Isolated splenic lymphoma: an elusive preoperative diagnosis

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Four patients underwent splenectomy for various clinical and radiological diagnoses and were found to have primary splenic lymphoma at surgery and histology. The diagnosis was classical Hodgkin's lymphoma, mixed cellularity type (one case); marginal zone B-cell non-Hodgkin's lymphoma (one case); and large B cell type non-Hodgkin's lymphoma (two cases). The first two patients had multiple nodules in the spleen measuring 0.1-0.5 cm while large cell lymphomas had large nodules (largest measuring 11 cm x 7 cm x 4 cm). The diagnoses were confirmed by immunohistochemical analysis. Mean follow up of these patients was 11 months; all patients received chemotherapy. One patient died, of causes not related to the disease process. [Indian J Gastroenterol 2000;19:184-186]

Key words: Hodgkin's lymphoma, large cell lymphoma, marginal zone lymphoma, splenectomy

The frequency of splenomegaly in patients with Hodgkin's disease is around 13%; patients presenting with only splenomegaly account for less than 1% of cases with Hodgkin's disease. Primary splenic lymphoma is extremely rare, accounting for <1% of all reported cases of extranodal lymphoma. Splenic involvement occurs late in the course of Hodgkin's disease.

We report four patients with splenomegaly, who underwent elective splenectomy for a presumptive diagnosis other than lymphoma, and were diagnosed to have primary splenic lymphoma on histology and immunohistochemistry.

Case Reports

Of 21 patients undergoing elective or emergency splenectomy in our unit between March 1996 and September 1999, four (age mean 43 years, range 14 to 72) were diagnosed to have primary splenic lymphoma.

The mean duration of symptoms in these four patients was 9 months (Table 1). Hemogram, blood cell counts and peripheral smear were normal in all, except for absolute lymphocytosis in one case (lymphocyte count 9540 x 10^6/L, with lymphocytes having cytoplasmic projections suggestive of hairy cell leukemia). Liver and renal profiles were normal in all patients. X-ray chest had no evidence of hilar adenopathy. CT chest was not done preoperatively as none of these cases was suspected to have lymphoma. Esophage-gastrodouenal endoscopy was normal in all. Ultrasonography and contrast-enhanced CT scan confirmed splenomegaly in all four; however, in cases 3 and 4 the radiological diagnosis was splenic hemangiomata and multiple splenic abscesses. Liver was normal in all the cases. Bone marrow examination in cases 1 and 2 was suggestive of erythroid hyperplasia and hairy cell leukemia, respectively.

Intraoperative examination of the abdomen and pelvis ruled out any lymphadenopathy. Liver and other intrabdominal organs were normal at the time of splenectomy. The mean maximum length of the excised specimen was 22 cm and mean weight was 1360 g. The intra-operative and gross pathological findings are given in Table 2.

Histology

All the slides were stained with hematoxylin and eosin.

Case 1: The spleen, hilar nodes and splenica showed infiltration of congested white pulp by nodular areas of polymorphs, lymphoplasmocytic cells, histiocytes and Reed-Steinberg cells. Evidence of classical Hodgkin's disease. Liver showed congestion with hemosiderin deposits.

Case 2: There were multiple nodules composed of uniform small non-cleaved lymphocytes, invading the trabeculae at places, with congested and focally infiltrated red pulp. The appearance was of nodular non-cleaved small lymphocytic cell type of non-Hodgkin's lymphoma. The neoplastic infiltrate was monomorphic and composed of small centrocyte-like lymphoid cells. The cells had scanty cytoplasm and oval to round, minimally

