Abstract

Lymphoid neoplasms are a heterogeneous group of hematological malignant diseases through clinical presentation, histology, evolution and prognosis, that require a large panel of clinical and laboratory investigations for the certainty of the diagnosis.

Objectives: Highlighting the place of laparatomy in diagnosing patients with suspected malignant lymphoma in which previous investigations have not elucidated the diagnosis.

Material and methods: We analyzed retrospectively patients with suspected malignant lymphoma that were sent to surgery for diagnostic laparatomy during January 2000–January 2010.

Results: There were 46 patients included in the study, 29 presenting abdominal tumor mass with retroperitoneal, pelvic or small intestine localization and mesenteric lymph nodes (18, 6, and 5, respectively). In all 29 patients with abdominal tumor mass a histological diagnosis was obtained from the sample taken during laparotomy. There were 23 cases of non-Hodgkin lymphoma and 6 cases of other malignancies. From 17 patients without abdominal tumoral mass only 5 were found having intra-abdominal malignancies: 3 cases had malignant lymphoma, 2 cases – undifferentiated carcinoma. A positive alternative diagnosis was developed in 9 patients from the 17 patients without abdominal tumor mass, and 3 patients remained undiagnosed after laparatomy.

Conclusions: The results of our study show that laparatomy performed for diagnosing patients with malignant lymphoma is useful in patients with abdominal tumor mass, while in patients without abdominal tumor mass there is a possibility for the diagnostic laparatomy to be negative or to highlight a non-malignant malignancy that can be diagnosed using other types of investigations.

Keywords: diagnostic laparatomy, histologic diagnosis, malignant lymphomas

Introduction

Malignant lymphomas and the non-Hodgkin lymphoma (NHL), especially, are a heterogeneous group of disorders with a wide variability in clinical...
manifestations, evolution and response to treatment. The correct histological diagnosis, completed with the immunohistochemical is essential because infectious diseases such as: infectious monocucleosis, toxoplasmosis or cytomegalovirus infection, may present a similar clinical picture with: fever, multiple peripheral lymph node involvement, presence of atypical lymphocytes in peripheral blood and/or in bone marrow. Also, some neoplasms or non-neoplastic diseases as “cat scratch” disease, tuberculosis, sarcoidosis or some autoimmune diseases may pose problems of differential diagnosis [1].

Usually, the diagnosis is established by biopsy of a peripheral lymph node or a mediastinal or extranodal location. For the patients with suspected lymphoma that have unavailable biopsy material, particularly for those presenting with primary abdominal injury that may include gastrointestinal tract, retroperitoneal lymph nodes, mesenteric lymph nodes or spleen, an elective diagnostic laparatomy is needed [1,2,3].

**Purpose**

Highlighting the role of laparatomy in diagnosing patients with suspected malignant lymphoma, in whom previous investigations did not elucidate the diagnosis.

**Materials and methods**

We analyzed retrospectively a total of 46 patients with suspected malignant lymphoma, addressed to surgery for diagnostic laparatomy between January 2000 – January 2010 to the Surgery Departments of the Municipal Emergency Hospital in Timișoara and the Department of General Surgery of the Emergency County Hospital „Dr. Constantin Opriș” in Baia Mare.

The study batch included 27 males and 19 females (Figure 1).

The median age of the patients who underwent laparatomy for diagnostic purposes was 46 years (17-72 year range) (Figure 2).

Of the 46 patients studied, 29 had palpable abdominal mass, other than liver or spleen, and 17 patients were without abdominal tumor mass.

All patients were addressed to surgery for laparotomy were previously investigated, without having the test results sustaining a diagnosis certainty.[4,5] Generaly, depending on the type of the disease, there were performed [6]:

**Laboratory tests:** Erythrocyte sedimentation rate; Serum lactate dehydrogenase; C-reactive protein; \( \beta_2 \) – microglobulin; ceruloplasmina; alkaline and acid serum phosphatase; liver function tests; renal function tests; Rheumatoid factor; Antinuclear factor; Coombs test; blood cultures; Serology for HIV, hepatitis and other infections.

