

Primary High-Grade Large Cell Type Gastric Lymphoma - eleven years survival and follow-up.

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Abstract

Primary gastric lymphomas are uncommon gastric tumors, which constitute approximately 2% of all primary gastric malignancies. The stomach is the most common extra-nodal site of non-Hodgkin's lymphoma. The incidence is appearing to be increasing. The diagnosis is often difficult due to its clinical similarity to peptic ulcer disease and stomach carcinoma. Primary high-grade diffuse large cell lymphoma of stomach is a rare pathology, which has a 5-year survival rate of approximately 56%. We would like to report on a patient with such a rare form of gastric lymphoma who has well survived more than 10 years and is healthy after meticulous treatment and rigorous follow-up.

CASE HISTORY

A 28-year-old Hindu male patient came with chief complaints of pain on ingestion of food, sensation of gaseous distension and an urge to vomit along with nausea since 3 months. He also gave a history of loss of weight and appetite since then. He used to eat hot, spicy and salty food daily from outside. He also used to drink very little water due to his busy work schedule. He had no other major medical illness nor had he undergone any kind of surgery. He had taken symptomatic treatment from his family doctor for the same problems initially but it did not relieve him of his symptoms. He finally came to our institute for further management.

On examination, the patient was thin built and poorly nourished. His vital parameters were within normal limits (WNL). On investigating, his hemoglobin was 11.1g%, WBC count 7200/cu mm, DC: N52/L43/E5, blood group: A rh (+ve), creatinine 0.5mg%, urine R/M: WNL.

The patient was subjected for upper GI scopy which revealed a nodular friable growth. It bled on touch involving almost the entire circumference of the stomach at its body. Multiple biopsies were taken and sent for histopathology study. On ultrasonography of abdomen and pelvis, the stomach wall showed an irregular, hypoechoic mass involving body of stomach, mainly greater curvature; lesser curvature and pylorus. Wall thickness measured almost 5.5cm. The rest of the viscera was WNL. Primary biopsy showed features of lymphoma. A decision to perform total

gastrectomy and oesophago-jejunal anastomosis with Roux-en-Y loop was taken.

Under general anesthesia, the patient was explored with midline incision and all findings were confirmed. Additionally, there were omental metastases. Total gastrectomy and oesophago-jejunal anastomosis with Roux-en-Y loop was done as decided earlier. The patient withstood the procedure well and his post-operative course was uneventful. Repeat upper GI scopy was carried out, which showed a nice anastomotic line at the terminal oesophagus which was dilated with the scope.

Histopathology of the specimen revealed poorly differentiated malignancy involving the distal 3/4 of the stomach which could be carcinoma or lymphoma and immunohistochemistry (IHC) was advised for further delineation. IHC showed primary high-grade diffuse large cell type lymphoma of the stomach. Chemotherapy was given consisting of cyclophosphamide, doxorubicin, oncovin and prednisolone (CHOP) which is the most useful and widely used chemotherapeutic regimen for any stage of lymphoma. No radiotherapy was offered to the patient. He was put on vitamin B-12 injections and protein supplements. The patient withstood the chemotherapeutic regimen well. At yearly follow-up, he was asymptomatic and healthy.

The patient presented with chronic calculous cholecystitis after 10 years. He was freshly investigated and he underwent laparoscopic cholecystectomy. Histopathology showed

cholelithiasis with a 12mm solitary calculus without any pericholecystic collection. Now, after one year, the patient is healthy and doing well. Repeat upper GI scopy revealed normal and healthy gastric mucosa.

DISCUSSION

There is always some or the other controversy that surrounds the treatment of gastric lymphoma, and therapeutic regimens also vary from center to center. Some institutes advocate surgery alone while others prefer non-operative treatment with radiation, chemotherapy or combination of both. Aggressive surgical resection has always been the mainstay of treatment. (1) Besides attempted cure, surgery provides the most accurate means of both grading and staging of the disease. (2) In the past, radical gastrectomy with en-bloc resection of spleen and regional nodes was performed almost exclusively to assure tumor-free margins.

