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Infiltration Pattern as a Diagnostic Clue in Hepatic Lymphoma: A Clinicopathological Study

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Research Article

Keywords: Hepatic lymphoma, Secondary, Diffuse, Cholestasis, Histopathology, Immunohistochemistry, Histological pattern

Posted Date: November 18th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10412826/v1

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Additional Declarations:
No competing interests reported.

Tables 1 to 4 are available in the Supplementary Files section.

Infiltration Pattern as a Diagnostic Clue in Hepatic Lymphoma: A Clinicopathological Study

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Running Title: Tertiary care experience on Hepatic lymphomas

Keywords: Hepatic lymphoma, Secondary, Diffuse, Cholestasis, Histopathology, Immunohistochemistry, Histological pattern

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Abstract word count: 325 words
Manuscript word count: 2456 words
Number of Tables: 4
Number of Figures: 2
References: 21

Ethics approval and consent to participate: NA
Consent for publication: Yes
Availability of data and materials: Data can be shared as per request
Competing Interests: None
Funding: None
Authors' contributions
Acknowledgements
Source of Funding: None.
Conflicts of Interest: The authors declare no conflicts of interest.
Data Availability: Data are available from the corresponding author upon reasonable request.
Declaration: I have not used AI assistance in the preparation of the manuscript

Abbreviations

PHL: Primary Hepatic Lymphoma

SHL: Secondary Hepatic Lymphoma

NHL: Non-Hodgkin Lymphoma

DLBCL: Diffuse Large B Cell Lymphoma

CLL/SLL: Chronic lymphocytic Lymphoma/Small cell Lymphocytic Lymphoma

ALCL: Anaplastic Large Cell Lymphoma

GGT: Gamma Glutamyl Transferase

ALP: Alkaline Phosphatase

IHC: Immunohistochemistry

Abstract

Background: Hepatic involvement in lymphomatous disease is frequently under-recognized. Infiltration can be either primary or secondary to systemic disease. Diverse morphological and biochemical presentations complicate the diagnosis.

Aim: To characterize the clinicopathological spectrum of hepatic lymphomas and to study the subtype-specific histomorphological patterns of hepatic lymphoma on liver biopsy.

Methods: Liver biopsy specimens diagnosed as lymphomatous infiltration between 2011 and 2025 were analyzed. Clinical and biochemical data were collected. Histopathological sections were reviewed for the pattern of lymphomatous infiltration. **Results:** The study included 65 cases, comprising 8 cases of primary hepatic lymphoma (PHL) and 57 cases of secondary hepatic lymphoma. Males were predominant (n=56; 86.2%), and the mean age at presentation was 49.5±20.0 years. Among all, Diffuse Large B-Cell Lymphoma (DLBCL) is the most common (n=40/65; 61.5%). On histomorphological analysis, the most prevalent infiltration pattern is diffuse (52.3%), followed by portal (18.5%) and nodular (12.3%). In DLBCL, diffuse is the dominant subtype–pattern pairing (26/40); aggressive B-cell-like Burkitt's lymphoma (4/4; 100%) and lymphoblastic lymphomas (2/2; 100%) also show an exclusively diffuse pattern. Hodgkin's lymphoma (2/2;100%), CLL/SLL (1/1; 100%), and T-cell-rich B-cell lymphomas (2/2; 100%) are exclusively portal. Peripheral T-cell lymphoma (2/2; 100%), hepatosplenic lymphoma (1/1; 100%), Anaplastic large cell lymphoma (3/4; 75%), and T-cell NHL are the T-cell lymphomas with an exclusive sinusoidal pattern. Mantle cell lymphoma shows a nodular pattern (1/1; 100%). Six cases (9.2%), primarily DLBCL with nodular or portal involvement, exhibited a cholestatic profile with markedly elevated GGT levels.

Conclusion:

Hepatic lymphomas have different patterns of infiltration and are subtype-specific. Primary hepatic lymphomas are diffuse and parenchymal-replacing, whereas secondary hepatic lymphomas are seeded in a portal and sinusoidal pattern. A sinusoidal pattern should prompt workup for a T-cell or NK-cell neoplasm. Patients presented with cholestatic presentation, which reflects nodular or portal bile duct compression and is a common mimicker of biliary or pancreatic disease. A low threshold for immunohistochemistry and retention of primary hepatic lymphoma in the differential are key to accurate diagnosis.

Keywords: Lymphoma, Infiltration, Pattern, Biopsy, Immunohistochemistry, Cholestatic.