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/sex</th>
<th>Duration</th>
<th>Hematology</th>
<th>Radiology</th>
<th>Presumptive diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14/M</td>
<td>6 months</td>
<td>PS: normal; BM: erythrocyte hyperplasia</td>
<td>USG &amp; CECT: Autoimmune</td>
<td>Autoimmune</td>
</tr>
<tr>
<td>2</td>
<td>47/F</td>
<td>2 years</td>
<td>PS: absolute lymphocytosis with villous lymphocytes; BM: hairy lymphocytes</td>
<td>USG: splenomegaly with no intra-abdominal lymphadenopathy</td>
<td>Hemolytic anemia</td>
</tr>
<tr>
<td>3</td>
<td>45/F</td>
<td>5 months</td>
<td>CECT: splenic SOL, hemangiomata</td>
<td>CECT: multiple splenic SOLs, Multiple splenic abscesses</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>72/F</td>
<td>15 days</td>
<td>CECT: splenic SOLs, Multiple splenic abscesses</td>
<td></td>
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PS: peripheral smear; BM: bone marrow; USG: ultrasonography; CECT: contrast-enhanced computed tomography; SOL: space-occupying lesion

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mally cleaved nuclei. Cells with nucleoli were not seen. Mitoses were extremely scanty. Hilus lymph node involvement showed perifollicular (marginal zone) pattern and a sinus pattern of the infiltrate was present.

**Case 3**: There were dense sheets of uniform-sized non-cleaved large lymphocytes, with obliteration of the white-red pulp demarcation in the tumor zone. Merging in the red pulp at the periphery, eliciting a minimal host response. Areas of necrosis, hemorrhage and cystic degeneration were evident, thus giving the picture of large cell lymphoma.

**Case 4**: The nodules revealed diffuse sheets of large pleomorphic lymphocytes with high mitotic activity, and areas of necrosis involving, the diagnosis being diffuse large cell type of non-Hodgkin’s lymphoma.

**Immunohistochemistry**

Four-micron-thick paraffin sections were immunostained using mouse monoclonal antibodies to CD20, CD45RO, CD3, CD15 and CD30, and rabbit polyclonal antibody to CD3 (DAKO, Denmark). The deparaffinized sections were treated in a microwave oven for ten minutes for antigen retrieval. The antigen-antibody reaction was localized by the avidin-biotin-peroxidase technique (Vecstain Elite ABC kits; Vector Laboratories, Burlingame, California).

Spleenic sections in case 1 showed patchy nodular involvement by a polymorphous infiltrate composed of large atypical cells expressing CD15 and CD30. They were negative for CD3, CD45RO and CD20. The background lymphoid cells surrounding these Reed-Sternberg cells were predominantly activated T-cells. A diagnosis of classical Hodgkin’s disease, mixed cellularity type was made.

Sections in case 2 showed lymphoid cells that expressed CD20 (Fig) and were negative for CD3, CD45RO and CD43. A diagnosis of non-Hodgkin’s lymphoma, marginal zone B-cell type was made.

Sections from cases 3 and 4 showed patchy nodular involvement by a monomorphic infiltrate of large nucleolated cells. While the infiltrate was composed purely of centroblasts in case 4, case 5 revealed a small proportion of immunoblasts in addition. Large areas of necrosis were seen in both cases. The large atypical cells expressed CD20 but were negative for CD3 and CD45RO, leading to a diagnosis of non-Hodgkin’s lymphoma of diffuse large B-cell type.

**Follow up**

All cases were started on chemotherapy (CHOP — cyclophosphamide, vincristine, prednisolone and Adriamycin — 6 cycles) and were followed up over a mean period of 11 months. Two patients expired, one (case 4) immediately postoperatively and the second (case 1) after re-exploration 5 months later for gangrenous small bowel obstruction. The other two cases did not develop any other evidence of extranodal lymphoma.

**Discussion**

The diagnosis of malignant lymphoma of the spleen may be missed if lymph node and bone marrow biopsies are negative. Fifteen percent of primary splenic lymphomas have been misdiagnosed to be hairy cell leukemia on bone marrow examination. Up to 3% have been treated as autoimmune hemolytic anemia.

Lymphomas involve the white pulp of the spleen, in contrast to the leukemias and histiocytomas which involve the red pulp. They involve all the malphigian bodies uniformly, and cause an increase in the number of white pulp nodules per unit area of the spleen, without associated germinal center formation.

