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Spectrum of Disease Entities in Splenectomy Specimen

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Introduction: We report here our results of Pathological assessment of 35 splenectomy cases.
Purpose of Study: To evaluate the subtle morphological change which is often missed due to lack of experience & knowledge.
Material and Methods: It was a non-interventional descriptive study, carried out in the Pathology department of PIMS. All available splenectomy, slides were reviewed from a period of Jan 2004 to April 2007. Slides were reviewed by two histopathologists & one hematologist.
Results: On re-examination there was change in 65% (n: 35) cases. Malaria was the most often missed diagnosis. In 31% (n: 11) cases malaria was suspected due to blackish-brown pigment in the macrophages. Out of these in 27% (n: 3) definite schizonts were seen and hence malarial spleen was confirmed. Littoral cell Hyperplasia was found in 20% (n: 7) cases which was previously diagnosed as Idiopathic Thrombocytopenic purpura in 2 cases ,congested Spleen in 4 cases and Littoral hyperplasia in 1 case. Extramedullary hemopoiesis has been in seen in 17% (n: 6) cases which were previously diagnosed as congested spleen in 4 cases, consistent with Thallasemia in 1 case and 1 case of essentially normal Spleen. Malignancy was picked up in 6% (n: 2) cases which were missed in initial examination.
Conclusion: Spleen still lingers as useless and "vestigial" organ in the minds of surgeons and the pathologists despite its very vital immunophysical defense activities. The spleen are too often removed before giving a therapeutic trial of proper antimalarial drugs in " idiopathic thrombocytopenia " and idiopathic splenomegaly .Possibility of malignancy is also missed often .Inadequate history and rather very cursory examination of splenic section results in missing vital diagnosis. Unnecessary splenectomies must be avoided while pathologist must examine this very precious organ very carefully. Needless to say that many of the diagnosis attained on splenic sections could have been obtained on FNAC of Spleen.
Key words: Spleen, Malaria, Littoral cell Hyperplasia. Histopathological examination of Spleen.

Introduction

The spleen is an important organ with active roles in immunosurveillance and other physical defense mechanism.[1] It is a discriminatory filter which is inserted into the blood stream. It clears the blood from aged blood cells and foreign particles and is the site of immune reactions to blood-borne antigens.[2] Spleen was considered, not essential for life that is why when there is trauma or any immunological disease the surgeons do not hesitate to perform a splenectomy. However the removal of the spleen exposes the patients to infections especially polysaccharide capsule bearing bacteria i.e. pneumococcal, Hemophilus Influenzae and meningococcus.[3] This attitude is not only of the Surgeons but even the Pathologists who do not see the slides very carefully and miss many morphological features. This is because the pathologists are not well versed with the normal histology as well as the pathological changes in this vital organ. Many times the subtle findings are overlooked.

It is pertinent that the importance of this organ should be realized both by the surgeons and pathologists. The surgeons and physicians must avoid unnecessary splenectomies.[4] Fine Needle Aspiration Cytology (FNAC) may be used when necessary. On the other hand the pathologist must pay close and careful attention to the sections.

Material and Methods

This is a retrospective study conducted at histopathology department of PIMS. We collected 35 cases of splenectomy from January 2004 to April 2007. All these cases were operated either at main hospital PIMS or children hospital. All these cases were reviewed by 2 histopathologists & one haematologist to arrive at a consensus.

All splenectomy specimens were fixed in 10% buffered formalin, routinely processed and embedded in paraffin. Slides were stained by Haematoxylin and eosin stain.

Following parameters were thoroughly and

meticulously examined

- Capsule
- Sub capsular hemorrhages
- White pulp whether increased or decreased
- Red Pulp
- Sinuses whether empty ,dilated or Congested
- Splenic cord (Cords of Bilroth), either cellular, fibrotic, congested
- Hemorrhages
- Fibrosis
- Pigment Hemozoin
- Hemosiderin
- Formalin Particles (artifact)
- Extramedullary hemopoiesis
- Eosinophils
- Atypical Infiltrate
- Storage cells
- Hemophagocytic cells
- Gamma Gandy bodies
- Littoral cells
- Schizonts

Results

Our 35 cases included 30 (85%) of adults and 5 (15%) cases of children. The age range of children (3 males and 2 females) was 4-12 years, while that of adults (19 males and 11 females) was 14-60 years.

Nearly half of the Splenectomies were carried out during the 2nd and 3rd decade of life i.e. 19(54%) patients.

In 23(65%) cases diagnosis was changed as shown in Table No. 1.