**Hematological:** Complete blood counts; Aspirates of bone marrow (including flowcytometry examination); Bone marrow biopsy (including immunohistochemistry)

**Radiology:** Chest Radiology; chest/abdomen/pelvis computed tomography (CT); Gastroscopy/colonoscopy/barium passage; Magnetic resonance imaging (MRI).

**Procedures:** liver biopsy; node biopsy; Mantoux reaction; Kveim test.

From previous investigations, before surgery admission, the imaging tests prevailed, all patients being previously investigated in this matter to determine the nature and extent of abdominal tumors and possible, hepatic or splenic determination. Abdominal and pelvic CT were performed, at least one abdominal ultrasound, and in 6 cases the investigation was continued with a MRI. From the 29 patients with abdominal tumor mass that had CT, 18 patients presented a retroperitoneal tumor mass, 6 patients – with pelvic tumor, and 5 patients – with tumor in the
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small intestine associated with mesenteric lymph node involvement (Figure 3). Patients that presented retroperitoneal tumor mass were investigated using extra imaging investigation to determine the extension and nature of the palpable tumor mass, the possible liver and spleen infiltration (CT, MRI, liver-spleen scintigraphy).

Also, all 46 patients had a bone marrow aspirate and biopsy performed before surgery, 27 patients being transfered from the Hematology Department of the Emergency Municipal Hospital from Timisoara were they had been diagnosed with suspected malignant lymphoma with primary abdominal damage. These investigations could not result in an hematologic or histologic diagnosis.

Nine patients had a percutaneous liver biopsy and three had a node biopsy. None of these explorations could confirm a histologic diagnosis.

A number of 17 patients presented clinical symptoms suggesting a malignant lymphoma with abdominal localization, but no abdominal tumor mass: 8 had splenomegaly, 2 had hepatomegaly, 3 hepatop-splenomegaly and 4 presented a normal abdominal examination, other than the previously presented (Figure 4).

Of the eight patients with splenomegaly, 3 presented with sensitivity and left upper quadrant abdominal pain. The latter were found during surgery with idiopathic splenic vein thrombosis (2 cases), and splenic cyst (one case). Six presented with symptoms of a systemic disease in which splenomegaly was one of the symptoms. Clinical symptoms in the remaining group are presented in Table I.

These patients were further investigated according to their mode of clinical presentation: bone marrow biopsy (5 patients) with nonspecific abnormalities and node biopsy (one patient) with lymphoid hyperplasia. One patient was treated, preoperatively, with a combination of chemotherapy due to rapidly progressive pulmonary infiltration.
From highlighting the abdominal determinations to surgery the median duration was 8.6 months (1-23 months range).

**Surgical protocol**

The approach was through a median xifo-cord incision. The muscle-aponeurotic plane was incised, and then entered the peritoneal cavity and the peritoneal cavity was fully explored. Partial or full ablation of the tumor formations was practiced, hepatic and lymph node biopsies depending on their presence (from the splenic, celiac, periportal, mesenteric, para-aortic, and iliac hilum) underwent biopsy of such lymph nodes and tumors on the small intestine that presented abnormalities during CT. In 15 patients classic splenectomy was performed as well. The spleen was first mobilized by spleno-renal ligament section and splenic artery, and then tied off behind the ligament 2-3 cm proximal to the hil. Once it was a safe situation, splenectomy was done in the routine manner by ligation and dissection of short gastric vessels, ligation and division of their twigs artery and splenic vein in the hil. A single drain was left in the splenic bed. Intraoperative, accessory spleens were searched and meticulous attention was paid to hemostasis and splenosis phenomenon. There was also installed a nose-gastric tube to prevent gastric ileus. For 31 patients the spleen was preserved. All patients had pieces sampled during surgery that were sent to histo-pathologic exam.

**Statistic method**

All data was in placed in Microsoft Access (Redmond WA) data base.

For the specific analysis of statistic bounds we used: weighted arithmetic mean of all items analyzed; calculation of average age per gender, subgroups defined by analyzed items; calculation of ponders (percentages) for all items analyzed; coefficient of rank correlation which takes values in closed periods (-1 and +1), the closer the coefficient value is to +1 or -1, the stronger the correlation is, in that direction (+) or the opposite (-1), the closer the coefficient value is to 0, the weaker the correlation is; calculation of survival parameters (by sex, age, biological parameters).

