Emergency presentation of intestinal lymphoma

Ann. Ital. Chir., 2012 83: 405-410

Gianluca Costa, Luca Lepre*, Simone Maria Tierno, Federico Tomassini, Barbara Frezza, Pietro Fransvea, Guido Pascarella, Sandro Mero*, Genoveffa Balducci

Università Roma Sapienza, Facoltà di Medicina e Psicologia
Dipartimento di Chirurgia,Azienda Ospedaliera "Sant'Andrea", Rome, Italy
**Azienda Ospedaliera "San Filippo Neri" Rome, Italy*

Emergency presentation of intestinal lymphoma

PURPOSE: *The aim of the present study was to evaluate the clinical features, management and outcome of patients submitted to emergency surgery because of intestinal lymphoma.*
METHODS: A *consecutive series of fourteen patients with gastrointestinal tract lymphoma referred for emergency surgery between March 2006 and May 2010 was retrospectively analyzed.*
RESULTS: *Patients including 9 males (64.2%) and 5 females (35.7%). The mean age of male and female was 55.4 ± 21.2 and 78.4 ± 9.0 respectively. The difference was statistically significant (p* <0.04*). Ileum was the most common location (13 cases, 86.6%) and a small bowel resection was the commonest surgical procedure performed. Presence of etiological risk factor for developing intestinal lymphoma was detected in 6 patients (40%). The overall morbidity rate was 40.0% (6 patients) and the mortality rate was 53,3% (8 patients). The estimated 12, 24, and 36-months overall survival rate was 56%, 33%, and 22% respectively.*
DISCUSSION: Our *study reports an elevated overall mortality accounting for 8 patients which were all but two of advanced stage; 6 patients died in the postoperative course. Univariate and multivariate analysis failed to show significant differences maybe because the total number of subjects was too small to reach statistical significance. However the Odds Ratio was significantly high for the presence of etiological risk factor (OR 7.50) and perforation as presenting symptom (OR 6.67).*
CONCLUSION: An *aggressive surgical attitude comprising an ample ileum resection is needed in almost all cases because an acute presentation is closely related with an advanced stage of the disease and with a high risk for anastomotic disruption, both conditions leading to a poor short and long-term survival.*

KEY WORDS: Emergency surgery, Intestinal lymphoma, Non-Hodgkin's lymphoma.

Introduction

The extranodal localization of lymphomas is relatively frequent and it arises in the gastrointestinal (GI) tract in 30-45% of the cases. However, the lymphomas are rare GI tumors accounting for only 1-4% of all malignancies. The stomach is the most common affected location (50-60%), followed by small bowel in 20-30% of the cases, and by colon and rectum in only 10-20% [1,2]. The almost unique variety of intestinal lymphoma is non-Hodgkin's lymphoma, whereas the Hodgkin's one occurs sporadically both as primary or secondary manifestation of the disease [1].

The preoperative diagnosis of these rare tumours is difficult because they may present nonspecific complaints such as vague abdominal pain, weight loss, nausea, vomiting, and in some cases palpable abdominal mass. A direct evidence of GI lymphoma is often bowel obstruction or perforation followed by acute abdomen symptoms. The aim of the present study is to evaluate the clinical features, management and outcome of patients submitted to emergency surgery because of intestinal lymphoma.

Pervenuto in Redazione Settembre 2011. Accettato per la pubblicazione Novembre 2011
Correspondence to: Gianluca Costa, MD, c\o Centro Studi sul Trauma, Via P. Galluppi 8, 00136 Rome, Italy (e-mail:gcosta@ospedalesantandrea.it).