However, with better understanding of tumor biology and increased use of adjuvant therapy, lesser procedures are now widely accepted. The goal of surgery is resection of all gross disease and involved lymph nodes, but in cases in which gastric lymphoma extends into the esophagus or duodenum, total resection may not be always mandatory. (3) Several surgeons have found no decrease in survival for patients with involved margins if adjuvant radiation therapy (RT) or chemotherapy were given concurrently. Currently, splenectomy is rarely done except in cases of direct tumor extension.

Resectability rates range from 60% to 85%. Five-year survival following potentially curative resection ranges from 50% to 87%. (4) Five-year survival in tumors judged non-resectable ranges from 6% to 40%. (5) It is important to note that the issue of resectability takes into account many factors at the time of operation including size and stage of the tumor, as well as the age and general status of the patient. Thus, whether or not a tumor is resectable is multifactorial, which affects the survival of the patient.

Operative mortality rates range from 2.3% to 25% and are generally higher for palliative procedures (6). This has been seen mainly in tumor-debulking surgeries. However, the necessity for debulking to avoid complications has more recently been questioned.

The role of radiotherapy (RT) in the management of gastric lymphoma is debatable. The use of RT as a single therapy for stage IE disease has been advocated by Burgers et al. (7). Their group found survival rates in stage IE patients treated

with radiation alone comparable to those treated with resection and radiation combined (both near 85%). In contrast, several surgeons have found little benefit to RT alone and demand need for further study.

Radiation therapy has also been advocated as adjuvant therapy for both potentially curative and palliative resections. As with the use of radiotherapy alone, the role of RT in the treatment of patients who have undergone partial or complete surgical resection is not firmly established. Several studies have found no significant improvement of overall survival rates with administration of radiation after attempted curative resection, mainly in early stage disease. Shimm et al. [14] found an increased survival with adjuvant radiation in patients with poor prognostic factors: penetration of the bowel wall, positive regional nodes or positive surgical margins.

Gastric lymphoma seems to be a more systemic disease with the majority of recurrences occurring at extra-abdominal sites. In the absence of obvious persistent local disease, the need for additional local therapy with RT is put in question by these reports. The need for systemic postoperative treatment, as is provided by chemotherapy, is apparent. As stated earlier, most primary gastric lymphomas are of the diffuse histiocytic or of the diffuse large-cell type. These subtypes seem to be quite responsive to current chemotherapeutic regimens. In addition, successful adjuvant chemotherapy allows for adoption of less aggressive surgical procedures, thus decreasing morbidity and mortality.

The results of most post-operative chemotherapy trials have been encouraging. For stages IE and IIE, several authors have found excellent 5-year disease-free survival for patients treated with chemotherapy after surgery (8). Therapeutic regimens usually include CHOP (cyclophosphamide, adriamycin, vincristine, and prednisone), CHOP-bleo (added bleomycin), COPP-bleo (cyclophosphamide, vincristine, procarbazine, prednisone, and bleomycin), or CVP (cyclophosphamide, vincristine, and prednisone). Perhaps the most marked improvement in survival has been in the management of advanced-stage disease.

The issue of whether chemotherapy, alone or in combination with RT, should be used in the absence of surgery remains largely controversial (9). Several surgeons have reported good results with only RT and chemotherapy, and cite the advantages of stomach conservation and avoidance of surgical morbidity. Maor et al. reported improvement in 5-year survival with the combination of chemotherapy and RT

compared with surgical therapy alone. In a study of 34 patients with stage IE and IIE disease (₃), 68% of patients treated with combined RT and chemotherapy were free of disease at five to fifteen years after diagnosis. There was no significant difference in survival between IE and IIE (₉).

It is important to note that the Ann Arbor staging system was used in this study without the addition of Musshof's criteria. Patients with a diagnosis of early stage gastric lymphoma made by endoscopic biopsy should initially undergo surgical resection (₇). Surgical therapy provides local control, which may not be covered by chemotherapy and allows for correction of possible errors in preoperative staging. Adjuvant chemotherapy should be considered even in early-stage disease, given that most failures of surgical therapy are extra-abdominal (₁₀).

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