



# Gastrosplenic Fistula: a Systematic Review

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## Abstract

Gastrosplenic fistula is an unusual complication of benign as well as malignant gastric and splenic pathologies. This pathology acquires an important clinical significance due to its rare association with life-threatening upper gastrointestinal haemorrhage. The aim of this article is to review the English-language literature in order to gain a better understanding of etiological factors, diagnostic evaluation, and management of gastrosplenic fistula. The systematic search of the literature was performed on PubMed and MEDLINE from January 1950 to September 2020 according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement. We retrieved 44 articles matching our selection criteria from the search. There were 3 case series, 37 case reports, and 4 review of the literature. In our appraisal of articles published in PUBMED, a total of 36 cases of malignant and 10 cases of benign gastrosplenic fistula could be identified. Gastrosplenic fistula is an exceptional complication of malignancies of the gastrointestinal tract. Lymphomas particularly arising from the spleen are the commonest cause. Gastric adenocarcinoma causing GSF is extremely rare. Most cases occur spontaneously, but at times, it can be secondary to tumour necrosis following chemotherapy.

**Keywords** Gastrosplenic fistula · Malignant and benign aetiology · Upper gastrointestinal haemorrhage

## Introduction

Gastrosplenic fistula (GSF) is an unusual complication of benign as well as malignant gastric and splenic pathologies. Lymphoma of the spleen being the most commonly incriminated aetiopathology [1, 2]. However, rarely, it can occur due to gastric lymphoma or adenocarcinoma. Its occurrence in association with benign pathologies is even rare. Though the presentation is often insidious, nevertheless, it may rarely present with catastrophic gastrointestinal haemorrhage requiring emergent embolization or surgical extirpation for control [3, 4]. Therefore, a high index of suspicion of GSF is warranted in all patients with gastrointestinal lymphomas presenting with upper gastrointestinal haemorrhage. Most cases occur spontaneously, though occasionally, they may complicate following a course of chemotherapy. In this study, we present and share a review of the English literature

devoted to GSF in order to gain a better understanding of the etiological factors, diagnostic evaluation, and management of this pathology.

## Methods

The search strategy, inclusion and exclusion criteria, and primary and secondary outcomes were defined before the search. The systematic search of the literature was performed on PubMed and MEDLINE from January 1950 to September 2020 according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement (Fig. 1). All resulting titles, abstract, and full text, when available, were read and kept for reference. Specific MeSH terms included “gastrosplenic fistula,” “malignant etiology,” “benign etiology,” “histopathology,” “imaging studies,” “endoscopy,” “chemotherapy,” and “surgical intervention.”

