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• REVIEW •

Primary gastric lymphoma

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Abstract

AIM: The purpose of this review is to describe the various aspects of primary gastric lymphoma and the treatment options currently available.

METHODS: After a systematic search of Pubmed, Medscape and MDconsult, we reviewed and retrieved literature regarding gastric lymphoma.

RESULTS: Primary gastric lymphoma is rare however, the incidence of this malignancy is increasing. Chronic gastritis secondary to *Helicobacter pylori* (*H pylori*) infection has been considered a major predisposing factor for MALT lymphoma. Immune histochemical marker studies and molecular biology utilizing polymerase chain reaction have facilitated appropriate diagnosis and abolished the need for diagnostic surgical resection. Advances in imaging techniques including Magnetic Resonance Imaging (MRI) and Endoscopic Ultrasonography (EUS) have helped evaluation of tumor extension and invasion. The clinical course and prognosis of this disease is dependent on histopathological sub-type and stage at the time of diagnosis. Controversy remains regarding the best treatment for early stages of this disease. Chemotherapy, surgery and combination have been studied and shared almost comparable results with survival rate of 70-90%. However, chemotherapy possesses the advantage of preserving gastric anatomy. Radiotherapy alone has been tried and showed good results. Stage IIIE, IVE disease treatment is solely by chemotherapy and surgical resection has been a remote consideration.

CONCLUSION: We conclude that methods of diagnosis and staging of the primary gastric lymphoma have dramatically improved. The modalities of treatment are many and probably chemotherapy is superior because of high success rate, preservation of stomach and tolerable complications.

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INTRODUCTION

Primary gastric lymphoma is a rare tumor, accounting for less than 5% of primary gastric neoplasms[1-5]. However it is the most common extranodal lymphoma, representing 4-20% of all extranodal lymphomas[6,7]. In the Middle East, stomach is the most common gastrointestinal site, with an incidence rate similar to that reported in the western literature[8-11]. However Turkish and Indian series suggested that intestinal lymphomas have been more predominant than gastric lymphoma in those regions[12,13].

Gastric lymphomas are prevalent in patients aged more than 50 years, however it still has been reported in the second decade of life[14,15]. Reported median age is 60-65 years and males are 2-3 times more affected than females[16-18]. Recently, several studies have shown an increase in the incidence among HIV infected and AIDS patients, affecting increasingly younger age groups[19-21].

PATHOLOGY

Malignant lymphomas affect the stomach as a primary tumor or as part of more wide spread disease process. Stomach is the most common site with secondary lymphoma[22,23]. 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.

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 *H pylori* infection[23-26]. Histologically and immunohistochemically MALT lymphomas are of the B-cell non-Hodgkins type (NHLs) and share many features in common, therefore they are denoted as malignant lymphomas of MALT. The association between *H pylori* chronic gastritis and MALT lymphoma has been confirmed in large population based studies where immunological evidence of *H pylori* infection has been shown to be more in patients with gastric lymphomas than in matched controls[24-26]. Other forms of gastric lymphomas are non-MALT type, although many may be initially MALT tumors. Rare tumors may be T cell in origin[27-30].

The histological classification may vary from low to high grade. Grading has been classified into low, intermediate and high grade. Other terminology of primary and secondary high-grade lymphomas has been adopted[24]. In the histology of secondary high-grade lymphomas, there is evidence of low-grade component. Various systems (Rappaport, Working formulation and Modified Kiel) have frequently been utilized for histological classification, Combination of two or three classification systems have also been commonly used[17,23,30,31].

A majority of primary gastric lymphomas are histologically of the diffuse histiocytic or large cell type[15,32,33]. Reports from Saudi Arabia have shown a predominance of diffuse large B-cell type[14,33]. Gastric maltoma represents up to one half of primary gastric lymphoma. In the last few years, the Revised European American Lymphoma (REAL) classification of lymphoid neoplasms has been widely used with the advantage of high reproducibility and clinical relevance (Tables 1,2)[32,34].

