradiotherapy. The second case is of a 34 years old Bahraini male whom presented with mild dyspepsia and in whom SRC was an incidental finding on initial endoscopic biopsy that was later confirmed by targeted biopsy. This patient was advised total gastrectomy but died due to delay in appropriate and timely interventions primarily due to his multiple consultations regarding the same matter.

## BACKGROUND

Gastric carcinoma (GC) is the 15<sup>th</sup> most common cancer in the USA and the 3<sup>rd</sup> most common cause of cancer-related death worldwide. The majority of GC patients present for medical attention in an advanced disease stage which makes cure for GC a real challenge. The incidence. The incidence of GC though found to be less than 2% in persons below the age of 35, was found to be more aggressive than in the other age groups.<sup>1</sup>

SRC is one of the sub types of adenocarcinoma that produce mucus, and owing to its characteristic infiltrative pattern and the associated high peritoneal carcinomatosis rate has shown to be a key independent

anticipator of poor prognosis.<sup>2-3</sup> Nonetheless, lesions that are diagnosed at an early stage demonstrated a favorable prognosis.<sup>4</sup>

This case report presents the course of two cases of SRC gastric carcinoma, both of which were diagnosed at an early stage, with their respective different outcome.

## CASE PRESENTATION

### Case 1

A 49 years old Bahraini lady presented with a history of abdominal pain since one year along with a change in bowel habits. Gastroscopy and colonoscopy were done in August 2014. Gastroscopy showed fundal gastric ulcer over the lesser curvature that had well defined margins with central depression. Microscopic examination of gastric biopsies revealed erosive gastritis. Gastric body mucosa showed features of moderately severe, chronic active (erosive) gastritis with prominent surface polymorph induced inflammation and pits abscesses. No apparent glandular atrophy was seen. However abnormal acidic mucin production was noted on special (Alcian blue/PAS) stain, signifying

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## Corresponding Author:

Mulazim Hussain Bukhari, Prof of Pathology, Punjab Medical University, Faisal Abad, Pakistan. E-mail: mulazim.hussain@gmail.com

an abnormal shift to the incomplete metaplasia. Pylori infection was noted on special (Warthin-Starry) stain. No equivocal evidence of dysplasia or neoplasia was found. Colonoscopy was negative. The patient received the standard triple therapy for Pylori infection (14 days of Amoxicillin, Clarithromycin and a proton pump inhibitor) followed by one month of proton pump inhibitor. Gastroscopy repeated one month after triple therapy showed persistence of gastric ulcer over the same location. (Figure 1). It was biopsied again. Microscopic examination confirmed eradication of H. Pylori but showed features of differentiated signet ring adenocarcinoma (Figure 2). The tumor was characterized by ill defined sheets and cords of mildly pleomorphic but large cells with both eosinophilic and clear bubbly cytoplasm with signet ring differentiation and foci of apparent intracellular (PAS/Alcian blue positive) mixed mucin production. No tumor cell necrosis was seen. Tumor cells were found within the lamina propria and the attached superficial part of the submucosa. Both computed tomography (CT) scans and positron emission tomography

(PET) scan were negative and the patient was referred for laparoscopic evaluation followed by subtotal gastrectomy on 16 October 2014. Postoperative pathology revealed a 3 x 2.5 cm ulcer on the lesser curvature showing poorly differentiated (grade 3) tubular adenocarcinoma. Lesion was invading lamina propria into muscularis propria. Five out of 22 examined perigastric lymph nodes were involved. Pathologic staging pT1a pN2 (Stage II), M0. Treatment was continued with concurrent chemotherapy and radiotherapy (CCRT)- (Capecitabine 1000 mg PO BD for 5 days per week with 5 weeks of radiation). Post treatment imaging showed no recurrence of the disease.

### Case 2

A 34 years old Bahraini gentleman with a short history of dyspepsia underwent gastroscopy, which showed mild antral gastritis. Endoscopic biopsies obtained were suggestive of gastric adenocarcinoma. Due to the unexpected findings gastroscopy was repeated by a different operator. After careful examination a small antral superficial ulcer was found and biopsied. Results confirmed the presence of SRC gastric adenocarcinoma. The patient was advised for total gastrectomy. PET scan was negative. Considering the mild presentation, diagnosis came as a surprise to the patient. Consequently, the patient kept obtaining several opinions. Investigations done at different hospitals were conclusive of the same diagnosis. But unfortunately by the time the patient agreed to undergo surgical resection, peritoneal metastatic deposits had taken place and due to unnecessary delay of 17 months between diagnosis and appropriate intervention, it led to death of the patient.