Patients and Methods

The clinical records of patients with gastrointestinal tract lymphoma referred for emergency surgery at the Department of Surgery of the Sapienza University "Sant'Andrea" Hospital in Rome, and at the Emergency Surgery and Trauma Care Unit of "S. Filippo Neri" Hospital in Rome between March 2006 and May 2011 were retrospective reviewed. Clinical charts of all patients were analyzed and data were recorded in a computerized database. Variables considered for analysis were sex, age, lymphoma's location and type, symptoms, associated disease, etiological risk factor, surgical procedure, stage, postoperative morbidity and mortality, and long-term outcome. Morbidity and mortality included both minor and major complications or death that occurred during the same hospitalization as a result of primary surgery. The type of lymphoma was classified according to the WHO classification system. Patients were staged according to the Paris staging system and to the Ann-Arbor staging system modified by Musshoff [3-5]. The latter was also used to calculated the International Prognostic Index. Patients not subjected to radical surgical treatment or submitted to limited resection received an adjuvant treatment. The patients discharged were subjected to a regular follow-up for median of 25 months (range 1-60) obtained by clinical outpatient examination, from the general practitioner or by mean of telephone calls. The long-term outcome was classified as good when patient was alive and no symptoms were referred; as poor when recurrence of the disease was evident or if patient died. Statistical analysis was carried out using the 17.0 version of the PASW Statistics Programme (SPSS Italy, Bologna) for MacOsX. The one-way analysis of variance (ANOVA) test, the chi-square test, and the t Student's test were used when appropriate for univariate comparisons. Survival rates were calculated using the Kaplan-Meier method and the generalized Wilcoxon's test was used to assess the differences between survival curves. Multivariate analysis was then performed with the stepwise logistic regression model using poor outcome as dependent variable. The significance level was set at $p < 0.05$.

Results

Fourteen patients were identified over the study period. Patients including 9 males (64.2%) and 5 females (35.7%). Demographics and clinical data of patients are summarized in Table I. One patient with a metachronous localization arising as first appearance in the appendix and after four months in the ileum (Case #8) was twice considered for statistical analysis. The mean age was 63.1 $\pm$ 21.0 years (range 27-88). The mean age of male and female was 55.4 $\pm$ 21.2 and 78.4 $\pm$ 9.0 respectively. The difference was statistically significant ($p < 0.04$). One patient had a synchronous localization (Case #9) as a matter in 86.6.% of cases ileum was the localization of the disease, followed by colon in 13.3%, and appendix in 6.6%. It was proved that the most common associated medical conditions were cardiovascular in 7 patients (46.6%), respiratory in 4 patients (26.6%), and chronic renal failure in 2 patients (13.3%). With regard to possible etiological risk factors 3 patients (20.0%) had a history of a previous non-Hodgkin's lymphoma in complete remission since more than five years and 3 patients (20.0%) were found to be in treatment with immunosuppressive agents, for autoimmune thrombocytopenia, for kidney transplantation, and for mediastinal lymphoma respectively. The most common presenting symptom was obstruction in 8 patients (53.3%). Other onset symptoms were perforation in 5 (33.3%) patients, haemorrhage in 1 patient (6.6%), and acute appendicitis in 1 patient (6.6%).

The surgical treatment was ileal resection in 13 patients (86.6%), Hartmann's procedure in 2 patients (13.3%), and appendectomy in 1 patient (6.6%); the patient with synchronous small and large bowel localization was submitted to Hartmann's procedure combined with ileal resection and cholecystectomy. In all but one patient the final histological examination revealed B-type non-Hodgkin's lymphoma while in the remaining patient the histopathological investigation revealed a recently described particular feature of lymphoproliferative disorder [6,7].

Twelve cases presented with evidence of spread to regional lymph nodes or beyond, with only two confined to the ileum (stage I; 13,3%); four showed involvement of regional lymph nodes (stage IIE1; 26,6%), five showed evidence of infiltration beyond regional lymph nodes (stage IIE2; 33,3%), three had spread to other organs within the abdomen (stage III; 20.0%). According to the Paris staging system 13 cases (86.6%) were T3 and 2 cases (13.3%) were T4.

