CASE SERIES

Splenectomy for diagnosis of lymphomas: A case series

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Abstract

Splenomegaly can be caused by various etiologies such as infections, congestion/ portal hypertension, auto-immune diseases, infiltrative diseases and malignancy. It requires extensive work-up of hematological, radiological and sometimes bone marrow studies to arrive at definitive diagnosis. However, in 3-36% of cases, cause of splenomegaly remains unknown despite extensive work up; among which lymphomas (16-44%) are an important cause. Hence splenectomy and pathological examination of the spleen might be the only option in this sub-set of patients to confirm the diagnosis. Here is a series of four cases of splenomegaly of unknown etiology presented to us over a period of 3 years who underwent laparoscopic splenectomy for diagnostic purpose. All these cases were diagnosed as Non-Hodgkin's lymphoma. Thrombocytopenia, anaemia and symptoms due to mass effect that these patients had prior to surgery were reversed. All patients were started on chemotherapy with-in 4 weeks of surgery.

Keywords: Splenomegaly, lymphomas, splenomegaly of unknown etiology, Non-Hodgkin's lymphoma, primary splenic lymphomas

Introduction

Splenomegaly is an important clinical finding that often brings the physician's attention to an underlying disorder. A diagnosis can be obtained by hematological, radiological, and sometimes bone marrow studies. However, in 3-36% of cases, cause of splenomegaly remains unknown despite an extensive work up [1]. The diagnosis in these patients can be obtained with splenectomy and histopathological examination of the spleen. The role of splenectomy as a diagnostic test in splenomegaly of unknown etiology is not yet well established. Cause for concern in these patients is due to the possibility of lymphomas (16-44%) [1-4].

Lymphomas are systemic diseases with life threatening implications, establishing a definitive diagnosis is very important. Fine Needle Aspiration Cytology (FNAC) is not a viable option considering the need for immuno-histochemical studies, risk of bleeding and false negative results [3]. Core biopsy is also not performed considering the high vascularity of the spleen [3].

Hence splenectomy is the only option left for establishing definitive diagnosis in a subset of population where diagnosis is not confirmed despite an extensive work-up. Currently splenectomy in hematological disorders is usually restricted to Immune Thrombocytopenic Purpura (ITP) and autoimmune hemolytic purpura refractory to medical management. However, in a subset of population with splenomegaly of unknown etiology splenectomy as a diagnostic modality maybe indicated. Here we present a series of 4 cases with splenomegaly of unknown

cause where splenectomy was done with a diagnostic intent and turned out to be lymphoma.

Case-1

Fifty-seven-year-old male patient came with complaints of generalized weakness and abdominal discomfort for past 3 months. He had history of weight loss and loss of appetite. Clinical examination revealed pallor and massive splenomegaly. He was evaluated with hematological, biochemical investigations, peripheral smears, Contrast Enhanced Computed Tomography (CECT) scan of abdomen and pelvis; which showed pancytopenia and massive splenomegaly with some areas of necrosis around the head and tail region of pancreas. However, serum amylase and lipase were not elevated. Bone marrow aspiration and biopsy showed a hyperplastic marrow but findings were inconclusive. Laparoscopic splenectomy was done; histopathologic and immuno-histochemical studies revealed the diagnosis of diffuse large B cell lymphoma

Case-2

Seventy-one-year-old female patient came with complaints of generalized weakness, anorexia and weight loss of 4 months duration. On evaluation, she was found to have pancytopenia with massive splenomegaly. Bone marrow biopsy showed lymphoid infiltration of marrow with differential diagnosis of Chronic Lymphocytic Leukemia (CLL) vs lymphoma. The case was discussed in multi-disciplinary tumor board meeting and it was decided to do splenectomy for arriving at final diagnosis. She underwent laparoscopic splenectomy and definitive diagnosis of T cell rich B cell lymphoma was established.

Case-3

Sixty-year-old male patient came with complaints of fatigue, weight loss and abdominal discomfort of 4 months duration. Clinical examination revealed anemia and massive splenomegaly. He was evaluated with routine blood investigations, peripheral smear, CECT abdomen and pelvis. Pancytopenia and massive splenomegaly were confirmed. Bone marrow biopsy showed hyperplastic marrow with erythroid hyperplasia, suspicious of Chronic Myeloid Leukemia (CML), however not confirmatory. After discussion in multi-disciplinary tumor board meeting patient was taken up for laparoscopic splenectomy; histopathologic and immuno-histochemical studies showed anaplastic diffuse large B cell lymphoma.

Case-4

Fifty-three-year-old male came with complaints of mass per abdomen, generalized weakness and weight loss since past 5 months. Clinical examination revealed anemia and massive splenomegaly. He was evaluated with routine blood investigations, peripheral smear. CECT abdomen and pelvis showed massive splenomegaly and retro-peritoneal fibrosis. Bone marrow biopsy showed hyperplastic marrow and the diagnosis remained inconclusive. He underwent laparoscopic splenectomy and the final diagnosis was B cell Non-Hodgkin's lymphoma.

