Case Report
Gastro-Splenic Fistula Related to Large B Cell Lymphoma

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Abstract: We report a case of spontaneous gastroscopic fistula in a 57 year old female who presented to the emergency department with abdominal pain and weight loss. From the physical examination, she had a palpable abdominal mass. A CT scan was performed and showed a mass involving the proximal greater curve of the stomach, infiltrating the spleen and pancreas. There was a 12 mm defect in the cardia of the stomach with gas entering the large mass but there was no free gas in the abdomen. The defect was a gastroscopic fistula. A gastroscopic biopsy confirmed the diagnosis of diffuse large B cell lymphoma. Surgical removal of the mass was not feasible; therefore she was treated with RCHOP chemotherapy, achieving complete remission.

Keywords: gastroscopic fistula (GSF); diffuse large B cell lymphoma (DLBCL)

1. Introduction
Gastroscopic fistula (GSF) is a rare disease entity resulting from gastric, splenic malignancies and rarely benign conditions. In the literature, there are 28 cases reported since 1962, first case report was from Belgium [1]. With chemotherapy there is a risk of fistula formation as a result of tumor necrosis and gastric wall invasion. The majority of the reported cases were treated with splenectomy and partial gastrectomy followed by chemotherapy [2,3]. When surgical options are deemed risky due to poor general conditions, the outcome is generally poor [3]. However our patient’s condition was complicated by gastro intestinal bleed and pulmonary embolism. Surgical intervention was not feasible and therefore she was treated with chemotherapy. This is the third case in the literature where chemotherapy was administered to a lymphoma patient with GSF, prior any surgical intervention. In the majority of the cases, GSF occurred during chemotherapy or after the completion of treatment.
If it was diagnosed prior the administration of chemotherapy, surgery was performed. In our case, chemotherapy was administered concomitantly with GSF.

2. Case Presentation

A 57 year old female presented to the emergency department with 6 weeks history of right upper abdominal pain. She had lost 6 kg in weight and was experiencing night sweats. On admission she was febrile and hypotensive. Her temperature was 40.0 °C and her oxygen saturation was 95% on room air with a blood pressure of 90/59 mmHg.

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

The physical examination revealed a palpable right upper quadrant mass and abdominal tenderness. Bowel sounds were normal and there was no generalized lymphadenopathy. Spleen tip was palpable.

Laboratory results were as follows:
- WBC: 20.0 × 10^9/L (normal:4.0–11.0), NE: 16.4 × 10^9/L (normal:2.0–7.5), LY: 1.4 × 10^9/L (normal 1.5–4.0), MO: 1.8 × 10^9/L (normal 0.2–0.8), HB: 82 g/L (normal 115–165), MCV: 77.6 fl (normal 76–100), RDW: 15.9% (normal 10.0–15.7), PLTS: 710 × 10^9/L (normal 150-450), crea: 56 umol/L (normal 46–92), urea: 5.2 mmol/L (normal 2.5–7.8), bili: 9 umol/L (normal 0–21), ALT: 31 IU/L (normal 3–53), ALP: 137 IU/L (normal 30–130), alb: 32 g/L (normal 35–50), amy: <30 IU/L (normal 30–110), CRP: 342 mg/L (normal 0–10), LDH: 1303 IU/L (normal 313–618), iron: 3.0 umol/L (normal 7.0–30.0), B2-microglobulin: 2.2 mg/L (normal: 1.2–2.4).

The CT scan revealed a 13.3 × 10.7 cm lesion of the large distal body and tail of pancreas. This communicated with the cardia of the stomach and contained multiple specks of gas. The lesion infiltrated the spleen which was difficult to identify separately. There was also a smaller 1.4 × 1.2 cm low attenuation lesion anterior to the larger lesion.

Additionally, a non-obstructing 2.6 × 2.5 cm soft tissue density mass involved the ileocecal valve (Figures 1 and 2).

![Figure 1. Early CT showing loss of stomach (*) wall integrity and fistulation into spleen (+). The fistulous tract is shown by the arrow.](image-url)
Figure 2. Image from a later CT showing complete breakdown of the stomach (*) wall continuity into a large collection replacing the spleen (+). Clear communication seen between the stomach and collection defined by the arrow.

A gastroscopy performed showed a malignant looking ulcer on the gastric fundus. Figure 3 shows the heterotypic population of lymphoma cells from the gastric biopsy.

Figure 3. Biopsy revealed lymphoma cells with round, oval, nuclei, multiple punctate nucleoli and scant cytoplasm (hematoxylin and eosin ×20).

Figure 4 shows gastric mucosa with infiltration by large lymphoid cells expressing a post germinal center phenotype and a high proliferation index. There was co-expression of CD30.
Immunohistochemistry testing showed BCL-2\(^+\) BCL-6\(^+\) CD10\(^-\) CD20\(^+\) CD23\(^-\) CD3\(^-\) CD30\(^+\) CD5\(^-\) CD79\(^+\) CyclinD1\(^-\) IRF4\(^+\) Ki67\(^{90\%}\) LMP-1\(^-\) expression.