The overall morbidity rate was 40.0% (6 patients), and the mortality rate was 53.3% (8 patients). Minor complications included infection of respiratory tract (33.3%), of urinary tract (6.6%), and wound infection (20.4%). Major complications included three ileal anastomotic leakage (20.0%), one pulmonary embolism (6.6%) and one severe acute pancreatitis (6.6%). Six patients died in the postoperative course. Four patients died of multiple organ dysfunction syndrome (MODS), two of which followed anastomotic leakage; two patient died on the fourth and on the fifth postoperative day of pulmonary embolism and of septic shock following severe acute pancreatitis respectively. The remaining two patients died at 2 and 3 months of diagnosis. Six of the 15 patients are alive and continued to be on follow-up with no evidence of recurrence. The estimated 12, 24, and 36-months overall survival rate was 56%, 33%, and 22% respectively (Fig. 1).

Univariate and multivariate analysis revealed no significant differences between the good and poor outcome

Table I - *Summary of clinical and demographic characteristics (Legends: MOF, Multi Organ Failure-DM,Diabetes Mellitus-AMI, Acute Myocardial Infarction-COPD, Chronic Obstructive Pulmonary Disease-CHT,Chemotherapy-CT, Computer Tomography).*

Case	Organ	Onset Symptoms	Age	Gender	Treatment	Post-operative outcomes	Follow-up	Complications	Associated Disease	Clinical Features	Type Of Lymphoma	Modified Ann Arbor staging system	Paris staging system
1	Ileum	Bowel obstruction	88	F	Ileal resection	Alive		None	Hypertension, COPD	Previous non Hodgkin lymphoma treated with radiotherapy Lymph Nodes +	Large B-cell Lymphoma	IIE2	T3 N2 M0
2	Ileum	Bowel obstruction	37	M	Ileal resection	Alive		None	None		Non-Hodgkin's B-Cell Lymphoma	I	T3 N0 M0
3	Ileum	Perforation	44	M	Ileal resection	Dead		Bilateral pleural effusion, MOF	Macular degeneration	Suspected multiple liver and retroperitoneal location (CT)	Non-Hodgkin's B-Cell Lymphoma	III	T3 N1 M2
4	Ileum	Bowel obstruction	38	M	Ileal resection		Died 3 months later for second-line therapy failure	Pleural effusion	None		Non-Hodgkin's B-Cell Lymphoma	IIE2	T3 N2 M0
5	Ileum	Bowel obstruction	27	M	Ileal resection +biopsy retroperitoneal swelling	Alive		Pleural effusion and surgical wound infection	None	Retroperitoneal swelling	Non-Hodgkin's B-Cell Lymphoma	IIE1	T3 N1 M0
6	Ileum	Intestinal Bleeding	39	M	Ileal resection	Alive		Surgical wound infection	None	Abdominal great vessels lymphadenopathy (ChT)	Non-Hodgkin's B-Cell Lymphoma	IIE2	T3 N2 M0
7	Ileum	Bowel obstruction	77	M	Ileal resection Appendectomy	Alive		anastomotic dehiscence	Hypertension, diverticulosis	Omentum and appendix location	Non-Hodgkin's B-Cell Lymphoma	I	T4 N0 M0
8	8.1 Appendix 8.2 Ileum	Acute appendicitis Bowel obstruction	81	M	Appendectomy Ileal resection	Dead		anastomotic dehiscence	Hypertension		Pheripheral Non.Hodgkin's T-Cell Lymphoma	I IIE1	T3 N0 M0 T4 N1 M0
9	Colon Ileum	Bowel obstruction	74	F	Hartmann's procedure and ileal resection + cholecystectomy	Alive		None	Hypertension, DM Type II, Alcoholic Cirrhosis		Non-Hodgkin's B-cell Lymphoma	IIE1	T3 N1 M0
10	Colon	Perforation	82	F	Hartmann's procedure	Dead			Autoimmune Thrombocytopenia, Hypertension, COPD, Chronic Atrial Fibrillation, AMI, DM Type II, Renal Failure,Cerebral Emhorrhage	Spleen and Liver metastasis	Mucocutaneus Hodgkin-like EBV+ Lymphoma	III	T3 N1 M2
11	Ileum	Perforation	54	M	Ileal resection	Dead		Severe Acute Pancreatitis	Renal Failure, Renal transplant		Non-Hodgkin's B-Cell Lymphoma	IIE2	T3 N2 M0
12	Ileum	Bowel obstruction	76	M	Ileal resection	Dead (IV post-operative day)		Pulmunary embolism		Previous non Hodgkin lymphoma treated with Chemyotherapy	Large B-cell Lymphoma	IIE2	T3 N2 M0
13	Ileum	Perforation	65	F	Ileal resection		Died 2 months later	Anastomotic dehiscence+Bronchopneumonia Acute renal faliure, septic shock	Hypertension, asthma, diverticulosis, Immunosoppresive neutropenia	Mediastinal B-cell Lymphoma treated with immunotherapy	Non-Hodgkin's B-Cell Lymphoma	III	T3 N3 M2
14	Ileum	Perforation	83	F	Ileal resection	Dead					Large B-cell Lymphoma	IIE1	T3 N1 M0