These methods were used because:
- they have a high grade of comparison – using data from the same source and at the same time for all patients;
- time stability of determination methods for the biological parameter;
- power of discrimination for rejection and containing features;
- data accessibility – their use in transversal and longitudinal analysis.

**Results**

A positive histologic diagnosis was obtained from the resulting material during laparatomy in all 29 patients.
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who had abdominal tumor mass. There were 20 cases of NHL and six cases of other malignancies and three cases of retroperitoneal fibrosis (Table II and Fig. 5).

Of 17 patients without palpable abdominal mass, only 5 were found with intra-abdominal malignancies: lymphoma – 3 cases, and undifferentiated carcinoma – 2 cases. There was a case of tuberculosis and one case of chronic active hepatitis, and in each of these patients the preoperative percutaneous liver biopsy was nonspecific. Laparatomy could not be followed by a histological diagnosis in 7 patients: four received preoperative chemotherapy and corticosteroids and had no histological evidence of residual malignant disease, two were considered to have atypical autoimmune disease, one had an atypical variant of juvenile chronic polyarthritis, and three remained undiagnosed, but with spontaneous regression of symptoms and signs (Figure 6).
Postoperative complications

Pulmonary complications were the most common morbidities. They occurred in 4 patients within 30 days after surgery and in 2 patients as a late complication. Pulmonary complications included atelectasis, pneumonia, bronchitis and pleural effusion [8].

Infectious complications were the second most common, frequent morbidity, 3 patients had early septic complications and 2 patients had late septic complications. Septic complications included central venous line sepsis, bacteriemia and urinary tract infections.

Pancratic damage was reported in one case, bleeding occurred in one case and one case also with prolonged ileus.

There were two deaths, one early after surgery by sepsis and one late (over 30 days after surgery with disease progression (carcinoma).

Discussion

The place of laparatomy in the initial diagnosis of malignant lymphomas was investigated by analyzing a group of 46 patients with suspected malignant lymphoma, addressed for diagnostic laparatomy. Intra-abdominal malignant tumor was found in 34 patients and 26 of them had malignant lymphoma. A positive alternative diagnosis has been developed in 9 patients of the 17 patients without abdominal mass, six patients remaining undiagnosed after laparatomy.

From the results of this study emerges the recommendation to investigate patients with suspected malignant lymphoma through laparatomy. Patients with abdominal tumor mass other than liver or spleen should undergo early laparatomy, unlike those without abdominal tumor mass, which should be pursued through an extensive screening program in which diagnostic laparatomy is used only as a final procedure.

From our study results that patients who were addressed to surgery for laparatomy as a diagnosis for malignant lymphomas belong to two categories: patients with a abdominal tumor mass, in which diagnostic laparatomy has an important purpose, and those without intra-abdominal tumor mass, which shows a significant risk that diagnostic laparatomy could be negative or show a nonmalignant disease that could be diagnosed using other techniques.

Patients with abdominal mass, other than liver or spleen should undergo early diagnostic laparatomy. Multiple radiological investigations are not necessary, they could rarely influence the decision to perform a laparatomy and frequently delaying the histological diagnosis and treatment. They have a particular value in the disease course monitoring during treatment [5,9].

Patients with primitive gastrointestinal lymphoma will require endoscopic evaluation of the gastrointestinal tract, imaging of the liver and spleen; they are not always necessary preoperatively but they are useful for staging lymphoma. Sometimes liver biopsy and multiple bone marrow biopsies are best performed during laparatomy. Also, abdominal and pelvic CT or bipedal limbography surgery can be performed after surgery as a basis to monitor the response of lymph nodes to treatment.

Extemporaneous examinations (sections on ice) should be performed during operation before attempting retroperitoneal tumor resection, and incision biopsy alone may be sufficient if a malignant lymphoma is diagnosed.

Patients without abdominal mass should follow an extensive program of investigation adapted to the presentation, in order to decrease the incidence of negative laparatomies. Patients with splenomegaly require hematological and serological investigations, while patients with heptomegaly should perform multiple liver biopsies for histological examination, in addition to screening for autoimmune diseases, infections or other malignancies [9,10].