Microscopically, low-grade lymphomas may not easily be distinguished from pseudolymphomas, a term used to describe the lymphocytic infiltration of the gastric mucosa, which may occur with chronic gastritis and peptic ulceration. Pseudolymphomas may mimic clinically and endoscopically gastric adenocarcinomas or lymphomas. Pathologists can differentiate between pseudolymphomas and lymphomas based on several histological characteristics which indicate malignant

changes, like prominent lymphoepithelial lesions (lymphoid infiltration of glands or crypts with partial destruction), Dutcher bodies and moderate cytologic atypia[35]. In cases which can not be diagnosed with histological differentiation, immunohistochemical marker studies or molecular biology utilizing polymerase chain reaction (PCR) may facilitate establishing an accurate diagnosis[36,37]. However, recent studies have indicated that the great majority of pseudolymphomas are in fact true lymphomas of low-grade malignancy using markers of clonality, and this term preferably has to be abandoned[37].

Table 1 The REAL classification of non-Hodgkin's Lymphomas

B-cell lymphomas
Precursor B-cell lymphomas:
B-lymphoblastic
Mature B-cell lymphomas:
B-cell CLL / small lymphocytic
Follicular
Marginal-zone-nodal
Extranodal marginal-zone (MALT)
Splenic marginal-zone
Lymphoplasmacytic
Mantle-cell
Diffuse large B-cell
Primary mediastinal large B-cell
Burkitt's like
Burkitt's
T-cell lymphomas
Precursor T-cell lymphomas:
T-lymphoblastic
Mature T-cell lymphomas:
Mycosis fungoides / sezary syndrome
Peripheral T-cell (many subtypes)
Anaplastic large T / null cell
Adult T-cell leukemia / lymphoma

Table 2 Histologic classification of gastrointestinal lymphomas

B-cell
Mucosa-associated lymphoid tissue (MALT)-type (extranodal marginal-zone lymphoma):
Low-grade
High-grade, with or without a low-grade component
Immunoproliferative small intestinal disease (IPSID):
Low-grade
High-grade, with or without a low-grade component
Lymphomatous polyposis (mantle-cell lymphoma)
Burkitt's and Burkitt's-like
Other types of low- or high-grade lymphoma corresponding to lymph node equivalents
T-cell
Enteropathy-associated T-cell lymphoma (EATCL)
Other types not associated with enteropathy

Macroscopically, gastric lymphomas may appear as ulcerated (single, multiple or diffuse), polypoid, granulonodular or infiltrative lesions[13,24,33]. Ulcerative type alone or combined with other lesions has been the most frequent endoscopic presentation of primary tumors. The lesion may vary from fine nodularity or normally looking mucosa to very advanced large fungating ulcerated mass[13]. Endoscopically, the differentiation between lymphomas and adenocarcinomas may not be easy, however early lymphomas tend to produce larger tumors than adenocarcinomas and may be multifocal as well[15]. Gastric lymphomas involve more frequently the antrum and corpus[33]. In a series, 46% of lesions are located at gastric body[24]. Entire gastric involvement has also been reported[18,24]. In advanced diseases tumors may spread to extraintestinal sites like central nervous system, bone, liver, kidneys, ovary and lungs[24].

CLINICAL PRESENTATION

The initial symptoms of upper abdominal pain and early satiety may be vague and nonspecific, leading to a delayed establishment of diagnosis up to several years[39]. Symptoms and signs may mimic that of other abdominal pathologies including peptic ulcer disease, gall bladder, pancreatic or functional disorders as well as other gastric neoplasms[15]. Other common symptoms included weight loss, nausea, vomiting, abdominal fullness and indigestion[30,31,33]. Weakness, night sweat, jaundice, fever and dysphagia occur less frequently[13,23,30]. Many patients came down late with advanced disease and complications may develop before diagnosis[38]. Twenty to thirty percent may present with bleeding in the form of hematemesis or melena while, gastric obstruction and perforation are less common[37,38]. Physical examination could be normal in 55%-60%[30]. Common signs include epigastric tenderness and palpable mass. The tenderness is encountered in 20%-35% and masses in 17%-25%[15,23,31]. Other uncommon findings included fever, hepatomegaly, splenomegaly, jaundice and lymphadenopathy. In one series, lymphadenopathy is found in 12%[24,30,31]. Signs of malnutrition may also appear in advanced disease[39].

DIAGNOSIS

Clinical presentation and radiological features are often nonspecific. Esophagogastroduodenoscopy (EGD) and biopsy are primary methods for diagnosis[15,40]. The diagnosis of low-grade MALT lymphoma by forceps biopsy is often difficult in early disease and reapeated endoscopies and biopsies may be required before final diagnosis is achieved[25].

