CASE REPORT

Primary gastric Burkitt lymphoma: a rare cause of life-threatening haematemesis

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SUMMARY

Lymphomas are the second most common gastric malignancy following gastric adenocarcinoma. The majority of gastric lymphomas are either mucosa-associated lymphoid tissue lymphomas or diffuse large B-cell lymphomas. Primary gastric Burkitt lymphoma is a subtype of non-Hodgkin's lymphoma and represents an aggressive and rare malignancy with only a small number of cases reported worldwide. Clinical and radiological presentation is non-specific and mimics other gastric lymphomas. Diagnosis is established with pathological evaluation. Due to the paucity of cases, treatment of this condition is not well studied and is extrapolated from paediatric and adult literature of Burkitt lymphoma not isolated to the stomach. We present the case of a male patient with primary gastric Burkitt lymphoma who initially presented with life-threatening haematemesis, later achieving complete remission with treatment. We discuss the epidemiology, presentation and management of gastric Burkitt lymphoma.

BACKGROUND

Lymphomas are the second most common gastric malignancy following gastric adenocarcinoma. The majority of gastric lymphomas are either mucosa-associated lymphoid tissue lymphomas or diffuse large B-cell lymphomas. Primary gastric Burkitt lymphoma is a subtype of non-Hodgkin's lymphoma (NHL) and represents an aggressive and rare malignancy with only a small number of reported cases worldwide. A 2014 report by Mitra *et al* reviewed the literature and found only close to 50 reported cases worldwide.¹ Due to the paucity of cases, treatment of this condition is not well studied and is extrapolated from paediatric and adult literature of Burkitt lymphoma not isolated to the stomach. We present the case of a male patient with primary gastric Burkitt lymphoma who initially presented with life-threatening haematemesis, later achieving complete remission with treatment. We discuss our patient's clinical course, from initial diagnosis, through treatment and finally complete remission in hopes of contributing to the limited literature on this rare gastric neoplasm.

CASE PRESENTATION

A 42-year-old male with no significant past medical history presented to the emergency department with complaints of epigastric pain, nausea and haematemesis which began 3 days prior to presentation. He reported a 30 pound weight loss over the

previous 6 months, progressive fatigue and intermittent subjective fevers.

On physical examination, he was tachycardic. His other vital signs were within normal limits. He appeared pale and in distress, his abdomen was soft, non-tender to palpation, non-distended with normal bowel sounds. Complete blood count was significant for a haemoglobin of 4.1 g/dL and a haematocrit of 14.3%, a mean corpuscular volume of 82.3 cu micron, a white blood cell count of $4.8 \times 10^9/L$, with 70.4% neutrophils, 23.2% lymphocytes, 3.7% monocytes, 1.2% eosinophils, 0.3% basophils and 1.2% large unstained cells. Uric acid level was 7.4 mg/dL and lactate dehydrogenase level was 256 U/L. A basic metabolic panel did not reveal any abnormalities. HIV and serum *Helicobacter pylori* antigen testing were negative. The patient underwent resuscitation with intravenous normal saline and transfusion with multiple units of packed red blood cells.

INVESTIGATIONS

Urgent upper endoscopy revealed a large, ulcerated mass on the lesser curvature of the stomach with stigmata of recent bleeding (figure 1). The ulcer extended from the incisura to the fundus. Multiple biopsies were obtained. A 1:10 000 solution of epinephrine was used to inject oozing sites. A CT scan of the abdomen revealed findings suggestive of malignant infiltration of the gastric antrum and pylorus (figure 2a,b).

Biopsies revealed gastric tissue infiltrated by sheets of atypical medium-sized lymphoid cells with fine chromatin and scant cytoplasm. The atypical lymphocytes infiltrated around gastric glands with scattered mitotic and apoptotic cells. The tumour cells showed Burkitt-like morphology with a starry sky pattern (figure 3). Histological examination and rapid urease test of biopsies were negative for *H. pylori*.

