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Confronting the Uncommon: Histiocytic Sarcoma of the Ileum and T-Cell Lymphoma of the Gallbladder - A Rare Case Series Illuminating Diagnostic and Therapeutic Challenges

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Abstract

Background: Gastrointestinal lymphomas, though uncommon, represent a significant subset of extranodal non-Hodgkin lymphomas. This article explores two rare types of gastrointestinal lymphomas: malignant T-cell lymphoma of the gallbladder and histiocytic sarcoma of the ileum.

Case 1: Malignant T-cell Lymphoma of the Gallbladder: A 54-year-old male presented with acute abdominal pain and pleural effusion, clinically diagnosed with acute cholecystitis. Pathological examination of the gallbladder revealed mucosal ulceration with diffuse infiltration by atypical lymphoid cells. Immunohistochemistry showed positive staining for TdT, BCL-2, and CD3. The diagnosis was malignant T-cell lymphoma-NOS (Not Otherwise Specified).

Case 2: Histiocytic Sarcoma of the Ileum: A 26-year-old male with a history of chronic diarrhea, initially diagnosed with inflammatory bowel disease (IBD), developed an obstructive ileal mass. Histological analysis of the ileum showed infiltration by atypical lymphoid cells with nuclear pleomorphism and multinucleated cells. Immunohistochemistry was strongly positive for CD68. The diagnosis was histiocytic sarcoma of the ileum.

Discussion: The gastrointestinal tract, particularly the small intestine, is a common site for extra nodal lymphomas, though rare forms such as gallbladder T-cell lymphoma and ileal histiocytic sarcoma present significant diagnostic challenges. Accurate diagnosis relies on comprehensive histopathological and immunohistochemical analysis. Treatment typically involves a combination of surgical resection, chemotherapy, and radiation, with histiocytic sarcoma often associated with a poor prognosis due to its aggressive nature.

Conclusion: These cases highlight the importance of thorough diagnostic evaluation in rare gastrointestinal lymphomas. The complexity of these conditions necessitates careful histological and immunohistochemical assessment to guide effective treatment strategies and improve patient outcomes.

Keywords: Histiocytic Sarcoma; Lymphoma; Chemotherapy

Abbreviations

IBD: Inflammatory Bowel Disease; IHC: Immuno histochemistry; GI: Gastro Intestinal; MALT: Mucosa-Associated Lymphoid Tissue; EATL: Enteropathy-Associated T-Cell Lymphomas; NHL: Non-Hodgkin's Lymphomas; DLBL: Diffuse Large B-Cell Lymphoma; MCL: Mantle Cell Lymphoma; FL: Follicular Lymphoma; HS: Histiocytic Sarcoma.

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Introduction

Gastrointestinal lymphomas comprise a group of distinct clinic pathological entities of B or T cell type, with primary gall bladder involvement of T-cell lymphoma and histiocytic sarcoma of small intestine being extremely uncommon. The Gastrointestinal tract is the common site of extra nodal non-Hodgkin lymphoma accounting for 30-40% of all extra nodal lymphomas. Here, we explore histiocytic sarcoma of the ileum and T- cell lymphoma of gall bladder.

Case Presentation

Case 1: Malignant T-cell Lymphoma of the Gallbladder

Patient: A 54-year-old male with acute abdominal pain, diagnosed with acute cholecystitis, and noted to have pleural effusion.

Clinical Presentation: The patient presented with symptoms of acute cholecystitis and was found to have pleural effusion.

Pathological Findings:

- **Gall Bladder Specimen:** The external surface was smooth, and the cut surface appeared bile-stained, firm, and grey-white. The thickness of the gall bladder wall ranged from 0.3 to 0.4 cm, without any presence of stones.
- **Histopathology:** Examination of the gall bladder wall revealed mucosal ulceration. A diffuse infiltration of small to medium-sized atypical lymphoid cells having nuclear membrane irregularity and scant cytoplasm. The infiltration extended into the muscular layer, reaching close to the serosa with a clearance of 0.1 cm (Figures 1 & 2). Pleural effusion for cytology showed atypical cells.

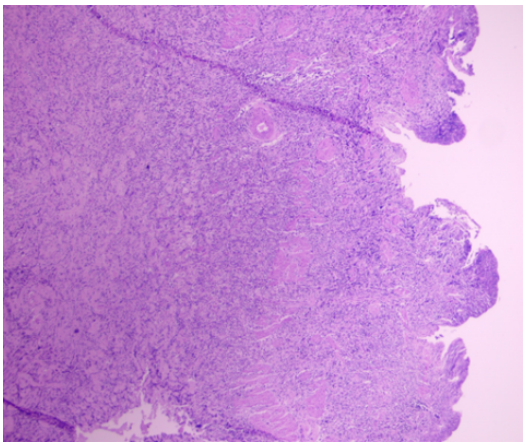

Figure 1: H&E (10x) Sections show wall of gall bladder with diffuse infiltration by atypical lymphoid cells.