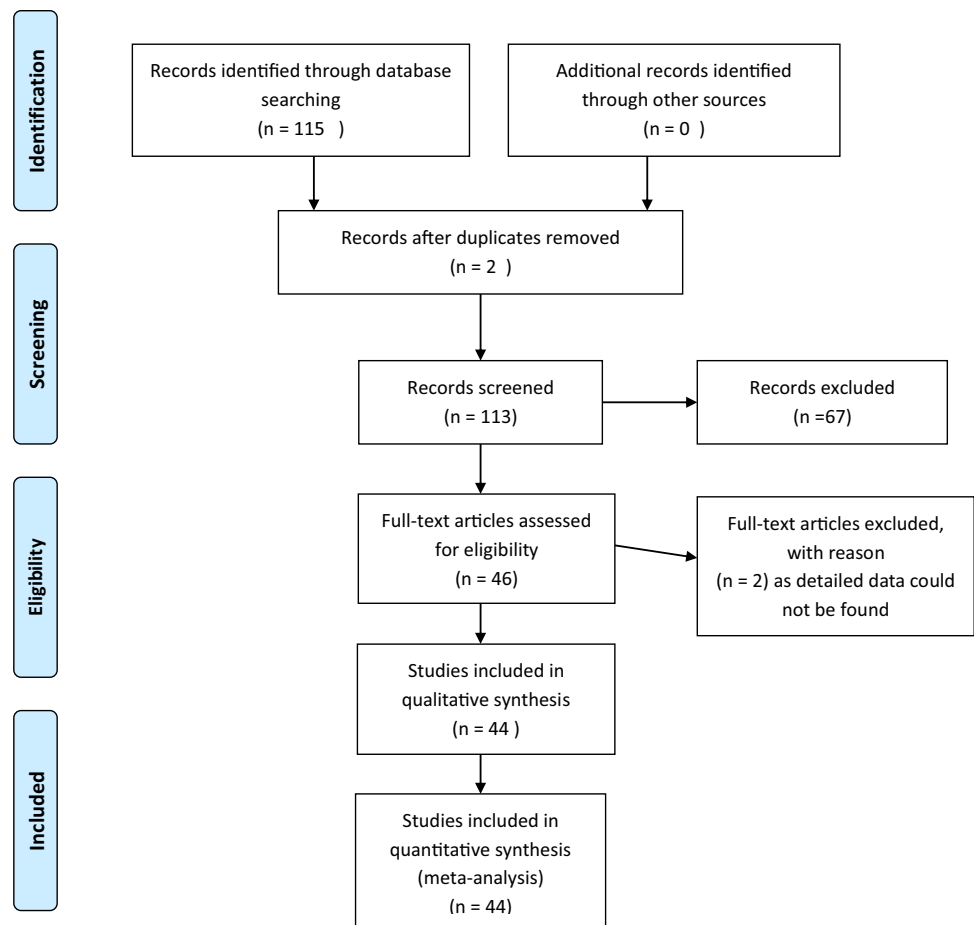
Observation prospective and retrospective studies, case series, and case reports on gastrosplenic fistula secondary to benign as well as malignant aetiology of stomach and spleen were included for the full review. Exclusion criteria included patients with a history of primary malignancy other than stomach and spleen and patients with a history of distal

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Fig. 1 PRISMA flow chart



gastrectomy or gastric pull through procedure (as surgery results in distortion of anatomy and the procedure itself can result in iatrogenic fistula formation).

Data were extracted by one author independently and then compared by the other author. The study author provided additional data if incomplete data were noted. Titles/abstracts considered potentially relevant were retrieved for review of the full manuscript. The list of full manuscript meeting inclusion criteria were compared, and any disagreements were resolved by discussion and consensus.

## Results

We retrieved 44 articles meeting our criteria from the search. Tables 1, 2, and 3 list articles matching the inclusion criteria. There were 3 case series, 37 case reports, and 4 review of the literature. In our appraisal of articles published in PubMed, a total of 36 cases of malignant GSF (Table 1) and 10 cases of GSF due to benign aetiologies could be identified (Table 2). Table 3 lists 22 articles with detailed description as the complete data of other reported cases was not available.

## Discussion

Gastrosplenic fistula (GSF) is one of the rare causes of upper gastrointestinal haemorrhage. The earliest case of GSF was reported by Scoville et al. in 1962 [5]. They described two patients of GSF due to splenic lymphosarcomas. One was a case of double fistula diagnosed at autopsy, and the other was suspected by virtue of the presence of air within an enlarged spleen at imaging studies, which the authors termed as “aerosplenomegalie.”

GSF can occur due to benign or malignant diseases, the commonest cause reported being a lymphoma of the spleen. Most of the cases were due to lymphomas (86.11%) 31/36. Of all causes of GSF due to lymphomas, the predominant primary site of lymphoma was spleen in 66.67% (24/36) followed by the stomach 16.67% (6/36). In one study, the authors failed to locate whether the source of primary was gastric or splenic in origin [3]. There were 2 cases due to adenocarcinomas [6, 7]. One patient developed GSF due to adenocarcinoma of the colon while receiving postoperative chemotherapy following local excision [8]. Isolated cases of GSF have also been reported

