Utility of surgical resection with or without radiation therapy in patients with low-grade gastric mucosa-associated lymphoid tissue lymphoma

The revised European and American classification of lymphoid neoplasms (REAL)[1] categorizes mucosa-associated lymphoid tissue (MALT) lymphomas as extranodal marginal zone B-cell tumors. The stomach is by far the most common site, and occurrence of gastric MALT lymphoma has been associated with Helicobacter pylori infection.[2]

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Anti-H. pylori therapy may lead to complete regression of early-stage primary gastric low-grade MALT lymphoma in approximately 50%-60% of cases.[3-6]

Here we review our experience in surgical treatment of stage IE and IIE gastric low-grade MALT lymphomas with or without radiotherapy and assess the safety and effectiveness of this therapeutic approach.

Between January 1986 to December 1998, 67 consecutive, unselected patients were diagnosed as having stage I or IIE (according to Ann Arbor system modified by Musshoff)[7] low-grade primary gastric MALT lymphoma. H. pylori infection was tested only in the 10 most recently recruited patients. The histopathologic diagnosis was based on the REAL classification.[1]

All these patients underwent subtotal or total gastrectomy, the latter being performed only in order to obtain microscopically tumor-free margins. Whenever careful pathologic examination of the surgical specimen revealed no evidence of intramural invasion (disease spread beyond the submucosa), perigastric lymph node involvement, or involvement of one or both surgical margins, patients were not submitted to subsequent radiotherapy. On the other hand, all patients who presented at least one of these three pathologic features were also treated with adjuvant radiotherapy 5 weeks after the resection. Treatment was delivered with cobalt 60 or 15 MV X-rays through shaped, parallel, opposed, anterior and posterior fields that minimally included the gastric bed and para-aortic lymph nodes. Simulation was done with oral and i.v. contrast medium to protect two-thirds of the left kidney from portal irradiation; the doses ranged from 3000 to 4000 cGy. No acute or late renal complications were observed. For patients with both positive lymph nodes and intramural invasion the whole abdominal approach was adopted. In patients treated with whole abdominal irradiation kidneys were shielded with posterior block to limit the dose to 1500 cGy; the dose was 3000 cGy.

Complete response (CR) and partial response (PR) were defined according the international criteria.[8] The Kaplan-Meier method was used to generate overall and relapse-free survival curves.[9]

Clinical and surgical characteristics at presentation are summarized in Table 1. In 38 (57%) patients, microscopically tumor-free margins were obtainable with subtotal gastrectomy (total gastrectomy being required in the remaining 29). Sixty-six (98%) patients obtained a CR, while the remaining patient achieved a PR. At the time of writing, 61 of the 66 (92.5%) patients who achieved CR are still in continuous CR at a median follow-up of 105 months (range, 38-180 months) in the absence of any maintenance therapy.

There have been five relapses at 24, 66, 74, 78, and 148 months. Three of these patients died from high-grade transformed disease. Intra-abdominal recurrences were found in 3 cases and extra-abdominal ones (neck plus mediastinum and rhinopharynx) in the remaining two. All relapsed patients underwent chemotherapy treatment. At 180 months, the projected 15-year relapse-free survival is 83% (Figure 1).

Table 1. Main clinical characteristics of the 67 patients with primary gastric MALT lymphoma.

Age	
Median	53 yr
Range	21-82 yr
Sex	38 males, 29 females
Systemic B-symptoms	1/66
Stage	
IE	41 (61 %)
IIE1	21 (32 %)
IIE2	5 (7 %)
Surgical features	
Positive surgical margins	27 (40 %)
Regional lymph node involvement	25 (37 %)
Intramural invasion	21 (31 %)

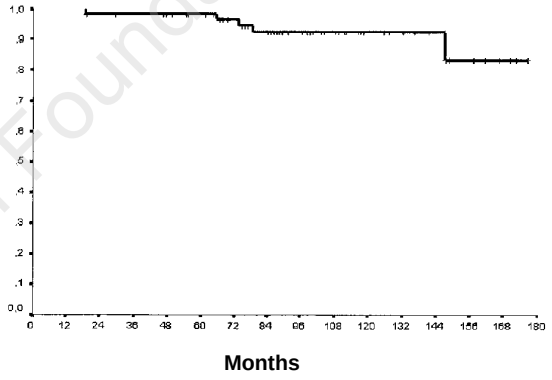

Figure 1. Relapse-free survival curve of all 66 patients with primary gastric MALT lymphoma who obtained a complete response after surgical tumor resection with or without radiation therapy.