groups maybe because the total number of subjects was too small to reach statistical significance. However the Odds Ratio was significantly high for the presence of etiological risk factor and perforation as presenting symptom. (Table II).

Discussion

The incidence of gastrointestinal lymphoma is low in comparison to other gastrointestinal malignancies such as carcinoma or stromal tumors (GIST). They are predominantly located in the stomach and more rare in the small and large bowel and they are proved to be non-Hodgkin lymphomas. These malignancies are more frequent in males between the fifth and seventh decades of age, being rare in the youngers [1,2,8,9].

The GI lymphoma frequently presents a growth similar to the anaplastic carcinoma, with localized or diffuse thickening into the intestinal wall and surface ulcers. The macroscopic aspect can be that of an annular lesion, of a simple organ wall thickening, or that of a ulcer growth

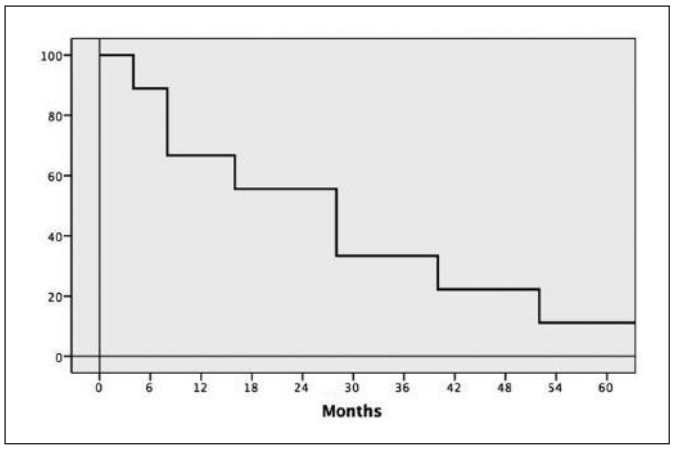

Fig. 1: Overall survival curve.

or of a polypoid growth. The main risk factors reported in the literature [1,2] are all conditions involving chronic alteration of the immune system, such as long-term administration of immunosuppressive agents in strong doses or HIV infection. In patients submitted to organ transplantation, as well as patients suffering from psoriasis and rheumatoid arthritis, the increased risk of lymphoma growth occurred more frequently than in other people. Association between NHL and inflammatory bowel disease (IBD) is still under debate [8,9,12-14].

Although in our series the age of the patients, sex and location of the disease showed a results similar to that reported in the literature [1,2], it could be notice that more than 30% of patients had age under the inferior limit of incidence. As regard to risk factors, three patients received a previous immunosuppressive therapy, while none of the patients had IBD or HIV infection.