**Table 1** Gastrosplenic fistula due to malignant aetiology ( $n = 36$ ); NHL: non-Hodgkin's lymphoma

Author/year	Site and type of primary	Cause
Kyang LS et al. (2020) [30]	Splenic lymphoma	Spontaneous
Yokoyama Y et al. (2020) [31]	Splenic, NHL	Spontaneous
Saito M et al. (2019) (2 cases) [32]	Splenic B-cell lymphoma	Spontaneous
Kang DH et al. (2017) [33]	Splenic T-cell lymphoma	Spontaneous
Gentili S et al. (2016) [34]	Splenic B-cell lymphoma	Spontaneous
Martinez JD et al. (2015)	Gastric adenocarcinoma	Spontaneous
Senapati J et al. (2014) [35]	Splenic B-cell lymphoma	Spontaneous
Ding YL et al. (2012)	Splenic, NHL	Spontaneous
Dellaportas D et al. (2011)	Splenic, NHL	Spontaneous
Moran M et al. (2011)	Gastric, NHL	Spontaneous
Jain V et al. (2011)	? Gastric ?? Splenic, NHL	Spontaneous
Rothermal LD et al. (2010)	Splenic, NHL	Spontaneous
Khan F et al. (2010)	Splenic, NHL	Spontaneous
García MA et al. (2009)	Gastric, NHL	Spontaneous
Maillo C et al. (2009)	Splenic, Hodgkins lymphoma	Spontaneous
Seib CD et al. (2009)	Splenic, NHL	Spontaneous
Palmowski M. et al. (2008)	Splenic, NHL	Post-chemotherapy
Aribas BK et al. (2008)	Splenic, NHL	Post-chemotherapy
Moghazy KM et al. (2008)	Splenic, NHL	Post-chemotherapy
Al-Ashgar HI et al. (2007)	Splenic, Hodgkins lymphoma	Spontaneous
Kerem M et al. (2006)	Gastric, NHL	Spontaneous
Puppala R et al. (2005)	Gastric, NHL	Spontaneous
Bird M A et al. (2002)	Splenic lymphoma	Spontaneous
Pizzirusso F et al. (2004)	Colonic cancer with splenic metastasis	Post-Chemotherapy for Carcinoma colon
Choi JE et al. (2002)	Splenic, NHL	Spontaneous
Yang SE et al. (2002)	Splenic, NHL	Spontaneous
Carolin KA et al. (1997)	Gastric, NHL	Post-chemotherapy
Blanchi A et al. (1995) (Case 1)	Splenic, NHL	Spontaneous
Blanchi A et al. (1995) (Case 2)	Splenic, NHL	Spontaneous
Delgado Sanchez MJ et al. (1994) [36]	Splenic lymphoma	Spontaneous
Hiltunen KM et al. (1992)	Gastric, high-grade centroblastic lymphoma	Post-chemotherapy
Krause R et al. (1990)	Gastric, adenocarcinoma	?Post-chemotherapy
Harris NL et al. (1984) [37]	Splenic, NHL	Spontaneous
Bubenik O et al. (1983)	Splenic, NHL	Post-chemotherapy
De Scoville A et al. (1967) (Case 1)	Splenic lymphosarcoma	Spontaneous
De Scoville A et al. (1967) (Case 2)	Splenic lymphosarcoma	Spontaneous

due to benign aetiologies, viz, peptic ulcers, Crohn's disease, trauma, and splenic abscess and splenic tuberculosis (Table 2). We could acquire the details on clinical characteristics, radiological features, pathological diagnoses, and therapeutic procedures in 22 cases of malignant GSF published in literature which have been enumerated in Table 3.

The development of internal fistulation in gastric malignancies is reported to occur in less than 1% of gastric cancers [9, 10]. GSF formation and perforation of viscus are considered to be unfavourable prognostic events, resulting from tumour progression or post-chemotherapy complications [11]. The close proximity of the stomach

and spleen as also the presence of a gastrosplenic ligament have been proposed to facilitate the formation of a GSF due to involvement by tumour growth, infection, or necrosis [2, 3, 12]. It is intriguing to note that despite the fact that adenocarcinomas of the stomach are commoner than primary gastric lymphomas, all the cases of malignant gastric GSF reviewed in our series were resultant to lymphomas and only two were due to an adenocarcinoma of the stomach [6]. A probable explanation is the absence of desmoplastic reaction in lymphomas when compared with adenocarcinomas, as also rapid growth and tumour necrosis which occurs in lymphomas [11]. The fistula most