Multiple and step biopsies are required because endoscopic findings may vary from subtle mucosal changes to gross lesions. These may include mucosal edema, friability, patchy redness, irregular patchy gray or whitish granularity, contact bleeding, superficial irregular erosions and ulcerations[33]. Repeated endoscopic biopsies are mandatory in case of clinical suspicion and negative or inconclusive histology. Furthermore, endoscopic mucosal resection enhances the histological yield[41]. Occasionally, rapid diagnosis by endoscopy can be made by detection of monoclonality in immunoglobulin heavy chain rearrangement of the lymphoproliferative disease by PCR[42]. It is reccommended that biopsy specimens should undergo histological, immunohistochemical and genotyping studies to make the diagnosis.

Radiological examinations can help establish diagnosis and determine the extent of the lesions. Gastric wall thickening, atypical ulcer deformities, obstruction and mass effect are enhanced features suggestive, but not specific for gastric lymphoma[30,31,38]. CT scan of the abdomen can identify the gastric wall thickening or mass lesions in 85% of cases. Sometimes it may show typical imaging features of more homogenous and pronounced mural thickening that can help differentiate lymphomas from adenocarcinomas[42,43]. On CT scan, three quarters of cases of low grade MALT lymphomas may present with infiltrative form and polyploid form in the remainder. Lymphadenopathy is detected in only 50%[43]. Conventional sonographic examination can be of value in identification of gastrointestinal involvement as well as abdominal lymph node enlargement in lymphoma staging. The MRI features include irregularly thickened mucosal folds, irregular submucosal infiltration, annular constricting lesion, exophytic tumor growth, mesenteric masses and mesenteric/ retroperitoneal lymphadenopathy[44]. EUS is a valuable

technique in assessing the extent and invasion of the lesion. By EUS, infiltrative carcinomas tend to show a vertical growth in the gastric wall, while lymphomas tend to show mainly a horizontal extension[45,46]. It is highly accurate in determining the depth of lymphomatous infiltration and the presence of perigastric lymph nodes, thus providing additional information for therapeutic planning. It can differentiate between lymphomas and carcinomas in early stages, but in advanced stages both have similar appearances. With the development of the above diagnostic methods, open surgery is rarely needed to confirm the diagnosis.

STAGING

After establishing the diagnosis of primary gastric lymphoma, staging is essential for planning treatment. It is also important to rule out systemic lymphoma with secondary involvement of the stomach. The staging process starts with endoscopy and step biopsy to rule out microscopic infiltration of nearby structures like the duodenum. Chest radiography may show gross lesions in the lungs and mediastinum. CT scan of chest, abdomen and pelvis permits assessment of nodal involvement above and below the diaphragm, and extension of the tumor outside the stomach. EUS may be employed for accurate estimation of both the depth of invasion and involvement of regional lymphnodes[45,46]. It is superior to CT scan in false negative cases. Bone marrow examination helps determine presence or absence of tumor spread. Indirect laryngoscopy is also helpful for excluding Waldeyer' s ring involvement, which is reported to be associated with gastric lymphoma[32].

Table 3 Staging classification according to Musshoff's criteria

Stage	Definition
IE	Lymphoma limited to the stomach
IIE_1	Involvement of stomach and contiguous lymph nodes
IIE_2	Involvement of stomach and noncontiguous subdiaphragmatic lymph nodes
III	Involvement of stomach and lymph nodes on both sides of diaphragm
IV	Hematogenous spread (stomach and one or more extralymphatic organs or tissues)

The Following subscripts may be added E=extranodal, S=splenic, A=asymptomatic, B=symptomatic.

Table 4 Modified Blackledge staging system for gastrointestinal lymphomas

Stage I	Tumor confined to gastrointestinal tract without serosal penetration: Single primary site Multiple, non-contiguous lesions
Stage II	Tumor extending into abdomen from primary site: Nodal involvement II_1 Local (gastric / mesenteric) II_2 Distant (paraaortic / paracaval)
Stage II_E	Penetration of serosa to involve adjacent 'structures': Enumerate actual site of involvement, e.g. stage II_E (pancreas), stage II_E (large intestine), stage II_E (post-abdominal wall) Perforation / peritonitis
Stage IV	Disseminated extranodal involvement or a gastrointestinal-tract lesion with supradiaphragmatic nodal involvement

Various staging systems have been used. The Ann Arbor staging for primary lymphomas has been modified by Musshoff, and utilized by several authors for staging gastric lymphomas (Table 3)[18,47,48]. Several alternative staging systems have been proposed, and the revised version of the Blackledge staging system has been recommended for general use (Table 4)[49,34]. Several authors have suggested that such staging modification may be of prognostic significance[50,51,53].