Introduction

Hepatic lymphoma spans a clinicopathological spectrum ranging from primary hepatic lymphoma (PHL) to secondary hepatic infiltration as part of systemic disease.

Primary hepatic lymphoma (PHL) accounts for 0.016% of all Non-Hodgkin lymphomas and is defined as lymphoma localized to the liver without evidence of extrahepatic disease at presentation. The liver is the second most common extranodal site involved in non-Hodgkin lymphoma (NHL), with autopsy series reporting hepatic infiltration in up to 50% of cases. [1]

Hepatic lymphomas are commonly B-cell-derived, with diffuse large B-cell lymphoma (DLBCL) as the predominant subtype. [2, 3]

Clinical presentations are non-specific and may include abdominal pain with constitutional symptoms such as fever, vomiting, and weight loss. Hepatomegaly, splenomegaly, and lymphadenopathy may be present to varying degrees. Patients may have abnormal liver function tests, and a subset may show a cholestatic biochemical profile characterized by disproportionate elevations of alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT), which can mimic primary biliary disorders or biliary obstruction. This pattern remains poorly characterized in the existing literature. [4]

On histopathological examination, the principal infiltration patterns of hepatic lymphoma include diffuse, portal, sinusoidal, and nodular, or mixed portal and sinusoidal. Each pattern has distinct morphological correlates and differential diagnostic considerations. [4]

Given the paucity of series from the Indian subcontinent, this study was undertaken to document the clinicopathological, biochemical, and histomorphological profile of hepatic

lymphomas over 15 years at a tertiary referral center in northern India, with specific attention to the subgroup presenting with a cholestatic biochemical phenotype.

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Material and methods

1. Study design and patient selection

This retrospective analysis was conducted from Jan 2011 to Dec 2025 at the Department of Pathology, SGPGIMS, Lucknow, a referral tertiary care hospital in northern India. All Clinical and laboratory records were obtained from the hospital information system. Sixty-eight cases of hepatic lymphoma were identified from the pathology department archives out of a total of 5,623 liver biopsies. Cases were further sorted according to the inclusion criterion of at least 6 portal tracts. Patients with inadequate biopsy samples (fewer than six portal tracts) or without immunohistochemistry were excluded. Sixty-five cases met the inclusion criteria and were included in the final analysis.

Among them, 8 cases met the criteria for PHL, defined as a liver-confined lymphoma at presentation with no or minimal involvement of the spleen, lymph nodes, peripheral blood, bone marrow, or other lymphoid tissues. The other 57 cases involved extrahepatic tissue(s) in addition to the liver and were grouped. All 65 liver biopsy specimens were reviewed by the hepatopathologists (NN) at SGPGIMS. Clinical information for the patients, including age, sex, presenting symptoms, and laboratory testing, was obtained through computerized database searches. Liver biopsy cases with inadequate tissue, missing clinical records, or insufficient immunohistochemical data were excluded.

2. Clinical and biochemical data

A detailed clinical evaluation and laboratory investigations were obtained from the Hospital Information System, including presenting complaints, hemogram, liver function tests, coagulation parameters, and viral markers. All parameters were recorded at the time of performing the liver biopsy.

The cholestatic subgroup of patients has markedly elevated GGT levels (greater than 400 U/L, approximately 6-7 times the upper limit of normal). Their clinical, biochemical, and histomorphological features were analyzed separately.

3. Histopathological evaluation

Liver biopsies comprising 6 or more portal tracts were considered adequate and included in the study. Tissue sections stained with hematoxylin and eosin (H&E), Masson's trichrome (MT), orcein, and Gomori's reticulin stain were reviewed for histological features, including diagnosis, infiltration pattern, duct damage, and sinusoidal dilatation. Lymphomatous infiltration was classified as diffuse, portal, sinusoidal, nodular, or mixed (portal + sinusoidal) according to established criteria. [5, 6] **Figure 1** shows the pictorial diagram and histopathology of different patterns of hepatic lymphomatous infiltration.

Immunohistochemical staining was performed as part of the diagnostic protocol on a Ventana Biosystems instrument. The immunohistochemistry (IHC) panel included CD20, CD3, CD5, CD10, CD23, CD30, CD56, DCL2, BCL6, MUM1, Ki67, ALK1, and MYC, and was applied as appropriate. Classification followed the 2016 and 2022 WHO guidelines. [7, 8] Cases confined to the liver at presentation were classified as primary hepatic lymphoma. In contrast, those with involvement as part of systemic disease identified on clinical staging investigations, including contrast-enhanced computed tomography, 18F-FDG PET-CT, and bone marrow examination, were defined as secondary hepatic lymphoma.

