Splenectomy for isolated splenomegaly; experience with twelve patients

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Summary:

Background: Changes in the indication for splenectomy in hematology, especially in hematological malignancies, has been observed in the last 10 – 15 years. Yet splenectomy, as a diagnostic tool, is still an option in the management of isolated splenomegaly.

Objectives: to describe the outcome of diagnostic splenectomy in the management of 12 patients presenting with isolated splenomegaly.

Patients and methods: Between August 2005 and July2012, Twelve patients underwent splenectomy for diagnostic purposes in the hematology unit / Baghdad Teaching Hospital. Analysis of these patients was done with a median follow up of 16 months (6 months -4 years).

Results: The median age was 46 years (range 25-68). The median duration of symptoms was 6.8 months (range 3-12) months. The median duration of follow up was 16 months. We had 8 females, and 4 males. Three patients were asymptomatic, but they had progressive enlargement of spleen over one month. The most common symptoms were malaise and abdominal pain, seen in 8 patients. The other less frequent symptoms were fever (5 patients), weight loss (5 patients), arthralgia (4 patients), while the bleeding manifestation was seen in one patient only. Anemia was seen in 5 patients, two had leucopenia, and two had thrombocytopenia. Focal lesions in the spleen were seen in two patients by ultrasound and CT scan. The results of bone marrow aspirate and biopsy, upper gastrointestinal endoscopy and serological tests for collagen vascular diseases all were unrevealing prior to splenectomy. The histopathological results were; Hodgkin disease(1 patient), intermediate grade Non-Hodgkin lymphoma(1 patient) , splenic marginal zone NHL(2 patients),Diffuse Large B Cell Lymphoma(1 patient), Gaucher's disease(1 patient), favor myeloproliferative disorders(1 patients), one patient had tuberculosis, while 4 patients ended with non-diagnostic results. Laproscopic splenectomy was done in one patient only. Postoperative complications were seen in 4 patients which were grade 1-2 bleeding and simple wound infection. During follow up one patient with undiagnostic reports proved to have collagen vascular disease & two patients developed lymphoma, and the last one developed features of myeloproliferative disorder.

Conclusion: splenectomy for isolated splenomegaly has a significant impact on the management of a significant proportion of those 12 patients. Other investigations which help in the diagnosis of collagen vascular diseases, myeloproliferative disorders& lymphoproliferative disorders are needed before proceeding for splenectomy.

Keywords: isolated splenomegaly, splenectomy, splenic lymphoma.

Introduction:

The patient with splenomegaly can present a diagnostic challenge. The list of conditions associated with splenomegaly is extensive. A patient presenting with splenomegaly may have a collection of signs, symptoms and test results that are common to various diseases, some are benign and self-limiting, some are due to infections and others are malignant. The list of initial investigations is long, and some are common to all patients, and others are done depending on the clinical picture. After this step, the diagnosis may be settled, or this step will just directs us to the second line of investigations, as an example JACK2 V617F mutation will establish the diagnosis of myeloproliferative disorder when the blood film is suggestive. The list of second line investigations is variable, but it may include bone marrow examination, immunophyenotyping, lymph node biopsy, and liver biopsy when the liver function is abnormal [1].

If the underlying cause behind splenomegaly remains unrecognized then this clinical situation is referred to as isolated splenomegaly [2]. The incidence of such clinical scenario even with the recent advances in investigations is around 7% to 15% of patients evaluated for splenomegaly or hypersplenism [3]. The underlying etiology behind this condition is variable, and the percentage of malignancy among such patients after splenectomy varied from 0% to 80% [4,5]. This wide range made the next recommended step in the management

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varied from wait and see approach, splenic biopsy, and splenectomy [2].
The purpose of this study was to describe the outcome of twelve patients subjected to diagnostic Splenectomy.

Patients and methods:
Between August 2005 and July 2012, twelve patients admitted to the Hematology Unit at Baghdad Teaching Hospital- Medical City. They were labeled as having isolated splenomegaly after a diagnostic work up which included complete blood picture, bone marrow aspiration and biopsy, liver function tests, virology screen for HBsAg, anti-HCV Ab, anti-HIV Ab (all done by ELISA method), a chest X-ray, abdominal Doppler ultrasound study, upper gastrointestinal endoscopy (to rule out portal hypertension) and abdominal computerized tomography.
Hypersplenism was defined as the presence of at least two cytopenias along with a normal or a hypercellular marrow. Leucopenia was defined as total white blood cell count less than 4000 / mm^3, thrombocytopenia was defined as platelet count less than 150,000 / mm^3, and anemia is considered if hemoglobin was less than 10 g/dl. Reversal of hypersplenism was defined as normalization of all three cytopenias within one month of Splenectomy [6]. All patients received pneumococcal vaccine at least 2 weeks prior to surgery. Splenectomy was carried out using a midline or left sub costal incision. One patient had his spleen removed using laparoscopic approach.