**Table 2** Benign causes of gastrosplenic fistula ( $n = 10$ )

Author	Year	Cause
Leeds IL et al. [38]	2016	Splenic abscess
Lee KJ et al. [39]	2015	Splenic tuberculosis
Ballas K et al. [40]	2005	Splenic abscess
Nikolaidis N et al. [41]	2005	Post-traumatic
Kryshtalskiy N et al. [42]	1991	Splenic abscess
Cary ER et al. [27]	1989	Crohn's disease of stomach
Glick SN et al. [43]	1987	Gastric ulcer perforation
Joffe N et al. [44]	1981	Gastric ulcer perforation
Immelman EJ. et al. [45]	1975	Gastric ulcer perforation
Stoica T et al. [46]	1973	Gastric ulcer perforation

often occurs spontaneously as was seen in 75% (27/36) patients reviewed in our series.

Perforation of malignant gastrointestinal lymphomas can occur following chemotherapy in 5% cases [13]. Perforations can occur either into the free peritoneal space or into an adjacent organ [9]. GSF reported after chemotherapy is less common and has been postulated to occur due to rapid lysis of the tumour, i.e., the rate of tumour destruction being far greater than the regenerative capacity of the gastric mucosal cells [12]. It has been postulated that spontaneous GSF secondary to lymphomas of stomach or spleen usually occurs in advanced terminal stage of the illness as opposed to post-chemotherapy GSF [12].

The presentation of GSF is largely innocuous often being incidentally detected in imaging studies for nonspecific abdominal pain with left upper abdominal pain being the most common presenting symptom [14]. Splenomegaly is reported to be present in 85% cases [15]. Unlike GSF resultant to benign aetiologies like peptic ulcer disease which commonly present with gastrointestinal (GI) bleed, malignant GSF infrequently present with clinical features of frank upper GI bleed as was seen in 18% patients in the series. Alternatively, patients can have occult haemorrhage presenting as heme positivity in stools [4]. Rarely, the haemorrhage can be exsanguinating necessitating an urgent angiographic embolization or emergency surgical extirpation to control the bleed [16–19]. Thus, a high index of suspicion of GSF is warranted in all patients with gastric or splenic lymphomas presenting with upper GI haemorrhage [2].

Endoscopy is the initial investigation of choice in patients with upper GI bleed. However, in the diagnosis of GSF, the findings are often deluding and therefore inferior to a CECT. Some authors have questioned the need for endoscopy in cases where the CT diagnosis is obvious [3]. Nevertheless endoscopy is useful for providing supportive evidence and helps in obtaining a biopsy as the lesion often ulcerates the stomach. Details of endoscopy were present in 19 patients in our reviewed series. The classical endoscopic finding is that

of an ulcer in the fundus or the greater curvature of the stomach and was seen in most cases. Alternatively, only irregular or distorted gastric folds may be visualized at times converging on the greater curvature to a bright red area with central ooze [9, 12, 20]. Seldom can one visualize the fistulous tract as a direct communication between the stomach and spleen as observed in 26% patients in our review [1, 3, 11, 12, 21]. The site of involvement is usually the fundus or the greater curvature possibly due to the relative proximity of the area to spleen. Endoscopic biopsy when attempted is confirmatory in most cases in the present review [2, 3, 12, 21–24]. Caution should be exercised as the mass could represent a splenic hematoma. Therefore, CECT before the endoscopic biopsy is valuable. Often, the gastric ulcer biopsy was positive irrespective of the primary site, i.e., stomach or spleen. It is noteworthy that most of the tumours were non-Hodgkin's lymphoma (NHL), i.e., 63.89% (23/36) particularly of diffuse large B cell type 58.33% (21/36), which is quoted as the commonest type of lymphoma in the stomach, constituting > 95% of all gastric lymphomas [13, 20]. This type of lymphomas is commonly incriminated in the pathogenesis of gastrointestinal fistulae by virtue of its aggressive growth pattern and infiltrative nature [9, 22, 24].