The criteria for establishing the diagnosis of primary splenic lymphoma include splenomegaly, absence of extrasplenic involvement, negative lymph node and liver biopsies, and post-splenectomy disease-free interval of 6 months. The commonest and true primary splenic lymphomas consist mainly of splenic marginal zone...
lymphomas. Among primary splenic lymphomas, Hodgkin's disease is rare. The diagnostic criteria for non-Hodgkin's lymphoma are however not as well defined as those for Hodgkin's disease.

Ahmann et al. staged primary splenic lymphomas as stage 1: disease confined to spleen, stage 2: disease involving the hilar nodes as well, stage 3: disease spreading to other intra-abdominal lymph nodes. Two-thirds of patients present in stage 2 or more.

Gorg et al. studied the pattern of splenic involvement in a series of 680 cases and identified four types, viz., diffuse (37%), focal small nodular type (39%), focal large nodular lesions (23%), and bulky disease (2%). As was seen in our series, high-grade and large cell lymphomas showed large or small nodular lesions, while low-grade lymphomas and Hodgkin's disease showed diffuse or small nodular pattern. The small lymphocytic type is the most difficult to diagnose in the absence of lymph node or bone marrow biopsy. These however run the most indolent course as opposed to the large cell type which has a more fulminant course, associated with tissue necrosis and degeneration.

The survival and prognosis of primary splenic lymphomas thus is not only dependent on the time of diagnosis and intervention but also on its histologic type and grading.

References

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BOOK REVIEW

The Pancreas. Edited by Prof J D Wig. Chandigarh: Azad Offset Printer. 2000. 703 pages

This book appears to be based on lectures delivered during a conference on the pancreas held at the Postgraduate Institute of Medical Education and Research, Chandigarh in 1999, with chapters contributed by those who participated.

The chapters on History of Pancreatic Surgery, Pathophysiology of Acute Pancreatitis, Prediction in Acute Pancreatitis, Damage Limitation Strategies in Acute Pancreatitis, Idiopathic Pancreatitis and Acute Biliary Pancreatitis, Radiological Intervention in Complicated Pancreatitis, and Pancreatic Necrosis are well written and informative. Prof YK Joshi and Prof Kartar Singh have laid emphasis on the value of nutrition in the management of pancreatic diseases, an aspect that is often neglected. Similarly, the chapters on Pathogenesis of Pain and Endoscopic Intervention in Chronic Pancreatitis are well presented and have given clear messages.

Frieds et al. have clearly discussed the place of various surgical procedures for chronic pancreatitis and have recommended the gold standard for surgery of chronic pancreatitis today. The most important contribution is the details about duodenum-preserving pancreatic head resection and the Frey procedure. Leak from pancreatico-jejunal anastomosis has been a major cause of morbidity following Whipple resection.

Prof John Howard has given some useful tips to prevent it.

The role of extended pancreatectomy and adjuvant therapy has been well discussed. The book has also covered some of the less known aspects of pancreatic diseases, such as pancreatic disease and parasites, tuberculosis, pseudocysts, trauma and transplantation. However, the chapter on prevention of complications following major pancreatic surgery deals only with the role of octreotide. The positive aspect of this chapter is that it has clearly defined the role of octreotide in prevention of postoperative pancreatic leak.

The main criticism of the book is repetitiveness of contents. Thus, a reader has to endure cytokines over five chapters, pancreatic necrosis over four, and nutrition, pathogenesis of pain and pancreatic trauma over two chapters each. This has crept in not only due to multiple authorship but also because of poor editing and a tendency by the editor to contribute too many chapters, many of which are repetitions. Instead, the editor could have given short expert comments at the end of each chapter.

Since the book has been edited by an Indian, I am rather disappointed not to see valuable Indian data, particularly on chronic pancreatitis, the so-called tropical pancreatitis. But, overall, medical and surgical gastroenterologists and postgraduate students will find the book useful.

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