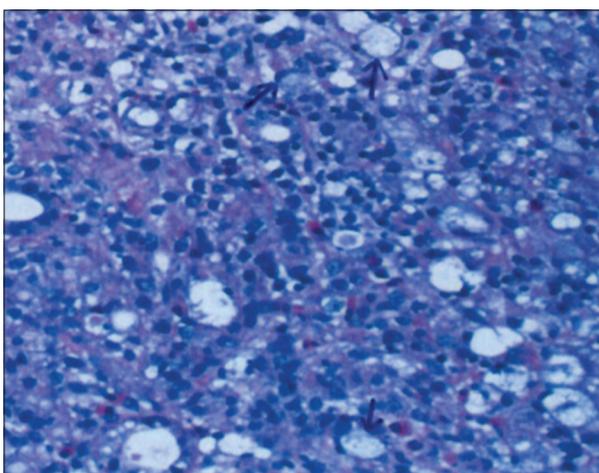
### DISCUSSION

Signet ring cell adenocarcinoma, a form of gastric adenocarcinoma, as declared by the majority of researchers has high invasive propensity with poor prognosis.<sup>3</sup> Having said that, the nature of SRC carcinoma remains controversial.<sup>2</sup> Some researchers, like Hyung WJ et al, stated that SRC has better survival rate and lower rate of lymph node metastasis when compared to non-SRC carcinoma.<sup>5</sup> Moreover, recent studies demonstrated that SRC carcinomas portend no worse prognosis compared to other forms of gastric carcinoma when adjusted for stage.<sup>4,6</sup>

Upon studying SRC lesions, it was found that those diagnosed at an early stage had a favorable prognosis, while those diagnosed at a later stage had much worse prognosis.<sup>2,4</sup> It was also observed that early lesions, restricted to the mucosal lining, had higher cure rates than within those with regional lymph node or distant metastasis.<sup>7</sup> The above findings suggest the urgent application of treatment early in the course of the disease leading to better outcomes. This



**Figure 1:** Lesser curvature fundal gastric ulcer with well-defined margins and central depression



**Figure 2:** Adenocarcinoma, Signet Ring Type: Ill-defined sheet of pleomorphic, poorly differentiated adenocarcinoma with apparent large cells containing eosinophilic and clear cytoplasm and signet ring differentiation (arrow). [H & E stain, MPF]

can also be appreciated on reviewing the outcomes of the cases presented above. As the first case (in which the disease was limited up to perigastric lymph nodes) responded well to treatment, while the second one (which developed peritoneal metastasis) ended with mortality as a result of the delay in treatment.

Diagnosis tend to be remarkably delayed among younger patients due to the low level of suspicion though they have high prevalence of the lesion thus posing diagnostic challenges.<sup>8</sup> As early diagnosis appears to play a crucial role in the management of SRC carcinoma, researchers have worked hard to improve the early diagnosis. One of the endoscopic signs that was found to be specific for the diagnosis of early SRC carcinoma is the “stretch sign” that is the “elongation of the architecture of the submucosa”.<sup>9</sup> This along with other signs can aid in the endoscopic diagnosis of early gastric cancer, knowing that early gastric cancer produces subtle mucosal changes in contrast to advanced cancer.<sup>10</sup>

One of the rare, however interesting, laboratory abnormalities that is found to be associated with gastric adenocarcinoma is thrombocytopenia.<sup>11,12</sup> It is believed that this phenomenon is mediated by immune mechanisms.<sup>13</sup> However this phenomenon was not noted in either of the cases presented here.

Treatment plan highly depends on the stage of the disease, therefore accurate locoregional staging is required to decide upon treatment modalities needed for each patient.<sup>14</sup> Endoscopic ultrasonography (EUS) is one of tools used for the diagnosis and staging of gastric cancer.<sup>14</sup> Various studies reviewed the accuracy of EUS-guided T-staging, which was found to be between 60 – 90%.<sup>14</sup> On the other hand, N-staging accuracies were found to be slightly lower, 50-80%.<sup>14</sup> However EUS influence on management is still controversial.<sup>14</sup> The disease of the first case presented earlier was staged through the following: endoscopic biopsy, preoperative laparoscopic exploration, PET and CT scans, and postoperative pathology examination.

Among the various lines of management of gastric cancer, curative resection has shown to be the most efficacious.<sup>6</sup> Curative resection generally includes lymphadenectomy.<sup>6</sup>

Regarding resection techniques used, many studies compared subtotal versus total gastrectomy with no observable difference in the survival rate.<sup>15-17</sup> Some suggest that subtotal gastrectomy is superior as it provides a better nutritional status and therefore better quality of life.<sup>17</sup> The latter complies with a study conducted in 200 which suggested that early SRC carcinomas may be managed through less invasive surgery for a better quality of life.<sup>5</sup>

Subtotal gastrectomy was chosen as the resection technique for the 1<sup>st</sup> case presented, and showed good results along with the following adjuvant chemoradiotherapy. It concluded that ESD is a safe and possible modality to treat undifferentiated early gastric cancer, however close follow-up is required due to the higher recurrence rates among patients managed with ESD than the rates for patients managed with surgery.<sup>6-17</sup>

## CONCLUSION

In conclusion, after comparing the clinical course and the consequent different outcomes of the two cases discussed above in this report, emphasis need to be made on the importance of the application of aggressive treatment as early as possible aiming for a better outcome. This can be made possible through the use of effective diagnostic tools and accurate staging methods followed by the selection of the appropriate treatment modalities.

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