Clinical features of intestinal lymphomas are characterized by non specific symptoms such as abdominal pain, nausea, vomiting, weight loss, alteration in bowel habits and palpable abdominal mass as well as in all neoplastic pathologies of the intestinal tract. In the rare cases of diagnosis established preoperatively the therapeutic approach is related to tumor stage. Surgery alone can be considered as an adequate treatment for patients with an early stage of disease while patients with high grade disease or advanced stage may enjoy prolonged survival when treated with adjuvant or neo adjuvant therapy [14-18].

In most of the cases, the lack of specific complaints accounts for the delay in the diagnosis that is only done after emergency surgical treatment because GI lymphomas frequently arise with acute abdominal symptoms due to perforation or, although more rarely, to bowel obstruction or bleeding. In such patients, the surgical resection involved segment, may resolve acute abdomen symptoms but only in rare cases could lead to the lymphoma extirpation. Contrary to the literature, in our series the most common clinical onset of the disease was

TABLE II - *Univariate analysis*

	p value	Odds Ratio (95% CI)
Etiological Risk Factor	0.072	7.500 (0.759-74.157)
Perforation	0.119	6.667 (0.487-91.331)

obstruction and final staging showed that the majority of patients presented an advanced stage as it is usually observed in face of emergency surgery. In all patients diagnosis has been done after surgical treatment and final histological examination which reveals in all cases a non-Hodgkin's lymphoma.

In case of an acute presentation of the disease as well as it is observed in elective surgery, short and long-term prognosis does not only depend on the radicality of the resection or on the tumor stage but it is deeply influenced by postoperative complications often linked to immuno-depressive status. Our study reports an overall mortality rate of 53.3% accounting for 8 patients which were all but two of advanced stage. Among these 6 patients died immediately in the postoperative period, and 2 other patients a few months after surgical treatment. Infection of surgical wound, ileal anastomotic dehiscence followed by pneumonia and acute renal failure are the most frequent complications observed in our study. The notable rate of anastomotic dehiscence could be related to the difficult performance of radical resection according to the microscopically spread of the lymphoma into the intestinal wall and considering a safety margin and the removal of locoregional lymphovascular tissue. Anastomotic healing could be affected also by the patient's immunodepression status.

The long-term prognosis or likelihood of recovery depends on the type of cancer, the overall health of the patient, and whether the cancer has spread to other regions or if it is only a localized disease. The literature [6,19-22] shows a significantly longer overall survival (85% at five years and 65% at ten years) for patients with localized lymphoma (stage IE and IIE) while an overall 5-year survival rate about of 33% for patients with extended disease (stage IIIE and IVE) with a study of Zinzani et al. [23] showing an overall survival rate of such patients less then 20%. According to the literature, in our experience the majority of patients were of advanced disease and survival rate is consistent with that reported by other authors.

Conclusion

GI lymphomas frequently present with acute abdominal symptoms which require emergency surgery. As lymphoma is one of the most frequent causes of emergency surgery for diseases concerning the ileum our recom-

mendation is to consider it and to adapt bowel resection in such a way as to make it as radical as is possible. It means that an aggressive surgical attitude comprising an ample ileum resection is needed in almost all cases because an acute presentation is closely related with an advanced stage of the disease and with a high risk for anastomotic disruption, both conditions leading to a poor short and long-term survival.