In patients with generalized disease a complex program of investigations for diagnosis and differential diagnosis has to be performed. For these patients, laparatomy is used as a final diagnostic step after exhausting other diagnostic exploration.

During laparatomy biopsies are executed from any organ or abnormal tissue, i.e. liver biopsy, multiple biopsies of lymph nodes and possible biopsy of abdominal muscles to allow the diagnosis of lymphoma, granulomatous disease or arteritis. If the spleen is normal and there is no other evidence of intraabdominal lymphoma, splenectomy is not necessary, because it probably doesn't influence the diagnosis.

Antibiotics and corticosteroids treatments should be performed only after laparatomy preferable because they can hide a definitive diagnosis and preoperative chemotherapy may also lead to a wrong diagnosis.

Traditionally, laparatomy was the only effective method for staging and diagnosis of these lymphomas [1,2]. Since the 1980s, with the development of diagnostic imaging techniques, CT and directed percutaneous biopsy (BPD) using CT and the recognition of morbidity associated with laparatomy other procedures of diagnosis than laparatomy became
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known [11]. Often, directed percutaneous biopsy can not provide adequate architectural informations because of limited tissue sampling [12]. In the 1990s laparoscopic diagnostic methods have been used to obtain tissue samples from the abdominal lymph nodes and abdominal extended masses [12,13,14].

The role of surgery in the diagnosis of malignant lymphoma is limited to tumor tissues diagnosis and occasionally in determining the stage of the tumor before treatment. When lymphadenopathy is confined to the abdomen, the diagnostic options are percutaneous biopsy directed through CT, surgical incisional or excisional biopsy or laparoscopic biopsy. Because of increased morbidity associated with laparatomy, or delay in diagnosis because of inadequate percutaneous biopsy material, laparoscopic lymph node biopsy was used increasingly for suspected intra-abdominal lymphoma [11,13,14].

The percutaneous CT-guided biopsy of retroperitoneal adenopathy is a reliable and accurate means of obtaining tissue for lymphoma diagnosis. Despite the availability and overall accuracy of percutaneous biopsies, some patients will require a bioptical surgical procedure to complete the diagnosis of lymphoma. Harvested tissue should be available for histological and immunohistochemical analysis [16].

Laparoscopic approaches have an important role when guided percutaneous biopsy fail to provide a definitive diagnosis. The proximity of large blood vessels, duodenum, or pancreas can lead to inadequate laparoscopic biopsy specimen, particularly in the para-aortic region. Para-aortic adenopathy is not a contraindication for laparoscopic biopsy. A better sampling of tissue samples and a higher laparoscopic experience with a more complete mobilization of the colon, duodenum, and pancreas should reduce the prevalence of false-negative results in these regions.

If laparotomy and laparoscopic lymph node biopsy is negative there are indicated: close clinical follow-up and abdominal and pelvic CT not to delay diagnosis. Laparoscopy with diagnostic purpose presents advantages such as: reduced postoperative pain, early resumption of activity, shorter recovery time, fewer postoperative complications and possibly earlier administration of definitive systemic therapy [17].

Laparoscopy is a reliable method to obtain adequate tissue from patients with suspected intra-abdominal lymphoma. Lately, this minimally invasive procedure is an optimum method for diagnosing lymphoma when directed percutaneous puncture had not success in establishing a definitive diagnosis of lymphoma.

Conclusions

Patients with palpable abdominal mass other than liver or spleen should undergo early diagnostic laparotomy.

For patients with retroperitoneal tumor mass urography and abdominal CT is recommended, the MRI having a particular value in monitoring disease response to treatment.

Extemporaneous examinations (sections on ice) should be performed during operation before attempting retroperitoneal tumor resection, if a malignant lymphoma is diagnosed, biopsy incision alone being sometimes sufficient for diagnosis.

Patients that don't present abdominal mass should follow an extensive program of investigation near the presentation of the disease, in order to reduce the incidence of negative laparatomies.

Any organ or abnormal tissue biopsies are executed during laparotomy, even multiple liver biopsies to allow positive and differential diagnosis.

References