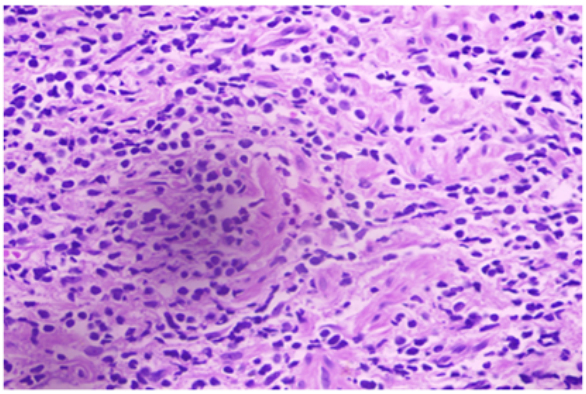

Figure 2: H&E (40x) Sections show wall of gall bladder with diffuse infiltration by atypical lymphoid cells.

- **Immunohistochemistry (IHC):** Positive staining was observed for TdT, Bcl2, CD3, and a high proliferative index. The remaining antibodies from the lymphoma panel yielded negative results (Figures 3 & 4).

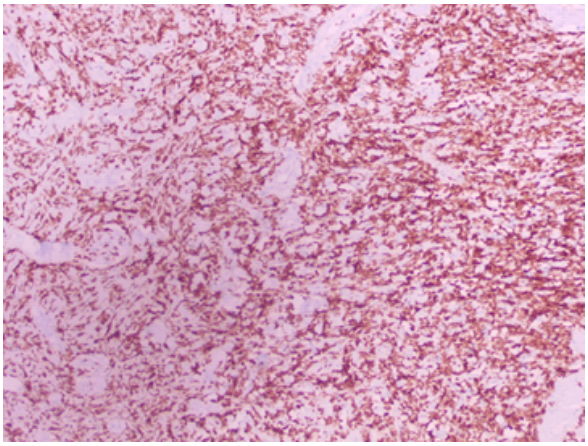

Figure 3: (IHC) Sections show diffuse positivity for CD3.

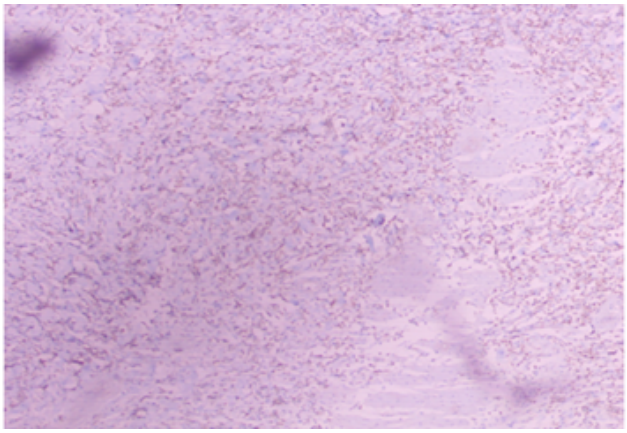

Figure 4: (IHC) Sections show diffuse positivity for Tdt.

Diagnosis: The diagnosis established was Malignant T-cell lymphoma-NOS (Not Otherwise Specified).

Case 2: Histiocytic Sarcoma of the Ileum

Patient: A 26-year-old male with a two-year history of chronic diarrhoea, initially diagnosed as inflammatory bowel disease (IBD).

Clinical Presentation: The patient's condition evolved with an acute abdomen due to an obstructive ileal mass.

Pathological Findings:

- **Ileal Segment Specimen:** The specimen showed a partially cut-opened segment with a dilated part. A circumferential mass was present on the ant mesenteric border.
- **Histopathology:** The ileal mucosa is infiltrated by atypical lymphoid cells arranged in diffuse, large sheets. These cells displayed nuclear pleomorphism, coarse chromatin, prominent nucleoli, and moderate cytoplasm. Large multinucleated pleomorphic cells were seen. There are areas of apoptosis and frequent mitotic figures. Foci of necrosis are seen. The tumour infiltrated the mucosal layer and was situated 0.1 cm away from the serosal margin. One out of the five examined lymph nodes showed a metastatic carcinomatous deposit (Figures 5 & 6).

