



# Don't Give Up! Gastric Cancer; Poorly Differentiated Diffuse Type Carcinoma is Curable: A Case Report

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## Abstract

**Introduction:** Diffuse-type gastric carcinoma with signet ring cells (SRC) is a poor-prognosis subtype of gastric cancer, highly malignant with stromal induction. Till now searching for molecularly targeted drugs for these cases is disappointing.

**Case Presentation:** A 59-year-old female diagnosed with gastric cancer was admitted to Aria Hospital in Rasht, Iran in 2011. She underwent a subtotal gastrectomy as complete tumor resection with free surgical margins and adequate lymph node dissection. Diffuse infiltrating carcinoma was poorly differentiated. SRC carcinoma, tumor invades at the serosal surface, vascular and perineurial invasion, but no regional lymph node metastasis was reported. Then, the patient received chemotherapy with Taxotere plus oxaliplatin and 5-fluorouracil (5 FU) for 6 cycles and 20 sessions of radiation. At present, 6 years after the initial surgery, the patient is alive without any recurrence.

**Conclusions:** In the current case report the vital role of a multi-disciplinary approach to save cancer patients' lives is strongly appreciated.

**Keywords:** Gastric Cancer, Diffuse Type Carcinoma, Curable

## 1. Introduction

Gastric cancer (GC) with the highest incidence and mortality rate in Eastern and Western Asia is the 4th most common cancer and the 2nd most frequent leading cause of cancer death accounting for over 700,000 deaths per year. In spite of significant advances in therapeutic strategies, it is still a global burden with a poor prognosis, which the median survival is only estimated as 9 - 11 months (1-3). Its risk factors include *Helicobacter pylori* and Epstein-Barr virus infections, dietary patterns, method of food preservation, smoking, and obesity (2, 4). The current case report aimed at emphasizing the fact that although cancer diagnosis is disappointing and remains as a life threatening condition, a positive attitude of patients toward heavy and long-term treatments and a multi-disciplinary approach with a good cooperation among internal specialist, pathologist, surgeon, anesthesiologist, oncologist, and psychiatrist provide favorable outcomes and better prognosis. The main message of the current work was "Don't give up to cancer!"

## 2. Case Presentation

The current paper reports a case of GC who is still alive 6 years after diagnosis in 2011 with no local recurrence or distal metastasis. A 59-year-old female with no history of disease or medication, complaining about some non-specific symptoms such as heartburn and nausea, but no weight-loss or abdominal pain referred to Aria Hospital in Rasht, Iran. The *Helicobacter pylori* testing as well as other routine lab tests, and the tumor markers were reported within the normal ranges. A diagnostic endoscopy was performed, but histological evaluation reported no dysplasia or malignancy. Pantoprazole was started and she was advised to attend for the next visit 1 month later. She was quite asymptomatic, but due to suspicious endoscopic view (Figure 1), the procedure was repeated. The 2nd pathological examination was determined as diffuse type carcinoma, poorly differentiated with signet ring cells (SRCs). Pelvic and abdominal computed tomography (CT) scans indicated no evidence of metastasis. She was admitted to Aria Hospital, a private general and referral center, to continue diagnostic and therapeutic interventions. She underwent a subtotal gastrectomy as complete tumor resection with free surgical margins of at least 4 cm and ad-

equate lymph node dissection (12 lymph nodes). The microscopic findings supported the following diagnosis. Diffuse infiltrating carcinoma poorly differentiated (SRC carcinoma) (Figure 2), tumor invade at the serosal surface, vascular and perineurial invasion, but no regional lymph node involvement was reported. She had an uneventful post-operative course and was discharged 5 days after the operation. Surgery was followed by chemotherapy with Taxotere plus oxaliplatin and 5-fluorouracil (5 FU) for 6 cycles of 6 days and radiation was performed for 20 sessions. She was affected by treatment related adverse effects such as hair loss, appetite loss, dry mouth, weakness, and numbness in the hands, feet, achy muscles, and anxiety, which were hardly tolerable. The next endoscopy and CT scan with contrast and tumor marker check were conducted after 6 months. Now, 6 years after surgery, she is symptom free and is regularly visited.