In non-contrast CT, the finding of an air fluid level in the spleen should raise the suspicion [12] CECT is the investigation of choice in the diagnosis of GSF [5, 9, 12, 14, 23, 26]. The classic depiction of a contrast filled tract between the spleen and the stomach is pathognomic of the disease [9, 22] (Fig. 2). Nevertheless, a fair presumption can be made from indirect evidences such as the presence of an oral contrast or air in the spleen, even in the absence of a demonstrable fistula tract. Loss of fat planes between adjacent organs is usually noted which can help in situations where the fistulous tract is not visualized. Rarely, CECT may mimic a splenic abscess and a retrograde CT cystography was deemed helpful [26]. Supportive evidence from an upper GI endoscopy is beneficial in indirect cases. CECT clinched the diagnosis in all except one reported case in the series. Though there was an indirect evidence of splenic enlargement in the patient, no GSF could be identified and patient had repeated episodes of hematemesis or melaena without a definite identifiable source. In one such case, repeated endoscopy, angiography, and isotope scan also failed to detect the source of bleed initially and resulted also in a negative laparotomy. The GSF was suspected subsequently from indirect detection of an area of ooze in endoscopy and confirmed at relaparotomy [19]. Upper gastrointestinal series and barium studies have also been quoted to demonstrate the fistula in an occasional patient [27].

Most authors opted for resectional surgery, viz, resection of spleen along with part or whole of stomach and adjacent organs as the treatment modality for GSF (Fig. 3). Infrequently, an insidiously detected GSF has been treated with

**Table 3** Presentation characteristics, radiological diagnosis, endoscopic features, surgical treatment, and final HPE in of malignant GSF (22 cases)

Author / Year	Malignant/ Benign	Site of primary	Cause	CECT Findings	Endoscopic findings	Endoscopic Biopsy	Surgery Done	Chemo	Post-surgery/ FINAL HPE
Dellaportas D et al. (2011)	Malignant	Splenic	Spontaneous Hematemesis	Gastrosplenic fistula	Ulcer gastric fundus	Diffuse large B Cell NHL	Enbloc resection	Given Nature??	Diffuse large B cell lymphoma (NHL)
Moran M et al. (2011)	Malignant	Gastric	Spontaneous	Gastrosplenic fistula	Ulcer with fistula gastric fundus	Malignant B cell NHL	Gastrectomy + Splenectomy	CHOP	Malignant B cell NHL
Jain V et al. (2011)	Malignant	? Gastric ?? Splenic	Spontaneous Melaina	Gastrosplenic fistula	Ulcer with fistula gastric fundus	Diffuse Large B cell Lym-phoma	Partial gastrectomy + Splenectomy	Given Nature??	Diffuse large B cell lymphoma (both from stomach and spleen)
Rothermal LD et al. (2010)	Malignant	Splenic	Spontaneous Heme positive in stool examination	Gastrosplenic fistula	Gastric ulcer	Moderate chronic gastritis	Sleeve gastrectomy + splenectomy + liver biopsy	CHOP	Large B cell lymphoma
Khan F et al. (2010)	Malignant	Splenic	Spontaneous hematemesis and melaina	Gastrosplenic fistula	Irregular Ulcer gastric fundus	Diffuse large B cell lymphoma	Not done	R -CODOXM/ VAC regimen	-
A García MA et al. (2009)	Malignant	Gastric	Spontaneous	Gastrosplenic Fistula	Ulcer greater curve stomach which sur-rounded a GSF	Chronic gastritis due to H. pylori infection, without malignancy	Total gastrectomy, splenectomy And distal pancreatectomy	Given Nature??	Diffuse large B cell lymphoma (NHL)
Maillo C et al. (2009)	Malignant	Splenic	Spontaneous (gastro-splenic and thoraco-splenic fistula Hematemesis	Gastrosplenic Fistula	Two regular ulcerated lesions in greater curvature next to cardia	NA	Urgent laparotomy splenectomy, partial gastrectomy, diaphragmatic primary repair, ICD and feeding jejunostomy	Not given	Splenic Large B cell lymphoma
Seib CD et al. (2009)	Malignant	Splenic	Spontaneous	Gastrosplenic Fistula	Not done	NA	Exploratory laparotomy adhesiolysis, splenectomy, and partial gastrectomy	Pre op given No post-operative given	Hodgkin's Lym-phoma classical type nodular-sclerosing
Palmowski M et al. (2008)	Malignant	Splenic (diffuse large B cell NHL)	Post-chemo-therapy	Follow up CT after chemotherapy showed gastrosplenic fistula	Not done	NA	Splenectomy with resection of greater curvature of stomach	Pre and post-op R-CHOP regimen	Normal splenic and gastric parenchyma, only avital tumour cells