In all 4 cases (Table 1), a definitive diagnosis was established only after diagnostic splenectomy. All the patients had uneventful post-operative recovery and all were started on appropriate chemotherapeutic regimens with-in 4 weeks of surgery. The resolution of hypersplenism and mass effect of spleen after splenectomy also facilitated the prompt commencement of chemotherapy.

Table 1: Series of 4 cases with splenomegaly of unknown cause where diagnostic splenectomy was done

Age/ Sex	Clinical Picture	Hematology	Imaging	Bone Marrow	HPE and IHC
57/M	C/o- Generalized weakness and Abdominal discomfort P/A – Splenomegaly+	Thrombocytopenia+ (Platelets-45,000) P. Smear – Microcytic, Hypochromic Anemia with Lymphopenia and Thrombocytopenia	CECT- Splenomegaly -Necrotic Head and Tail of pancreas	Biopsy- Hyperplastic marrow with increased eosinophilic precursor	Diffuse large B cell lymphoma
71/F	C/o -Generalized weakness P/A – Splenomegaly+	Pancytopenia (Hb-7.5 TC-2200 Platelets-26,000) P. Smear – Pancytopenia	CECT- -Mild Hepatomegaly -Massive Splenomegaly	Biopsy- Suspected lymphoid infiltration of bone marrow, requires further evaluation	T cell rich B cell lymphoma
60/M	C/o- -Fatigue -Abdominal Discomfort P/A- Massive Splenomegaly	Anemia (Hb-8.7g/dl) P. smear- Leucoerythroblastic anemia with Thrombocytopenia	CECT- Massive splenomegaly	Biopsy – Hyperplastic marrow with erythroid hyperplasia, mild increase in eosinophil precursors and plasmacytosis	Anaplastic diffuse large B cell lymphoma
53/M	C/o- Mass per abdomen loss of weight and generalized weakness P/A – Splenomegaly+	Anemia (Hb -8.7 TC-4200 Platelets-1,46,000) P. smear – Dimorphic Anemia	CECT- -Grade III Hepatosplenomegaly with dilated portal vein, splenic vein and SMV-Enhancing soft tissue attenuating lesion in the retroperitoneum extending from the level of the celiac artery to the perirectal region, encasing vascular structure, rectum, seminal vesicles, kidneys and proximal ureters-Likely acute benign retroperitoneal fibrosis. -Minimal Ascites	Biopsy- Hyperplastic marrow with mild plasmacytosis	B cell, Non-Hodgkin's lymphoma

Discussion

Splenomegaly can be caused due to infections, congestion/ portal hypertension, auto-immune diseases, infiltrative diseases and malignancy [3-4]. The various causes of splenomegaly are listed in Table 2.

Among the various hematological causes for splenomegaly, lymphomas account for 16-44% cases. Other hematological causes in the decreasing order of incidence are CML (8-29%), CLL (10-20%), haemoglobinopathies (7-12%) and myelofibrosis (9-16%) [1-4]. Work-up of these patients include complete hemogram with peripheral smear, Erythrocyte Sedimentation Rate (ESR), coagulation profile, serology for HIV, renal function tests, liver function tests, urine analysis and imaging (ultrasonography/CECT abdomen) [3]. In selected groups of patients, malaria testing, hemoglobin electrophoresis, upper GI endoscopy, reticulocyte count, vitamin B12, bone marrow aspiration, bone marrow biopsy and other specific

Table 2: Various diseases causing splenomegaly and incidence [1-4]

Category	Groups	Examples
Infection (Incidence: 9-36%)	Acute	Infectious mononucleosis, viral hepatitis, septicemia, typhoid, cytomegalovirus, toxoplasmosis
	Sub-acute/Chronic	Tuberculosis, subacute bacterial endocarditis, brucellosis, syphilis, HIV
	Tropical/Parasite	Malaria, leishmaniasis, schistosomiasis
Hematological (Incidence: 16-66%)	Myeloproliferative	Myelofibrosis, chronic myeloid leukemia (CML), polycythemia vera, essential thrombocytosis
	Lymphoma	Non-Hodgkin lymphoma (NHL), Hodgkin lymphoma
	Leukemias	Acute leukemia, chronic lymphocytic leukemia (CLL), hairy cell leukemia, prolymphocytic leukemia
	Congenital	Hereditary spherocytosis, thalassemia, HbSC disease
	Others	Autoimmune hemolysis, megaloblastic anaemia
Congestive and Inflammatory (Incidence: 4-10%)	Congestive	Splenic/portal/hepatic vein thrombosis or obstruction, congestive cardiac failure
	Collagen diseases	Systemic lupus erythematosus, rheumatoid arthritis (Felty's)
	Granulomatous	Sarcoidosis
Hepatic (Incidence: 9-41%)		Cirrhosis
Infiltrative (Incidence: 1-6%)		Gaucher's disease, amyloidosis
Others (Less common)	Miscellaneous	Cysts
	Neoplastic	Haemangioma, metastases (lung/breast carcinoma, melanoma)

investigations might be warranted based on the suspected cause of splenomegaly [3].