Table No. 1: Revised Diagnostic Groups in Comparison with Previous Diagnosis

Previous Diagnosis	Revised Diagnosis
Congested Spleen/Vascular congestion/Ruptured spleen (n:20)	Malarial Spleen (n:1)
	Littoral Cell Hyperplasia (n:4)
	Congestive Spleen (n:6)
	Fibrosis (n:3)
	Obstructive Change (n:1)
	Atypical Cells (n:2)
	Hemophagocytosis (n :1)
	Hyperplasia with Red cell eaten by macrophages (n:1)
	Ruptured Spleen (n:1)
Consistent with Hypersplenism (n:2)	Congestion and Fibrosis (n:3)
Hydatid Cyst (n:1)	Hydatid Cyst(n:1)
Hemosiderosis/ Thallaesemic spleen (n:2)	Marked Hemosiderosis (n:2)
Marked Extramedullary hemopoiesis with gamma gandy Bodies (n:1)	Malaria with Extramedullary hemopoiesis (n:1)
Normal Spleen / Accessory Spleen (n:2)	Hyperplastic White Pulp (n:2)
Storage Disorder Consistent with Gaucher (n:1)	Storage Disorder Consistent (n:1)
Littoral Cell Hyper plasia with white Pulp Hyperplasia (n:1)	Littoral Cell Hyper plasia (n:1)

Splenic Abscess (n:1)	Malaria leading to hemorrhage and fibrosis (n:1)
Fibrosis and hyperplasia of white pulp (n:1)	Hemorrhage, fibrosis and Gamma Gandy Bodies (n:1)
Idiopathic Thrombocytopenic Purpura (n:2)	Littoral Cell Hyperplasia (n:2)

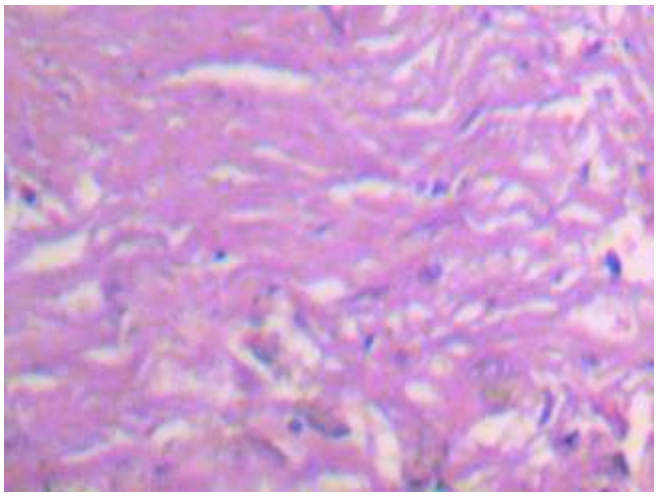

Fig. 1: Marked Fibrosis in the Red Pulp (H & E x 200)

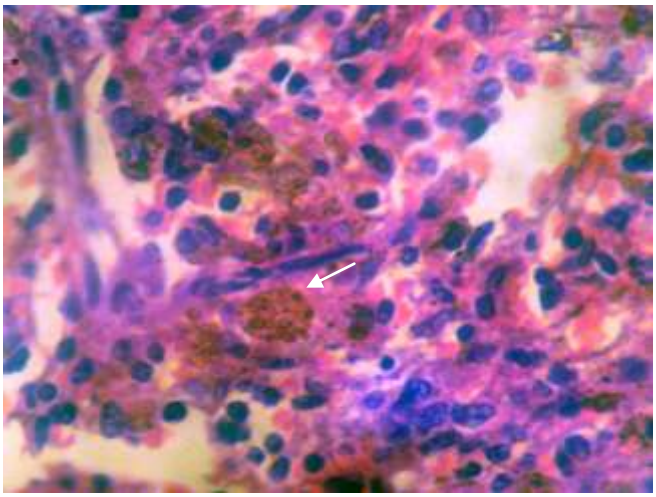

Fig. 2: Hemosiderin Laden Macrophages in Trabeculae (H & E x 1000M)

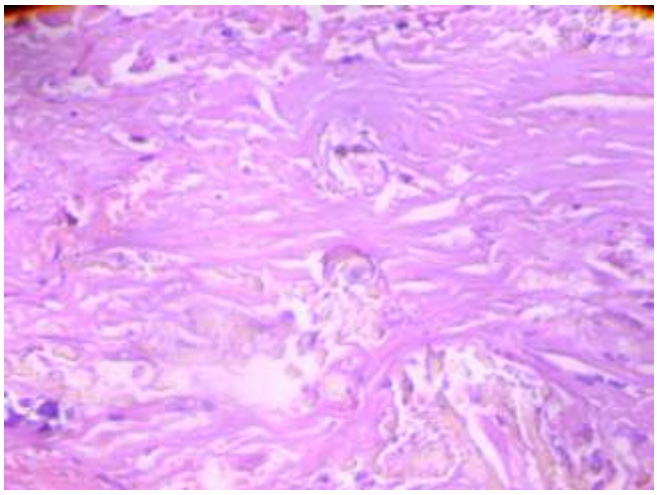

Fig. 3: Gamma-Gandy Body (H & E 400)

