DOI: 10.7860/JCDR/2024/62199.19126

Case Report

Pathology Section

# Primary Splenic Hodgkin Lymphoma and its Prognosis: A Report of Two Cases

SAYANTAN DE[1], MOUMITA SENGUPTA[2], DEBASHIS BHATTACHARYA[3], MADHUMITA MONDAL[4], MAMATA GUHAMALLICK SINHA[5]



## ABSTRACT

Primary Splenic Lymphomas (PSL) constitute an extremely uncommon variety of splenic neoplasm and can present with grave complications such as splenic rupture. Hodgkin Lymphomas (HL), a type of hematopoietic neoplasm, are typically diagnosed between the ages of 20 and 30 years and present with supra-diaphragmatic lymphadenopathy, often accompanied by systemic B symptoms. A histopathological diagnosis involving Reed-Sternberg (RS) cells in an inflammatory background is crucial. However, other differentials such as reactive hyperplasia, infectious mononucleosis, anaplastic large cell lymphoma, or various other lymphomas may mimic Hodgkin disease both clinically and histologically. Therefore, accurate diagnostic evaluation of Hodgkin lymphoma is crucial, especially as it is highly curable with combination chemotherapy, even in higher stage disease. In this report, the authors present two cases of primary splenic HL diagnosed through histopathological and immunohistochemical examination of splenectomy specimens from January 2020 to December 2021 at the Department of Pathology, IPGME&R, Kolkata, India. While reporting the histopathological sections, the authors also considered other differentials such as reactive changes, tuberculosis, and other non-Hodgkin lymphomas. Both patients were male, aged 10 years and 18 years, and presented with abdominal distension and fever, without any palpable peripheral lymph nodes, for the last six months to one year. After chemotherapy, the patients were regularly monitored to identify any signs of recurrence or relapse. Therefore, the initial recognition and proper diagnosis of Hodgkin lymphoma presenting in the spleen may vary in clinical presentation and morphology, but early accurate diagnosis carries a good prognosis, as survival is best determined by its histopathological type.

**Keywords:** Haematopoietic neoplasm, Splenectomy, Supra-diaphragmatic lymphadenopathy

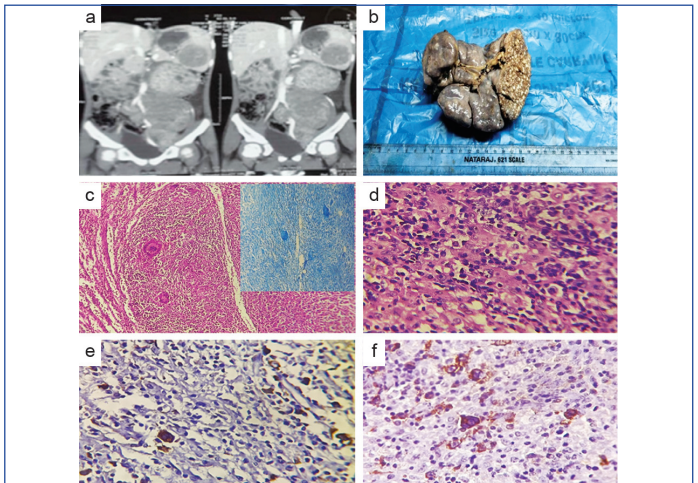
## CASE REPORT

### Case 1

A 10-year-old boy presented with fever and abdominal swelling for the last year. He had decreased appetite and mild weight loss without any palpable lymph nodes. The fever was mild and continuous in nature, without an evening rise in temperature. He had undergone routine blood investigations and fever work-up, including tests for malaria, dengue, typhoid, and others. Sputum for Acid Fast Bacilli (AFB) was negative. The erythrocyte sedimentation rate was elevated (110 mm/h) using the Westergren method. Tests for Hepatitis B and C, Human Immuno-deficiency Virus (HIV), and Epstein Barr Virus (EBV) serum were negative. Ultrasound showed splenomegaly. A Computed Tomography (CT) scan revealed a large mass in the spleen, determined to be neoplastic in nature [Table/Fig-1a]. Subsequently, a splenectomy was performed, and the specimen was sent for Histopathological Examination (H&E).