It is reported that despite an extensive work-up, about 3-36% of patients require splenectomy for definitive diagnosis [1]. Historically, diagnostic splenectomy was associated with considerable post-operative morbidity and mortality. However, with improved peri-operative management, anesthetic practices and surgical techniques, the outcomes are much better, with morbidity rates of up to 12% and mortality rates of less than 1% [5]. Laparoscopic splenectomy is associated with early recovery and is now well accepted surgical procedure [6]. All our patients had an uneventful recovery after surgery and were discharged in 5-7 days. Diagnostic splenectomy is finding a role in the diagnosis and staging of lymphoma and was also found to have the added benefits of reversal of hypersplenism and palliation of mass symptoms in lymphoma patients [5]. All our patients had features of hypersplenism. Laparoscopic splenectomy was diagnostic and reversed the hypersplenism in our patients.

In a study by Pottakat *et al*., 41 patients over 15 years had undergone splenectomy for diagnostic purpose. Among them 39% patients had congestive splenomegaly, 34% had lymphoma, 2% had lymphoma with tuberculosis and 12% had tuberculosis. They concluded that splenectomy still had a role to play in pathological diagnosis of idiopathic splenomegaly [1]. In another study done over 10 years by Hangge *et al*., 35 patients with no definitive pre-operative diagnosis underwent splenectomy and among them 13 patients were diagnosed with lymphomas. They have concluded that splenectomy was useful diagnostic tool in selected patients with splenomegaly without a definitive pre-operative diagnosis [2]. In another study by Carr *et al*., 18 patients over 7 years had undergone splenectomy for diagnostic purpose. Among them 4 patients had sarcoidosis, 6 had congestive splenomegaly, one had Castleman's disease and the remaining 7 (39%) had lymphomas. They concluded that a high percentage of patients with splenomegaly of unknown etiology will have primary lymphoma of the spleen and that splenectomy is both diagnostic and therapeutic and should be considered for all patients with idiopathic splenomegaly [7]. It was reported in a study by Naples *et al*. that of the 68 patients who underwent splenectomy for diagnostic purpose 34 patients (50%) had malignant etiology with lymphomas accounting for 30 of those cases. The remaining 34 patients had benign etiology. They concluded that splenectomy is an effective diagnostic modality in determining a pathological cause for idiopathic splenomegaly [8]. Even a recent study form US National cancer database suggests that though the proportion of patients undergoing diagnostic and therapeutic splenectomy for splenic lymphomas has significantly decreased from 69% in 2004 to 44% in 2013; it still has a significant diagnostic role [9]. We followed these same principles in our decision to perform splenectomy for diagnostic purpose in our patients.

A study from Western Europe reported their approach in patients of unexplained splenomegaly. They have suggested an algorithm for these patients in which the initial hematological, biochemical and microbiological blood work-up along with imaging in the form of CT scan or MRI is done. Positron Emission Tomography (PET) CT is done if this initial work-up does not yield diagnosis. Targeted biopsies taken when indicated; and after all that, if still the diagnosis is not known they suggest diagnostic splenectomy [10].

All our patients had an extensive work-up for the cause of splenomegaly. There was high suspicion of lymphoma in all these cases but confirmation was lacking. All these cases were discussed in multidisciplinary tumor board who recommended splenectomy for confirming the diagnosis. All of them were vaccinated with polyvalent pneumococcal, meningococcal and Hemophilus influenza B vaccines 2 weeks prior to surgery. All patients underwent laparoscopic splenectomy and spleen was recovered in a bag through Pfannenstiel incision. Patients were discharged with-in 5-7 days after surgery. There were no peri-operative complications reported in any of our patients.

Post-operatively platelet counts were checked on post-operative day 7 and day 14. Platelet counts more than 5 lac per cubic millimeter warranted tablet aspirin 75-150 mg once daily till the platelet counts normalized. All our patients were started on chemotherapy with-in 4 weeks of surgery.

Conclusion

Patients with splenomegaly need extensive work-up for diagnosis of the underlying cause. If the diagnosis is still inconclusive and there is a high suspicion of malignancy/ lymphoma, splenectomy can be considered as a valid diagnostic modality.

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How to cite this article:
Chodisetti S, Santosh KKY, Bhat PKR, Shruthi, CJ Sorake. Splenectomy for diagnosis of lymphomas: A case series. *J Krishna Inst Med Sci Univ* 2023; 12(2): 138-143

Submitted: *31-Jan-2023* ***Accepted:*** *18-Mar-2023* ***Published:*** *01-Apr-2023*