Immunohistochemical studies showed that the atypical cells were 100% positive for Ki-67, as well as positive for PAX5, BCL6, CD10; and negative for cyclin D1 and BCL2 (figure 4A,B). An Epstein-Barr virus (EBV) in situ hybridisation study, with appropriate controls, was negative. Flow cytometry detected a kappa restricted CD20+, CD19+, CD10+ clonal B-cell population with a high S fraction (40%) by DNA analysis. Cytogenetic study was positive for rearranged MYC gene. DNA analysis demonstrated high tumour cell-associated S-phase fraction (40%), consistent with a highly aggressive tumour nature.

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Figure 1 Upper endoscopy images of large, ulcerated mass on the lesser curvature of the stomach with active bleeding.

Staging workup: Bone marrow biopsy did not reveal evidence of involvement by lymphoma. Lumbar puncture was performed, and cerebrospinal fluid cytology was negative for malignant cells. CT scan of the chest, abdomen and pelvis did not reveal evidence of disease outside the stomach. Due to the urgency of the patient's condition at diagnosis, as well as the unavailability of inpatient positron emission tomography (PET) CT scans at our institution, a PET CT scan was not performed. A brain MRI was not performed due to the lack of clinical symptoms and a negative lumbar puncture analysis and cytology.

The patient was diagnosed with stage I gastric Burkitt lymphoma.

TREATMENT

On diagnosis, the patient received initial treatment with dose-adjusted R-EPOCH chemotherapy consisting of rituximab, etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin. He also received prophylactic intrathecal methotrexate.

OUTCOME AND FOLLOW-UP

The patient was scheduled for and completed six cycles of chemotherapy. He tolerated therapy well, without development of tumour lysis syndrome. He had no recurrence of abdominal pain

and did not require further blood transfusions due to haematemesis. A PET/CT scan after his third cycle showed a decrease in the size of his tumour. A PET/CT scan after his sixth cycle found no evidence of residual or recurrent lymphoma ([figure 5](#)), the bulky gastric wall mass seen on prior examinations was not present and the patient was found to be in complete remission.

DISCUSSION

Burkitt lymphoma is an aggressive subtype of B-cell NHL with three variants: endemic, sporadic and immunodeficiency associated. Endemic Burkitt lymphoma primarily affects children in endemic areas in Africa where EBV is the causative agent. It has a tendency for extranodal localisation affecting the mandible, kidneys, ovaries and gastrointestinal tract. Sporadic cases are found in the rest of the world with localisation primarily to the abdomen, particularly the ileocecal area.² While the stomach is a common extranodal site of presentation for other types of NHL, primary gastric Burkitt lymphoma is extremely rare.³ The incidence of Burkitt lymphoma in the USA is 0.3 per 100 000, but that of primary gastric Burkitt lymphoma is unknown with likely underreporting and misidentification.⁴

Published literature involving gastric Burkitt lymphoma is limited, consisting primarily of case reports and case series. Significant variability exists in presentation, site, age and associated features between reported cases. There appears to be a male predominance with a male-to-female ratio ~2.5–6.3:1.⁵ On presentation, patients may complain of abdominal pain or present with haematemesis, obstruction or perforation. On endoscopy, the lesions are frequently described as deep ulcerations or ulcerated masses. Immunohistological studies of tissue obtained endoscopically confirm the diagnosis. While the relationship between HIV and EBV infection in Burkitt lymphoma has been well established, the aetiology of primary gastric Burkitt lymphoma is unknown. Sporadic reports show association with EBV, *H. pylori* and hepatitis B virus; however, the paucity of cases makes it difficult to prove a causal relationship. Isolated cases have reported remission with eradication of *H. pylori* infection.⁶

Burkitt lymphoma is a high-grade lymphoma with a growth fraction close to 100% and a doubling time of 25 hours.² It frequently demonstrates a complete response to intensive

Figure 2 (A) Axial CT scan of the abdomen showing findings suggestive of malignant infiltration of the gastric antrum and pylorus (white arrow). (B) Coronal CT scan of the abdomen showing findings suggestive of malignant infiltration of the gastric antrum and pylorus (white arrow).