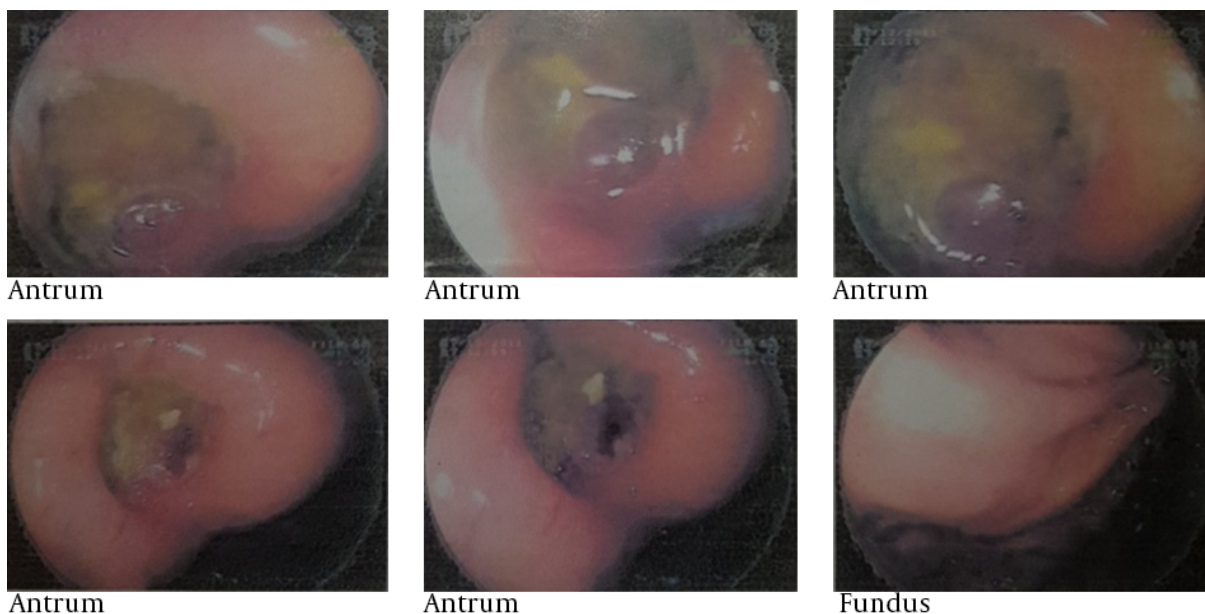
### 3. Discussion

Confirming the valuable improvements in cancer management guidelines, the current study results were compared with those of several studies from 2003 to 2017 investigating the pathological complete response rate and median survival time of advanced gastric cancer cases. In 2003, following available treatments, the pathological complete response was 0% and the median survival time was 7.3 months. Progresses in this field significantly improved the patients' outcomes; therefore, in 2008 the results showed that 1.1% of the cases had the pathological complete response and 13 months as the median survival time and in 2013 it increased to 21% and 17.3 months. Kazuhiro Tada reported a 58-year-old male diagnosed with advanced gastric cancer (T3N1M0), histologically differentiated tubular adenocarcinoma; estimated with a 5-year survival rate as 15%. After 3 courses of chemotherapy with S-1 plus cisplatin (SP), he underwent a total gastrectomy with lymph node dissection of the splenic hilum. A rare outcome with a complete recovery of the pathology was reported in the next examination and after 7 years he was not affected by any local recurrence or metastasis (5). Better clinical outcomes are expected following further researches in this field. Based on the New American Joint Committee on Cancer, tumor size (T), lymph node involvement (N), and metastasis (M) of the case (T3, N0, M0) presents stage IIB (6). According to American Cancer Society, the overall survival rate in GC is about 29% and the 5-year survival rate for GC at this stage is estimated as 33% (7, 8). In these cases a complete response to even powerful chemotherapy regimens is rare (5). Shimonosono et al. (9) reported, an 80-year-old woman suffering from

