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Case Report

Burkitt's Lymphoma of the Stomach: A Case Report and Review of the Literature

Neil Watson[1,2], Vincenzo Cassibba[1], Marco Casini[1], Andrea Mega[3], Martina Tauber[4], Andrea Iori[3], Raimondo Di Bella[1] and Andrea Piccin[1]*

[1]Haematology Department, San Maurizio Regional Hospital, Italy

[2]University of Edinburgh, United Kingdom

[3]Gastroenterology Department, San Maurizio Regional Hospital, Italy

[4]Pathology Department, San Maurizio Regional Hospital, Italy

***Corresponding author:** Andrea Piccin, Haematology Department and Bone Marrow Transplant Unit, San Maurizio Regional Hospital, Bolzano/Bozen, South Tyrol, Italy, Tel: 393472736692; Fax: 390471908703; Email: apiccin@gmail.com

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Abstract

Sporadic Burkitt's Lymphoma (BL) is a subtype of Non-Hodgkins Lymphoma (NHL). In contrast to other types of NHL, sporadic Burkitt's lymphoma usually affects the ileocaecal area of small bowel. We report a case of sporadic BL affecting the stomach, which represents an under-reported manifestation of the disease. This is followed by a review of the literature on gastric Burkitt's lymphoma.

Keywords: Burkitt lymphoma; Gastric présentation; Helycobacter pylori; Gastric resection

Introduction

Sporadic Burkitt Lymphoma (BL) is an aggressive subtype of B cell Non-Hodgkin Lymphoma (NHL) which is rare in adults. The disease typically manifests in the Gastrointestinal (GI) tract, usually at the ileocaecal area [1]. The pathogenetic hallmark of BL is rearrangement of the c-MYC oncogene, an important regulator of cell proliferation and apoptosis. While the stomach is the commonest extra nodal site of presentation for other types of NHL [2], gastric presentation of sporadic BL is rare. The true prevalence of gastric BL is unclear due to a paucity of reports, and it may be under-recognized by clinicians. Correct diagnosis of BL is crucial, as prompt management is imperative and outcomes differ from other types of NHL. We report a case of sporadic BL presenting with gastric erosion in an adult male and we compare our findings with previous reports.

Case Description

Case #1

A 23 year old man presented in January 2013 to the Accident and Emergency Department of San Maurizio Regional Hospital of Bolzano, Italy, complaining of a three months history of abdominal pains, and increasing asthenia, fever, night sweats and weight loss of 10Kg. Examination revealed diffuse pallor, tachycardia, and marked epigastria pain. There was no lymphadenopathy, hepatosplenomegaly or palpable masses. Baseline full blood count revealed hemoglobin 7.5 g/dl (12-18), white cell count 8.7 x10^9/L (4.8-10.8), neutrophils 60.2% (40-74), lymphocytes 24.7% (19-48%), monocytes 11.7 (0.2-1), eosinophils 2.5 % (0-0.7), basophils 0.9% (0-0.2%), platelet count 496 x10^9/L (130-400). Other results included Erythrocyte Sedimentation Rate (ESR) 46mm (<25), prothrombin time 0.95 (<1.2), creatinine 0.58mg/dl (0.7-1.2), LDH 1121 IU (<225), protein 5.1g/dl (6.6-8.3), triglycerides 204 mg/dl (30-150). Serological studies shown: CMV IgG+ IgM-, HSV1/HSV2 IgG+ IgM-, VZV IgG+ IgM-, HAV IgG+ IgM-, HCV Ab-, HIV Ag/Ab-, HBs-Ag -ve, HBsAb+, HbcAb+, HbeAg-, HbeAb+, HBV DNA not elevated, EBV Ig G– IgM-.

An Oesophago-Gastroduodenoscopy (OGD) demonstrated a large gastric ulceration involving two-thirds of the body of the stomach and duodenum (Figure 1 OGD).