Figure 3 H&E staining at different magnifications showing gastric tissue infiltrated by sheets of atypical medium-sized lymphoid cells with fine chromatin and scant cytoplasm. The atypical lymphocytes infiltrate around gastric glands with scattered mitotic and apoptotic cells. The tumour cells show Burkitt-like morphology with a starry sky pattern.

chemotherapy and prognosis is generally good, particularly in young patients with early-stage disease. Older patients have higher mortality and greater risk of central nervous system (CNS) involvement. Chemotherapy with CNS prophylaxis is therefore the recommended modality of treatment. The role of surgery in management of this condition is not clear. In previously reported cases, surgical intervention was reserved for complications such as perforation, severe uncontrollable bleeding, obstruction or other emergent indications. Long-term survival

with combination chemotherapy has been shown to approach 40%–80%.⁷

Primary gastric Burkitt lymphoma is aggressive and carries a poor prognosis if untreated. The standard of care chemotherapeutic regimen for the treatment of this condition has not yet been established. An intensive, frequent multi-agent chemotherapeutic regimen that includes CNS prophylaxis is required. Older individuals have worse outcomes, especially with more advanced disease, making early diagnosis and treatment essential.

Figure 4 (A) Immunohistochemical studies showed that the atypical cells were 100% positive for Ki-67, as well as positive for PAX5, BCL6, CD10. (B) Immunohistochemical studies showed that the atypical cells were BCL2 negative.

Figure 5 (A) Axial CT scan with resolution of previous gastric wall mass. (B) Overlay of fluorodeoxyglucose (FDG) PET scan on CT with no abnormal uptake in the gastric wall.

Primary gastric Burkitt lymphoma is managed similarly to other non-gastric presentations of Burkitt lymphoma. Current adult chemotherapy regimens have been extrapolated from the paediatric literature. Different chemotherapeutic regimens are used by providers; common regimens include HyperCVAD (hyperfractionated cyclophosphamide, vincristine, doxorubicin and dexamethasone with or without rituximab alternating with high-dose methotrexate and cytarabine), CODOX-M-IVAC (cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate with ifosfamide, cytarabine, etoposide and intrathecal methotrexate) and dose-adjusted EPOCH (dose-adjusted infusional etoposide, vincristine and doxorubicin, with oral prednisone and bolus dose-escalated cyclophosphamide chemotherapy).

A prospective, non-randomised trial that included 53 patients with newly diagnosed Burkitt lymphoma treated with the CODOX-M/IVAC regimen demonstrated a 2-year progression-free and overall survival rate of 64% and 67%, respectively.⁸ A prospective single-arm trial of HyperCVAD in 31 patients with newly diagnosed Burkitt lymphoma demonstrated complete remission in 86% and 3-year overall survival of 89%.⁹ Finally,

in an uncontrolled prospective trial where 19 patients received dose-adjusted EPOCH, the rates of freedom from progression of disease and overall survival were, respectively, 95% and 100%.¹⁰ The CODOX-M-IVAC regimen is highly toxic, primarily to the bone marrow, with patients expected to have a prolonged hospital stay during therapy. Older patients with lower fitness levels may better tolerate the relatively less toxic dose-adjusted EPOCH regimen. Data comparing these chemotherapeutic regimens are limited as there have been no head-to-head trials comparing them to each other.

Contributors FA, JJF and NP all contributed to the authorship of the manuscript as well as patient care, with JJF and NP focusing on the discussion section and FA on the case presentation and management, as well as final draft review. MM was the attending physician who reviewed the final draft, provided guidance and final remarks.

Competing interests None declared.

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Learning points

- ▶ Burkitt lymphoma is an aggressive subtype of B-cell non-Hodgkin's lymphoma with three variants: endemic, sporadic and immunodeficiency associated.
- ▶ Primary gastric Burkitt lymphoma is a rare, highly aggressive malignancy.
- ▶ While the relationship between HIV and Epstein-Barr virus infection in Burkitt lymphoma not isolated to the stomach has been well established, the aetiology of primary gastric Burkitt lymphoma is unknown.
- ▶ Gastric Burkitt treatment has not been studied due to the paucity of cases; current treatment is extrapolated from paediatric literature for Burkitt lymphoma as well as studies of Burkitt lymphoma not isolated to the stomach in adults.
- ▶ The main stay of treatment is multi-agent chemotherapy as well as central nervous system (CNS) prophylaxis due to high likelihood of CNS involvement or relapse.
- ▶ Treatment must be initiated rapidly after diagnosis, as prognosis is otherwise very poor due to rapid doubling time.

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