There were no operative deaths. Only 4 (6%) surgical complications were noted (2 cases of anastomotic and 2 cases of intestinal obstruction after radiotherapy). In our series of 67 consecutive unselected patients with stage IE or IIE disease, surgery with or without radiation therapy (depending on the pathologic features) produced very favorable results. The initial CR rate was as high as 98%. After a median follow-up of 105 months, only five relapses have been recorded. The projected 15-year relapse-free survival is 83%.

Excellent results have recently been reported for low-dose radiotherapy alone in patients with low-grade MALT stomach lymphomas without H. pylori infection, or in whom it persists after antibiotic therapy.[10] However, the use of radiotherapy in lieu of surgical resection must be considered in the context of its toxicity. Although moderate-dose radiotherapy (35–45 Gy) can produce high local control rates, the dose required to control unresected disease is higher than that used in adjuvant settings (30 Gy).

In conclusion, this report provides evidence that surgical

treatment with or without radiotherapy provides a safe and effective option for patients with stage IE-IIE low-grade gastric MALT lymphomas. In terms of long-term relapse-free survival, our results compare very favorably with those from historical series in which antibiotic treatment was used as front-line therapy.[3-6] We think that the use of antibiotic therapy might be limited to particular situations (e.g., elderly patients, patients not eligible for surgery). In any case, surgery with or without radiotherapy remains the elective therapeutic procedure for patients who are refractory to, or who have relapsed after, antibiotic treatment.

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Allogeneic blood stem cell transplantation in advanced chronic myeloid leukemia - high response rate associated with increased chronic graft-versus-host disease

Twenty-four patients with advanced chronic myeloid leukemia in second chronic phase or in accelerated phase underwent allogeneic blood stem cell transplantation. After a median follow-up of 38 months (range: 4-69) 17 patients (70.8%) are alive, including 15 patients (62.5%) who are disease-free, whereas 4 patients (16.7%) have relapsed. Chronic graft-versus-host disease occurred in 13 of 21 (61.9%) patients at risk.

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Allogeneic stem cell transplantation remains the only curative option and induces long term molecular and cytogenetic remission in patients with advanced chronic myeloid leukemia (CML).[1] Single center series or international registries observed an overall survival of 20-25 % for patients transplanted in accelerated phase and a further decrease to about 10 to15 % for those transplanted in blast crisis.

Between 3/1997 and 8/2002 24 patients underwent peripheral blood stem cell transplantation (PBSCT) from either family or unrelated donors at our institution (Table 1). Accelerated phase and blast crisis were defined (by the presence of 10% to less than 20%, ≥ 20% blasts in marrow or peripheral blood, respectively) according to the WHO definition of CML.[2] The standard transplant-preparative regimen of 12 Gray (Gy) fractionated total body irradiation (TBI) in combination with a dose of 120mg/kg bodyweight of cyclophosphamide iv. was used in 18 patients (75%). Two patients (8.3%) received 8 Gy TBI and 120 mg/kg bodyweight cyclophosphamide, combined with a dose of 20 mg/kg anti-thymocyte globulin (Fresenius®) and 140 mg/m^2 fludarabine. One patient received 16 mg/kg bodyweight busulfan, 120 mg/kg cyclophosphamide and 200 mg/m^2 thiotepa. A reduced conditioning regimen with fludarabine (6×30 mg/m^2) busulfan (8 mg/kg bodyweight) and anti-thymocyte globulin (4×10 mg/kg bodyweight) was used in 3 patients (12.5%) due to prior radiotherapy or significant comorbidity.[3] All patients received 5 µg/kg granulocyte colony-stimulating factor (G-CSF) subcutaneously beginning on day +1 after PBSCT. Twenty patients (83.3%) received standard immunosuppression with cyclosporine 3 mg/kg bodyweight in combination with methotrexate on days 1, 3, 6 and 11. Seven patients who had matched unrelated donors or mismatched unrelated donors were additionally treated with 2 i.v. mycophenolate mofetil starting on day +10.

All patients showed leukocyte engraftment on a median of day +13.5 (range: 8-20) and 23 (95.6%) patients had platelet engraftment >20,000 ×10^9/L on a median of day +18 (range: 13-29). One patient died early on day +34 due to severe graft-versus-host disease (GvHD) and ongoing pancytopenia after initial myeloid engraftment. Acute GvHD ≥ was observed in 12 patients (50%) with 3 patients (12.5%) having grade III or IV. Limited and extensive chronic GvHD occurred in 6 (28.6%) patients each. Three patients (14.3%) developed de novo limit-