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Case Report

PRIMARY GASTRIC LYMPHOMA: CASE REPORT WITH REVIEW OF LITERATURE

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ABSTRACT
Stomach is the most common site of lymphoma in gastrointestinal tract, which can be either primary or secondary to lymphoma at other sites. Mucosa associated lymphoid tissue (MALT) lymphomas and diffuse large B cell lymphomas (DLBCL) are commonly encountered in stomach. Most of the gastric lymphomas are found secondary to chronic inflammation induced by Helicobacter pylori infection. Primary lymphomas of stomach carry a better prognosis and hence correct diagnosis is important. We report a case of primary gastric lymphoma of DLBCL type which was negative for H. pylori infection, in a 45 year old male.

Keywords: *Stomach, Lymphoma*

INTRODUCTION
Gastrointestinal tract (GIT) is the most common extranodal site involved by lymphoma accounting for 5%-20% of all cases (Ghimire *et al.,* 2011). Although virtually lymphoma can arise from any region of the gastrointestinal tract, stomach is the most commonly involved site (60%-75%) in gastrointestinal tract followed by small bowel, ileocecal region and rectum (Herrmann *et al.,* 1980; Papaxoinis *et al.,* 2006). Gastric lymphoma accounts for 3%-5% of all malignant tumors of the stomach (Ferrucci *et al.,* 2007). Malignant lymphomas affect the stomach as a primary tumor or as part of more wide spread disease process, which is more common (Al-Akwaa *et al.,* 2004). Generally lymphomas are considered as "primary" in the gastrointestinal tract when the initial symptoms of the disease are in the abdomen indicating a disturbance of the gastrointestinal function, or when the bulk of the disease is in the stomach (Al-Akwaa *et al.,* 2004). Non-Hogdkin's lymphoma (NHL) is the most frequent gastric tumour after adenocarcinoma while Hodgkin's lymphomas (HL) are uncommon in stomach, whether primary or secondary (Ferrucci *et al.,* 2007; Venizelos *et al.,* 2006). Most gastric lymphomas are thought to arise in the mucosa or submucosa from the so-called mucosa-associated lymphoid tissues (MALT), which usually develop after chronic inflammation induced by Helicobacter pylori infection (Al-Akwaa *et al.,* 2004). Although all histological kinds of nodal lymphoma can arise from the stomach, the majority of them are of the B-cell origin, and mucosa associated lymphoid tissue (MALT) lymphoma and diffuse large B- cell lymphoma (DLBCL) account for over 90%. MALT lymphoma comprises up to 50% of all primary lymphomas involving the stomach. Primary gastric lymphomas (PGLs) are generally seen in elderly age group (above 50 years) (Ghimire *et al.,* 2011). We present a case of PGL of DLBCL type, without any evidence of H. pylori infection, in a 45 year old patient.

CASES
A 45 year old male patient presented with complaint of on and off pain in upper abdomen of 6 month duration for which he was being treated with antacids mainly. His physical examination was unremarkable. Due to the chronicity and resistant nature of his pain an upper gastrointestinal endoscopy was performed, which revealed two polypoidal masses in the body of stomach. An endoscopic biopsy was performed, although only small amount of tissue could be taken, and was sent for histopathological examination which showed few small nests of round to oval cells with fine nuclear chromatin. A provisional diagnosis of adenocarcinoma was made.

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Later a total gastrectomy was performed along with dissection of lymph nodes along greater and lesser curvature. Gross examination of opened up stomach showed a polypoidal mass of size 3cm in the body along greater curvature and two smaller masses of size 1 cm each, one in body and other in antrum, along lesser curvature. An ulcer was also seen adjacent to the larger mass. Adequate sections were taken from the masses and ulcer and they revealed diffuse proliferation of neoplastic lymphocytes replacing the gastric epithelium including the muscle layer and focally involving the serosa. (Figures 1& 2) This morphology was consistent with DLBCL.