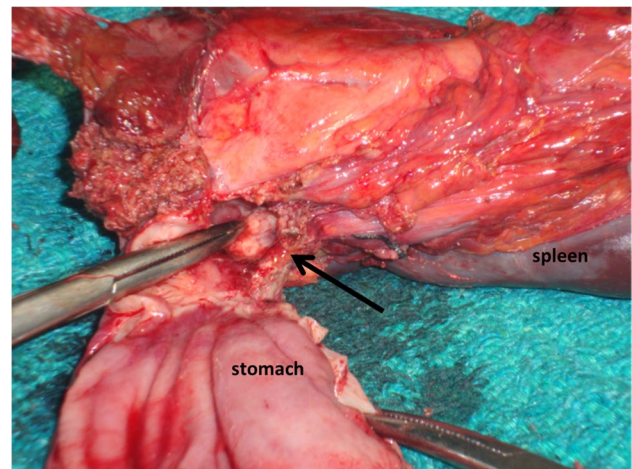
**Table 3** (continued)

Author / Year	Malignant/ Benign	Site of primary	Cause	CECT Findings	Endoscopic findings	Endoscopic Biopsy	Surgery Done	Chemo	Post-surgery/ FINAL HPE
Aribas BK et al. (2008)	Malignant	Splenic (large B cell NHL)	Post-chemo-therapy	Retrograde CT cystography showed gastrosplenic fistula	Not done	NA	Splenectomy, fistula resection and gastric wedge resection	Pre-op CHOP & MINE	Splenic abscess
Moghazy KM et al. (2008)	Malignant	Splenic (differentiated histiocytic lymphoma)	Post-chemo-therapy	Gastrosplenic fistula	Follow up endoscopy showed spontaneous fistula closure	NA	Splenic artery embolization, followed by splenectomy and gastric resection	Given Nature??	NA
Al-Ashgar HI et al. (2007)	Malignant	Splenic	Spontaneous	Gastrosplenic Fistula	Opening in lateral part of fundus with blind end	NA	Laparoscopic excision of fistula tract, partial gastrectomy	Doxorubicin, bleomycin, Vinblastine Dacarbazine	Hodgkin's lymphoma classical type nodular-sclerosing
Kerem M et al. (2006)	Malignant	Gastric (diffuse B cell NHL)	Spontaneous	Gastrosplenic fistula	Not done	NA	Splenectomy, proximal gastrectomy, oesophago-gastrostomy, and pyloroplasty	CHOP	Diffuse B cell NHL
Puppala R et al. (2005)	Malignant	Gastric lymphoma	Spontaneous	Gastrosplenic fistula					
Pizzirusso F et al. (2004)	Malignant	Splenic	Post-chemo-therapy for Ca colon	Gastrosplenic fistula			Resection of the spleen and the greater gastric curvature		Adenocarcinoma Colon
Choi JE et al. (2002)	Malignant	Splenic	Spontaneous	Gastrosplenic Fistula	Deep ulcer like opening in the gastric fundus	Diffuse large cell type malignant lymphoma	Splenectomy, gastric wedge resection, distal pancreatectomy	Pre-op given Nature??	Diffuse large cell type malignant lymphoma
Bird MA et al. (2002)	Malignant	Splenic	Spontaneous Hematemesis				Splenic artery embolization, followed by splenectomy and gastric resection		
Yang SE et al. (2002)	Malignant	Splenic	Spontaneous	Gastrosplenic Fistula	ulcerated lesions	Diffuse Large B cell Lymphoma (NHL)	splenectomy and a partial resection of gastric fundus	Pre and post-op CHOP	NA
Carolyn KA et al. (1997)	Malignant lymphoma	Gastric	Post-chemo-therapy	Post-chemo-evidence of GS fistula	Pre chemo:- gastric ulcer in fundus Post-chemo follow up: evidence of GS fistula, closed by 4th cycle	Poorly differentiated large cell lymphoma	Exploratory laparotomy and splenectomy	Pre-op CHOP	No evidence of fistula, no malignancy in spleen and lymph nodes