**Figure 4.** Hematoxylin and eosin stained section (top left) shows gastric mucosa with infiltration of the lamina propria by sheets of large lymphoid cells. On immunohistochemistry, they are positive for CD20, bcl2 and bcl6, express a post germinal center phenotype (IRF4 positive, CD10 negative) and show a high proliferation index (Ki67—90%). There is co-expression of CD30. The images were taken on an a Nikon Eclipse 80i microscope with Plan Apo lens \(\times20\) magnification, using a Nikon DSFi1 camera and DS-L2 Nikon digital sight system.
FISH was carried out on thin paraffin sections. (Dako probe sets) and the lymphoid cells had no evidence of an MYC gene rearrangement.

Her stage was IVB, with a revised IPI of 3 and CNS IPI risk score suggested a 10% risk of CNS relapse within 2 years.

The patient was started on intravenous antibiotics and there were multiple discussions regarding the management of her case.

Surgical treatment of the gastro splenic fistula was not considered feasible. The collection resulting from the fistula was contained but surrounded by an inflammatory phlegmon. The fistula itself could not be repaired and surgical treatment would have involved at least a total gastrectomy, splenectomy and distal pancreatectomy. This would not remove the whole mass and would have been very high risk in her clinical condition. It would have been non curative and delayed potentially curative chemotherapy.

Following lengthy MDT discussions it was decided to administer six cycles of RCHOP with three cycles of intrathecal methotrexate and high dose methotrexate at the end.

During the patient’s hospital stay, she had two events of gastric bleeding with an approximate blood loss of 600 mL. Prophylactic tinzaparin was stopped. Four days after the gastric bleed she was considered stable so she received her first cycle of RCHOP. The team appreciated that there were major risks of complications from the administration of RCHOP, however it was deemed to be the most appropriate treatment option for our patient.

On day +9 post RCHOP and whilst being on prophylactic Tinzaparin for five days, the patient became significantly hemodynamically compromised.

She collapsed whilst returning from the bathroom. Oxygen saturation was 88% and patient became hypotensive with a blood pressure of 75/60 mmHg.

We decided to proceed with CT scans to exclude cerebral bleeding, to review the lymphoma and to rule out a pulmonary embolism.

Regarding the lymphoma, the large mass in the upper abdomen had increasing locules of gas and clear communication was seen with the stomach.

Unfortunately, the CT scan also revealed multiple pulmonary emboli involving the right main pulmonary, right upper and lower lobe and main left lower lobe arteries. The main pulmonary artery was not dilated. The patient had a small peripheral wedge shaped area of opacification in the left lower lobe, ground glass changes in the upper lobes bilaterally, which was concerning for pulmonary infarction. She also had a right internal iliac vein thrombus and thrombus in the left femoral vein. Following discussion with the Acute Care Team it was decided that thrombolysis with alteplase was considered a reasonable option even though the risk for a lethal bleed was apparent. This was discussed with the patient who agreed to proceed.

Thrombolysis was beneficial in this case and there were no bleeding complications afterwards.

The patient completed six cycles of RCHOP, three cycles of intrathecal methotrexate (cytospin at diagnosis was clear) and high dose methotrexate in the end.

The end of treatment PET CT scan showed complete remission. The patient is still in remission 2 years post completion of treatment (Figure 5).
The patient was started on intravenous antibiotics and there were multiple discussions.

**Figure 5.** End of treatment Axial PET image showing excellent response with minimal non-specific residual FDG activity in spleen considered likely post inflammatory.

### 3. Discussion

Gastro-splenic fistula is a rare complication seen mainly in gastric and splenic lymphomas [4–23]. The treatment is usually surgical, followed by chemotherapy. Al-Ashgar et al. recommend avoiding extensive open laparoscopic procedures and suggest simple laparoscopic fistulectomy with partial gastric resection [22].

One of the most feared complications of GSF is massive hematemesis, which can be lethal.

By reviewing the literature, massive hematemesis has been reported in 2 lymphoma cases with erosion of gastric contents into the splenic circulation [15,17]. In the event of GSF massive bleeding, Moghazy KM suggests splenic artery embolization, followed by splenectomy and gastric resection [10].

Diffuse Large B cell Lymphoma seems to have a tendency to invade the gastric wall and cause widespread necrosis causing fistulation with the adjacent organs [19]. Also, Crohn’s disease [23] and benign gastric ulcers [24–27] are known causes.

In our case, the patient received no surgical treatment and underwent chemotherapy. This is the first case in the literature where chemotherapy has been given first. The fistula resolved with continued chemotherapy. There are also other reports in the literature where fistulas resolved post chemotherapy [4]. Early diagnosis of GSF may be life-saving but can be challenging and should be considered in every DLBCL patient undergoing routine abdominal imaging. Abdominal CT seems superior to other radiological tests for diagnosing GSF [13].

We thought that this case was worth mentioning, as GSF is recognized as a rare complication of gastric or splenic lymphoma.

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