Biopsies of the lesions were performed. On histological sections an extensive atypical lymphoid infiltrate was observed. The tumor shows a diffuse monotonous pattern of growth and invades the glandular tissue in the lamina propria and deeply the sub mucosa. The cells were medium-sized cells with rounded nuclei and scanty

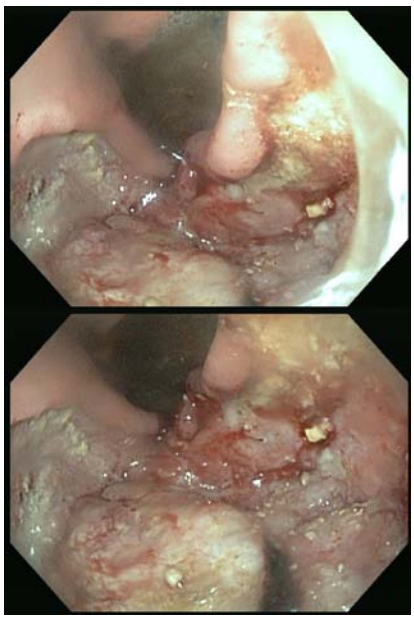

Figure 1: OGD 29/01/2013.

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cytoplasm. Multiple apoptotic bodies were observed (Figure 2 ABC Histology).

Immunohistochemically the tumor cells were positive for CD20, CD 10, Bcl-6, MUM-1 and variable weakly for Bcl-2. The proliferation index (MIB/Ki67) was close to 100%. Staining for CD3, cytokeratin PAN (epithelial), CD56, synaptophysin, CD34, TDT, EBV and BCL1 were all negative. No EBV or EBV-encoded RNA (EBER) was detected. The FISH analsysis revealed a translocation of the MYC locus (8q24) using break apart (Dakocytomation). Helicobacter pylori were not detected in the biopsies. The bone marrow biopsy demonstrated an atypical infiltration with medium-sized cells and "*starry sky*" appearance in about 65% of the cellularity. A final histological diagnosis of Burkitt lymphoma with infiltration of the bone marrow was made.

The proliferative index (MIB1/Ki67) was 95% (Figure 3 ABCD immuneshistochemistry). Staining for CD3, cytokeratin PAN (epithelial), CD56, synaptophysin, CD34, TDT and BCL1 were all negative. Fluorescent In-Situ Hybridization (FISH) revealed a translocation of the MYC locus (8q24). A CT-scan (31.01.13) of thorax was unremarkable, while CT-scan of abdomen showed thickening of gastric walls with ulcers on the greater curve and liver lesions suggestive for neoplastic infiltrations on the IVa and the VII liver segments. An Ann Arbour stage IVE+B was therefore given. The patient was transferred to the haematology ward and started on the BFM German protocol GMALL-B-ALL/NHL 2002. In February 2013 he received the first a course of chemotherapy (prephase: cyclophosphamide 200mg/m^2 i.v. days 1-5; prednisolone 60mg/m^2 PO on day 1-5), followed by a II° course of chemotherapy (cycle A1: Rituximab© 375mg/m^2 i.v. day 7; dexamethasone 10mg/mg/m^2 PO days 8-12; vincristine 2mg iv day 8; ifosfamide 800mg/m^2 iv days 8-12; methotrexate 1500mg/m^2 iv day 8; etoposide 100mg/m^2 i.v. day 11-12; cytarabine 2x150 mg/m^2 iv day 11-12; cytarabin 40mg and methotrexate 15mg intrathecal day 8 and 12), which was well tolerated. In March2013 he received the III° course of chemotherapy (cycle B1

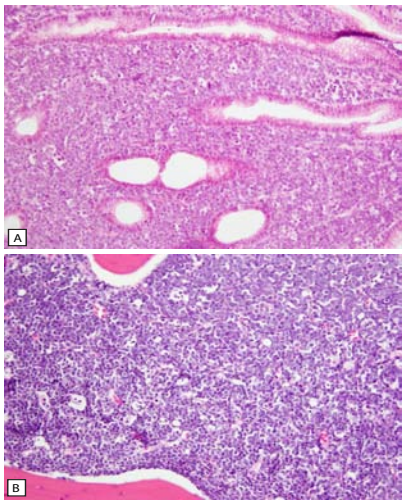

Figure 2: Histology.
A: Gastric musocsa with diffuse infiltration by medium-sized neoplastic lymphoid cells, HE, 20x.
B: bone marrow biopsy with extensive infiltration by the tumour cells with starry sky pattern, HE, 20x.

