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Peripheral T-Cell Lymphoma with Hodgkin-Like Morphology: A Diagnotic Pitfall in Resource-Limited Settings

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ABSTRACT

Lymphomas are malignant hematological neoplasms characterized by the clonal proliferation of tumor lymphocytes. Peripheral T-cell lymphomas (PTCLs) are a heterogeneous group of aggressive non-Hodgkin lymphomas, often difficult to diagnose due to their morphological and morphophenotypic polymorphism. Some forms can mimic classic Hodgkin lymphoma, thus posing a significant diagnostic challenge.

We report the case of a 31-year-old woman presenting with a mediastinal mass and cervical lymphadenopathy. Histological examination revealed a nodular architecture with large Reed–Sternberg-like cells and polymorphous inflammatory background rich in eosinophils, suggestive of classical Hodgkin lymphoma, nodular sclerosis subtype. However, immunohistochemical analysis revealed a T-cell phenotype (CD3+, CD5+, CD4+), with CD30, CD15 and GATA3 expression in large atypical cells along with EBV positivity. CD 20 and AE1/AE3 were negative. The overall profile was consistent with a peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS).

By highlighting the challenges posed by Hodgkinoid morphology, this report advocates for a rigorous morpho-immunophenotypic integration to avoid misdiagnoses with critical therapeutic implications.

Keywords

Diagnostic pitfall, Hodgkin-like morphology, Immunohistochemistry, Peripheral T-cell lymphoma, Resource-limited settings.

Introduction

Accounting for 10–20% of adult non-Hodgkin lymphomas, Peripheral T-cell lymphomas (PTCLs) are among the most diagnostically challenging hematologic malignancies due to their marked heterogeneity [1]. A major challenge arises when PTCLs present with Hodgkinoid morphology and markers (CD30+, CD15+), mimicking classical Hodgkin lymphoma [2,3]. This diagnostic dilemma is exacerbated in resource-limited settings where specialized diagnostic panels are restricted. Here, we report a case of PTCL initially suggestive of Hodgkin lymphoma to discuss the critical importance of extensive immunophenotyping in distinguishing these entities and ensuring appropriate therapeutic management.

Case Report

A 31-year-old woman presented with cervical lymphadenopathy associated with progressively worsening respiratory symptoms. Clinical examination revealed firm, non-tender cervical nodes. Imaging demonstrated a large anterior mediastinal mass associated with cervical lymphadenopathy. A cervical lymph node biopsy was performed.

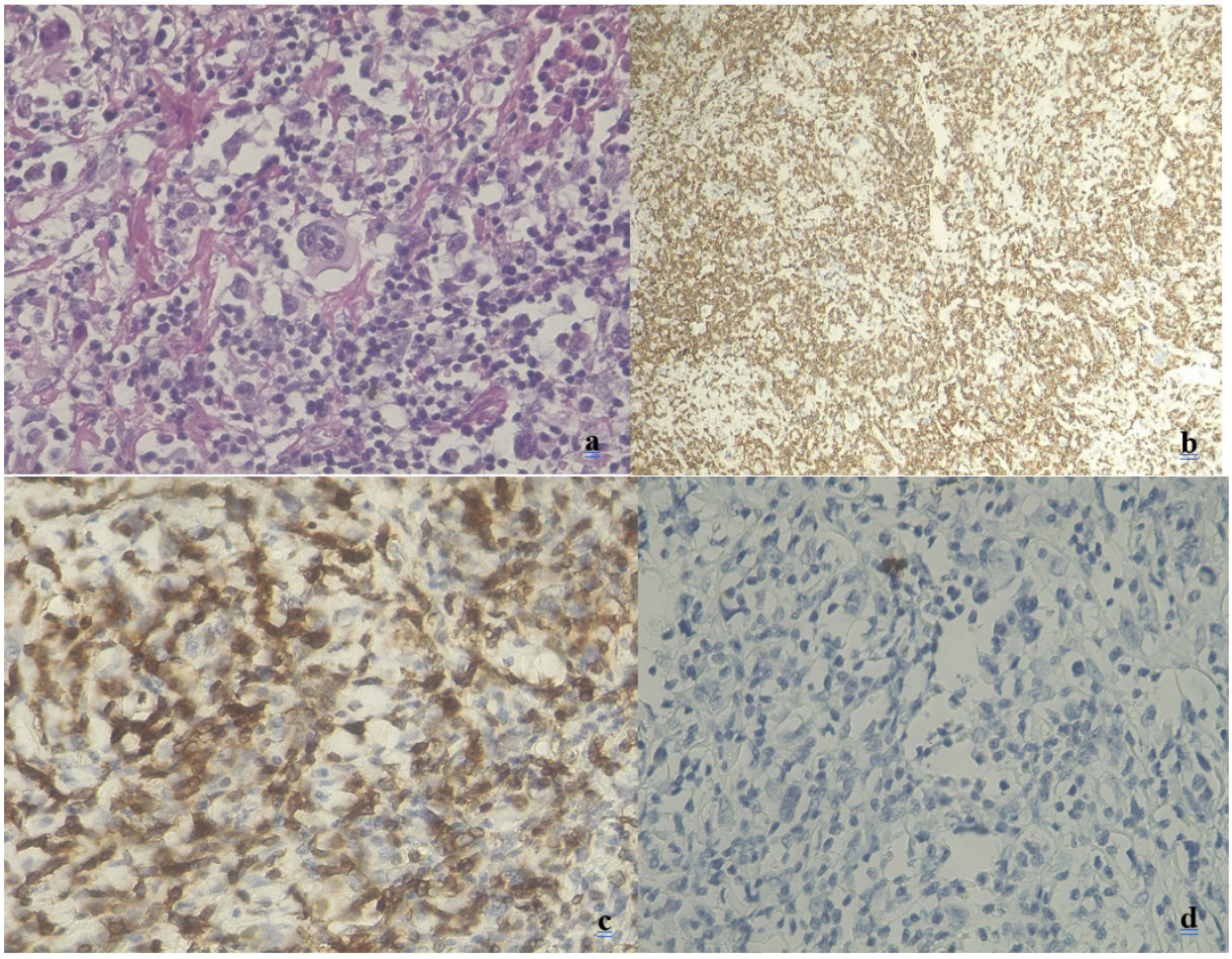
Histological examination showed a nodular architecture intersected by fibrous bands. The parenchyma was infiltrated by a polymorphous inflammatory background comprising lymphocytes, eosinophils, and histiocytes, interspersed with large atypical bi- and multinucleated cells morphologically resembling Reed-Sternberg cells. These findings initially suggested classical Hodgkin lymphoma, nodular sclerosis subtype (Figure 1a).