4. Statistical analysis

SPSS software (SPSS, Chicago, IL) was used to perform statistical analysis. Quantitative variables are indicated as the mean ± standard deviation. Categorical variables are represented as frequencies (%). The independent-samples t-test is used for normally distributed variables, and the Mann–Whitney U test for non-normal data. Fisher's exact test was used to compare categorical variables. A p-value of <0.05 was statistically significant.

Results

1. Demographics and clinical features

The study comprises 65 histologically confirmed cases of hepatic lymphoma. Cases fall into Primary Hepatic Lymphoma (PHL, n=8; 12.3%) and Secondary Hepatic Lymphoma (SHL, n=57; 87.7%) based on the absence or presence of extrahepatic/systemic disease at presentation. Age ranged from 3 to 83 years, with a median of 53 years (mean: 49.5 ± 20.0), and a male-to-female ratio of 6.2:1 (56 males, 9 females). Age was comparable between PHL and SHL (mean 49.9 ± 9.9 vs 49.5 ± 21.1 years).

Most patients presented with right abdominal pain (60%). Few patients presented with weight loss (30%) and fever or chills (10%). Primary hepatic lymphomas exhibited higher rates of hepatomegaly (87.5% versus 36.8%) and splenomegaly (75% versus 40.4%).

Lymphadenopathy was common in both groups (75% versus 63.2%). Details are given in **Table 1**

2. Biochemical parameters

Mean hemoglobin was 10.2±2.4 g/dL (median 10 g/dL), indicating anemia in most of the hepatic lymphoma cases along with a deranged liver function test. On comparative analysis of PHL and SHL, serum albumin was 2.83±0.8 g/dL (median 2.8 g/dL), consistent with hepatic dysfunction, and was significantly lower in primary hepatic lymphoma (median 2.05 g/dL) compared to secondary hepatic lymphoma (median 2.90 g/dL), p=0.033. No other laboratory parameters, including hemoglobin, total leucocyte count, platelet count, bilirubin (total/direct), transaminases, alkaline phosphatase, GGT, or total protein, showed a statistically significant difference between the two groups. Laboratory parameters are given in **Table 2**

3. Lymphoma subtypes and histological infiltration patterns

3.1 Histological diagnosis

All lymphoma diagnoses were established based on histological and immunohistochemical findings in liver tissue obtained by needle biopsy. DLBCL dominated (n=40, 61.5%), followed by T-cell NHL (n=6; 9.2%), Burkitt lymphoma (n=4; 6.2%) and ALCL (n=4; 6.2%). Other subtypes were lymphoblastic lymphoma (n=2; 3.1%), Hodgkin lymphoma (n=2; 3.1%), T-cell-rich B-cell lymphoma (n=2; 3.1%), and peripheral T-cell lymphoma (n=2; 3.1%). Hepatosplenic lymphoma, mantle cell lymphoma, and small cell lymphocytic lymphoma comprised a single case each (n=1; 1.5%).

DLBCL was the dominant subtype, accounting for 87.5% of PHL and 57.9% of SHL cases. Although DLBCL was more frequent in PHL, the difference between DLBCL and the pooled non-DLBCL subtypes was statistically non-significant (Fisher's exact test, p=0.139). This may reflect the limited number of cases of primary hepatic lymphoma.

3.2 Histological pattern of infiltration

The most common histological pattern of infiltration was diffuse infiltration of atypical lymphoid cells into hepatic parenchyma and portal tracts (n=34; 52.3%). Portal infiltration was the next most common pattern (n=12; 18.5%), followed by the nodular pattern (n=8;

12.3%). Six cases demonstrated dilated sinusoids with atypical lymphoid cells (n=6; 9.2%). A mixed pattern involving portal tracts and sinusoids was observed in five cases (7.7%; n=5). A diffuse pattern of infiltration predominated in PHL (7/8; 87.5%) compared to SHL (27/57; 47.4%). Portal- and sinusoidal-restricted infiltration was observed exclusively in the secondary hepatic lymphoma group, consistent with the pathophysiology of systemic lymphoma seeding the liver via portal or sinusoidal routes. The histological architectural pattern of hepatic infiltration is given in **Table 3.**