TREATMENT

The modalities of treatment for gastric lymphomas have been a controversial subject, and the best regimen has not been standardized. However, options of treatment depend on the histologic classification and stage of the disease. Some centers adopt surgery alone, while others advocate non-surgical treatment with radiation, chemotherapy or both.

SURGERY

Traditionally, aggressive surgical resection has been the main stay of treatment because it can collect definitive tissues for pathologic examination, allow exploration of the abdomen, reduce tumor burden and obviate the concern that gastric hemorrhage or perforation would complicate medical treatment of lymphomas. More recently, radical gastrectomy is disputed and considered unnecessary. Lesser procedures are now accepted where resection of the gross disease and involved lymphnodes will provide adequate results[39,52,53]. Several reports have shown a superior outcome when surgical resection is undertaken in the early stages of the disease with a 5-year survival rate of 80%-93%[54,55].

Kazaya *et al* advocated wide resection of early gastric tumor and extensive lymph node dissection[15]. Other authors also found surgery alone to be an adequate treatment for stage 1E or pure MALT lymphomas with a survival rate of >95%, provided staging is performed after radical gastrectomy[56]. In a large series of patients treated according to *H pylori* status, tumor grade and stage, surgical resection remained the treatment of choice in patients with stage IIE, low-grade lymphoma and non-responders of stage IE treated by eradication for *H pylori*, however the author advised further studies to compare surgical with conservative treatment[57].

A prospective study from France, has found that in stages I E and II E, the complete response, survival rate and disease free survival rates were similar to those who underwent complete resection, partial or no surgery prior to administration of chemotherapy. The survival rates of 60% with surgery alone compared to 85% if adjuvant chemotherapy was given, were reported[40]. In a retrospective study of 92 patients from Italy in different stages who underwent surgical resection when it was feasible, the ten-year actuarial survival rates were 100% and 80% for stage IE and IIE respectively compared with 21% and 0 for stage IIIE and IVE[58].

Surgical resection with clear margins is advised in order to maximize the chance of cure[39,55,59]. On the contrary, other reports have found no difference in survival, whether the margin of resection was clear or not, as long as post-operative chemotherapy had been given[60,61].

The mortality and morbidity related to surgery were similar if not more than those related to non-surgical treatment for stage I and II. Therefore, aggressive surgery is not indicated due to increased morbidity which is outweighing the benefit gained in terms of survival[60-62] and gastrointestinal organ preservation may provide substantial advantage for the quality of life in these patients[39]. Resectability rates ranged from 60%-88%, and the 5-year survival ranged from 50%-87%[55,60]. Debulking of advanced disease was associated with the high morbidity and mortality and low response rates of 6%-40%[63]. Operative mortality was between 3%-25% with higher rates

for palliative procedures which were performed for symptomatic relief, removal of tumor mass and avoidance of hemorrhage or perforation related to other mode of therapy[63]. In a prospective study of 208 patients, there was no difference in therapeutic outcome in surgically or conservatively treated patients, even after complete resection, the authors concluded that surgery favored by most authors in treatment of primary gastric lymphoma should be reassessed[64].

CHEMOTHERAPY

The effect of chemotherapy alone as a sole treatment for gastric lymphomas is still debatable. The needs behind trying chemotherapy were the considerable morbidity and mortality associated with resection[63]. Stomach conservation, and avoidance of postoperative complications such as myocardial infarction, gastrointestinal bleeding, enterocutaneous fistula and malabsorption syndrome were important factors that obviated the choice of chemotherapy. Initial trial in a small number of patients in stage I E and II E has shown excellent results by combination of chemotherapy and radiotherapy with a survival rate of 70% and few complications[52]. Salvgnol *et al* reported a survival rate of 71% in patients treated by chemotherapy[55]. Another recent study on aggressive gastrointestinal lymphoma found primary chemotherapy with or without radiotherapy useful and induced a complete response in 81% of patients, with fewer complications compared with surgery including less risk of perforation or bleeding[65]. Other reports showed no apparent difference in survival between patients treated by chemotherapy or surgery and chemotherapy with survival rates of 67% and 60%, respectively. There has been no report of serious adverse effects such as bleeding or perforation in chemotherapy-treated patients of intermediate and high grade non- Hodgkin lymphomas[60]. In a report from Italy, 17 patients with resectable large cell lymphoma treated primarily by chemotherapy with or without consolidation radiotherapy, only two failed in the first line therapy and 15 were free of disease at 6 years[66]. Consolidation radiotherapy might improve the efficacy of chemotherapy. None of the patients experienced acute treatment related morbidity or mortality from local complications[68]. In three recent trials with variable chemotherapy regimens, the survival rates of 82%-88% in stage IE and IIE, high grade lymphoma with only few and manageable complications were found[65,67,68].