On gross examination, the spleen measured 15×8×6 cm, with the cut-section showing multiple small whitish nodules involving the majority of the splenic tissue [Table/Fig-1b]. Haematoxylin-Eosin stained sections revealed splenic tissue with the presence of a nodular mixed inflammatory infiltrate composed of small lymphocytes, plasma cells, with scattered admixed large abnormal cells having oval to occasionally multilobated nuclei, vesicular chromatin, prominent nucleoli, and abundant cytoplasm, consistent with Reed-Sternberg (RS) cells and mononuclear variants. There were also multiple Langhans giant cells present with the formation of granulomas [Table/Fig-1c,d]. Thus, based on morphology, HL was suspected, with a differential diagnosis of non-Hodgkin lymphomas such as diffuse large B-cell lymphoma, ALK positive lymphoma, peripheral T-cell lymphoma, and infectious aetiologies like tuberculosis and infectious mononucleosis also to be considered.

Results of immunohistochemical staining confirmed the presence of HRS cells: CD30 and CD15 were strongly positive, along with dim positivity of PAX5 [Table/Fig-1e,f]. Background cells showed expression of CD45, CD20, and CD4. To rule out other non-Hodgkin lymphomas, ALK, EMA vimentin, BCL6, BCL2, and ki67 staining were performed, which were negative on tumour cells. No acid-fast bacilli were detected in the acid-fast stain (Ziehl-Neelsen) smear. Therefore, the diagnosis of HL was confirmed. Postoperatively, a bone marrow biopsy revealed a reactive marrow. The patient




**[Table/Fig-1]:** a) Computed Tomography (CT) scan picture showed splenic enlargement with approx. size of 150×70×70 mm and have heterogeneously hypodense lesion with lobulated outline along with mild patchy post-contrast enhancementin spleen; b) Splenectomy specimen showing small nodule; c) H&E 100X-Normal splenic architecture in left with granuloma formation (Inset: AFB negative); d) H&E 400X-mixed inflammatory infiltrate composed of small lymphocytes, plasma cells with scattered admixed large abnormal cells having oval to occasionally multilobated nuclei, vesicular chromatin, prominent nucleoli and abundant cytoplasm-RS cells and mononuclear variants; e) CD15 Positive in RS cells (400X); f) CD30 Positive in RS cells (400X).

received chemotherapy, and there was no recurrence of lymphoma in other sites after being regularly followed-up for one year.

### Case 2

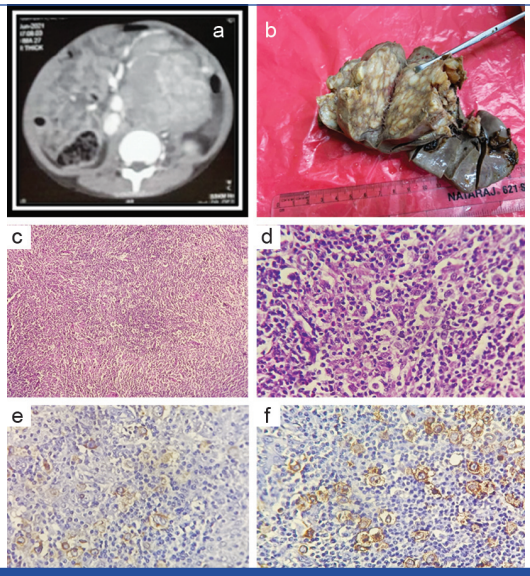
An 18-year-old male patient was admitted to the hospital with progressive abdominal swelling and a dragging sensation for six months. The patient also reported low-grade fever, significant weakness, decreased appetite, pallor, and weight loss. Routine blood investigations, biochemical, and microbiological parameters were conducted. The haemoglobin was 9 g/dL, and the Erythrocyte Sedimentation Rate (ESR) was 100 mm/hour using the Westergren method.

On examination, splenomegaly was found with no palpable lymph nodes. A CT scan revealed a large mass in the spleen, likely neoplastic in nature [Table/Fig-2a], following which a splenectomy was performed. On gross examination, the spleen measured 15×7×6 cm, with the cut section showing a whitish homogenous area involving almost the entire spleen [Table/Fig-2b].

Microscopically, the splenic architecture was replaced by a mixed inflammatory infiltrate composed of small lymphocytes, plasma cells, neutrophils, and numerous eosinophils, with scattered admixed large abnormal cells having oval to occasionally multilobate nuclei, vesicular chromatin, prominent nucleoli, and abundant cytoplasm, consistent with RS cells and mononuclear variants [Table/Fig-2c,d]. Primarily based on morphology, HL was diagnosed, although other non-Hodgkin lymphoma varieties like anaplastic large B-cell lymphoma, diffuse large B-cell lymphoma, T-cell lymphoma, and other infectious aetiologies like cytomegaloviral infection were also considered in the differential diagnosis.