**Table 3** (continued)

Author / Year	Malignant/ Benign	Site of primary	Cause	CECT Findings	Endoscopic findings	Endoscopic Biopsy	Surgery Done	Chemo	Post-surgery/ FINAL HPE
Blanchi A et al. (1995) (Case 1)	Malignant	Splenic	Spontaneous	Suspected gastrosplenic fistula	Direct communication between fundus of stomach and ulcerated splenic cavity	NA	Resection of spleen, tail of pancreas and involved stomach	Given Nature??	B cell high grade centroblastic lymphoma
Blanchi A et al. (1995) (Case 2)	Malignant	Splenic	Spontaneous	gastrosplenic fistula	Ulcerated cavity fundus	B cell high grade centroblastic lymphoma	Not done	Given Nature??	NA
Delgado Sánchez MJ, (1994)	Malignant	Splenic lymphoma	Spontaneous	gastrosplenic fistula					

**Fig. 2** CECT showing gastrosplenic fistula (arrow)**Fig. 3** Resected specimen showing gastrosplenic fistula (arrow)

chemotherapy alone and followed up with endoscopy but such reports are usually confined to post-chemotherapy GSF and can be considered anecdotal till definitive evidence is available to support the advocacy of non-operative strategies [19, 22, 23]. The potential danger imminent in pursuing a non-operative therapy is the risk of it culminating in a catastrophic haemorrhage. It has been reported that gastric juice can cause erosion of splenic vessels and result in massive bleeding [22], requiring emergent surgery or embolization to control bleeding [16, 18, 19]. In one patient, a case of GSF complicating a primary gastric lymphoma, non-operative therapy was adopted in view of associated comorbidities; however, the patient succumbed 2 months following diagnosis [25].

Reports exist of upper GI haemorrhage resultant to GSF during chemotherapy in cases of splenic lymphoma raising concerns whether all such cases merit a routine

pre-chemotherapy endoscopic evaluation of the stomach [14]. Surgery provides a definitive tissue diagnosis in cases where a prior histological diagnosis could not be ascertained [9]. The extent of gastric resection is controversial with authors variably resorting to a wedge excision, a sleeve resection of greater curvature, or a partial or total gastrectomy. A splenectomy is routinely added to the procedure which may rarely need an additional distal pancreatectomy [1, 9, 24]. However, in one reported case, the authors refrained from a splenectomy and only excision of the fistulous tract along with a partial gastrectomy was performed [28]. Rarely, GSF following chemotherapy has been treated with an isolated splenectomy without gastric resection [23]. Splenic artery embolization followed by splenectomy and gastric resection may be a prudent choice in massive bleed due to a GSF [17, 18]. Though, most authors performed the operation through an open approach; reports of successful excision of the fistulous tract along with gastrectomy using the laparoscopic approach have also been published [29]. It is noteworthy that in most patients undergoing a surgical resection, following chemotherapy residual malignancy is rarely demonstrable [11, 19, 23, 29].

## Conclusion

Gastrosplenic fistula is an exceptional complication of malignancies of the gastrointestinal tract. Lymphomas particularly arising from the spleen are the commonest cause. Gastric adenocarcinoma causing GSF is extremely rare. Most cases occur spontaneously, but at times, it can be secondary to tumour necrosis following chemotherapy. CECT is superior to endoscopy in diagnosing GSF and is the investigation of choice. An iconic depiction of the fistulous tract or contrast and air in the spleen is pathognomic. Endoscopy usually demonstrates an ulcer in the region of gastric fundus or greater curvature and can provide with a tissue biopsy prior to definitive management. Most cases are due to NHL, diffuse B cell, or histiocytic type. Resectional surgical therapy is advocated to circumvent acataclysmal bleed and includes splenectomy along with segmental, partial, or total gastrectomy depending on the extent of involvement of the organ. The limitation of this study is that the detailed data of all the reported cases could not be retrieved.

## Declarations

**Conflict of Interest** The authors declare no competing interests.

**Statement of Informed Consent** Not applicable.

**Statement of Human and Animal Rights** Not applicable.

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