Riassunto

I linfomi primitivi gastro-intestinali sono dei tumori rari, rappresentando l'1-4% di tutti i tumori del tratto gastroenterico. Di questi solo il 20-30% sono localizzati all'intestino tenue e il 10-20% al colon e al retto. Il quadro clinico è caratterizzato da una sintomatologia aspecifica rappresentata da dolore addominale scarsamente localizzato, perdita di peso, nausea, vomito e talvolta dalla presenza di una massa addominale palpabile. Più frequentemente tale patologia si manifesta direttamente con una complicanza quale l'occlusione o la perforazione intestinale, con conseguente quadro di addome acuto.
Questo studio è stato effettuato analizzando retrospettivamente 14 pazienti operati in regime di urgenza nel periodo di tempo compreso tra il 1 Marzo 2006 e Gennaio 2010. È stata valutata la sede d'insorgenza e il tipo di linfoma, il sintomo d'esordio e il tipo di intervento chirurgico effettuato. Sono state inoltre valutate le eventuali patologie associate ed i tassi di mortalità e morbilità
L'età media della popolazione è stata di 63, 1 anni (range 27-88) con una prevalenza del sesso maschile (9 pazienti, 64,2%) rispetto a quello femminile (5 pazienti, 35,7%). L'organo più frequentemente interessato dalla malattia è stato l'ileo (13 pazienti, 86,6%), seguito dal colon (2 pazienti 13.3%), ed infine dall'appendice (1 paziente, 6.6%). I quadri clinici d'esordio sono stati l'occlusione intestinale (8 pazienti 53.3), la perforazione (5 pazienti 33.3%) l'emorragia (1 paziente 6.6%) e l'appendicite acuta (1 paziente 6.6%). Tutti i casi osservati sono stati rappresentati da linfomi non-Hodgkin. Le patologie più frequentemente associate sono state quelle cardiovascolari (46,6%), quelle respiratorie (26,6%), l'insufficienza renale (13,3%). Per quanto riguarda i fattori di rischio in 3 pazienti (20%) è stata riscontrata una pregressa storia clinica di linfoma di Hodgkin in completa remissione da più di 3 anni ed in altri 3 (20%) pazienti era in atto un trattamento immunosoppressivo per piastrinopenia autoimmune, trapianto renale e linfoma mediastinico Il trattamento chirurgico in urgenza è stato di resezione ileale (13 pazienti, 86,6%), Hartman (2 paziente, 13.%) ed appendicectomia (1 paziente, 6.6). La morbilità è stata del 40.0% (6 pazienti) e la mortalità è risultata del 53.3% (8 pazienti). Il tasso di sopravvivenza complessivo a 12, 24 e 36 mesi è stato rispettivamente del 56%, 33% e 22%.

I linfomi intestinali sono più frequenti nei pazienti di sesso maschile, con un picco di incidenza tra i 50 e i 70 anni, mentre risultano essere rari nei bambini. I principali fattori di rischio riportati in letteratura sono rappresentati da tutte le condizioni che comportano un'alterazione cronica del sistema immunitario. Tutt'ora oggetto di discussione è l'associazione tra linfomi e malattie infiammatorie croniche intestinali. Nella maggioranza dei casi, la diagnosi viene posta tardivamente a causa della scarsa specificità della sintomatologia e spesso viene formulata solo dopo il riscontro istologico sul pezzo operatorio, in seguito ad un intervento chirurgico eseguito in urgenza per addome acuto
L'analisi della nostra esperienza non ha evidenziato differenze statisticamente significative forse perché il numero dei pazienti era troppo ridotto per raggiungere un significatività statistica. Il rischio relativo (Odds Ratio), tuttavia, è risultato sensibilmente elevato per il fattore presenza di fattori di rischio e per il fattore perforazione intestinale quale sintomo di esordio della malattia. La prognosi immediata e a lungo termine non dipende soltanto dalla radicalità della resezione o dalla stadio del tumore ma è anche profondamente influenzata dalle possibile complicanze post-operatorie spesso correlata ad uno stato di immunospressione.
Considerando che i linfomi sono una delle principali patologie che interessano il piccolo intestino e che portano ad un intervento chirurgico d'urgenza, la nostra raccomandazione è quelle di effettuare una resezione sufficientemente ampia in modo da ottenere la migliore radicalità possibile. Ciò significa che un intervento chirurgico aggressivo si rende necessario nella maggioranza dei casi in quanto una presentazione acuta è strettamente legata ad uno stadio avanzato della patologia associato ad un elevato rischio di deiscenza dell'anastomosi, fattori entrambi responsabili di una ridotta sopravvivenza sia a breve che a lungo termine.