Immunohistochemical analysis demonstrated a neoplastic T-cell phenotype: CD3+ (Figure 1b), CD5+ (Figure 1c), CD4+, focal CD8+, with a Ki-67 index of 20%. The atypical large Hodgkinoid cells were CD30+, CD15+ and GATA3+, but they remained negative for B-cell : CD20 (Figure 1d) and epithelial (AE1/AE3) markers. Diffuse EBV expression was observed. All of these findings were consistent with a peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS), with a Hodgkin-like morphology.

Discussion

In resource-limited settings, the diagnosis of lymphoma continues to rely predominantly on conventional histopathological examination using hematoxylin and eosin (H&E) staining. However, peripheral T-cell lymphomas (PTCLs) are known for their extreme morphological polymorphism, which can mimic both reactive processes and other lymphomatous entities, most notably classical Hodgkin lymphoma [1,2]. In this context, morphology alone is frequently insufficient for a definitive diagnosis, significantly increasing the risk of misdiagnosis.

Our case underscores the diagnostic dilemma faced when morphology mimics classical Hodgkin lymphoma. The presence of a nodular sclerotic architecture, coupled with large atypical Reed–Sternberg-like cells within a background rich in eosinophils,



a. Hematein eosin stain; b. CD 5 positivity; c. CD3 positivity; d. CD20 negativity.
Figure 1: peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS), with a Hodgkin-like morphology.
Source: Departement of Pathology, Clinical Biology Center, Institut Pasteur Madagascar.

was initially highly suggestive of the nodular sclerosis subtype of classical Hodgkin lymphoma. Similar morphologic presentations have been documented in Hodgkinoid variants of PTCL, highlighting the deceptive nature of morphology alone [2,3].

Current literature demonstrates that certain PTCLs can aberrantly express markers classically associated with classical Hodgkin Lymphoma, particularly CD30 and CD15. This overlap exacerbates diagnostic confusion when immunohistochemical panels are restricted [3,4]. Alikhan et al. described PTCLs cases featuring Reed–Sternberg-like cells that expressed CD30 and occasionally CD15, closely mimicking classical Hodgkin lymphoma [4].

The GATA3 positivity noted in this instance represents an additional diagnostic pitfall. Although GATA3 is a transcription factor involved in T-cell differentiation and frequently expressed in various PTCLs, it can also be expressed in a subset of classical Hodgkin lymphoma cases, thereby limiting its specificity when interpreted out of context [5].

Similarly, diffuse EBV positivity represents a diagnostic pitfall. While EBV is commonly associated with classical Hodgkin lymphoma, its presence is also reported in certain PTCLs, particularly in the setting of immune activation or immunosuppression [6,7]. Consequently, the detection of EBV alone is insufficient to ddistinguish between these two entities.

In resource-limited settings, restricted access to molecular techniques, specifically T-cell receptor clonality studies, imperatively requires a rigorous, integrated morpho-immunophenotypic analysis. This case underscores the imperative of systematically including a broad panel of T-cell markers (such as CD3, CD5 and CD4) whenever classical Hodgkin lymphoma is suspected, particularly if the clinical or morphological presentation exhibits any atypical features.

Beyond its diagnostic implications, this observation reminds Pathologists that morphology, regardless of how suggestive it may appear, should never be interpreted in isolation in lymphoid pathology. Only a comprehensive and meticulous immunophenotypic approach can ensure diagnostic precision, which is the sine qua non for selecting the appropriate therapeutic strategy and improving patient outcomes.

Conclusion

Peripheral T-cell lymphomas with Hodgkin-like morphology represent a complex diagnostic challenge in pathology, particularly in resource-constrained settings where hematoxylin and eosin staining remains the cornerstone of diagnosis. This case report highlights the critical need for an integrated morpho-immunophenotypic approach whenever classical Hodgkin lymphoma presents with atypical features. Even without access to molecular studies, the judicious application of a targeted immunohistochemical panel can reliably secure the diagnosis. By serving as a practical reference, this case underscores a fundamental principle in hematopathology: morphology alone is seldom sufficient for a definitive diagnosis, and meticulous immunophenotypic correlation is essential to ensure appropriate patient management.

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