In other series, chemotherapy alone compared with surgical resection alone, has shown no significant difference in the matter of survival. The overall 2-year survival was 67% and 81%[69-71].

In patients with comorbid factors and increased risk of surgery-related morbidity and mortality, chemotherapy offered an effective or equally effective mode of treatment to surgical resection 57% *vs* 58%[71].

The fear of chemotherapy-related complications, for instance, bleeding and perforation, has been disputed, and less significant compared with surgical resection[65,67-69]. Some authors reported the incidence of chemotherapy-related bleeding between zero and three percent and no perforation[60,72]. Therefore, chemotherapy has been suggested and adopted as a primary mode of treatment. Combined chemotherapy comprising cyclophosphamide, doxurubicin, vincristine and prednisolone (CHOP), has been the preferable and the most effective regimen for all tumor stages[31,65]. Several other regimens have also been used with almost similar efficacy and comparable toxicity[75]. While cyclophoshamide, vincristine and prednisolone (COP) were adopted for low grade lymphomas, high grade tumors were treated with doxurubicin, teniposide, cyclophosphamide and prednisolone (AVmCP). The latter two regimens combined with surgical resection have shown the survival rates of 80% and 100%, respectively[73].

COMBINED THERAPY

Multimodal therapy, combining resection with chemotherapy and occasionally radiotherapy have been commonly and widely accepted in many centers. It has significantly improved the 5-year survival[10,27,55,59,60,74]. Combination of radical surgery followed by chemotherapy has been associated with a significantly improved outcome in comparison with chemotherapy alone[73]. Lin *et al* have compared surgery, surgery with adjuvant chemotherapy and chemotherapy alone and found the 5-year survival rates of 57%, 76% and 58% compared with 0% in the untreated group. They recommended surgery when feasible with adjuvant chemotherapy as the mainstay of treatment for gastric lymphoma[71]. A Chinese study has suggested that chemotherapy plays a role in improving survival rates post-surgical resection[53]. A prospective study from France in 1990 reported a 100% survival in patients with high-grade tumors who underwent resection and adjuvant chemotherapy. A recent series has shown the superiority of combined surgery and chemotherapy to single mode with survival rates between 86%-94% for stages IE and IIE[53,59,66]. In these series the survival rates were higher for those who had complete resection, resection was the most important variable and major determinant of prolonged complete remission[59,60]. Survival was higher in low-grade lymphomas, although the initial response might be superior in high grade lymphomas[59]. Combined radical surgery and chemotherapy depending on the histologic grading were also associated with prolonged remission[73].

Resection of the tumor with clear margins is thought to have a better prognosis than with diseased margins[52,74,75]. However, other authors have found insignificant difference between the two procedures as long as post-operative chemotherapy was administered, and the extent of the disease at time of surgery, full thickness disease and lymph node involvement were important determining factors[39].

On the contrary, other studies reported no significant difference in outcome in groups treated with single or combined mode of treatment[57,62,70,72].

The stage and histologic grade of the disease play a role in the selection of the treatment modality, in addition to the comorbid disease and age of the patients.

Early stages of the disease regardless of the histological grade may be controlled by chemotherapy or chemotherapy and radiotherapy with the advantage of gastric conservation and avoidance of post-operative mortality and morbidity[54,62,65-67,69,74]. On the other hand, surgery is advocated as the first option with adequate control of the disease[57-59, 61], and occasionally with the necessity of wide resection and extensive lymph node dissection[15,78], however, adjuvant chemotherapy is indicated to control the local and distant disease if any[75,78].

In advanced stages of gastric lymphoma (stage IIIE, IVE) the behaviour of the tumor has the same manner as other advanced non-Hodgkin lymphomas, therefore combined chemotherapy is considered the treatment of choice for locally advanced or disseminated aggressive disease. In a prospective study of 700 patients with aggressive lymphoma treated with intensive chemotherapy, no difference in outcome was observed between patients with an advanced aggressive nodal lymphoma and the subset of patients (15%) in which the lymphoma was deemed to occur in the gastrointestinal tract[40].

