Splenomegaly - A Diagnostic Dilemma

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Abstract

Splenic marginal zone lymphoma is a rare form of malignant neoplasm, a subtype of Non-Hodgkin's Lymphoma. It is usually present in middle age group with unexplained splenomegaly, abdominal pain, fatigue and weight loss. It is also known as Primary Splenic Lymphoma. Splenectomy is usually chosen as a mode for both diagnosis and treatment. Here we present a case of a 37 years old female with massive splenomegaly who was later diagnosed to have primary splenic lymphoma.

Keywords: Splenomegaly, Primary splenic lymphoma, Non-Hodgkin's lymphoma.

Introduction

Massive splenomegaly is often a diagnostic dilemma for physicians. It can have many differentials including infectious and non-infectious causes. Some of these causes can be malaria, typhoid, tuberculosis, kala-azar and portal hypertension. There can also be hematological causes like leukemia, lymphoma and myeloproliferative diseases. [1] Here we describe a patient with a rare form of lymphoma as a cause of her splenomegaly. Kraemer *et al* (1984) has defined PSL as lymphoma presenting with splenomegaly, least bicytopenia and in the absence of peripheral lymphadenopathy. [2]

Case Report

A 37 years old female, farmer by occupation, resident of a rural place in Western Maharashtra, presented to us with a 6 months history of fever which was of low grade, intermittent and associated with chills. She also complained of generalized pain in abdomen with no aggravating or relieving factors. The patient gave history of reduced appetite and a significant weight loss of 6 kg in 4 months. She was admitted in an outside hospital for almost a month where she was investigated. Her investigations were suggestive of anemia with a hemoglobin of 9.5gm/dl, TLC-14,700 cells/cu.mm and platelet count of 3,67,000 cells/cu.mm. Ultrasonography of abdomen and pelvis done outside showed a well-defined solid mass of heterogenous echotexture in the splenic parenchyma.

CT scan of the abdomen done outside was also suggestive of mild splenomegaly with well-defined heterogeneously enhancing partially necrotic soft tissue with hypo-density in spleen representing a neoplastic etiology, but there was no evidence of lymphadenopathy.

Pet CT scan was suggestive of enlarged conglomerated and discrete peripancreatic and gastrosplenic lymph nodes s/o lymphomatous nodal tissue.

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But the histopathology of the USG guided biopsy of splenic lesion done outside was suggestive of necrotizing acute inflammation.

Bone marrow biopsy done outside was negative for any granulomatous lesion or epitheloid cells.

She had received ceftriaxone for 2 days, followed by metronidazole, piperacillin and tazobactam for 3 days, levofloxacin and cefixime for 7 days but there were no relief in her symptoms. Hence, she was referred to our hospital for further management.

There was no history of cough, dyspnea, hemoptysis, rash, contact with positive tuberculosis patient, joint pains or bone pains.

On examination, she was afebrile, with a pulse of 90 beats per minute and a blood pressure measuring 120/70mm of Hg. There was no generalized lymphadenopathy.

Systemic examination revealed tender splenomegaly of 9 cm below the left costal margin, hard in consistency. Other systems were normal on examination.

On history, the differentials made were:

1 Infectious Etiology- Tuberculosis/Malaria
2 Meliodosis
3 Lymphoma/Leukemia
4 Immunocompromised status
5 Kikuchi disease
6 Staphylococcal infection

Investigations

The complete blood count showed a normal hemoglobin and platelet count. Her total leucocyte count was 35,300 cells/cu.mm (N-85%, L-06%, M-4%, E-4%, B-0%). The peripheral blood smear showed normochromic normocytic picture with neutrophilic leukocytosis with shift to left up-to band stage.

She presented with raised creatinine of 1.84 mg/dl, and urea of 47 mg/dl. HIV, HBsAg, anti-HCV were negative.

Her liver function tests were normal. Random Blood sugar was 124 mg/dl.

Her peripheral smear did not show any malarial parasite. Her serum leptospirosis IgM was negative. Also, urine cultures were negative for growth of any organism. Her blood cultures even after keeping for prolonged incubation did not grow any organism. Incidentally, serum Typhifast IgM was positive.