Results:

Table (1) The main presenting symptoms:

Main presenting symptoms	**Number of patients**
Asymptomatic but progressive splenomegaly	**3**
Malaise and abdominal pain	**9**
Marked weight loss*	**6**
Arthralgia	**3**
Bleeding tendency	**1**
Dizziness	**1**
Sicca syndrome	**1**
Fever & Night sweat	**1**

*Defined as loss of more than 10%of body weight over 6 months.

Table (2) The blood count abnormalities:

Laboratory abnormality	Number of patients
Anemia (Hb <10 g/dl)	5
Thrombocytopenia (PLT <150 X 10^9/l)	2
Leucopenia (WBC <4 X 10^9/l)	3
Hypersplenism (>1 cytopenia)	2

Table (3) The main histopathological findings of the removed spleen

No.	Diagnosis	Age	Gender	Duration of symptoms (months)	Follow up duration post Splenectomy (months)
1.	Gaucher's disease	50	Female	12	48
2.	Congestive splenomegaly	68	Female	8	12
3.	Essential thrombocythemia	35	Male	3	36
4.	Hodgkin's lymphoma	32	Female	3	12
5.	Marginal zone lymphoma	50	Male	8	6
6.	Marginal zone lymphoma	65	Female	9	12
7.	Non-Hodgkin's lymphoma, Intermediate grade	30	Female	4	10
8.	Unrevealing histopathology	45	Female	6	12
9.	Unrevealing histopathology	50	Female	8	9
10.	Unrevealing histopathology	46	Female	9	12
11.	Unrevealing histopathology	40	Male	6	6
12.	Tuberculosis	25	Male	12	2

The median age was 46 years (range 25-68). The median duration of symptoms was 6.8 months (range 3-12). The median duration of follow up was 16 months (range 2-48). Table (1) shows the main presenting symptoms. Three patients (25%) were asymptomatic but had progressive splenomegaly over one month that was discovered accidentally. The most common symptoms were malaise & abdominal pain seen in eight (67%) patients. The other less frequent symptoms were fever seen in five (42%) patients, weight loss in five (42%) patients, arthralgia in four (33%) patients, while bleeding manifestations were seen in only one (8%) patient. Table (2) shows the incidence of abnormal blood counts. Anemia was seen in five (42%) patients, thrombocytopenia in two (17%) patients, leucopenia in two (17%) patients and hypersplenism in two (17%) patients. Focal lesions in the spleen by abdominal ultrasound were reported in two (17%) patients. The results of bone marrow aspiration and biopsy were unrevealing as well as upper gastrointestinal endoscopies and serological tests for collagen vascular disease. Table (3) shows the outcome of those 12 patients. The histopathological results were: Hodgkin's lymphoma 1 patient,

intermediate grade non-Hodgkin's lymphoma 1 patient, splenic marginal zone non-Hodgkin's lymphoma 2 patients, Gaucher's disease 1 patient, and in favor of essential thrombocytosis 1 patient. The last patient with positive result of the splenic examination was proved to have tuberculosis, where there was granuloma and the PCR was positive for Acid Fast Bacilli. One patient had congestive splenomegaly. Postoperative complications were seen in four (33%) patients mainly grade 1-2 bleeding and simple wound infection. Four (33%) patients remained undiagnosed after splenectomy.

After a follow up period of 6-12 months for the four patients with unrevealing histopathology following splenectomy, one patient (number 8) started to complain from Sicca syndrome and arthralgia, abnormal lymphocytes in the peripheral blood and a flowcytometry study had revealed T-Cell Non-Hodgkin's Lymphoma (low grade). The other female (number 9) with unrevealing histopathology was a 50 years old female presented with huge splenomegaly. Six months after splenectomy, she was presented with cerebrovascular accident without a cardiovascular risk factor; a diagnosis of vasculitis was made. The third patient (number 10) with non-diagnostic histopathology was 46 years old female with thrombocytosis; her JAK2 study was negative as well as her test for Philadelphia chromosome. Six months later, she developed cervical lymphadenopathy and lymph node biopsy revealed myeloproliferative disorder. Another female patient (number 11) is a 40 years old with significant B symptoms. Her splenic histopathology showed vascular malformation. She developed generalized lymphadenopathy about six months post splenectomy and her lymph node biopsy had revealed high grade B-Cell Non-Hodgkin's lymphoma.

The improvements in the cytopenias were seen in all the patients after a variable time, but no patient needed supportive transfusion after the surgery.