References

1. Ghimire P, Wu GY, Zhu L: *Primary gastrointestinal lymphoma*. World J Gastroenterol, 2011; 17(6):697-707.

2. Stanojevic GZ, Nestorovic MD, Brankovic BR, Stojanovic MP, Jovanovic MM, Radojkovic MD: *Primary colorectal lymphoma: An overview.* World J Gastrointest Oncol, 2011; 15; 3(1):14-18.

3. Ruskoné-Fourmestraux A, Dragosics B, Morgner A, Wotherspoon A, De Jong D: *Paris staging system for primary gastrointestinal lymphomas.* Gut, 2003; 52(6):912-13.

4. Boot H: *Diagnosis and staging in gastrointestinal lymphoma*. Best Pract Res Clin Gastroenterol, 2010; 24(1):3-12.

5. Pileri SA, Agostinelli C, Sabattini E, Bacci F, Sagramoso C, Pileri A Jr, Falini B, Piccaluga PP: *Lymphoma classification: The quiet after the storm*. Semin Diagn Pathol, 2011; 28(2):113-23.

6. Di Napoli A, Giubettini M, Duranti E, Ferrari A, Guglielmi C, Uccini S, Ruco L: *Iatrogenic EBV-positive lymphoproliferative dis-*

order with features of EBV+ mucocutaneus ulcer: Evidence for concomitant TCRÁ/IGH rearrangements in the Hodgkin-like neoplastic cell. Virchows Arch, 2011; 458(5):631-36. Epub 2011.

7. Dojcinov SD, Venkataraman G, Raffeld M, Pittalunga S, Jaffe ES: *EBV positive mucocutaneus ulcer.A Study of 26 Cases Associated with various sources of immunosuppression.* Am J Surg Pathol, 2010; 34(3):405-17.

8. Wong MT, Eu KW: *Primary colorectal lymphomas.* Colorectal Dis, 2006; 8:586-91.

9. Gonzalez QH, Heslin MJ, Davila-Cervantes A, Alvarez-Tostado J, De los monteros AE, Shiore G: *Primary colonic lymphoma*. Am Surg, 2008; 74:214-16.

10. Aithal GP, Mansfield JC: *The risk of lymphoma associated with inflammatory bowel disease and immunosuppressive treatment*. Aliment Pharmacol Ther, 2001; 15:1101-108.

11. Bebb JR, Logan RPH: *Does the use of the immunosuppressive therapy in inflammatory bowel disease increase the risk of developing lymphoma*? Aliment Pharmacol Ther, 2001; 15:1843-849.

12. Kwon JH, Farrel RJ: *The risk of lymphoma in the treatment of inflammatory bowel disease with immunosuppressive agents*. Oncology/Hematology, 2005; 56:169-78.

13. Ramasamy KA, Vignaraja R, Hastings AG, Bessell EM, Snape J: *A case of primary non-Hodgkin's lymphoma of the transverse colon presenting as inflammatory bowel disease*. Eur J Gastroenterol Hepatol, 2002; 14(12):1401-403.

14. Gobbi PG, Ghirardelli ML, Cavalli C, BaldiniL, Broglia C, Clò V, et al.: *The role of surgery in the treatment of gastrointestinal lymphomas other than low grade MALT lymphoma*. Haematologica, 2000; 85:372-80.

15. Dalal L: *Primary multifocal non-Hodgkin Lymphoma of the colon successfully treated with chemotherapy*. Gastrointest Endosc, 2008; 68:1005-06.

16. Feng L, Zhang G, Hu Z, Zou Y, Chen F, Zhang G, Tang L: *Diagnosis and treatment of 81 patients with primary gastrointestinal lymphoma*. Zhong Nan Da Xue Xue Bao Yi Xue Ban, 2009; 34(7):582.