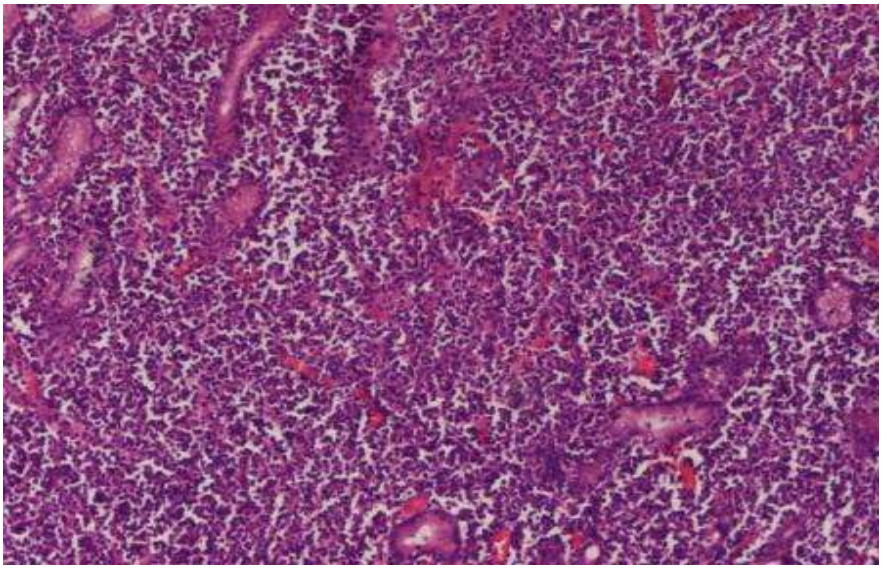

Figure 1: Diffuse Large B Cell Lymphoma: Diffuse proliferation of neoplastic lymphocytes replacing the gastric epithelium including the muscle layer and focally involving the serosa. H and E x10