Distinct subtype-specific associations were observed. DLBCL displayed all infiltration patterns but was predominantly diffuse (26/40; 65.0%); the remainder showed portal, nodular, or mixed patterns. Burkitt and lymphoblastic lymphomas were exclusively diffuse (4/4 and 2/2, respectively). Classical Hodgkin lymphoma, T-cell-rich B-cell lymphoma, and chronic lymphocytic lymphoma or small lymphocytic lymphoma (CLL/SLL) were confined to a portal pattern. A sinusoidal pattern was restricted to T-lineage and NK-cell neoplasms — peripheral T-cell lymphoma (2/2), hepatosplenic T-cell lymphoma (1/1), ALCL and T-cell NHL. In contrast, mantle cell lymphoma showed a nodular pattern. **Figure 2** shows histopathology and immunohistochemistry of various hepatic lymphomas.

4. *Cholestatic presentation: cases with markedly elevated GGT*

Six cases in the study cohort had markedly elevated GGT levels, ranging from 409 to 1210 U/L (mean 824.5±371.7 U/L). Liver biopsy showed nodular and portal infiltrations in four of six cases (66.7%). Details were given in T**able 4.**

Two cases presented with elevated GGT; however, total bilirubin levels were normal or near-normal. The remaining two cases show raised GGT and elevated total bilirubin levels. All four cases on liver biopsy exhibited nodular infiltration, suggesting bile duct compression by lymphoma as the mechanism for cholestatic presentation.

Discussion

Hepatic lymphoma presents significant diagnostic challenges due to its wide morphological and biochemical spectrum. The male predominance observed in this cohort (male-to-female ratio of 6.2:1) exceeds that reported in most Western series, where the ratio is 1.5:1 to 2:[9, 10]. This skew may reflect referral bias of the center and could be due to a high prevalence of chronic hepatitis B (HBV) infection in males in the Indian subcontinent. [3] The broad age distribution (3–83 years) aligns with published reports and reflects the diverse biological subtypes encompassed within this diagnostic category.

The proportion of PHL in our study (n=8; 12.3%) is notably higher compared to the conventionally cited figure of <1% of all extranodal lymphomas. This could be reflecting a highly selected biopsy cohort at a tertiary care referral center.

The most common chief complaint among patients was right upper quadrant pain (60%), consistent with the reported frequency of 39-70% across the published literature. [11] Primary hepatic lymphomas exhibited higher rates of hepatomegaly (87.5% versus 36.8%) and splenomegaly (75% versus 40.4%) than secondary hepatic lymphomas. This is supported by the observations that hepatomegaly predominated in PHL and reflects a dominant hepatic parenchymal involvement and congestive portal hypertension. [9]

Hematological and biochemical parameters are comparable between the two groups, except serum albumin, which was significantly lower in primary hepatic lymphoma (median 2.05 g/dL versus 2.90 g/dL; p=0.033). This again reflects more extensive hepatic parenchymal replacement and synthetic dysfunction in PHL, where tumor infiltration is typically confined to the liver and predominates.[12]

Diffuse large B-cell lymphoma was the dominant subtype across both groups, accounting for 61.5% of all cases (7/8 PHL and 33/57 SHL). In a systematic review, Lei et al. reported DLBCL as the dominant subtype in PHL, and Bronowicki et al. similarly reported DLBCL as the most frequent subtype of primary and secondary hepatic lymphoma. [2, 13, 14] The liver has a rich population of sinusoidal endothelial cells and Kupffer cells, which may support B cell homing and immune evasion. This may explain the predominance of B-cell NHL in hepatic lymphoma. [15]

The spectrum of non-DLBCL subtypes in this series, including Burkitt lymphoma, ALCL, T-cell NHL, peripheral T-cell lymphoma, and hepatosplenic lymphoma, collectively illustrates the morphological range that can be recognized and characterized through liver biopsies. The single case of hepatosplenic T-cell lymphoma (HSTL) in this cohort required a high index of suspicion on hematoxylin and eosin sections, followed by immunohistochemical confirmation. Caution is warranted whenever sinusoidal lymphoid infiltration is encountered without lobular architectural distortion. [7]