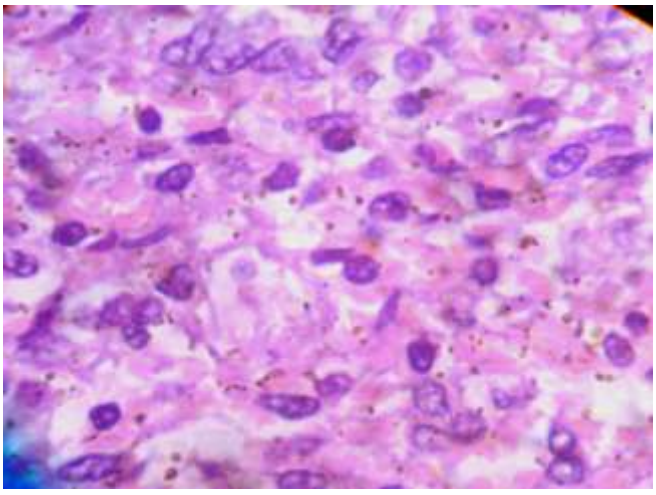

Fig. 4: Hemozoin Pigment in Red Pulp (H & E x 1000M)

Previously in 20 (57%) cases the diagnosis of vascular congestion or congested spleen was rendered. After reviewing only 6 (30%) remained with diagnosis as congested spleen, while the rest got more specific diagnosis.

We found blackish brown pigment along with hemorrhage and congestion in 11 (31%) cases. Out of these 3 (27%) cases were labeled as malarial spleen, as these cases along with hemozoin pigment also showed schizont. In the rest, (8 cases) it was very difficult to differentiate whether it is haematoxylin or hemozoin pigment.

Littoral Cell Hyperplasia was found in 7(20%).Among these 4 cases were previously diagnosed as congested spleen, 2 cases as Idiopathic thrombocytopenic purpura and 1 cases remained

unchanged.

6% (n: 2) cases contained atypical cells. One was suggested as Leukemia / Lymphoma and the other was of Chronic Myeloid Leukemia (CML).

Extramedullary hemopoiesis was seen in 6 (17%} cases. This included 4 cases of congested spleen, 1 of Thallaesemia and 1 of normal spleen.

Hemophagocytosis was missed in one case of congested Spleen.

Other important morphological changes were fibrosis, hemorrhage, gamma gandy bodies.

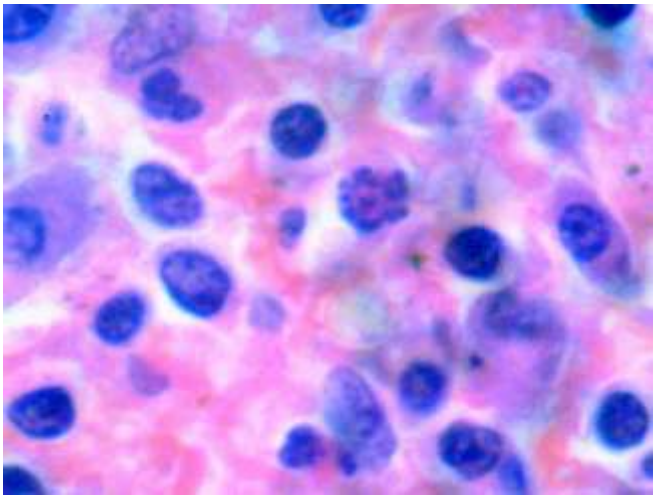

Fig. 5: Malarial Spleen showing Schizont (H & E x 1000)