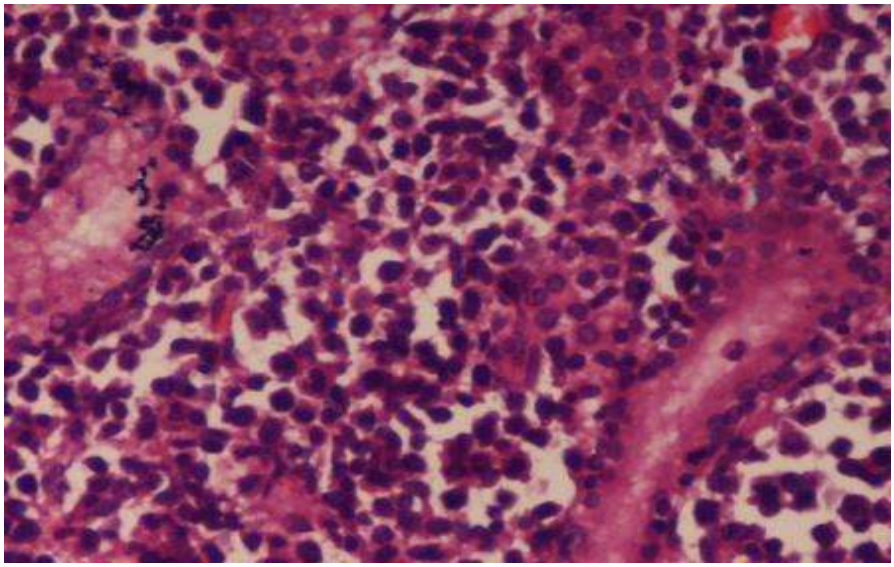

Figure 2: High power of Figure 1

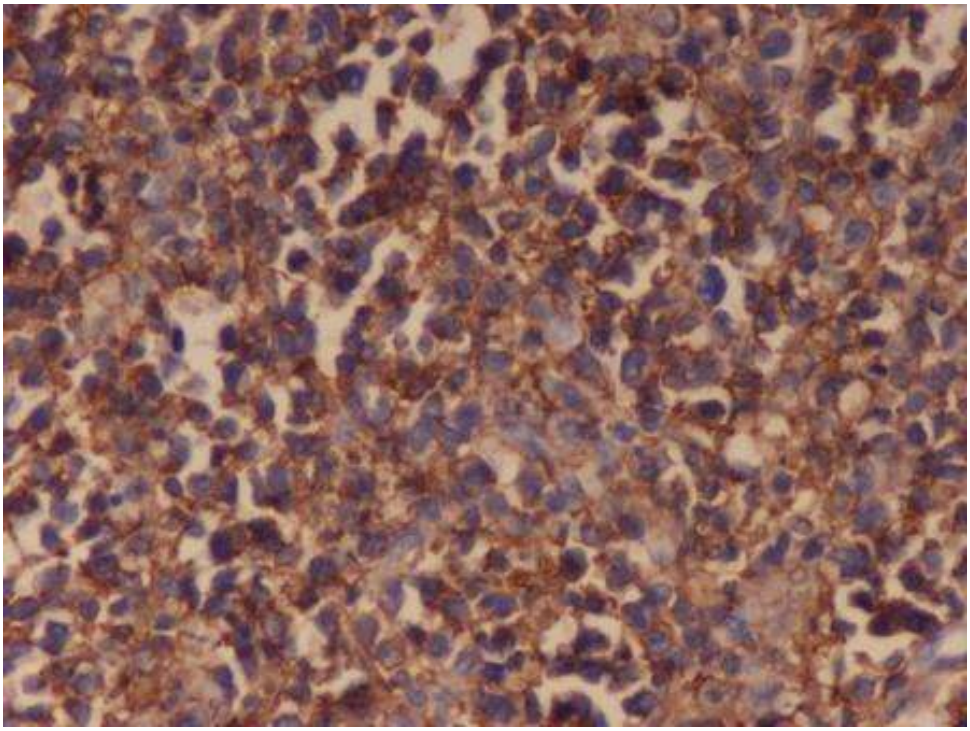

Figure 3: The lymphoma cells show intense cytoplasmic positivity for CD20. CD 20 immunostain x 40

The lymphoma cells were positive for CD20 immunostain, revealing their B cell lineage (Figure 3). The margins of resection were free and submitted lymph nodes showed only reactive features. Sections from normal appearing gastric mucosa showed features of gastritis but there was no evidence of H. pylori infection. As stomach was the predominant site of involvement without evidence of involvement of any other organ and blood counts were normal, a final diagnosis of PGL of DLBCL type was made. Since the resection margins and lymph nodes were free and there was no other evidence of metastasis, no further management (like chemotherapy or radiotherapy) was carried out. The patient is on regular follow up since 6 months and is doing well.

DISCUSSION

GIT is the most common extranodal site involved by lymphoma with the majority being non-Hodgkin type (Ghimire *et al.,* 2011; Ahmad *et al.,* 2003). However, according to some authors central nervous system is the most common extranodal site, followed by GIT (Ferrucci *et al.,* 2007). In GIT, the most common site is stomach (Ghimire *et al.,* 2011; Ferrucci *et al.,* 2007). Although the incidence of gastric carcinoma has reduced, the incidence of primary gastric lymphoma is increasing (Ghimire *et al.,* 2011). Dawson's criteria are used for labeling primary gastrointestinal lymphoma, that include (1) absence of peripheral lymphadenopathy at the time of presentation; (2) lack of enlarged mediastinal lymph nodes; (3) normal total and differential white blood cell count; (4) predominance of bowel lesion at the time of laparotomy with only lymph nodes obviously affected in the immediate vicinity; and (5) no lymphomatous involvement of liver and spleen (Dawson *et al.,* 1961). Secondary gastric lymphoma generally presents as advanced, disseminated non-Hodgkin's lymphoma requiring chemotherapy for treatment. On the other hand, PGL manifests as early, localized disease with a high potential for cure (Ahmad *et al.,* 2003).

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The age of occurrence of most gastric lymphomas is over 50 years with median age of 60-65 years with a relative predilection in males (Ghimire *et al.,* 2011; Al-Akwaa *et al.,* 2004). In a study done by Gisbert *et al.,* (2006) on gastric MALT lymphoma, the mean age of patients was 61 ± 14 years; 62% were males, 30% were smokers, and 16% had a history of alcohol abuse. Clinical symptoms of gastric lymphoma are nonspecific and indistinguishable from other benign and malignant conditions (Ghimire *et al.,* 2011; Al-Akwaa *et al.,* 2004). The most common complaints are epigastric pain, weight loss, nausea, vomiting, followed by abdominal lump, bleeding, perforation and obstruction. Gastric antrum is the site most commonly involved, followed by body and cardia in decreasing order (Ghimire *et al.,* 2011; Al-Akwaa *et al.,* 2004; Gisbert *et al.,* 2006).