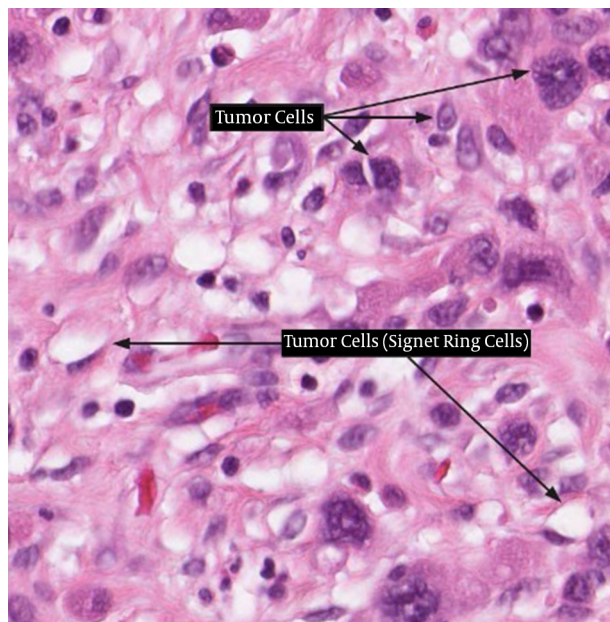
stage IV gastric cancer, poorly differentiated adenocarcinoma with perigastric lymph node metastasis. Her chief complaint was epigastralgia. In spite of tumor size reduction after administration of paclitaxel and S-1, a regrowth was observed in abdominal CT after the fourth chemotherapy course. Therefore, second line chemo-radiotherapy (CRT) was started with another regime. Then distal Gastrectomy with D2 lymphadenectomy with curative intent was performed. They suggested that intensive chemo-radiotherapy prior to gastrectomy in advanced gastric cancer, could increase the chance for a curative surgery (9).

In another report, by Abe et al. (10) a 66-year-old man with early gastric cancer, a well differentiated adenocarcinoma, tumor free margins with no lymph-vascular invasion was presented. She underwent a curative surgery. However, unexpectedly she developed a local recurrence and distal metastasis after 7 years, resistant to CRT and died. They recommended that maybe in early gastric cancer cases treated with endoscopic sub mucosal dissection the need for close monitoring and careful follow-ups by annual esophagogastroduodenoscopy and computed tomography (10).

In the current case, pathological diagnosis of the biopsy specimen was determined as diffuse-type gastric carcinoma poorly differentiated into SRC, which added more risk. Diffuse-type gastric carcinoma is a poor-prognosis subtype of gastric cancer, highly malignant with stromal induction. Till now results of searches on molecularly targeted drugs for these cases are disappointing (3, 11). SRC includes 15.1% - 28.2% of GC histological types. Not supporting the previous knowledge, it is determined that in early stages, SRC is not characterized by a poor prognosis with a gastric wall infiltration potential. Nevertheless, studies showed conflicting results. Beomell et al., indicated that the risk of lymph node metastasis (LNM) was higher in SRC, compared with mucosal cancer. In fact, the prognosis and outcomes of SRC remain controversial. In contrast, Imamura T. et al., reported that GC had a more favorable prognosis compared with other types. Thus, less invasive approaches such as endoscopic resection are not generally approved (12). It is shown that in cases of poorly differentiated GC known as a high risk type for LNM, the presence of SRC results in lower frequency of metastasis. On the whole, SRC seems a strong predictor for a better prognosis. Several justifying reasons are discussed in the current studies. It is suggested that SRC is found in younger patients and due to the typical enriched intracytoplasmic mucin and peripheral dense nuclei are easily discovered. Chael et al., found that mixed SRC behavior, similar to the current case, was more aggressive compared with the pure ones. Several factors including age, tumor stage, comorbidities, anesthesia, and surgical techniques



**Figure 1.** Endoscopic view: A large gastric ulcer, necrotic slough in the floor with irregular margin



**Figure 2.** Diffuse-type gastric carcinoma with signet ring cells

may affect prognosis after surgery. Obviously, similar to the other fields of medicine lots of gaps in knowledge remain in this issue. Nevertheless, a part of assumed factors for this success are discussed here. Firstly, GC is often di-