Most notably, diffuse infiltration was the predominant pattern of PHL in this series (7/8; 87.5%), compared with SHL (27/57; 47.4%), consistent with the findings by Avlonitis and Linos et al. [14]. This finding suggests the biological behavior of PHL, in which the lymphoma arises within the hepatic parenchyma and expands by replacing hepatocytes in a sheet-like fashion. In contrast, the portal pattern, sinusoidal infiltration pattern, and mixed sinusoidal and portal infiltration pattern are exclusive to secondary lymphomas in our study,

suggesting hematogenous or lymphatic seeding of the liver by systemic lymphomas, thereby involving the portal and sinusoidal areas. In our cohort, sinusoidal infiltration was observed in T-cell NHL and hepatosplenic lymphoma, consistent with the well-established association of intrasinusoidal growth with T-lineage and NK-cell neoplasms documented in the literature. [7, 13]

The cholestatic subgroup (GGT > 400 U/L; N = 6; 9.2%) represents the clinically instructive finding of this study. Cholestasis due to lymphomatous infiltration may result from bile duct compression, bile ductular reaction, or bile duct loss. In our series, the three cases with high GGT values displayed a nodular histological pattern, suggesting focal bile duct compression. Hubscher and Abdalian et al., in their studies, described nodular and periportal infiltration as likely causes of a cholestatic picture. [4, 16] Three cases in the study show high GGT (1210 U/L, 679 U/L, 409 U/L); however, the bilirubin is near-normal (0.8 mg/dL, 1.3 mg/dL, 1.0 mg/dL). This finding suggests the well-described biochemical dissociation observed in infiltrative liver disease, wherein enzyme induction (ALP/GGT) in the periportal biliary epithelium precedes bilirubin excretion, the extent of which depends on the degree of obstruction. [17, 18] Three cases with markedly elevated GGT (415, 1048 U/L, 1186 U/L) showed markedly elevated bilirubin (T Bilirubin 12.0 mg/dL, 26.3 mg/dL, and 22 mg/dL) and presented with clinical jaundice and represent true biliary obstruction. The nodular growth pattern and portal restrictive pattern produce mass-forming, expansile lesions that compress the biliary radicles, resulting in hyperbilirubinemia. [19, 20] These cases were initially prompted to undergo investigations for biliary or pancreatic disease before liver biopsy to establish the diagnosis. Several case reports have described lymphoma-associated cholestasis that mimics primary sclerosing cholangitis or cholangiocarcinoma. A practical implication of the results is that routine GGT measurement in the liver biopsy workup for lymphoma is warranted. Disproportionate elevation of GGT relative to transaminases prompts consideration of a nodular or portal infiltration pattern and directs the pathologist's attention to duct compression, damage, and duct loss. Dargent et al. conducted a study and advocated quantifying GGT in hepatic lymphomas as a marker of biliary involvement. [21] The retrospective study design and absence of follow-up data are limitations. Nevertheless, this study represents one of the largest single-center series of biopsy-diagnosed hepatic lymphomas from the Indian subcontinent. It provides a detailed clinicopathological characterization, including analysis of a cholestatic subgroup.

Conclusion

This series establishes diffuse large B-cell lymphoma as the predominant hepatic lymphoma subtype and shows that the architectural pattern of infiltration is subtype-specific rather than random. Primary disease produces a diffuse, parenchyma-replacing pattern, whereas secondary infiltration seeds the liver in portal and sinusoidal areas. A sinusoidal pattern should raise suspicion of a T-cell or NK-cell neoplasm and needs prompt confirmatory immunohistochemistry. Cholestatic subgroup driven by nodular or portal bile duct compression can mimic biliary or pancreatic disease and is flagged by a disproportionate rise in GGT. Recognizing these subtype–infiltration pattern associations, keeping a low threshold for immunohistochemistry, and retaining primary hepatic lymphoma in the differential are key to timely, accurate diagnosis.