Discussion:

The main aim of this study was to describe the role of splenectomy in the management of patients who had presented with isolated splenomegaly. Lymphoma that presents with splenomegaly without peripheral lymphadenopathy occurs in less than 1% of cases [7], but the incidence of lymphoma in such presentation is high as reported by several centers that treat hematological malignancies, and they recommend splenectomy in isolated splenomegaly, for diagnosis and treatment [7, 8, 4]. This study showed that 67 % of our patients had a hematological disorder as a cause of their splenomegaly (various types of lymphomas and other hematological disorders). This finding goes with the reported experience with splenectomy carried out for idiopathic splenomegaly that showed an incidence of malignancy ranging from 39%-80% in the pathological specimen [4, 5]. This high incidence of lymphoma in such presentation, with the positive impact on the overall management of patients, where splenectomy had corrected the different degrees of cytopenias, these two factors seem to make the argument against splenectomy weak. Anna et al reviewed the approach to isolated splenomegaly in 2009 [9] and they noticed that while there is a significant rate of identifying lymphoma at diagnostic splenectomy, many patients presenting with isolated splenomegaly will not have malignancy, and they recommend to adopt wait and see policy in young patients, who are asymptomatic, no significant cytopenia, mild splenomegaly, and their disease is of short duration. If there is progressive splenic enlargement, new symptoms, or progressive blood abnormalities then reassessment should be done [2]. In this study, all patients either they were symptomatic, or they had progressive disease which justified splenectomy.

Anna et al. in their review of the management of splenomegaly had discussed thoroughly the ideal interventional steps and whether to consider splenic biopsy rather than splenectomy. They had described two methods of splenic biopsy; fine needle aspiration, and splenic core biopsy. Although they concluded that both methods represent safe options for undiagnosed patients with isolated splenomegaly, and potentially avoiding diagnostic splenectomy, but on reviewing the studies that evaluate the safety and productivity of these tools, there were significant limitations and false negative results. [2] The recent addition of immunophenotyping (by flowcytometry, and immunohistochemistry) has made positive impact on the yield of the both methods of splenic biopsy, although still there is a considerable debate in this area [2]. The limited availability of the new facilities in the diagnosis has made the splenectomy a reasonable option in our hospital. [10, 11]

Two of our patients had focal hypoechoic lesions in the spleen on preoperative imaging studies. In a study including forty one patients with isolated splenomegaly, Pottakat et al found that 39% of their patients had focal lesions in the spleen, and that 31% of them had only hemorrhage and necrosis as a result of the venous congestion and repeated ischemia and infarction in the grossly enlarged spleen [6]. Although malignant splenic lesions are hypoechoic on ultrasonography in 97% of the cases, infarcts can also produce a similar picture [12]. Computed tomography findings alone are not helpful in the differentiation of different low attenuation lesions [13], so overemphasis on the presence and nature of splenic lesions seen on abdominal imaging for therapeutic decisions may be misleading in significant proportion of patients presenting with undiagnosed splenomegaly.

Although Gaucher's disease can be diagnosed easily by bone marrow studies, all suspected diagnoses are confirmed by the determination of the acid B-glucosidase activity in the isolated leucocytes or

cultured fibroblast. A study reported a case that was presented with isolated splenomegaly with focal mass and hypersplenism, the diagnosis was made by splenectomy which may also have a role in relieving hypersplenism in this disease. [8]

A major operative complication was bleeding that occurred in 33% of the cohort. It was slightly higher than that reported by others. Various series have quoted 14-48% incidence of postoperative complications and 2-5% mortality after elective splenectomy [14,15]. The significant proportion of patients with cytopenias and the resultant immunosuppression may be a possible explanation for the higher incidence of hemorrhagic and infectious complications after splenectomy.

One patient had been subjected to laparoscopic splenectomy. Progress in surgery has made it possible to perform splenectomy under video laparoscopic control with equal results to that of classic open splenectomy. Therefore this approach is likely to be the procedure of choice especially when the spleen is small. Furthermore, recent articles had explored the role of hand assisted laparoscopic splenectomy even when the spleen is large. [16]

The diagnosis of two patients with myeloproliferative disease after splenectomy seems odd. However, in both symptomatic patients, the blood films were not suggestive of this diagnosis, as well as there was no opportunity for JAK2 mutation testing.

Conclusion:

Splenectomy in isolated splenomegaly has a significant impact on the management of a significant proportion of those 12 patients. Other investigations which help in the diagnosis of lymphoproliferative disorders, collagen vascular diseases and myeloproliferative disorders are needed before proceeding for splenectomy.

Author contribution:

The concept of the study was contributed by Dr. Mohammed Saleem who also prepared the critical revision. The study design and the acquisition of data analysis were done by Dr. Ahmed Al Safar, while Dr. Mazin Abbas arranged the data interpretation and drafting of the manuscript.

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