agnosed in advanced stages since the initial symptoms are vague and overlap with other benign conditions. Also, easy and inexpensive inspection methods and specific markers are not available (1). Thus, paying proper attention to such symptoms and essential examinations can lead to early diagnosis. Secondly, the accurate recognition of histological type of GC is crucial to determine the appropriate treatment planning. The achieved data from the first endoscopy revealed the absence of malignant cells and only inflammation was reported, which is not clear whether the site of biopsy or histological examination caused this misdiagnosis. Third, in the current study, according to the patient condition, the treatment strategies followed the latest guidelines and in terms of the aspects of anesthesia, careful management was performed. It is well established that stress response due to surgery and general anesthesia can promote cancer recurrence by suppressing immune system through natural killer cell inactivation (13). In addition, some anesthetics such as morphine, fentanyl, and volatile agents disturb immune function. In contrast, propofol positively affects the degradation of inhibitor of growth 3 (ING3) leading to suppression of migration, invasion, and growth of gastric cancer cells (14). When general anesthesia is supplemented by regional anesthesia, the use of anesthetics and also the severity of stress response are limited, resulting in earlier recovery time and better outcomes (13, 15). In anesthesia management of the current case, the total intravenous anesthesia (TIVA) was selected,

suspicious agents were avoided, and acute pain, which is a main trigger for immune suppression, was controlled by the patient controlled analgesia (PCA). Forth, patients with cancer are faced to mood disorders, anxiety, pain, somatic symptoms, fear of death, feeling of helplessness, and dependency. It is not easy to cope with this life threatening diagnosis and it is reported that after lung cancer, GC is associated with the highest rate of suicide. In fact, stress and psychiatric comorbidities related to cancer result in poor response to treatment and increased recurrence rate (16). Obviously, psychiatrist's vital role to help such patients to stand with hope and strength during all setting of cancer management is appreciated.

### 3.1. Conclusion

The current case encountered a cured case of GC with presumed poor prognosis. In this report, the patient's belief towards treatment strategies and the role of a multi-disciplinary approach are strongly highlighted.