References

1. El-Fattah, M.A., Non-Hodgkin Lymphoma of the Liver: A US Population-based Analysis. J Clin Transl Hepatol, 2017. **5**(2): p. 83-91.
2. Lei, K.I., Primary non-Hodgkin's lymphoma of the liver. Leuk Lymphoma, 1998. **29**(3-4): p. 293-9.
3. Salmon, J.S., et al., Non-Hodgkin's lymphoma involving the liver: clinical and therapeutic considerations. Clin Lymphoma Myeloma, 2006. **6**(4): p. 273-80.
4. Abdalian, R. and E.J. Heathcote, Sclerosing cholangitis: a focus on secondary causes. Hepatology, 2006. **44**(5): p. 1063-74.
5. Loddenkemper, C., et al., Frequency and diagnostic patterns of lymphomas in liver biopsies with respect to the WHO classification. Virchows Arch, 2007. **450**(5): p. 493-502.
6. Jaffe, E.S. and S. Pittaluga, Aggressive B-cell lymphomas: a review of new and old entities in the WHO classification. Hematology Am Soc Hematol Educ Program, 2011. **2011**: p. 506-14.
7. Alaggio, R., et al., The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia, 2022. **36**(7): p. 1720-1748.
8. Swerdlow, S.H., et al., The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood, 2016. **127**(20): p. 2375-90.
9. Noronha, V., et al., Primary non-Hodgkin's lymphoma of the liver. Crit Rev Oncol Hematol, 2005. **53**(3): p. 199-207.
10. Ugurluer, G., et al., Primary Hepatic Lymphoma: A Retrospective, Multicenter Rare Cancer Network Study. Rare Tumors, 2016. **8**(3): p. 6502.
11. Ippolito, D., et al., Diagnostic approach in hepatic lymphoma: radiological imaging findings and literature review. J Cancer Res Clin Oncol, 2020. **146**(6): p. 1545-1558.
12. Mastoraki, A., et al., Primary hepatic lymphoma: dilemmas in diagnostic approach and therapeutic management. Indian J Hematol Blood Transfus, 2014. **30**(3): p. 150-4.
13. Bronowicki, J.P., et al., Primary lymphoma of the liver: clinical-pathological features and relationship with HCV infection in French patients. Hepatology, 2003. **37**(4): p. 781-7.

14. Avlonitis, V.S. and D. Linos, Primary hepatic lymphoma: a review. Eur J Surg, 1999. **165**(8): p. 725-9.
15. Shetty, S., P.F. Lalor, and D.H. Adams, Liver sinusoidal endothelial cells - gatekeepers of hepatic immunity. Nat Rev Gastroenterol Hepatol, 2018. **15**(9): p. 555-567.
16. Hubscher, S.G., M.A. Lumley, and E. Elias, Vanishing bile duct syndrome: a possible mechanism for intrahepatic cholestasis in Hodgkin's lymphoma. Hepatology, 1993. **17**(1): p. 70-7.
17. Pratt, D.S. and M.M. Kaplan, Evaluation of abnormal liver-enzyme results in asymptomatic patients. N Engl J Med, 2000. **342**(17): p. 1266-71.
18. Sharma, U., D. Pal, and R. Prasad, Alkaline phosphatase: an overview. Indian J Clin Biochem, 2014. **29**(3): p. 269-78.
19. Odemis, B., et al., Biliary tract obstruction secondary to malignant lymphoma: experience at a referral center. Dig Dis Sci, 2007. **52**(9): p. 2323-32.
20. Chaudhari, D., et al., Obstructive jaundice as an initial manifestation of non-hodgkin lymphoma: treatment dilemma and high mortality. Case Rep Med, 2013. **2013**: p. 259642.
21. Dargent, J.L. and C. De Wolf-Peeters, Liver involvement by lymphoma: identification of a distinctive pattern of infiltration related to T-cell/histiocyte-rich B-cell lymphoma. Ann Diagn Pathol, 1998. **2**(6): p. 363-9.

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Acknowledgements: None

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(III) Collection and assembly of data: Neha Nigam, Kavita Tiwari, Nirbhay Kumar, Amit Rastogi
(IV) Data analysis and interpretation: Neha Nigam, Chhagan Bihari
(V) Manuscript writing: Neha Nigam, Nandita Chaudhary
(VII) Final approval of manuscript: All authors

Figure 1: Histomorphological patterns of hepatic lymphomatous infiltration with corresponding schematic diagrams. The upper row (A–F) shows H&E-stained liver biopsy photomicrographs of the different patterns, and the lower row shows the matched schematic of each. The key denotes the portal tract, bile duct, hepatic artery, portal vein, hepatocytic cords, and atypical lymphoid cells. **(A)** Normal architecture, no atypical infiltrate. **(B)** Diffuse: sheets replacing parenchyma and portal tracts. **(C)** Portal: confined to the portal tract. **(D)** Nodular: discrete aggregate. **(E)** Sinusoidal: cells within the sinusoids. **(F)** Mixed portal and sinusoidal.