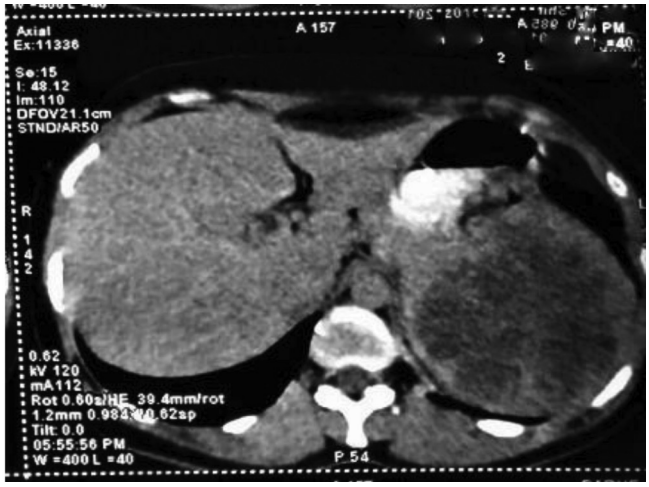

Figure 1: CT scan done outside showed splenomegaly with well-defined rounded 9x9x7cm sized heterogenously enhancing lesion

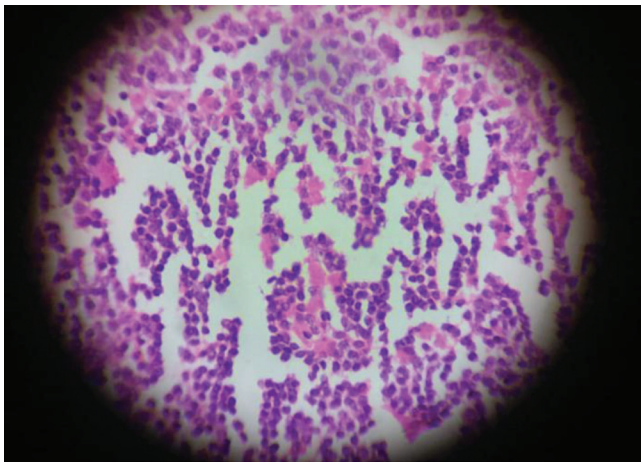

Figure 2: High power view showing a tumor arranged in form of island. Individual tumor cells are small, round with hyperchromatic nuclei and scant amount of cytoplasm.

Chest radiograph was normal. Repeat USG at our hospital showed well lobulated heterogenous predominantly solid lesion in spleen which was not drainable.

Upper GI endoscopy and colonoscopy was done to rule out any tubercular lesion and it was found to be normal.

Patient was begun on injection Meropenem 1gm 8 hourly, but when her fever spikes did not subside, an infectious disease opinion was sought.

Due to her farming occupation and hence exposure to fresh water in paddy fields, tender splenomegaly and leukocytosis, we thought of an infectious etiology such as meliodosis and hence was taken on injectable ceftazidime 2 gm 8 hourly as it is relatively more specific for it. But even when antibiotics were given for approximately 2 weeks, she continued to have fever

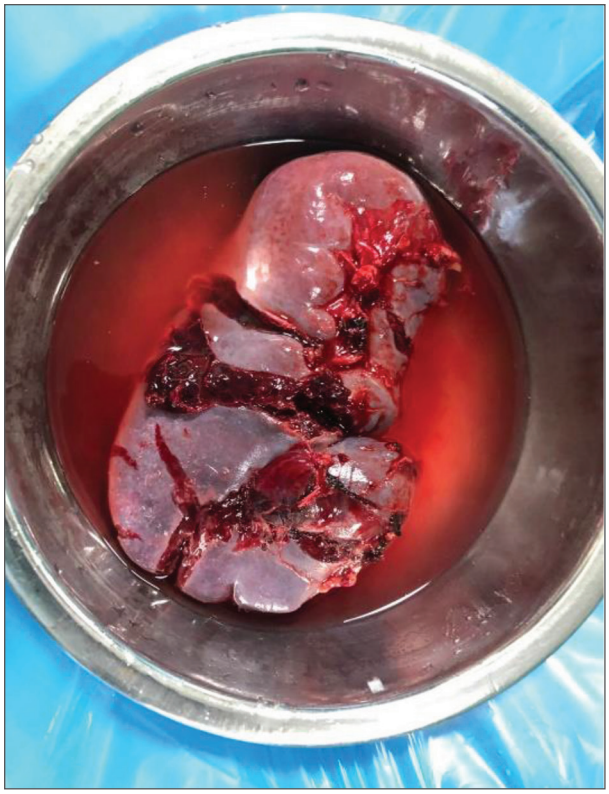

Figure 3: Gross specimen of the biopsied splenic tissue post exploratory laparotomy.