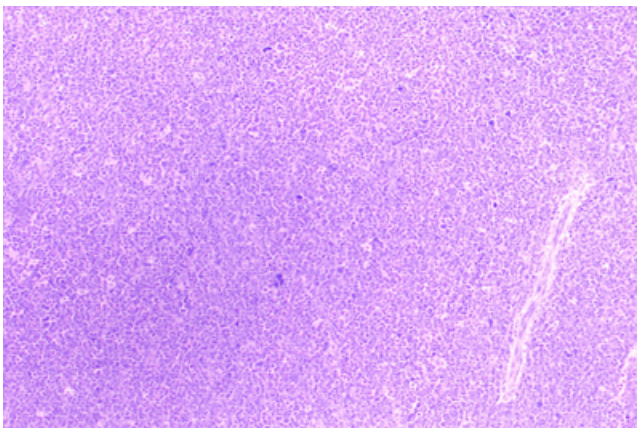

Figure 5: (H&E), 10x Sections show wall of ileum infiltrated by diffuse sheets of atypical cells.

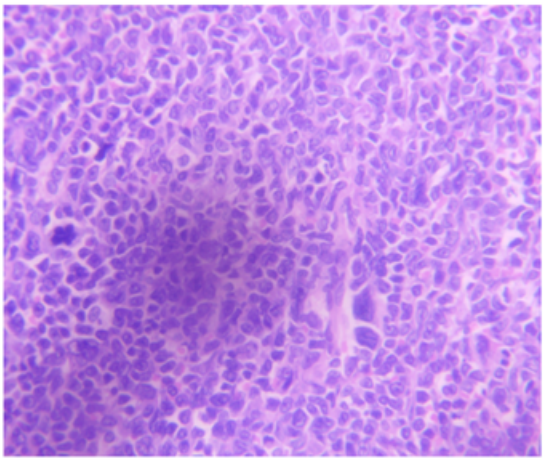

Figure 6: (H&E), 40x Sections show wall of ileum infiltrated by diffuse sheets of atypical cells.

- **Immunohistochemistry:** Strong diffuse positivity was observed for CD68, along with a high proliferative index. The remaining antibodies from the lymphoma panel produced negative results (Figure 7).

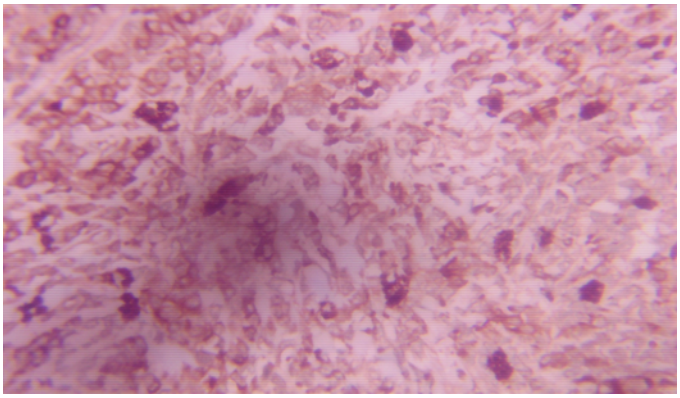

Figure 7: IHC, CD 68 (40x) atypical cells show diffuse positivity for CD68.

Diagnosis: The Final Diagnosis was Histiocytic Sarcoma of the Ileum

Both cases underscore the presence of uncommon and aggressive lymphomas within the gastrointestinal tract. The accuracy of diagnosis was achieved through meticulous pathological analysis and the application of immunohistochemical staining. These instances emphasize the necessity of thorough examination and IHC testing for the precise diagnosis and categorization of rare tumors, thereby aiding in the formulation of appropriate treatment strategies.

Discussion

The mucosal lining of the gastrointestinal (GI) tract serves as a critical defense mechanism against invading pathogens. Within this mucosal layer, mucosa-associated lymphoid tissue (MALT) orchestrates specific immune responses in both the epithelium and lamina propria. Prolonged exposure to inflammation and antigenic stimulation resulting from autoimmune and inflammatory disorders can ultimately lead to the clonal expansion of cells and the eventual development of extranodal GI lymphomas [1]. For instance, individuals with a genetic predisposition to gluten intolerance, such as coeliac disease, elicit immune responses upon exposure to gluten peptides presented by HLADQ2 and HLADQ8-positive antigen-presenting cells. These immune reactions can lead to damage of the intestinal epithelium by intraepithelial T-cell lymphocytes, which in turn can undergo malignant transformation, giving rise to aggressive enteropathy-associated T-cell lymphomas (EATL) in the small bowel [2].