MALT lymphomas have aroused special interest because regression of the tumor has been reported after *H pylori* eradication. Standardization of therapy is not yet available and is still a subject of controversies. The initial results were shown in five of six patients with low grade MALT lymphomas who had regression of the tumor after eradication of *H pylori*[77]. Thiede and associates studied a total of 120 patients with early gastric MALT lymphomas treated with amoxycillin and

omeprazole, a complete remission rate of 81% was achieved with partial response in 9%[78]. Zucca and colleagues, in a large multinational cooperative study, treated 233 patients with antibiotics and randomized them to observation alone or maintenance with chlorambucil. Complete remission was documented in 62% and partial response in 12% with a 6-month median time to lymphoma regression. At a 40-month follow-up, a total of 15 (13%) cases had relapse[79]. Manfred reported regression of reactive lymphoid infiltrates after *H pylori* eradication, without endoscopic or histolgical regression in MALT lymphomas[26]. It is not yet known which stages of MALT lymphomas respond to *H pylori* eradication. Although it seems that eradication therapy is an adequate option of treatment taking into consideration the utility of endosonography in determining the invasion of the disease[80].

Surgical resection, radiotherapy or chemotherapy and their combination have proven to be effective treatment modalities. Radiotherapy was tried as a local form of treatment in a small number of patients, resulting in a survival rate of 93%. Surgery, radiotherapy and antibiotics were compared and similar results were found[81].

Radiotherapy

In most instances, radiotherapy is used as an adjuvant to surgery, chemotherapy or both. It has rarely been tried as a single mode of therapy[31,81]. However, limited trials have suggested that radiotherapy can be utilized as a primary mode of treatment with reasonable outcome[78,81].

Radiotherapy has been studied in comparison with other treatment modalities for stage IE and IIE with comparable outcome of 80%-89% survival[13,31,68]. Higher survival rates (93%) have been reported in early stages of MALT lymphomas not responding to antibiotics[83]. Radiation was used post-operatively in high- and low-grade lymphomas, for any residual tumors in stages I and II to improve the disease free survival[9,57]. Combined chemotherapy might improve the chance of stomach conservation which may approach 100%[72]. Total gastrectomy has not improved the survival in patients in whom radiotherapy has been utilized as the primary mode of therapy with a survival rate of 84%. Contradictory studies have found the combined radiotherapy with either resection or chemotherapy to be of no significant difference in both modalities with a survival rate of 82%-88%[9,68,81].

PROGNOSIS

The prognostic factors in early stages were evaluated and defined in several studies. Good prognosis was associated with low grade disease, age below 65 years, free surgical margins in cases of resection, and achievement of initial complete remission[49,50,53]. In advanced diseases, good prognosis was found in low-grade histology, initial complete response, and in general the prognosis is the same as non-gastrointestinal lymphoma[50]. The grade of the disease also plays an important role in prognosis with better survival in low-grade disease rather than primary or secondary high-grade taking into consideration the stage[17]. Five-year survival rates were reported to be 91% for low-grade, 73% for secondary high-grade and 56% for primary high-grade tumors[17]. Debulking of the disease has not significantly altered the prognosis[50,53,61,64].

CONCLUSION

Due to the rarity of primary gastric lymphoma, many aspects of this neoplasm are still controversial. The incidence of the disease is increasing and HIV-infected people are more vulnerable. Universally, gastric lymphoma is the commonest gastrointestinal lymphoma except in a few countries where small intestinal lymphoma has been reported to be more common. On many occasions, patients present late, however with the availability of sophisticated diagnostic tools, the diagnosis can be made early and the classification and staging can be assessed accurately. The REAL classification despite being complex, has met a general agreement among pathologists and facilitated reproducibility. Most of the gastric lymphomas are primarily MALT type in origin. The best treatment for primary gastric lymphoma has not yet been exactly identified. It seems that for advanced disease, i.e., stage III and IV, combined chemotherapy and radiotherapy is superior since surgery is associated with failure of complete resection and significant morbidity and mortality. Most recent reports have advocated conservative treatment for early stages IE and IIE with the advantage of stomach conservation. On the other hand, many centers are still considering tumor resection as a better option. *H pylori* eradication with close observation has been considered adequate to treat early MALT lymphoma. Randomized trials are still needed to clarify whether conservative, surgical or combined treatment is more appropriate for treatment of localized gastric lymphoma.

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