spikes hence was planned for exploratory laparotomy and biopsy. She was vaccinated with Influenza vaccine prior to her surgery. It was performed and splenic biopsy was done along with supra-pancreatic and splenic hilar lymph nodes. During exploratory laparotomy, spleen was found to be adhered to liver with necrotic tissue in the upper pole. Histopathology of the biopsied specimen showed large foci of necrosis with proliferation of histiocytes suggestive of fibrinoid necrosis with no evidence of atypia/ malignancy with possibility of Kikuchi's disease. Pus and Tissue cultures were negative for any growth. Hence a second opinion was sought that showed diffuse lymphoid infiltrates positive for CD20 and Bcl-2 and c-MYC on IHC, suggestive of High-grade large B cell lymphoma (Histiocyte rich)

Patient was started on chemotherapy – R DA POCH regimen 7 cycles done. She received her last chemotherapy 2 months back. Mid chemotherapy, a repeat scan done in February 2020 showed no change in tumor size hence patient was started on radiation therapy with 27 cycles done and last one completed on 1st July 2020. Post radiotherapy, PET scan showed regression in size and metabolic activity in mid and upper pole and exophytic lesion of spleen. Patient is stable at present with no fever spikes, no abdominal pain and increased appetite with weight gain.

Discussion

Spleen is usually involved as a part of multisystem involvement in infection and hematological malignancy and very rarely as a primary organ involvement. Though the histopathology report was suggestive of Kikuchi's disease, the points which were not in favour of the same were that:

1 Kikuchi usually resolves in 1-2 months span unlike the above prolonged history of 6 months.

2 Kikuchi usually presents with leucopenia while in above case patient presented with leukocytosis. It is also difficult to explain transient renal disease for Kikuchi.

3 Usually Kikuchi disease is associated with autoimmune diseases such as SLE but since this patient didn't have those manifestations it was less likely to be that.

Splenic Marginal Zone Lymphoma is a rare form of indolent B cell lymphoma accounting for <2% of Non-Hodgkin's Lymphoma. It affects the spleen, bone marrow and the peripheral blood. [3] It is usually a slow growing tumor, but transformation into a malignancy can happen in a small fraction of the patients. [4] Malignant transformation usually involves the bone marrow, liver, central nervous system. [5]

Patient presents with a lymphocytosis with or without cytopenias (usually bicytopenia) and splenomegaly. Clinically patients usually present in the age group above 50 years with unexplained splenomegaly, anemia, thrombocytopenia, abdominal discomfort, early satiety and have lymphocytosis. Lymphadenopathy with fever, weight loss and night sweats are usually rare symptoms.

It is postulated to arise from a post-germinal center, memory B cell of splenic type. Pathogenesis is incompletely understood but it is attributed to mutations in oncogenes and tumor suppressor genes (such as Notch pathway, NF-kB pathway, MYD-88 and KLF-2). Infection with Hepatitis C is a risk factor for the disease and treatment of Hepatitis C can result in regression of lymphoma. They are also associated with autoimmune conditions such as Sjogren's, SLE, pernicious anemia.

Diagnosis has been difficult in the earlier stage due to absence of specific symptoms, hence histopathological examination of the biopsy sample is essential for a definitive diagnosis. On histopathology, the lym-

phoma cells usually replace the white pulp or proliferate in the marginal zone of the spleen along with a patchy or a diffuse infiltration in the red pulp of the spleen. [6] Flow cytometry of the peripheral blood is also essential for the diagnosis: malignant lymphocytes will be positive for surface immunoglobulin CD19 and CD29 and will lack CD5 and CD10. It is used to differentiate it from Hairy Cell Leukemia by the absence of CD25, CD103 and Annexin A1. [6] Treatment of choice for symptomatic patients is splenectomy. Novel therapies are also found to be considered such as with anti-CD20 antibody – Rituximab. Splenectomy is both diagnostic and therapeutic. It is associated with overall response rate of 85% and an estimated progression free survival at 5 years of 92 and 73% respectively.[4]

Conclusion

Though primary splenic lymphoma comprises a lesser percentage of Non-Hodgkin lymphoma, it should be ruled out in a patient with complaints of abdominal pain, fever, and splenomegaly. Histopathology and immunohistochemistry of the biopsied specimen are the most useful to arrive at a diagnosis.

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