17. Lee J, Kim WS, Kim K, Ko YH, Kim JJ, Kim YO, Chun HK, Lee WY, Park JO, Jung CW, IM YH, Lee MH, Kang WK, Park K: *Intestinal lymphoma: Exploration of the prognostic factors and the optimal treatment*. Leuk Lymphoma, 2004; 45(2):339-44.

18. Samel S, Wagner J, Hofheinz R, Sturm J, Post S: *Malignant intestinal non-Hodgkin's Lymphoma from the surgical point of view*. Onkologie, 2002; 25:268-71.

19. Gou HF, Zang J, Jiang M, Yang Y, Cao D, Chen XC: *Clinical prognostic analysis of 116 patients with primary intestinal non-Hodgkin lymphoma*. Med Oncol, 2010.

20. Koch P, del Valle F, Berdel WE, Willich NA, Reers B, Hiddemann W, Grothaus-Pinke B, Reinartz G, Brockmann J, Temmesfeld A, Schmitz R, Rübe C, Probst A, Jaenke G, Bodenstein H, Junker A, Pott C, Schultze J, Heinecke A, Parwaresch R, Tiemann M; German Multicenter Study Group Primary gastrointestinal non-Hodgkin's lymphoma: *I. Anatomic and histologic distribution, clinical features, and survival data of 371 patients registered in the German Multicenter Study GIT NHL 01/92*. J Clin Oncol, 2001; 19(18):3861-873.

21. O'Boyle CJ, Kerin MJ, Feeley K, Given HF*: Primary small intestinal tumours: Increased incidence of lymphoma and improved survival*. Ann R Coll Surg Engl, 1998; 80:332-34.

22. Wang T, Gui W, Shen Q: *Primary gastrointestinal non-Hodgkin's lymphoma: Clinicopathological and prognostic analysis*. Med Oncol, 2010; 27(3):661-6. Epub 2009.

23. Zinzani PL, Magagnoli M, Pagliani G, Bendani M, Gherlinzoni F, Merla E, Salvucci M, Tura S: *Primary intestinal lymphoma: Clinical and therapeutic features of 32 patients.* Haematologica, 1997; 82:305-08.

24. Ara C, Coban S, Kayaalp C, Yilmaz S, Kirimlioglu V: *Spontaneous intestinal perforation due to Non-Hodgkin's lymphoma*. Dig Dis Sci, 2007; 52(8):1752-756.

25. Allen AW, Donaldson G, Sniffen RC, Goodale F: *Primary malignant lymphoma of the gastrointestinal tract*. Ann Surg, 1954; 3(140):428-37.

26. Bairey O, Ruchlemer R, Shpilber O: *Non-Hodgkin lymphoma of the colon*. Haematology, 2006; 8:832-35.

27. Daum S, Ullrich R, Heise W, Dederke B, Foss HD, Stein H, Thiel E, Zeitz M, Riecken EO: *Intestinal non-Hodgkin's lymphoma: a multicenter prospective clinical study from the German Study Group on Intestinal non-Hodgkin's Lymphoma*. J Clin Oncol, 2003; 21(14):2740-746.

28. Dughayli MS, Baidoun F, Lupovitch A: *Synchronous perforation of non-Hodgkin's lymphoma of the small intestine and colon: A case report*. J Med Case Reports, 2011; 5(1):57.

29. Turan M, Karadayi K, Duman M, Ozer H, Arici S, Yildirir C, Koçak O, Sen M: *Small bowel tumors in emergency surgery*. Ulus Travma Acil Cerrahi Derg, 2010; 16(4):327-33.

30. Zemsky L, Katz H, Edelman M, Makower D: *Hodgkin's Disease involving large bowel*. Clin Colorectal Canc, 2001; 3(1):185-86.