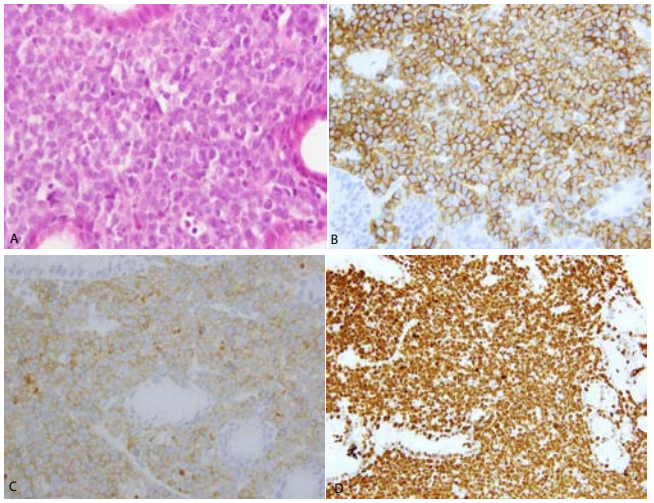

Figure 3: Immunohistochemistry.
A: gastric biopsy with medium-sized tumour cells, HE, 60x.
B: tumour cells are positive for CD20, 40X.
C: tumour cells are positive for CD10, 40X.
D: nearly 100% of tumour cells are Ki67 positive, 20x.

BFM: Rituximab© 375mg/m^2 i.v. day 28; dexamethasone 10mg/m^2 PO day 29; vincristine 2mg i.v. day 29; cyclophosphamide 200mg/m^2 i.v. day 29 -33; methotrexate 1500mg/m^2 iv day 29; adriamycin 25mg/m^2 i.v. day 32-33; cytarabin 40mg and methotrexate 15mg intrathecal 29,33). Prophylactic lamivudine was also administered because positive hepatitis B serology (see above).

On day +22 (30.4.13) of cycle III, the patient developed hematemesis leading to hypovolaemic shock. He was transfused with 2 units of RBC, 1 unit of PLT, and 600 mls of fresh frozen plasma to correct a prolonged PT (1.33). A new OGD demonstrated a 30mm gastric oozing ulcer at the lesser curvature of the stomach (Figure 4). However, the extent of the lesion had largely improved on endoscopy according to the gastro-enterologist. Haemostasis was achieved and the patient returned to the ward.

At the moment the patient is undergoing an IV° cycle of chemotherapy with peripheral blood stem-cell collection in case an autologous transplantation becomes necessary. The possibility of performing an allogeneic transplantation is being evaluated. Gastrectomy was not considered because the bleeding settled after the second OGD.

Discussion

Burkitt´s lymphoma is an aggressive form of B-cell NHL. The US incidence is 0.3 per 100,000 [3]. While BL is the commonest NHL in childhood, it accounts for >5% of adult lymphomas, and is thought to be under-researched in adults [4]. The sporadic (non-endemic) form encountered outside of Africa usually presents with an abdominal mass, most commonly localized at the ileocaecal region; it is rare for BL to manifest primarily in the stomach or duodenum [1,5]. The prevalence of this is unknown due to a paucity of published literature, consisting mostly of case reports and small case series (summarized in Table 1). Reviews are outdated by two decades. Cases display much heterogeneity in disease presentation, gastric site, patient age, and associated features such as infection. Gastric BL is prone

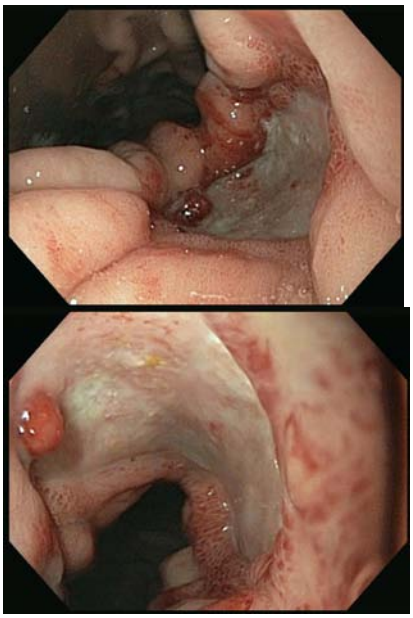

Figure 4: OGD 30/4/2013. Ongoing GI bleed.

to developing complications such as perforation and haematemesis, with some patients requiring surgery [6-8].