The geographical distribution of GI lymphomas reveals gastric involvement in 74.8% of cases, while the small bowel and ileocaecal regions contribute 8.6% and 7.0% respectively. Some instances involve lymphomas appearing in multiple sites (6.5%). Notably, extra nodal GI B-cell lymphomas are more prevalent, accounting for 80% of cases, and often exhibit heightened responsiveness to chemotherapy, carrying a more optimistic overall prognosis. Importantly, GI lymphomas constitute a minority of GI malignancies, ranging from 1% to 4%, yet play a more substantial role within the spectrum of non-Hodgkin's lymphomas (NHL), accounting for 10% to 15%, and an even more significant proportion of extra nodal NHLs (30% to 40%). Thus, the GI tract emerges as the primary site for extra nodal lymphomas [3]. Among the various sites within the GI tract, the small and large intestines are the secondarily affected regions, with the ileum being the most commonly involved segment. Various lymphoma subtypes are known to afflict the intestines, including MALT lymphoma, diffuse large B-cell lymphoma (DLBL), mantle cell lymphoma (MCL), follicular lymphoma (FL), and intestinal T-cell lymphoma [4-6].

Clinical presentations of GI lymphomas encompass diverse symptoms, such as fever, abdominal pain, diarrhoea, hematochezia, and weight loss. Diagnostic imaging techniques, like abdominal CT scans, frequently reveal indicators such as bowel wall thickening, obstruction, or mucosal ulceration [7,8].

Uncommon Manifestations: Gallbladder Lymphomas and Histiocytic Sarcoma

Primary lymphomas originating in the gallbladder are exceedingly rare and typically manifest as right upper quadrant pain. The predominant forms are often MALT lymphomas or DLBL, with sporadic occurrences of other B-cell and lymphoblastic lymphomas. Conversely, histiocytic sarcoma (HS) represents an exceptionally rare histiocytic disorder, the underlying etiology of which remains uncertain. Despite being categorized as a "sarcoma," it shares histopathological features with mature histiocytes. The clinical presentation of HS is notably diverse and correlates with the specific organs involved. Given its aggressive behaviour, grim prognosis, and the lack of a standardized treatment approach, diagnosing and managing HS poses intricate challenges for medical practitioners [9-12].

Chemotherapy remains the cornerstone of treatment for many lymphomas, including T-cell lymphomas. Standard regimens often involve combinations such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin). However, the efficacy of these regimens in rare subtypes, such as T-cell lymphoma of the gallbladder, is not well-documented. For histiocytic sarcoma, aggressive chemotherapy regimens have been used, although optimal protocols are yet to be established. Case reports suggest that treatments similar to those for high-grade B-cell lymphomas may be beneficial [13].

Radiotherapy is not typically a first-line treatment for these malignancies but may be utilized in localized disease or as palliative care. For instance, there have been instances where radiotherapy has been employed to manage symptoms or reduce tumor burden in T-cell lymphomas, especially in cases of localized involvement [14]. Comparing the treatment outcomes of these rare lymphomas with more common gastrointestinal lymphomas like diffuse large B-cell lymphoma (DLBCL) or mucosa-associated lymphoid tissue (MALT) lymphoma is essential. DLBCL, which is more frequently encountered, has a well-established treatment protocol and generally offers better prognosis compared to the aggressive nature of histiocytic sarcoma and T-cell lymphomas. Studies have shown that the 5-year survival rate for DLBCL can be as high as 60-70% with appropriate therapy, while outcomes for histiocytic sarcoma remain

poor, often underlining a median survival of less than a year post-diagnosis [15]. Recent advancements in targeted therapies and immunotherapy present promising avenues for treatment. Agents targeting specific mutations or pathways (e.g., CD30-directed therapies for anaplastic large cell lymphoma) are being explored in clinical trials, and may offer hope for patients with T-cell lymphomas [16].

Conclusion

Diagnostic Hurdles and Therapeutic Approaches

Accurately diagnosing HS and T-cell lymphomas in the gallbladder often proves intricate due to shared morphological and immunophenotypical attributes. Both histiocytic sarcoma of the ileum and T-cell lymphoma present diagnostic challenges. Following surgical interventions, supplementary treatments are typically recommended to address any residual cancer cells. These interventions may involve chemotherapy, radiation therapy, or a combination thereof. Notably, histiocytic sarcoma of the ileum is associated with an unfavourable prognosis due to its aggressive nature and propensity for metastasis. The scarcity of cases involving these conditions makes the collection of comprehensive, long-term outcome data challenging [17].

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