Figure 2 (A–Y): Hepatic lymphoma subtypes with immunohistochemistry. Diffuse Large B-Cell Lymphoma, non-GCB type: diffuse infiltration of large atypical lymphoid cells with increased mitoses (A, B; H&E, ×200 and ×400). Immunohistochemistry shows

the tumour cells to be positive for CD20 (C; IHC, ×200), with background reactive CD3-positive T cells (D; IHC, ×100); CD10 is negative and MUM1 is positive (E, F; IHC, ×100). Peripheral T-Cell Lymphoma: diffuse infiltration of atypical, angulated lymphoid cells (G, H; H&E, ×100 and ×400) that are positive for CD3 (I; IHC, ×100) and negative for CD20 (J; IHC, ×100). T-Cell-Rich B-Cell Lymphoma: large atypical lymphoid cells (arrowheads) in a background of reactive lymphoid cells (K, L; H&E, ×100 and ×400); the large atypical cells are positive for CD20 and PAX5 (M, N; IHC, ×400 and ×200), CD3 highlights the background reactive T cells (O; IHC, ×100), and CD30 is negative (P; IHC, ×200). Hepatosplenic T-Cell Lymphoma: atypical lymphoid cells within dilated sinusoids (Q; H&E, ×400). Hodgkin Lymphoma (mixed cellularity): liver biopsy shows portal lymphomatous infiltration (T; H&E, ×100), with Reed–Sternberg cells (U; H&E, ×400); the atypical cells are positive for CD15 and CD30, negative for CD20, with CD3 highlighting the background reactive T cells (V–Y; IHC, ×200 and ×100).

Figures

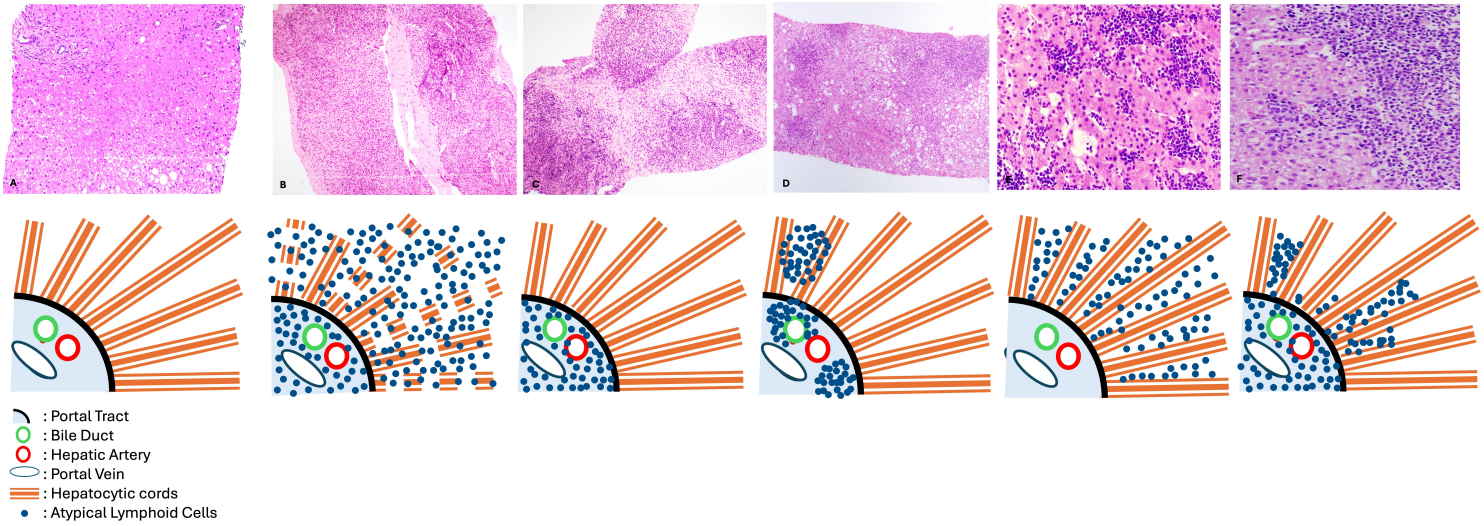


Figure 1

Histomorphological patterns of hepatic lymphomatous infiltration with corresponding schematic diagrams. The upper row (A–F) shows H&E-stained liver biopsy photomicrographs of the different patterns, and the lower row shows the matched schematic of each. The key denotes the portal tract, bile duct, hepatic artery, portal vein, hepatocytic cords, and atypical lymphoid cells. **(A)** Normal architecture, no atypical infiltrate. **(B)** Diffuse: sheets replacing parenchyma and portal tracts. **(C)** Portal: confined to the portal tract. **(D)** Nodular: discrete aggregate. **(E)** Sinusoidal: cells within the sinusoids. **(F)** Mixed portal and sinusoidal.