These RS cells were positive for CD15 [Table/Fig-2e] and CD30 [Table/Fig-2f], and weakly positive for PAX5, while CD20, CD45, and CD4 were positive for background cells. Other markers like ALK, EMA, vimentin, BCL6, BCL2, and ki67 were also used to exclude other non-Hodgkin lymphomas. Therefore, the diagnosis of HL was confirmed, and the patient received a chemotherapy regimen. Bilateral bone marrow aspiration and biopsy showed a reactive marrow. The patient was regularly followed for six months for any recurrence of the neoplasm or any involvement of other sites.

The summary of both cases of the present case report are depicted in [Table/Fig-3].




**[Table/Fig-2]:** a) CT scan showed irregularly marginated heterogeneously hypodense lesion with lobulated outline and mild patchy post-contrast enhancement noted in spleen with increase in size approximately measuring 160 mm×80 mm×70 mm; b) Gross picture of splenectomy specimen; c,d) H&E 100X and 400X- Splenic architecture was replaced by mixed inflammatory infiltrate composed of small lymphocytes, plasma cells, neutrophils and numerous eosinophils, with scattered admixed large abnormal cells having oval to occasionally multilobate nuclei, vesicular chromatin, red nucleoli and abundant cytoplasm, consistent with RS cells and mononuclear variants; e) CD15 Positive in RS cells(400X); f) CD30 Positive in RS cells (400X).

## DISCUSSION

The PSL is a rare malignant tumour, accounting for only about 1% of all malignant neoplasms and representing about 1% of all malignant tumours. The incidence of splenic lymphoma has been gradually increasing in recent times, making it the most common primary splenic malignancy [1]. Hodgkin's disease in this location is particularly unusual. It is more prevalent in lymph nodes such as cervical, axillary, mediastinal, and para-aortic sites [2,3].

PSL has been defined as a neoplasm that involves only the spleen, with or without involving splenic hilar lymph nodes, while maintaining the architecture of other organ systems. B cell non-Hodgkin lymphoma is the predominant type of PSL. Secondary involvement of the spleen as part of systemic involvement of haematological neoplasms with the inclusion of abdominal lymph nodes is more prevalent than isolated splenic malignancy [4]. In the present case report, both cases presented with isolated splenomegaly without involvement of other organs or lymph nodes and there was no other haematological neoplasm.

By definition, PSL is described as a lymphoma involving only the spleen and hilar lymph nodes, but not other sites, and there will be no relapse within six months following splenectomy. PSL is a lymphoma with splenic involvement in which splenomegaly is the chief complaint. PSL can present with a variety of symptoms, including fever, night sweats, weight loss, weakness, and upper abdominal pain with a dragging sensation. Pancytopenia can also be a feature, with laboratory findings of elevated Erythrocyte Sedimentation Rate (ESR) and beta-2 microglobulin. The principal clinical finding is splenomegaly [5]. A painless, enlarging, palpable lymph node is a common mode of presentation. Mediastinal and neck node involvement are seen in about 60% of patients, followed by splenic, axillary, abdominal, hilar, or inguino-femoral region involvement [6].

In the present report both cases presented with fever, decreased appetite, abdominal swelling, and a dragging sensation due to enlargement of the spleen, initially revealed by clinical palpation. Routine complete blood count was unremarkable, but the ESR value was increased, and other diagnostic workups for fever, such as viral markers, urine culture, and blood culture, came back as negative. There were no other palpable lymph nodes, but mild pallor was noted. On imaging, splenomegaly was evident with the presence of a splenic mass. Following splenectomy, on microscopic examination, Hodgkin lymphoma was provisionally suspected, but other differentials such as anaplastic large cell lymphoma or other non-Hodgkin lymphomas, tuberculosis, or reactive changes were also considered before arriving at the final diagnosis.