Radiological findings like gastric wall thickening, ulcer deformities, obstruction, mass effect etc, are helpful but not specific for lymphoma (Ghimire *et al.,* 2011; Al-Akwaa *et al.,* 2004). Endoscopy cannot distinguish gastric lymphoma from the more common gastric carcinoma (Ghimire *et al.,* 2011). The three main patterns that can be recognized at endoscopy include ulceration, diffuse infiltration, and polypoid mass, which are, however, not specific (Ghimire *et al.,* 2011; Ahmad *et al.,* 2003). Endoscopy, however, is an indispensable tool for the initial diagnosis and follow-up of cases as well as for obtaining biopsy specimens (Ghimire *et al.,* 2011). Biopsy, taken mainly via endoscopy, is primary method for diagnosis, and frequently repeat endoscopic biopsies are needed for correct diagnosis (Ferrucci *et al.,* 2007; Al-Akwaa *et al.,* 2004; Ahmad *et al.,* 2003). In our case, the patient was a 45 year old male who presented with just upper abdominal pain and the endoscopy had revealed polypoidal masses. Since carcinoma is more common, a provisional diagnosis of the same was made at first instance when very small biopsy tissue was available revealing malignant cells.

The most common histological subtypes are diffuse large B-cell and marginal zone B-cell NHL of the mucosa-associated lymphoid tissue (MALT)-type (Ferrucci *et al.,* 2007). Whether all diffuse large B-cell gastric lymphomas are derived from previous low-grade MALT lymphomas is still an open question that is not yet resolved unequivocally (Ghimire *et al.,* 2011; Ferrucci *et al.,* 2007). Rare tumors may be T cell in origin (Al-Akwaa *et al.,* 2004). The hallmark of MALT lymphoma is the lymphoepithelial lesion that results from tissue invasion by atypical lymphocytes as well as reactive lymphoid follicles (Ghimire *et al.,* 2011; Al-Akwaa *et al.,* 2004). The tumor B-cells can express the surface immunoglobulin and pan-B antigens (CD19, CD 20, and CD79a), the marginal zone-associated antigens (CD35 and CD21, and lack CD5, CD10, CD23) and cyclin D (Ghimire *et al.,* 2011; Ferrucci *et al.,* 2007). Lymphoepithelial lesions can be identified by using anti-CD20 antibodies (Ferrucci *et al.,* 2007). DLBCL, a heterogeneous group of tumors which are clinically, histologically, immunophenotypically, cytogenetically variable and can be divided into 3 subgroups, namely germinal-center B-cell-like, activated B-cell-like, and primary mediastinal DLBCL according to the gene expression patterns with each having a different prognostication (Ghimire *et al.,* 2011; Hans *et al.,* 2004).

H. pylori plays a role in the development of most MALT lymphomas. However, its exact mechanism has not been fully understood, although a chronic inflammation may enhance the probability of malignant transformation via B cell proliferation in response to H. pylori mediated by tumor-infiltrating T cells (Ghimire *et al.,* 2011; Hussell *et al.,* 1996). H. pylori may play a similar role in development of DLBCL and few studies have shown complete remission after eradication therapy alone (Hussell *et al.,* 1996). MALT lymphoma can therefore be divided into H. pylori positive or negative, based on the presence of H. pylori (Ghimire *et al.,* 2011). Our case did not show any evidence of H. pylori infection; hence it was H. pylori negative.

The modalities of treatment for gastric lymphomas have been a controversial subject, and the best regimen has not been standardized (Al-Akwaa *et al.,* 2004). Historically, therapeutic strategies in gastric lymphomas have been, for a very long while, based on surgery, followed by radiotherapy or postoperative chemotherapy, but this approach has been questioned over the last two decades (Ferrucci *et al.,* 2007). Management of early stage H. pylori positive MALT type of gastric lymphoma is to eradicate H. pylori with antibiotics and proton pump inhibitors (Ghimire *et al.,* 2011; Ferrucci *et al.,* 2007; Ahmad *et al.,*

2003). No definite guidelines have been advocated for the treatment of advanced or H. pylori negative MALT-type of gastric lymphoma. Although surgery has been used as its initial treatment, recent studies showed that radiotherapy alone can achieve a complete remission with a 5-year disease free period (Ghimire *et al.,* 2011; Ferrucci *et al.,* 2007). In our patient total gastrectomy with lymph node dissection was performed, with good results.

Conclusion

It can be concluded that PGLs present early with non-specific symptoms, and as localized disease, so they can be treated early with favorable results. The age of presentation is above 50 years but they can even present earlier. Although H.pylori infection is generally associated but it is not always the case. So a correct diagnosis of PGL is important due to its better prognostic implications as they can be treated by surgery alone.

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