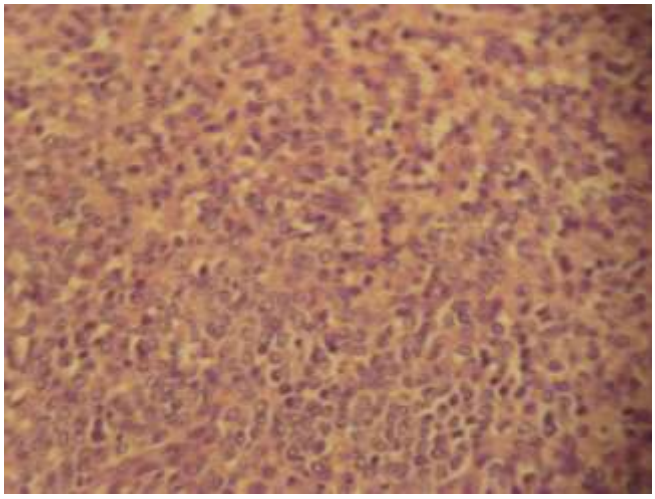

Fig. 6: Littoral Cell Hyperplasia (H & E x 200)

In one case there was vascular transformation possibly due to obstruction. In Thallasemic patients, the two cases, which we evaluated, spleen was loaded with tons of hemosiderin both extracellular and intracellular (macrophages). Hemosiderin is different from hemozoin. Hemozoin is granular and blackish in color, while hemosiderin is blackish-brown in color. The diagnosis remained unchanged in cases of storage disorder and Hydatid cyst.

Discussion

From our study it is quite evident that spleen is an organ which is often neglected both by surgeons as well as by the pathologist. It seems that when the role of spleen has been well established it is not considered by many as an essential organ for life in adult individuals. How ever there are many studies that quote that it is the only organ that removes un-opsonized encapsulated bacteria from the blood stream and its removal will expose the person to serious infections particularly pneummococal septicemia which is often life threatening.[3]

Many pathological changes during the histopathological examination of the spleen are missed because they are subtle and pathologists are not very familiar with the normal histology of spleen as well as the pathological changes which can occur. This might be because the pathologist take little interest and surgeons are not eager to know the exact diagnosis after splenectomy.[5]

So far the histopathology of congestive splenomegaly has been little explored. Probably because the findings tend to be repetitive and non specific.[6] In the histopathological analysis of 23(65%) cases of congestive splenomegaly, we found varied morphologic changes. There were hemorrhages, congestion of sinuses and fibrosis along with hemosiderin laden macrophages and gamma-gandy bodies (Fig. No. 1, 2, 3). These changes in literature have been characterized as sclero-congestive or fibro-congestive, implying that there is progressive fibrosis of the splenic cords due to the prolonged congestion and ischemia. As a matter of fact, the spleen diagnosed

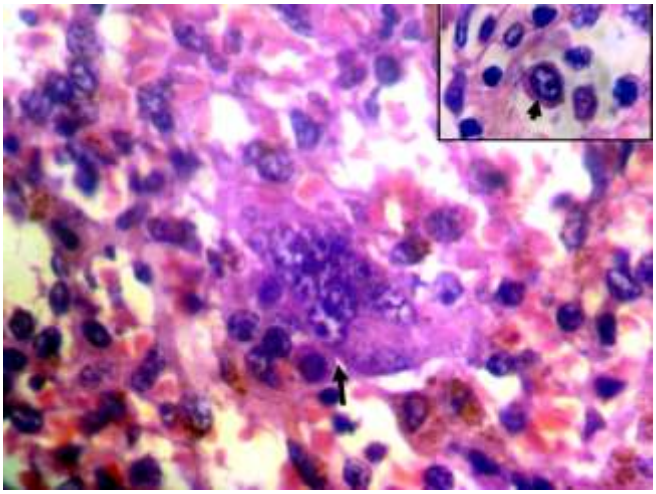

Fig. 7: Extramedullary Hemopoiesis showing Megakaryocyte (Arrow) Inset shows Normoblast (Arrowhead) (H&Ex1000)

as congested or ruptured may have some underlying simple pathology but due to subtle changes it can be missed easily.[7]

Congestive splenomegaly may be accompanied by signs of hypersplenism along with fibrous thickening of the capsule, which is frequent. There is marked dilatation of veins and sinuses, hemorrhages, fibrosis of the red pulp and accumulation of hemosiderin containing macrophages. The lymphoid follicles become inconspicuous.

Iron incrustation of the connective tissue and sclerosiderotic nodules Gamma–Gandy bodies develop as a result of focal hemorrhages.[7]

Because fibrosis is commonly present in advance cases, the condition is also termed as fibro congestive splenomegaly.

Therefore it is necessary that pathological change should be assessed systematically and all minor changes should also be recorded to reach to a final conclusion.

Best Practice Guideline for the Routine Pathology Evaluation of the Immune System by Haley et al says that the separate compartments in each lymphoid organ should be evaluated separately. Descriptive rather than interpretive terminology should be used to characterize changes within those compartments. Therefore, the (Periarteriolar Lymphoid Sheath) PALS, lymphoid follicles, marginal zone, and red pulp should be evaluated separately for changes in size and cellularity. Germinal center development within the lymphoid follicles should be noted as increased or decreased.[8, 9] Typical cellular changes that can be observed after exposure to an immunomodulatory agent are an alteration in the size and density of the PALS and/or marginal zone, and a change in the number of follicles with germinal centers.