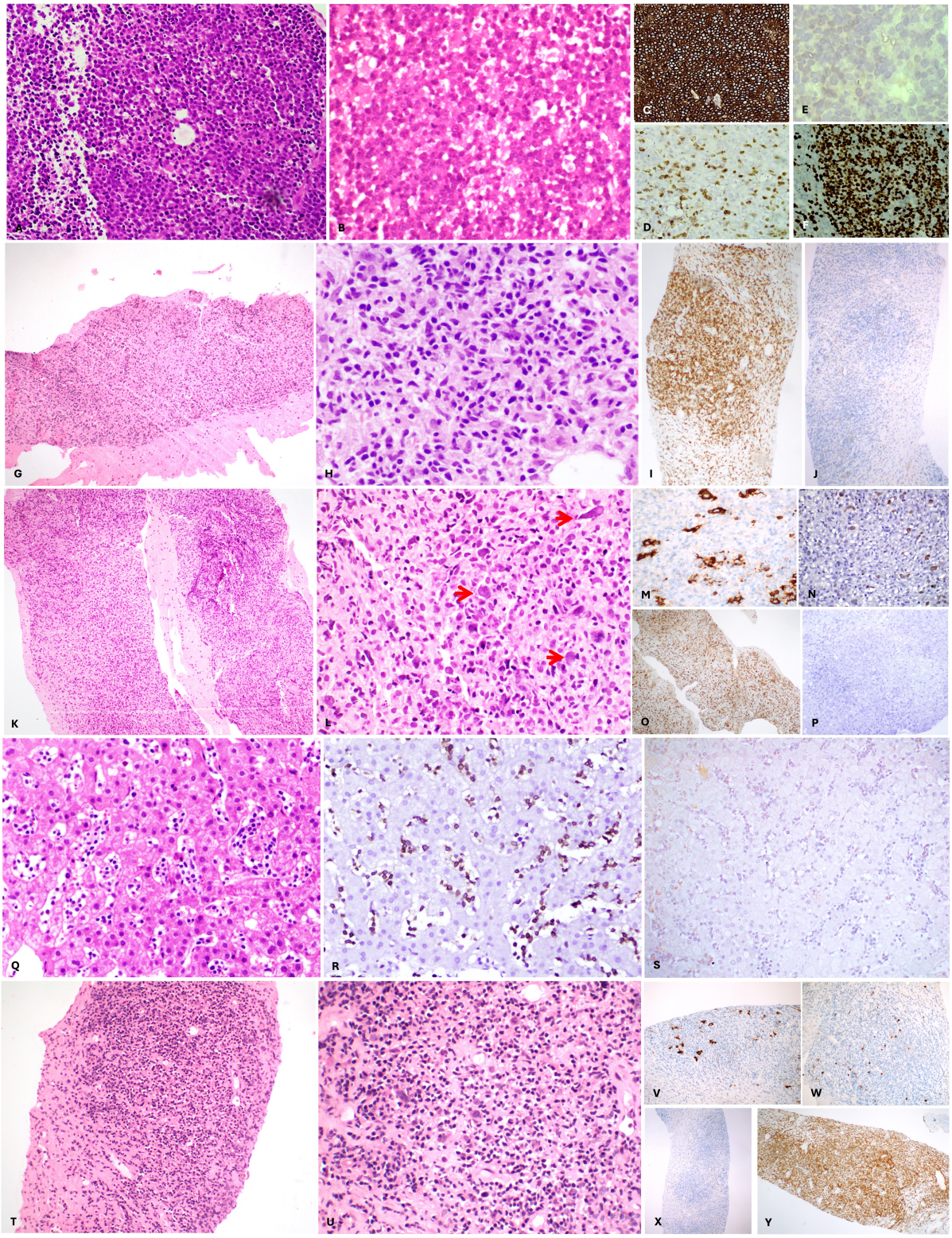


Figure 2

(A–Y): Hepatic lymphoma subtypes with immunohistochemistry. Diffuse Large B-Cell Lymphoma, non-GCB type: diffuse infiltration of large atypical lymphoid cells with increased mitoses (A, B; H&E, ×200 and ×400). Immunohistochemistry shows the tumour cells to be positive for CD20 (C; IHC, ×200), with background reactive CD3-positive T cells (D; IHC, ×100); CD10 is negative and MUM1 is positive (E, F; IHC, ×100). Peripheral T-Cell Lymphoma: diffuse infiltration of atypical, angulated lymphoid cells (G, H;

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