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### Footnotes

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### References

- Burlaka AP, Ganusevich I, Gafurov MR, Lukin SM, Sidorik EP. Stomach Cancer: Interconnection between the Redox State, Activity of MMP-2, MMP-9 and Stage of Tumor Growth. *Cancer Microenviron.* 2016;**9**(1):27-32. doi: [10.1007/s12307-016-0182-5](https://doi.org/10.1007/s12307-016-0182-5). [PubMed: [26905073](https://pubmed.ncbi.nlm.nih.gov/26905073/)].
- Van Cutsem E, Sagaert X, Topal B, Haustermans K, Prenen H. Gastric cancer. *Lancet.* 2016;**388**(10060):2654-64. doi: [10.1016/S0140-6736\(16\)30354-3](https://doi.org/10.1016/S0140-6736(16)30354-3). [PubMed: [27156933](https://pubmed.ncbi.nlm.nih.gov/27156933/)].
- Chang KK, Cho SJ, Yoon C, Lee JH, Park DJ, Yoon SS. Increased RhoA Activity Predicts Worse Overall Survival in Patients Undergoing Surgical Resection for Lauren Diffuse-Type Gastric Adenocarcinoma. *Ann Surg Oncol.* 2016;**23**(13):4238-46. doi: [10.1245/s10434-016-5357-2](https://doi.org/10.1245/s10434-016-5357-2). [PubMed: [27364501](https://pubmed.ncbi.nlm.nih.gov/27364501/)].
- Torre LA, Siegel RL, Ward EM, Jemal A. Global Cancer Incidence and Mortality Rates and Trends-An Update. *Cancer Epidemiol Biomarkers Prev.* 2016;**25**(1):16-27. doi: [10.1158/1055-9965.EPI-15-0578](https://doi.org/10.1158/1055-9965.EPI-15-0578). [PubMed: [26667886](https://pubmed.ncbi.nlm.nih.gov/26667886/)].
- Tada K, Etoh T, Shitomi Y, Ueda Y, Tojigamori M, Shiroshita H, et al. A case of advanced gastric cancer achieved a pathological complete response by chemotherapy. *Surg Case Rep.* 2017;**3**(1):68. doi: [10.1186/s40792-017-0344-9](https://doi.org/10.1186/s40792-017-0344-9). [PubMed: [28500392](https://pubmed.ncbi.nlm.nih.gov/28500392/)].
- Dikken JL, van de Velde CJ, Gonen M, Verheij M, Brennan MF, Coit DG. The New American Joint Committee on Cancer/International Union Against Cancer staging system for adenocarcinoma of the stomach: increased complexity without clear improvement in predictive accuracy. *Ann Surg Oncol.* 2012;**19**(8):2443-51. doi: [10.1245/s10434-012-2403-6](https://doi.org/10.1245/s10434-012-2403-6). [PubMed: [22618718](https://pubmed.ncbi.nlm.nih.gov/22618718/)].
- Survival Rates for Stomach Cancer, by Stage.* American Cancer Society; 2016. Available from: <https://www.cancer.org/cancer/stomach-cancer/detection-diagnosis-staging/survival-rates.html>.
- Washington K. 7th Edition of the AJCC cancer staging manual: stomach. *Ann Surg Oncol.* 2010;**17**(12):3077-9.
- Shimonosono M, Ishigami S, Arigami T, Uenosono Y, Uchikado Y, Kita Y, et al. A case report of curative distal gastrectomy for stage IV gastric cancer after chemoradiotherapy in a patient with a gastrojejunal gastric bypass. *Surg Case Rep.* 2016;**2**(1):131. doi: [10.1186/s40792-016-0259-x](https://doi.org/10.1186/s40792-016-0259-x). [PubMed Central: [PMC5106419](https://pubmed.ncbi.nlm.nih.gov/PMC5106419/)].
- Abe S, Oda I, Nakajima T, Suzuki H, Nonaka S, Yoshinaga S, et al. A case of local recurrence and distant metastasis following curative endoscopic submucosal dissection of early gastric cancer. *Gastric Cancer.* 2015;**18**(1):188-92. doi: [10.1007/s10120-014-0341-7](https://doi.org/10.1007/s10120-014-0341-7). [PubMed: [24477418](https://pubmed.ncbi.nlm.nih.gov/24477418/)].
- Kakiuchi M, Nishizawa T, Ueda H, Gotoh K, Tanaka A, Hayashi A, et al. Recurrent gain-of-function mutations of RHOA in diffuse-type gastric carcinoma. *Nat Genet.* 2014;**46**(6):583-7. doi: [10.1038/ng.2984](https://doi.org/10.1038/ng.2984). [PubMed: [24816255](https://pubmed.ncbi.nlm.nih.gov/24816255/)].
- Imamura T, Komatsu S, Ichikawa D, Kawaguchi T, Kosuga T, Okamoto K, et al. Early signet ring cell carcinoma of the stomach is related to favorable prognosis and low incidence of lymph node metastasis. *J Surg Oncol.* 2016;**114**(5):607-12. doi: [10.1002/jso.24377](https://doi.org/10.1002/jso.24377). [PubMed: [27562147](https://pubmed.ncbi.nlm.nih.gov/27562147/)].
- Wang J, Guo W, Wu Q, Zhang R, Fang J. Impact of Combination Epidural and General Anesthesia on the Long-Term Survival of Gastric Cancer Patients: A Retrospective Study. *Med Sci Monit.* 2016;**22**:2379-85. [PubMed: [27386842](https://pubmed.ncbi.nlm.nih.gov/27386842/)].
- Yang C, Gao J, Yan N, Wu B, Ren Y, Li H, et al. Propofol inhibits the growth and survival of gastric cancer cells in vitro through the upregulation of ING3. *Oncol Rep.* 2017;**37**(1):587-93. doi: [10.3892/or.2016.5218](https://doi.org/10.3892/or.2016.5218). [PubMed: [27840947](https://pubmed.ncbi.nlm.nih.gov/27840947/)].
- Wigmore TJ, Mohammed K, Jhanji S. Long-term Survival for Patients Undergoing Volatile versus IV Anesthesia for Cancer Surgery: A Retrospective Analysis. *Anesthesiology.* 2016;**124**(1):69-79. doi: [10.1097/ALN.0000000000000936](https://doi.org/10.1097/ALN.0000000000000936). [PubMed: [26556730](https://pubmed.ncbi.nlm.nih.gov/26556730/)].
- Faye AD, Gawande S, Tadke R, Kirpekar V, Bhawe S. Focusing on Psychiatric aspects of cancer: A need of the day? *Panacea J Med Sci.* 2016;**6**(3):117-24.