The aetiology of sporadic BL is unclear. A number of reports have demonstrated BL arising in association with H. Pylori infection [7-10]. Notably, one group demonstrated concomitant remission of gastric BL with HP eradication alone (no chemotherapy was initiated) [9]. In our case no HP was detected. HP has been established as a causative agent in MALT lymphoma where its eradication leads to lymphoma regression [11-13], and has also been associated with DLBCL, both through evolution from MALT, and spontaneous DLBCL; here eradication also promotes healing [14]. The low incidence of gastric BL means that insufficient data exists to establish any causative association. Such a link might lead to improved management of BL in a similar manner as in MALT and DLBCL.

Our patient's serology showed prior resolved acute HBV infection. This is significant as HBV has been implicated in studies as an oncogenic agent in various subtypes of NHL [15-17] and cases have reported BL associated with HBV infection [18,19]. Causative links have not been firmly established. It has been shown that HBV can persist in tissues, undetectable by serology, and therefore the presence of ongoing HBV infection in NHL cases may be under-recognized [15,20]. Further exploration of the role of the virus in NHL development is necessary to establish a causative role. EBV is the causative agent in endemic BL, and is present in a minority of sporadic BL cases. Our patient´s pathology samples were negative for EBV suggesting this was not a causative agent.

Chemotherapy is highly effective in BL and is the mainstay of management. The role of surgery is restricted to managing complications. Three of the cases of gastric BL previously reported required surgical resection of the stomach, and other published cases required management of GI perforation [21,22]. Our case presents a dilemma, as radical surgery on a BL patient has risks due to the chemotherapy-induced neutropaenia, and the damaged oozing mucosa. Furthermore, gastrectomy carries several complications and impairs the quality of life of a young patient, so where possible we believe that a conservative approach restricted to chemotherapy should be followed. Published studies on this condition are lacking, therefore more reports should be encouraged to identify patients' characteristics and dictate the best management. Serological screening including HP should be carried out and, if positive, eradication therapy should be prescribed.

Conclusion

BL affecting the stomach remains rare and likely under-reported. No up to date review articles exist in the literature and while sporadic reports show associations with EBV, HP and HBV, no causal relationship is established (Table 1). Such a link would improve understanding of pathogenesis, and potentially offer additional treatment options as has been shown for DLBCL and MALT tumours. Finally, there is no clear guidance on when to perform surgery for gastro duodenal BL. Published cases vary; generally operating in

Table 1: Previous case reports on Gastric Burkitt´s Lymphoma.

Study	Age	Gender	Site	Appearance	Notable features	Surgery	Outcome
Angotti et al 2012 [23]	4	M	Stomach anterior and posterior walls	Ulcerated masses		No	Undisclosed
Ziade et al 2012 [24]	15	F	Stomach, duodenum, jejunum	Raised, ulcerated tumours	EBV +ve; Krukenberg tumour	No	Remission
Colovic et al 2011 [6]	30	M	Antrum	Ulcero-infiltrative lesion		Subtotal distal gastrectomy	Remission
Ergun Met et al 2011 [25]	42	F	Mid portion of ant wall	Large Ulcer	Subsequent perforation	Closure	Remission
Kesik et al 2010 [7]	7	M	Antrum	Ulcerated masses	HP positive. EBV/HBV -ve Perforation	Semi-total gastrectomy for perforation; oesophago-jejunostomy	Remission
Baumgartner et al 2009 [9]	30	F	Lesser curvature of antrum	Ulcer 5x5cm	Remission with HP eradication	No	Remission
Chogle et al 2009 [26]	11	M	Body of somach	Deep ulcers	HIV positive	No	Death
Chieng et al 2009 [27]	9	M	Greater curve of gastric body, duodenum	Multiple raised ulcerated tumours	Presented as protein losing enteropathy	No	Remission
Grewal et al 2007 [28]	12	M	Proximal lesser curvature	Ulceration, thickened walls	HP infection	No	
Sharma et al 2001 [29]	35	M	Fundus, body and pylorus	Thick folds, lack of distensibility	Nil	No	Death
Shannon et al 2000 [30]	53	M	anterior wall of duodenum	Ulcer, perforation	HP +ve, perforation	Partial gastrectomy	

emergency circumstances (for instance, several had perforations). We believe that this is an appropriate role, as data are lacking on curative resections. Further case reports are warranted to improve our understanding and management of this disease.

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Author's Contribution

NW designed the study, reviewed the literature and wrote the manuscript; AP, VC, MC and SC were involved in patient management and reviewed the manuscript. AM performed OGD studies, GN performed histological studies.

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