Measures of follicle cellularity and germinal center development have been reported to be the most sensitive predictors for potential immunotoxicity whereas subtle changes in the red pulp are often difficult to detect. We examined trabeculae, Littoral cells, sinusoids, sinusoidal cells, hemorrhages, necrosis, fibrosis and pigment in the red pulp very carefully paying attention to minor details.[8]

Another important observation that was made is that malaria is often under recognized.[10] It is the commonest cause of pathological rupture of the spleen in the tropics. We found scattered granular Black pigment (hemozoin) (Fig. 4) along with congestion and hemorrhages in 11 (31%) cases. 3 (27%) cases in which the pigment was blackish brown and granular and showed the schizont (Fig. 5), we labeled them as malaria. In 8 cases the pigment was all over the slides and it was brownish in color, it was very difficult to differentiate whether it is hemozoin or artifact.

The spleen plays an important role in areas where malaria is common such as in Pakistan, producing antibodies against the malarial parasite. The splenic involvement in malaria causing splenomegaly makes it more prone to complications such as rupture as several of our cases had rupture.[11]

Most cases of pathological rupture of the spleen in malaria occur during acute infection. Lack of prior immunity to malaria appears to be a major predisposing factor. Splenic rupture is more common with Falciparum Vivax than Falciparum malariae and results from acute, rapid enlargement of the spleen. Chronically enlarged spleens are less vulnerable to rupture.[10]

7(20%) cases of Littoral cell hyperplasia were identified. 2 cases were previously diagnosed as of Idiopathic thrombocytopenic purpura (ITP) (Fig. 6). In ITP there are anti-platelet antibodies produced by spleen. These antibody coated platelets are removed by spleen. Prominence of histiocytes in red pulp (Littoral cell Hyperplasia) are the result of phagocytosis of platelets and of incompletely degraded membrane derived phospholipids. The phagocytosis of platelets by splenic histiocytes can be better appreciated in touch preparation. How ever presence of foamy macrophages is not pathogomonic of this disorder. Sheets of macrophages were variable ranging from small nodules to large foci.

They can be found in spleens of ITP or in other patients as we saw in 4 cases of congested splenomegaly where they can be incidental finding without clinical significance. Splenectomy in ITP is done in patients who don't response to steroids or immunosuppressive therapy. It is difficult to predict the effect splenectomy will have in individual case. However patients with prominent secondary follicles have a higher rate of antiplatelet antibodies production and exhibit a better initial response with a great increase of platelets post operatively.[7] We found extramedullary haemopoeisis in 6(17%) cases, which is a well established function of spleen and it can take over whenever required (Fig. 7).[12]

Extramedullary haemopoiesis is a reactive process that results from either marrow failure (myelofibrosis or infiltrative disease) or ineffective circulating mature blood elements. The spleen is the most common sites of involvement by this

process. It was seen in 6 cases, including 4 cases of congested spleen, 1 case of Thallasemia and one case of essentially normal spleen. Frequently, congestion leads to hypoxia and stimulate extramedullary hemopoiesis. Secondary signs of chronic anemia serve as supportive evidence of extramedullary hemopoiesis. However, tumor like lesions still needs further work up in search of definitive diagnosis. A reactive condition may be confused with malignancy.[7]

Our study included 2 cases of Thallasemia patients, and the spleens were loaded with hemosiderin both extracellularly and intracellularly. Iron overload is one of the major causes of morbidity in all patients with severe forms of Thallasemia, regardless of whether they are regularly transfused or not. This iron overload leads to organ damage.[13]

We had 2(6%) cases of malignancy that were missed, one case was of leukemic / lymphoma, other was of CML. Marked congestion perhaps hemorrhages along with fibrosis masked the neoplastic element and a quick diagnosis of congestion was rendered. This again highlights the importance of meticulous examination and familiarity with the pathological changes in the spleen.

Conclusion

We examined 35 cases of Spleen. In 65% cases the diagnosis were modified after careful and meticulous examination. May be these diagnosis could have been made on FNAC and Splenectomy could have been altogether avoided. Similarly, malarial etiology perhaps warrants an anti-malarial therapy in Idipathic thrombocytopenic Purpura and splenomegaly. The Pathologists must try to be familiar with normal and pathological Spleen. Each compartment must be looked very carefully. Larger studies in this regard are needed.

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