| Cases | Age | Gender | Chief complains | Gross | Microscopy | IHC | Follow-up |
|---|---|---|---|---|---|---|---|
| Case 1 | 10 year | Male | Abdominal swelling for last one year with fever, decreased appetite and mild weight loss for one year | 15×8×6 cm with cut section showed multiple small whitish nodule | Nodular mixed inflammatory infiltrate admixed with RS cells and mononuclear variants and presence of Granuloma AFB-negative | CD15 and CD30 positive in RS cells. | Bone Marrow-Reactive Marrow Chemotherapy given and no recurrence for one year |
| Case 2 | 18 year | Male | Abdominal swelling with low-grade fever,decreased appetite,pallor and weight loss for six months | 15×7×6 cm with cut section whitish homogenous | Splenic architecture replaced by mixed inflammatory infiltrate composed of numerous eosinophils, with scattered RS cells | CD15 and CD30 positive in RS cells. | Bone marrow-reactive marrow chemotherapy given and no recurrence for six months |

**[Table/Fig-3]:** Summary of total two cases of primary splenic Hodgkin Lymphoma (HL).

The most common finding of PSL on diagnostic radiological observations is hypodense splenic lesions on contrast-enhanced CT scans [5]. The prognosis of patients with PSL can significantly improve with splenectomy [7]. In this case report, both patients were primarily treated by surgical removal of the spleen after the confirmation of a splenic mass on radiology. HL is a hematopoietic neoplasm diagnosed in individuals aged 20-30 years, characterised by the presence of RS cells in an inflammatory background. Patients present with fever, night sweats, and lymphadenopathy. Even in cases presenting in higher and advanced stages, it is highly curable with a combination of the ABVD (Adriamycin – Bleomycin – Vinblastine- Dacarbazine) chemotherapeutic regimen and radiation therapy [6].

HL is usually categorised into two subdivisions based on histomorphology and immunohistochemistry: classical HL (cHL) and Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL). Further, cHL is divided into nodular sclerosis, mixed cellularity, lymphocyte-rich, and lymphocyte-depleted types. The malignant HRS cells in all subtypes of cHL exhibit a characteristic immunophenotypic pattern of CD30 (with its membrane and/or 'dotlike' staining), CD15, PAX-5 positivity, and CD45 negativity. FDG-PET (18 fluorodeoxyglucose positron emission tomography) plays a key role in staging and prognosis. Although there are other work-ups like physical examination, chest X-rays, chest and abdominal CT scans, and bone marrow biopsy, which are helpful for Ann Arbor staging. Along with Hodgkin R-S cells, there is the presence of non-neoplastic T lymphocytes, plasma cells, macrophages, mast cells, and eosinophils. R-S cells arrange their survival and expansion through many cytokines and chemokines, which interact with the non-neoplastic surrounding microenvironment [8].

In presently discussed two cases, both patients aged under twenty and male underwent splenectomy. Clinically, fever, decreased appetite, and upper abdominal distension were the most significant complaints. On H&E of splenic sections, the presence of diagnostic RS cells and their mononuclear variant and lacunar variant were revealed. In the first case, it was the nodular sclerosis variety, and in the second case, there were plenty of eosinophils, lymphocytes, and plasma cells. Provisionally, HL was diagnosed, and immunohistochemical examination was done to confirm the diagnosis and exclude other mimickers of Hodgkin's disease, such as diffuse large B-cell lymphoma, anaplastic large cell lymphoma, or other non-HL. In both cases, RS cells showed CD15, strong CD30, and weak PAX-5 positivity. In the background, T cells and B cells were positive for CD4 and CD20, respectively, on IHC.

The presentation of this extremely uncommon lymphoma can vary from vague symptoms to grave complications such as hypersplenism and splenic rupture, along with ascites. A precise histopathological diagnosis combined with immunohistochemistry is of utmost importance [5,9]. In this case report there was no history of splenic rupture or ascites at the time of presentation.

HL can be associated with a granulomatous reaction characterised by the presence of histiocytes, Langhans giant cells, and necrosis. Consequently, it is sometimes misdiagnosed as an infectious granulomatous reaction. The recognition of Hodgkin and Reed/Sternberg (HRS) cells in microscopy, along with immunohistochemical expression of CD15 and CD30, allows confirmation of the diagnosis of HL. To exclude concomitant tuberculosis, an acid-fast stain must be performed on histological specimens [10].

In this case series, one case revealed plenty of Langhans giant cells with granuloma formation in the splenic region. However, AFB staining revealed no acid-fast organism, but immunohistochemistry of CD15 and CD30 confirmed the diagnosis of HL. Postoperatively, for staging, a bone marrow examination was performed to exclude involvement of the bone marrow by lymphoma cells, and it revealed a normocellular marrow uninvolved by any malignancy.

The treatment of HL has an excellent prognostic impact even on incurable disease. Stage-adapted treatment consisting of chemotherapy and/or radiotherapy as a first-line treatment results in cure rates of approximately 80% [11]. In advanced stage disease, it is highly treatable with combination chemotherapy, radiation, or combined modality treatment. Although the mainstay of therapy for over the last 30 years has been the same ABVD chemotherapeutic regimen [6]. Both patients received chemotherapy of the ABVD regimen after diagnosis, and they are being regularly followed-up to identify any treatment failure or history of relapse.

## CONCLUSION(S)

Primary splenic lymphoma, especially HL, is very rare in presentation. Sometimes, the coexistence of granuloma may lead to an inappropriate diagnosis. Therefore, careful H&E, along with immunohistochemistry and other ancillary investigations, are of utmost importance for a better prognosis and survival of patients with splenic HL.

## REFERENCES


[1] Pan X, Ren D, Li Y, Zhao J. The effect of surgery on primary splenic lymphoma: A study based on SEER database. Cancer Med. 2021;10(20):7060-70.
[2] Bal MS, Singh K, Mohanvir G, Nishit BV, Bodal VK. Primary splenic hodgkin's lymphoma: A case report. Research and Reviews: J. Med. Health Sci. 2014;4(3):38-41.
[3] Wright MF, Mason E. Classic Hodgkin lymphoma. PathologyOutlines.com website. https://www.pathologyoutlines.com/topic/lymphomanonBclassic.html. 2023.
[4] Siddiqui MMR, Rahman MM, Masum MHA, Khan AW, Haque ME, Saeed A. Primary Splenic Lymphoma (PSL): A rare presentation of lymphoma. Anwer Khan Mod Med Coll J. 2018;9(2):152-53.
[5] Healy NA, Conneely JB, Mahon S, O'Riardon C, McAnena OJ. Primary splenic lymphoma presenting with ascites.Rare Tumors. 2011;3(2):e25.
[6] Shanbhag S, Ambinder RF. Hodgkin lymphoma: A review and update on recent progress. CA Cancer J Clin. 2018;68(2):116-32.
[7] Pan X, Ren D, Li Y, Zhao J. The effect of surgery on primary splenic lymphoma: A study based on SEER database. Cancer Med. 2021;10(20):7060-70.
[8] Gobbi PG, Ferreri AJ, Ponzoni M, Levis A. Hodgkin lymphoma. Crit Rev Oncol Hematol. 2013;85(2):216-37.
[9] Ingle SB, Hinge Ingle CR. Primary splenic lymphoma: Current diagnostic trends. World J Clin Cases. 2016;4(12):385-89.
[10] Szumera-Ciećkiewic A, Prochorec-Sobieszek M, Lech-Marańda E. Hodgkin's lymphoma mimicking tuberculosis in cervical lymph nodes. Pol J Pathol. 2014;65(1):83-88.
[11] Momotow J, Borchmann S, Eichenauer DA, Engert A, Sasse S. Hodgkin Lymphoma-review on pathogenesis, diagnosis, current and future treatment approaches for adult patients. J Clin Med. 2021;10(5):1125.



**PARTICULARS OF CONTRIBUTORS:**
1. Senior Resident, Department of Pathology, IPGMER, Kolkata, West Bengal, India.
2. Associate Professor, Department of Pathology, IPGMER, Kolkata, West Bengal, India.
3. Assistant Professor, Department of Pathology, IPGMER, Kolkata, West Bengal, India.
4. Assistant Professor, Department of Pathology, IPGMER, Kolkata, West Bengal, India.
5. Professor and Head, Department of Pathology, IPGMER, Kolkata, West Bengal, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Madhumita Mondal,
Qr. No. C-12, 242, AJC Bose Road, Kolkata-700017, West Bengal, India.
E-mail: rgkarmadhumita@gmail.com



**PLAGIARISM CHECKING METHODS:** [Jain H et al.]
- Plagiarism X-checker: Dec 13, 2023
- Manual Googling: Jan 14, 2023
- iThenticate Software: Feb 07, 2024 (12%)

**ETYMOLOGY:** Author Origin

**EMENDATIONS:** 7

**AUTHOR DECLARATION:**
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Dec 10, 2022**
Date of Peer Review: **Jan 17, 2023**
Date of Acceptance: **Mar 17, 2023**
Date of Publishing: **Mar 01, 2024**